EMBRACING INTERDISCIPLINARY APPROACHES IN AGING RESEARCH
Social and Institutional Pathways to Dementia

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Outline

(1) Overview of SDoH and Conceptual Frameworks

(2) Midlife social factors

- Financial well-being: poverty, income volatility, wages, food security

(3) Datasets and methodologies

(4) Future directions

Measures of Social Determinants of Health (SDoH)

Food Insecurity

Residential Segregation

Neighborhood Characteristics
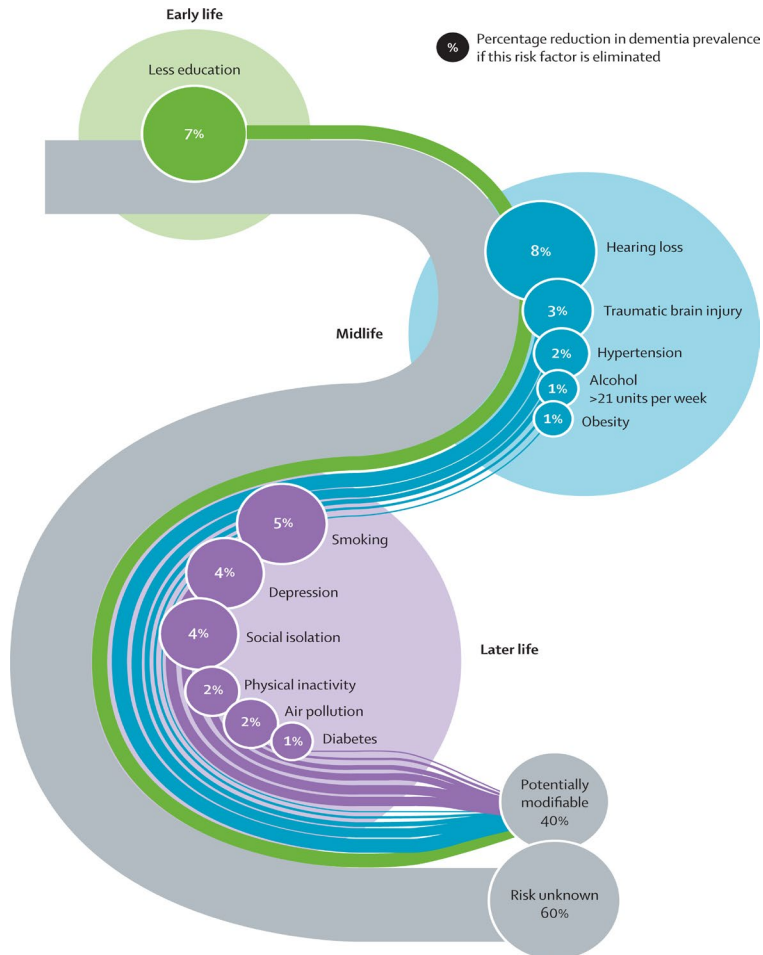
Wealth

Occupation

Income

Education

Poverty Ratio

Deprivation Index
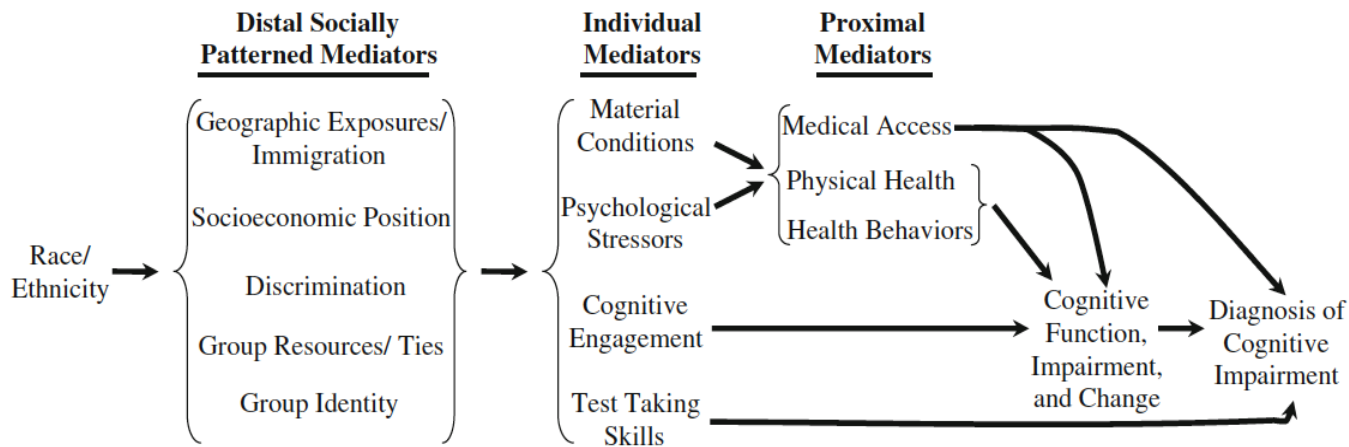
Immigration

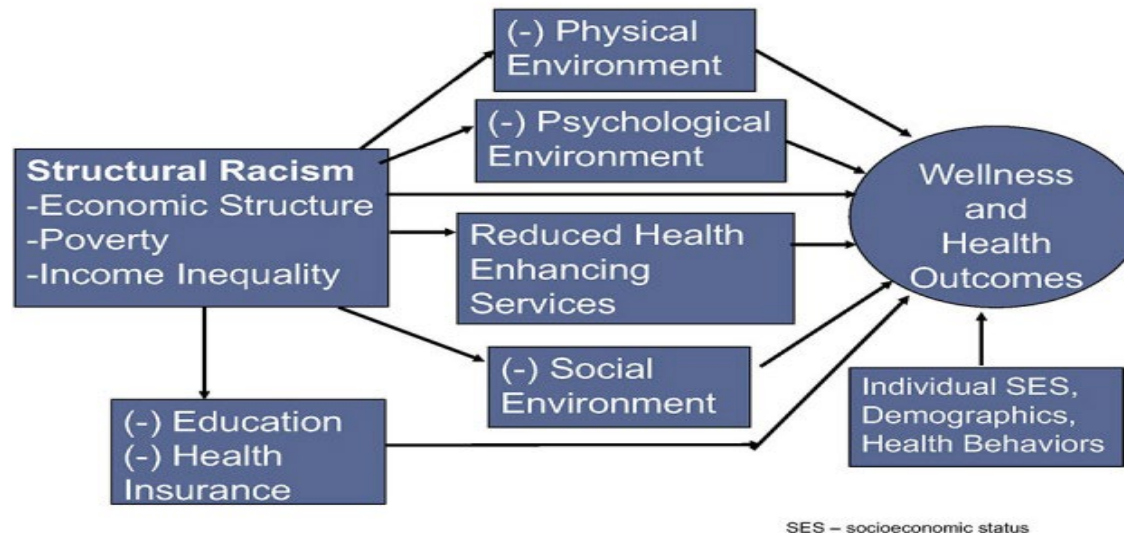Financial insecurity

Report by Lancet Commission

Where are the social and institutional determinants?

Livingston G, et al. Dementia prevention, intervention, and care: 2020 Report of the Lancet Commission. Lancet. 2020

Frameworks

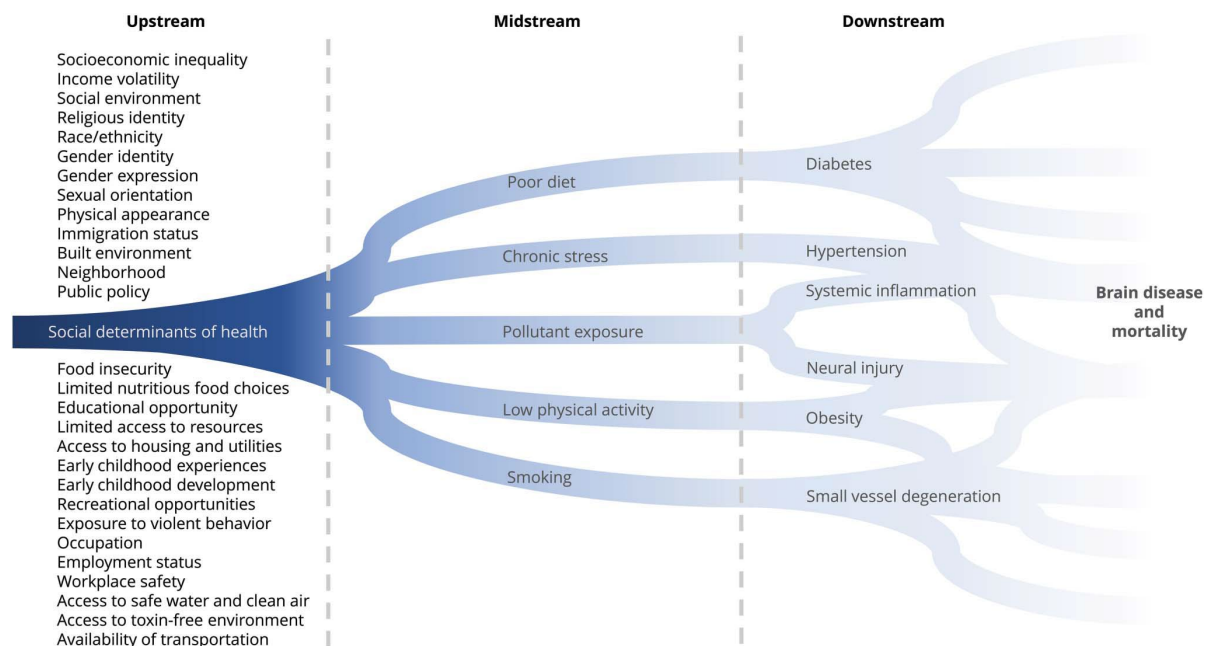M.M. Glymour and J. Manly, 2008, *Neuropsychology Reviews*

Beech 2021, Front Public Health. Adapted from Wen et al. 2003

Social determinants of health (SDoH)

SDoH : "*underlying community-wide social, economic, and physical conditions in which people are born, grow, live, work and age*" and "*the fundamental drivers of these conditions*"

- Impact of SDoH accumulates over the life course

- Many SDoH arise from systems governed by racialized and gendered rules …

- …and could thus be promising targets for intervention to reduce dementia disparities

Upstream

Socioeconomic inequality
Income volatility
Social environment
Religious identity
Race/ethnicity
Gender identity
Gender expression
Sexual orientation
Physical appearance
Immigration status
Built environment
Neighborhood
Public policy

Social determinants of health

Food insecurity
Limited nutritious food choices
Educational opportunity
Limited access to resources
Access to housing and utilities
Early childhood experiences
Early childhood development
Recreational opportunities
Exposure to violent behavior
Occupation
Employment status
Workplace safety
Access to safe water and clean air
Access to toxin-free environment
Availability of transportation

Midstream

Poor diet
Chronic stress
Pollutant exposure
Low physical activity
Smoking

Downstream

Diabetes
Hypertension
Systemic inflammation
Neural injury
Obesity
Small vessel degeneration

Brain disease and mortality

Salinas 2019 "Social health and brain health" *Neurology*

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Financial well-being in peak working and earning years (i.e. midlife)
Poverty, Income Volatility, Low Wage Earning, Food Insecurity

➤ Persistent socioeconomic inequalities mean many working age Americans will enter retirement in worse financial standing than in prior decades.

➤ From 2020 to 2021 the percent of older Americans (65+) living below the federal poverty level increased from 8.9% to 10.3%, placing a million more seniors into poverty.

➤ While financial well-being is acknowledged as a social determinant of health, **rarely** are its effects on cognitive and aging-related outcomes like dementia considered.

➤ There are straightforward policy options to intervene and alleviate poverty, income volatility, food insecurity etc.

National Council on Aging. 2022
Creamer J et al. *Poverty in the United States: 2021.*

Policy relevant exposures
Poverty, Income Volatility, Low Wage Earning, Food Insecurity

JOURNAL ARTICLE

Association of Low Hourly Wages in Middle Age With Faster Memory Decline in Older Age: Evidence From the Health and Retirement Study FREE

Katrina L Kezios ✉, Adina Zhang, Soohyun Kim, Peiyi Lu, M Maria Glymour, Tali Elfassy, Adina Zeki Al Hazzouri

American Journal of Epidemiology, Volume 191, Issue 12, December 2022, Pages 2051–2062, https://doi.org/10.1093/aje/kwac166
Published: 21 September 2022   Article history ▾

JAMA | Original Investigation

History of Low Hourly Wage and All-Cause Mortality Among Middle-aged Workers

Katrina L. Kezios, PhD; Peiyi Lu, PhD; Sebastian Calonico, PhD; Adina Zeki Al Hazzouri, PhD

RESEARCH ARTICLE
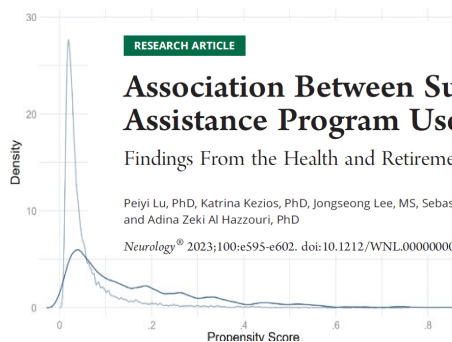
Association Between Supplemental Nutrition Assistance Program Use and Memory Decline
Findings From the Health and Retirement Study

Peiyi Lu, PhD, Katrina Kezios, PhD, Jongseong Lee, MS, Sebastian Calonico, PhD, Christopher Wimer, PhD, and Adina Zeki Al Hazzouri, PhD

Neurology® 2023;100:e595-e602. doi:10.1212/WNL.0000000000201499

Kezios K,,,Zeki Al Hazzouri. JAMA 2023; 329(7): 561-573
Lu P,,,Zeki Al Hazzouri. Neurology, 2023; 100(6):e595-e602.
Lu P,,,Zeki Al Hazzouri. JAMA Network Open 2023, 6(7): e2321474.
Kezios k,,,Zeki Al Hazzouri. AJE 191(12): 2051-2062; 2022

Poverty & Income Volatility

➢ Income is dynamic

➢ **Income volatility** (sudden and unpredictable change in income)

➢ **# Income Drops:** drops greater than 25% of previous period and lower than the average for all measurements

➢ Income volatility has been on the rise and is at record high since 1980

Dynan K, Elmendorf D, Sichel D. The evolution of household income volatility. The Journal of Economic Analysis & Policy. 2012
Hardy B. Income instability and the response of the safety net. Contemp Econ Policy. 2017

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FINDINGS: Sustained Poverty, Income Volatility, & Brain Health, CARDIA.

Total Brain Volume

DSST
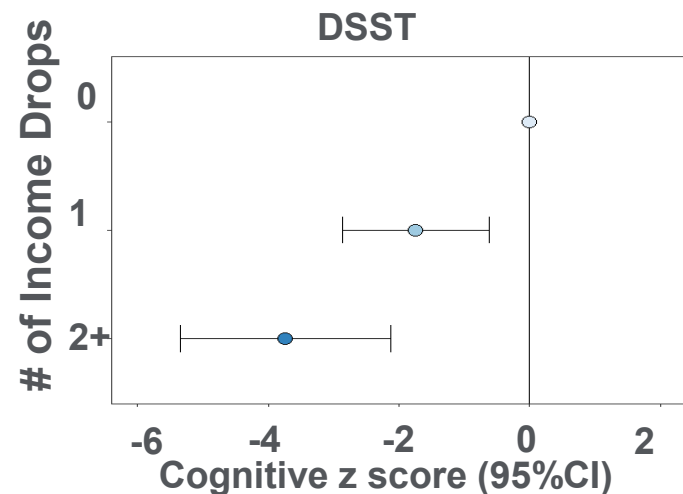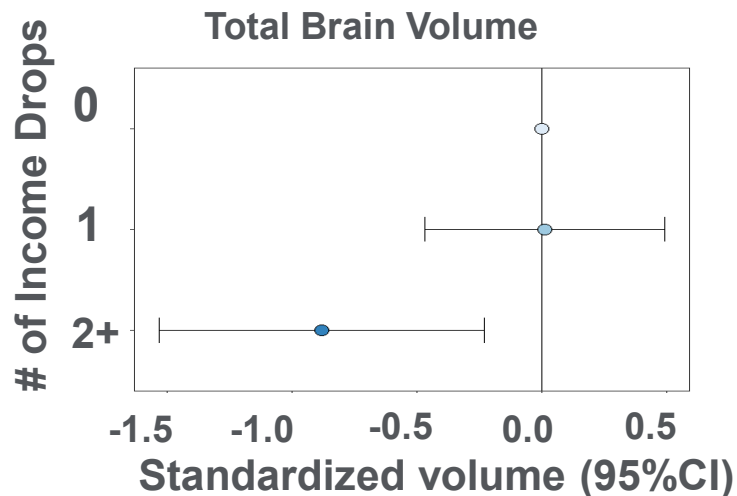
|	
Verbal memory (N=3,363)	**1 less points**
All-time	**-0.26 (-0.41, -0.11)**
≥1/3	-0.08 (-0.18, 0.02)
<1/3	0.03 (-0.05, 0.11)
Never	Ref
Processing speed (N=3,368)	**~12 less points**
All-time	**-0.61 (-0.75, -0.47)**
≥1/3	**-0.25 (-0.34, -0.15)**
<1/3	**-0.10 (-0.17, -0.02)**
Never	Ref
Executive function (N=3,350)	**~4 less points**
All-time	**-0.25 (-0.41, -0.10)**
≥1/3	**-0.13 (-0.24, -0.03)**
<1/3	-0.02 (-0.10, 0.07)
Never	Ref

Sustained Poverty (1990-2010) and Cognitive Function (2010)

Zeki Al Hazzouri A,,,Yaffe K. AJPM, 52(1): 1-9, 2017.
Grasset L,,,Zeki Al Hazzouri. Neurology, 93(20): e1890-e1899, 2019.

FINDINGS: Sustained Poverty, Income Volatility, & Brain Health, NLSY79
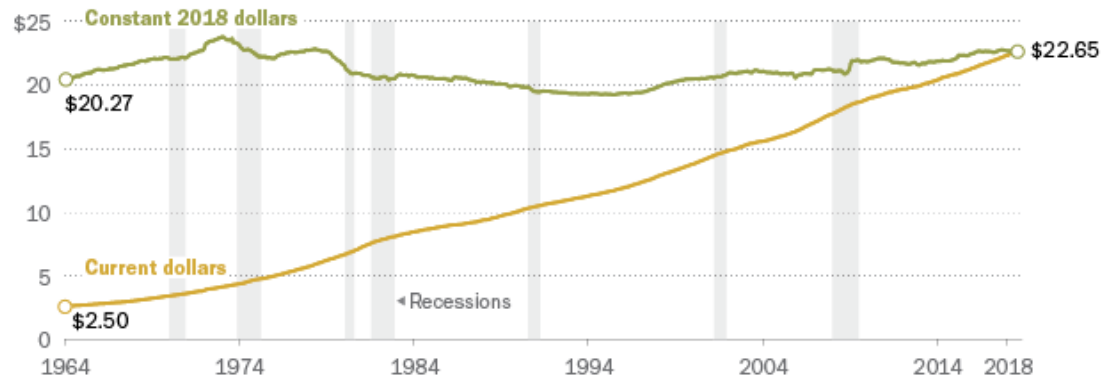
Poverty History	Global cognition (β, 95% CI)
Never	--
Sometimes	0.00 (-0.08, 0.09)
Often	**-0.15 (-0.24, -0.05)**
Always	**-0.41 (-0.56, -0.26)**

Time in Poverty and Risk for Cognitive Impairment
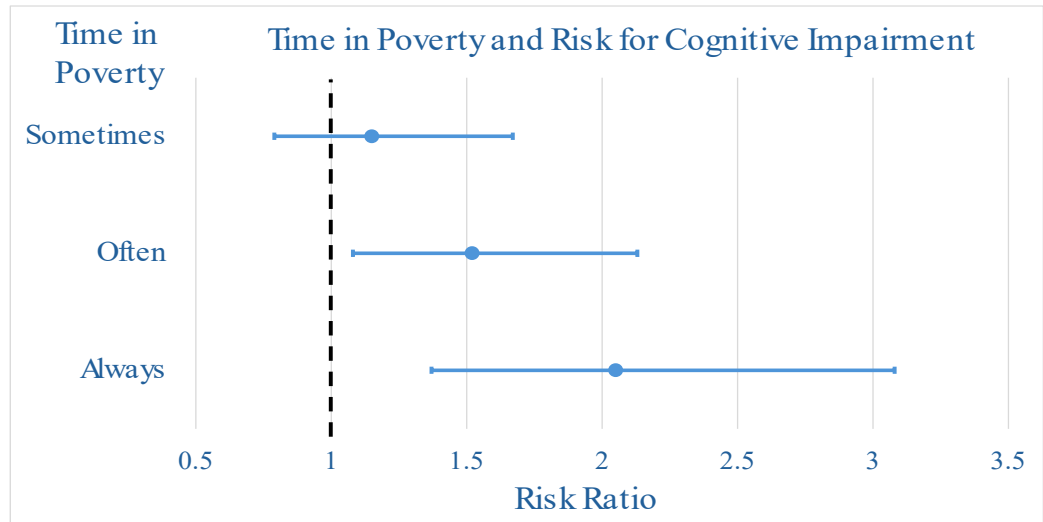
Colvin, Kezios, Zeki Al Hazzouri. In progress.

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Hourly Wages

Average hourly wages in the U.S., seasonally adjusted

$25
Constant 2018 dollars
20   $20.27
15
10
5   Current dollars
$2.50   ◄ Recessions
0
1964   1974   1984   1994   2004   2014   2018 $22.65

Source: U.S. Bureau of Labor Statistics
PEW RESEARCH CENTER

Why low wage?

44% of workers aged 18-64 in the US labor market earn low hourly wages

Low wage jobs → **health risks**
- e.g., limited flexibility, low job control, minimal or no health and financial benefits, exposure to workplace hazards, job stress, employment volatility, exploitation

Policy levers exist to change/improve wage
- could improve health outcomes & inequalities

- In the US, the federal minimum wage has remained $7.25 per hour since 2009 and has not kept pace with inflation

- Low-wage workforce has increased over the past 2 decade. Currently more than 53 million workers are earning low wages

Ross & Bateman. 2019. *Meet the low wage workforce*. Brookings Institute
Leigh & DeVogli. 2016. *Low Wages as Occupational Health Hazards.* J Occup Environ Med.
Desilver. 2018. *For most U.S. workers, real wages have barely budged in decades*. Pew Research Center

# FINDINGS: Low wages and memory decline. HRS

Translation

Workers with sustained low wage exposure experienced ~1 excess year of memory aging per 10-year period compared with never low-wage workers

AAIC>24

PRESS RELEASE

Lower Socioeconomic Status in Childhood, Persistent Low Wages Linked to Risk for Dementia and Faster Memory Decline

β_{time}: -0.12

$\beta_{sustained*time}$: -0.014
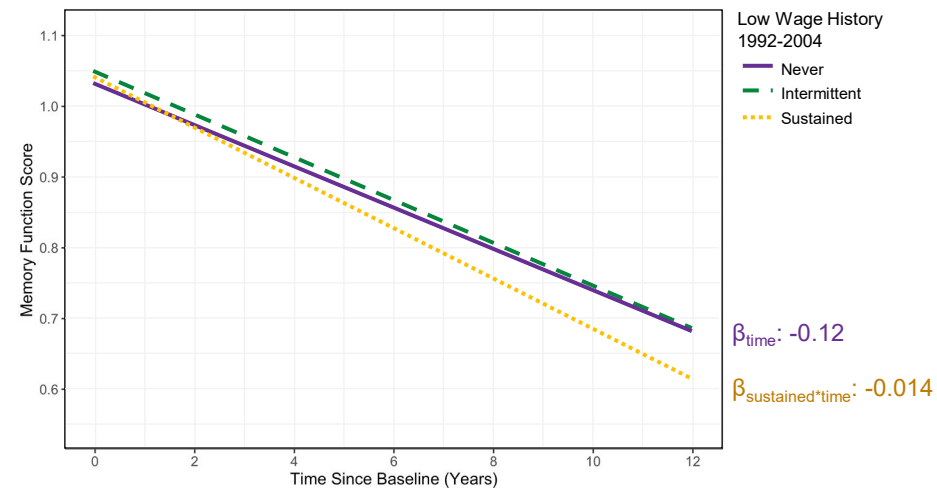
Kezios k,,,Zeki Al Hazzouri. AJE 191(12): 2051-2062; 2022

Food Insecurity

Senior Hunger Statistics:

1 in 15
US seniors
Faced hunger

5.2 million
seniors aged 60+ faced
hunger in 2020

6.8%
of all seniors
experience food insecurity

- In 2020, about 5.2 million (6.8%) older Americans aged 60 and above were food insecure.
- That is about **1 in 15** older Americans lives in food insecurity. Source: Feeding America
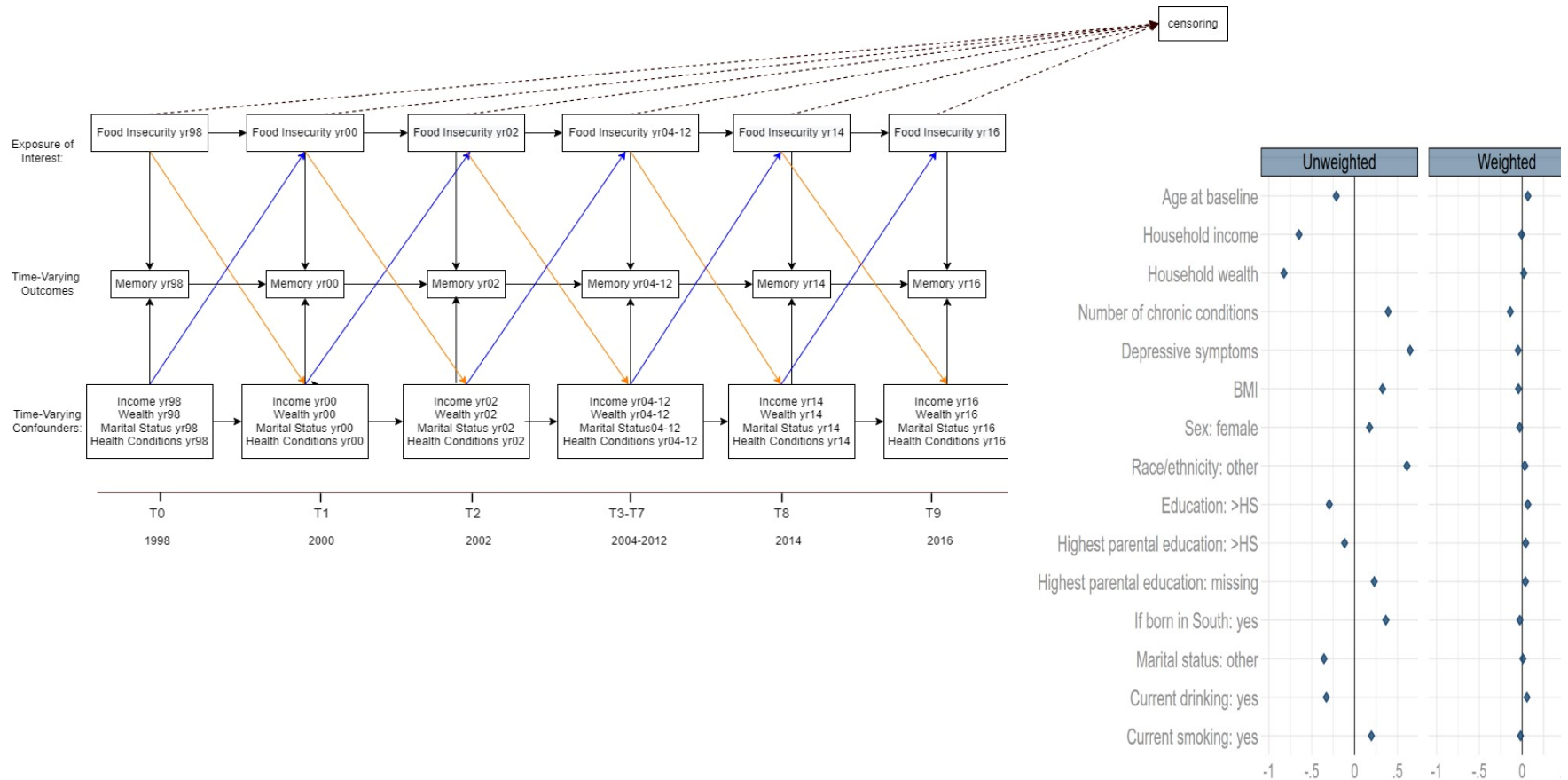
What is food insecurity?

- Inadequate and unreliable access to food for healthy life
- A marker of low income or poverty
- longstanding public health issue in the United States

1 in 5 older adults

experience at *least* one of the following:

Food insecurity | Skipped meals | Difficulty paying bills | Medication cut-backs | Dissatisfaction with finances

FRAC
Food Research & Action Center

Levy, H. (2015). Income, poverty, and material hardship among older Americans. RSF, 1(1): 55-77.

Source: Food Research & Action Center

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# FINDINGS: Food insecurity and memory decline, HRS

Lu P,,,Zeki Al Hazzouri. JAMA Network Open 2023, 6(7): e2321474.

FINDINGS: Food insecurity and memory decline, HRS

Predicted memory function trajectory for food-secure and food-insecure participants, based on marginal structural models, HRS, 1998-2016 (N=12,609)

Food-insecure people had a 0.65 excess years of cognitive aging than food-secure people over a decade.
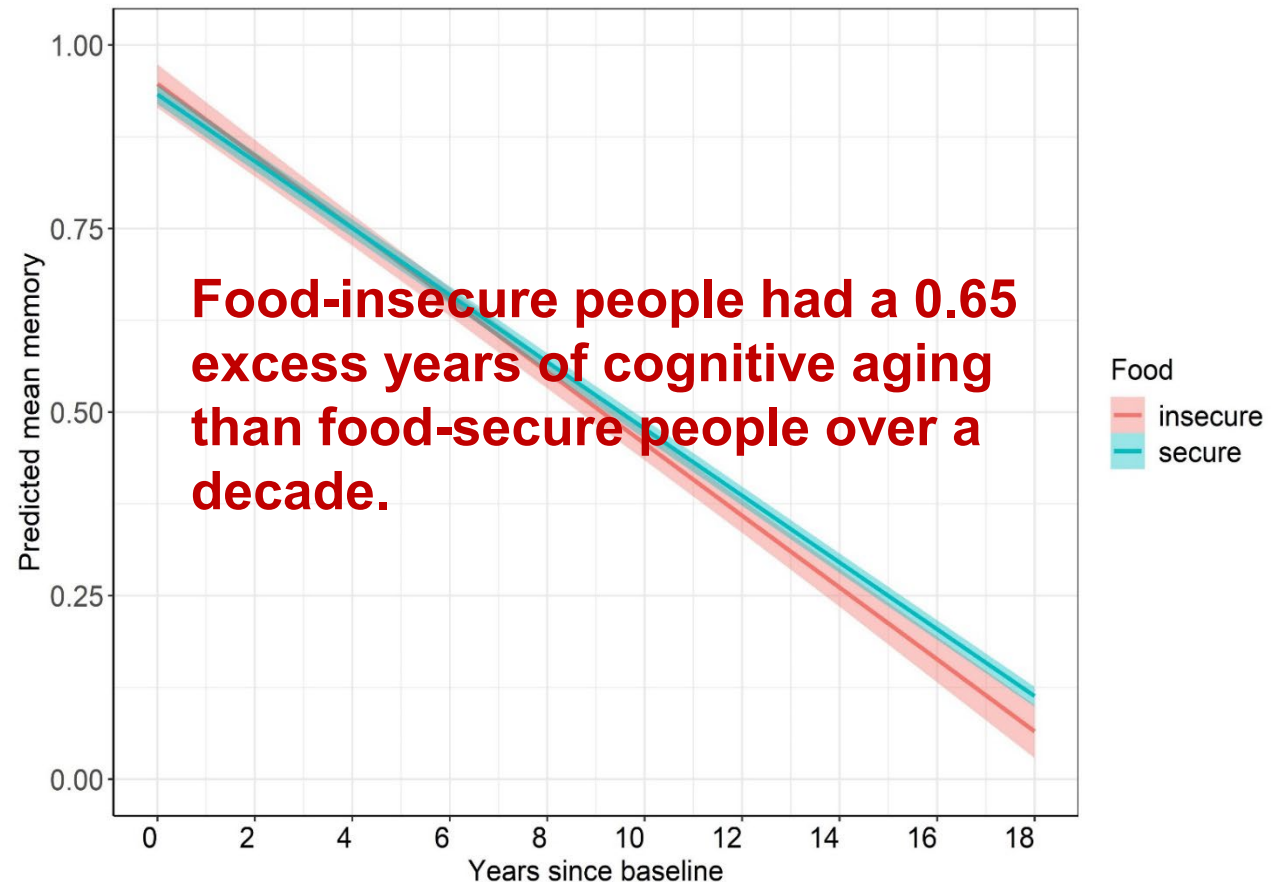
Lu P,,,Zeki Al Hazzouri. JAMA Network Open 2023, 6(7): e2321474.

SNAP

➢ One of the largest social safety net programs targeted at food insecurity and 'bandwidth poverty'.

➢ In 2021, more than 4.8 million older Americans participated in SNAP.
   o However, this only accounted for less than half (~48%) of the *eligible* older adults.

Mechanisms underlying the SNAP-cognition link
➢ Reduce stress related to financial difficulty
➢ Increase the purchasing power and investment in other health preserving behaviors

McGovern EK. 7 Facts About Older Adults and SNAP. 2021
Vigil A. *Trends in supplemental nutrition assistance program participation rates: fiscal year 2010 to fiscal year 2017.* Alexandria, VA: USDA;2019.

SNAP *Eligible*

We constructed the SNAP eligibility variable using established federal criteria

There are known pre-existing differences between SNAP users and non-users, even when SNAP eligible

We calculate a propensity to "use SNAP" --- to untangle the effect of SNAP from the conditions that made someone participate in SNAP
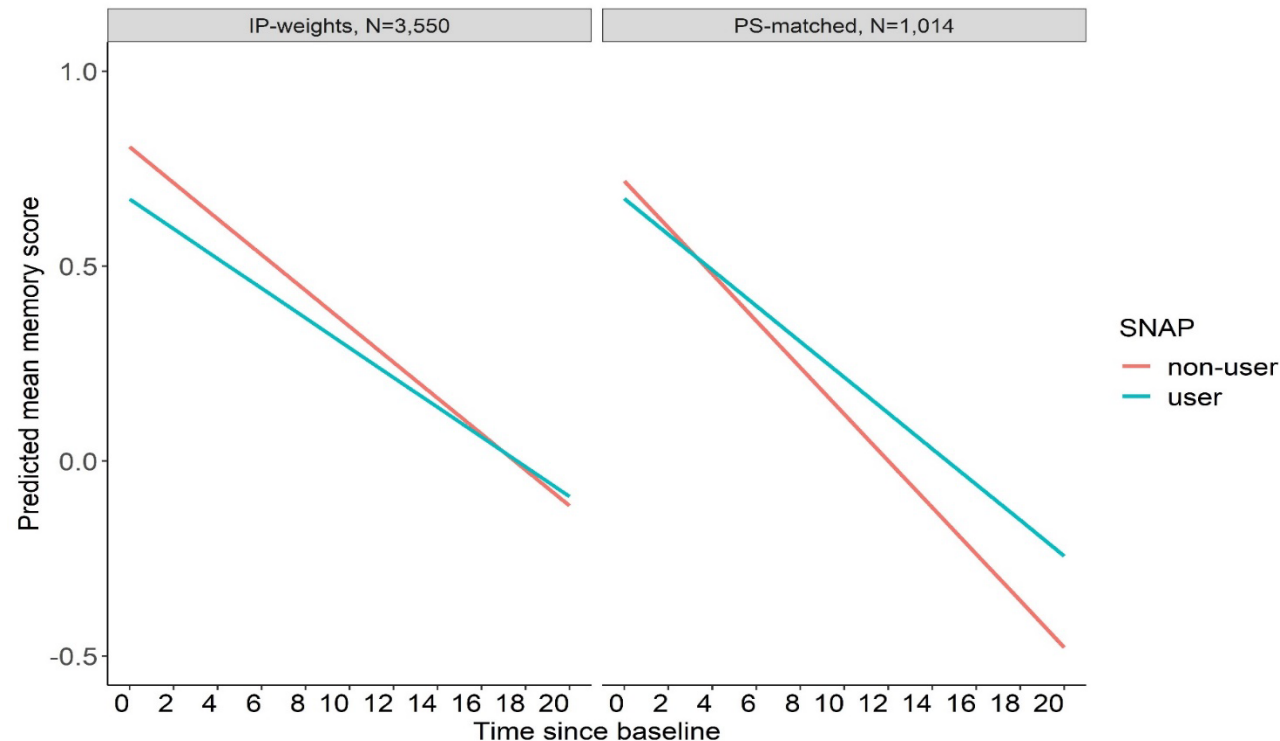
Inverse probability treatment weighting and propensity score matching

FINDINGS: SNAP Use in 1996 is Associated with Slower Memory Decline Among SNAP-eligible US Older Adults, HRS

▪As an example, based on IP weighted linear mixed models, the annual memory decline rate:

- ○ SNAP users: β= -0.038 standardized units [95%CI=-0.044, -0.032]
- ○ SNAP non-users: β= -0.046 [95%CI=-0.049, -0.043]

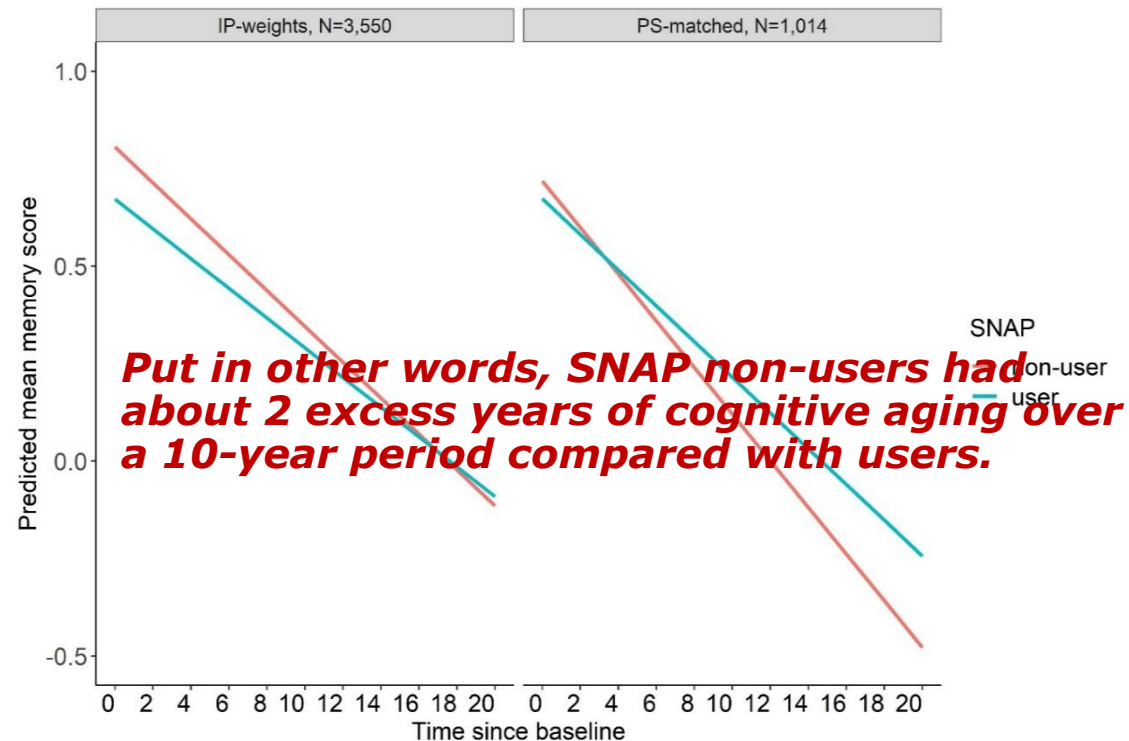Comparison of the predicted memory function trajectory in 1996-2016 between SNAP users and non-users in 1996

Lu P,,,Zeki Al Hazzouri. Neurology, 2023; 100(6):e595-e602.

FINDINGS: SNAP Use in 1996 is Associated with Slower Memory Decline Among SNAP-eligible US Older Adults, HRS

- As an example, based on IP weighted linear mixed models, the annual memory decline rate:
  - SNAP users: β= -0.038 standardized units [95%CI=-0.044, -0.032]
  - SNAP non-users: β= -0.046 [95%CI=-0.049, -0.043]

IP-weights, N=3,550   PS-matched, N=1,014

Put in other words, SNAP non-users had about 2 excess years of cognitive aging over a 10-year period compared with users.

Comparison of the predicted memory function trajectory in 1996-2016 between SNAP users and non-users in 1996

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Cognitive Decline & Dementia: a life course perspective
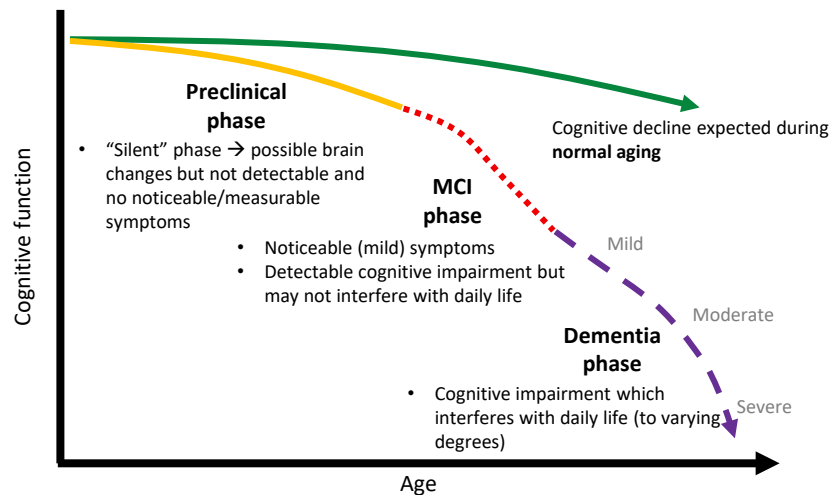
adapted from Sperling et al. *Alzheimers Dement* 2012
and Alzheimer's Association Facts and Figures 2020 Report
and UCI Mind webpage on Mild Cognitive Impairment

- **Dementia**: loss of memory, language, problem-solving, and other thinking abilities severe enough to interfere with daily life
  - Major public health burden
  - Documented disparities by race/ethnicity and gender

- Pathology may begin many years prior to diagnosis

- **Goal**: identify earlier-life factors associated with later accelerated cognitive decline, especially in high risk groups
  - Could provide opportunities to intervene to prevent dementia, delay onset, or slow disease progression
  - Could help reduce dementia disparities

Datasets

CARDIA Study and NLSY79: rich in midlife SDoH

HRS: rich in SDoH (close to retirement) and has established cognitive battery

Challenge #1: limited midlife exposure period

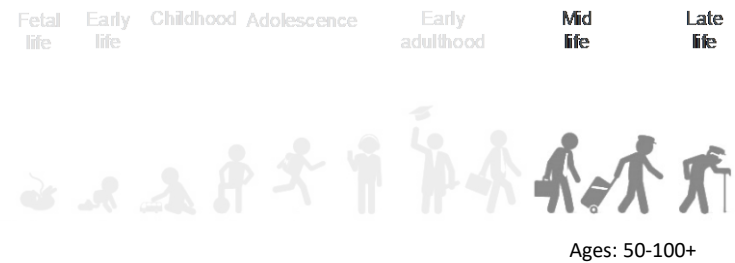| Birth year	Survey year													
	1992	1994	1996	1998	2000	2002	2004	2006	2008	2010	2012	2014	2016	2018
1958				40	42	44	46	48	50	52	54	56	58	60
1957				41	43	45	47	49	51	53	55	57	59	61
1956				42	44	46	48	50	52	54	56	58	60	62
1955				43	45	47	49	51	53	55	57	59	61	63
1954				44	46	48	50	52	54	56	58	60	62	64
1953				45	47	49	51	53	55	57	59	61	63	65
1952	40	42	44	46	48	50	52	54	56	58	60	62	64	66
1951	41	43	45	47	49	51	53	55	57	59	61	63	65	67
1950	42	44	46	48	50	52	54	56	58	60	62	64	66	68
1949	43	45	47	49	51	53	55	57	59	61	63	65	67	69
1948	44	46	48	50	52	54	56	58	60	62	64	66	68	70
1947	45	47	49	51	53	55	57	59	61	63	65	67	69	71
1946	46	48	50	52	54	56	58	60	62	64	66	68	70	72
1945	47	49	51	53	55	57	59	61	63	65	67	69	71	73
1944	48	50	52	54	56	58	60	62	64	66	68	70	72	74
1943	49	51	53	55	57	59	61	63	65	67	69	71	73	75
1942	50	52	54	56	58	60	62	64	66	68	70	72	74	76
1941	51	53	55	57	59	61	63	65	67	69	71	73	75	77
1940	52	54	56	58	60	62	64	66	68	70	72	74	76	78
1939	53	55	57	59	61	63	65	67	69	71	73	75	77	79
1938	54	56	58	60	62	64	66	68	70	72	74	76	78	80
1937	55	57	59	61	63	65	67	69	71	73	75	77	79	81
1936	56	58	60	62	64	66	68	70	72	74	76	78	80	82
1935	57	59	61	63	65	67	69	71	73	75	77	79	81	83

Exposure period (1992 subcohort)
Exposure period (1998 subcohort)
Outcome period (1992 subcohort)
Outcome period (1998 subcohort)

Kezios K,,,Zeki Al Hazzouri. JAMA 2023; 329(7): 561-573
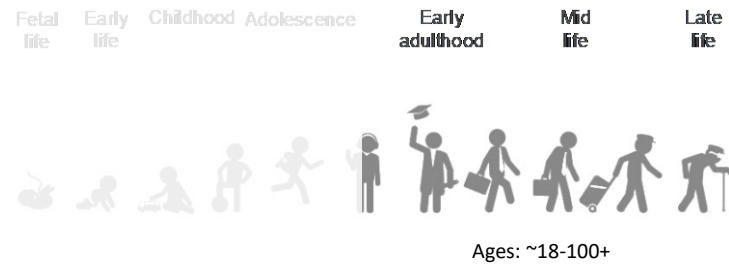
Life course research

Not capturing the full working life course

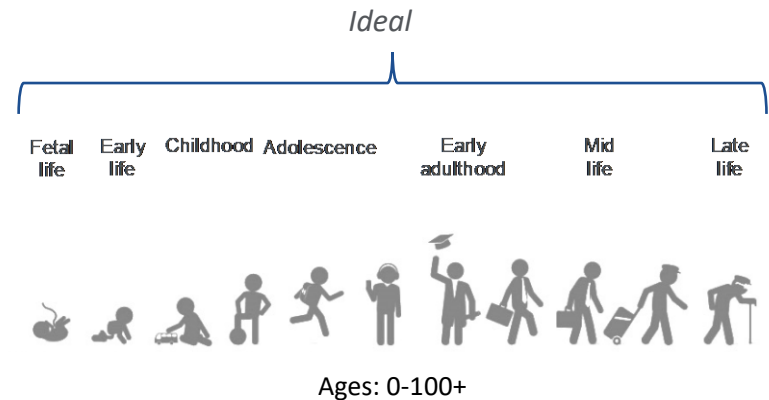- **What I have**: inference about midlife (50+) low wage earning

- **What I want**: inference about low wage earning over the entirety of working years

Fetal life   Early life   Childhood   Adolescence   Early adulthood   Mid life   Late life

Ages: 50-100+

Fetal life   Early life   Childhood   Adolescence   Early adulthood   Mid life   Late life

Ages: ~18-100+

Key challenge in life course research

Issue in life course research in general

- Many longitudinal cohorts have excellent exposure or outcome information but not always both and typically not frequently and repeatedly measured across the *full* life span (ideal)

Ideal

Fetal life   Early life   Childhood   Adolescence   Early adulthood   Mid life   Late life

Ages: 0-100+

- How to address it?

Can we get what we want via longitudinal cohort pooling?

Longitudinal (or "life course") cohort pooling

- Pooling multiple longitudinal cohorts covering different life periods and partially overlapping in age

- Imputing exposure values for individuals at unobserved time points based on individuals in other cohorts
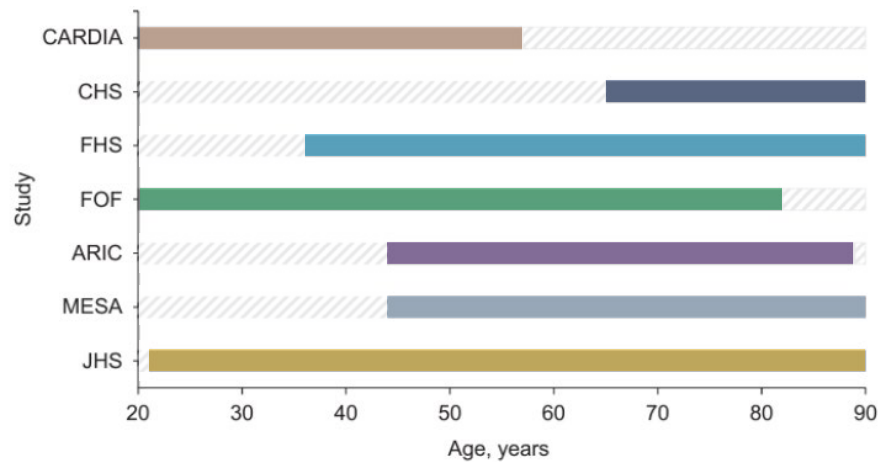
adapted from Ning et al. *Am J Epidemiol.* 2021

Life course synthetic cohorts: a potential solution?

Pool multiple data sources spanning different but overlapping periods of the life course to create one combined cohort with longer follow-up than any one cohort could provide alone
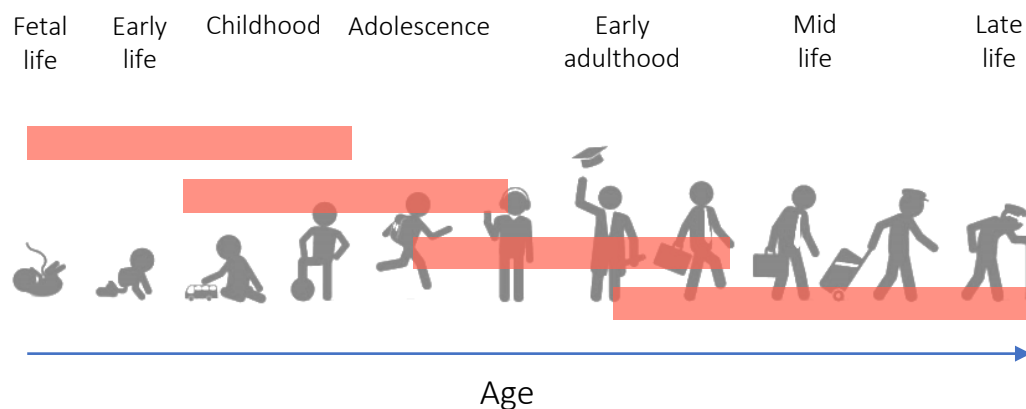
SYNBAD: A pooling initiative (R01AG072681)

HRS: 1992-Present; N = 43,216

REGARDS: 2003-Present; N = 30,239

CARDIA: 1985-2015; N = 5,115

NLSY1979: 1979-2018; N = 11,530

Add Health: 1994-2018; N = 20,745

BHS: 1973-2010; N = 12,138

Muscatine: 1970-Present; N = 11,377

NHANES

| 0 | 10 | 20 | 30 | 40 | 50 | 60 | 70 | 80 | 90 |
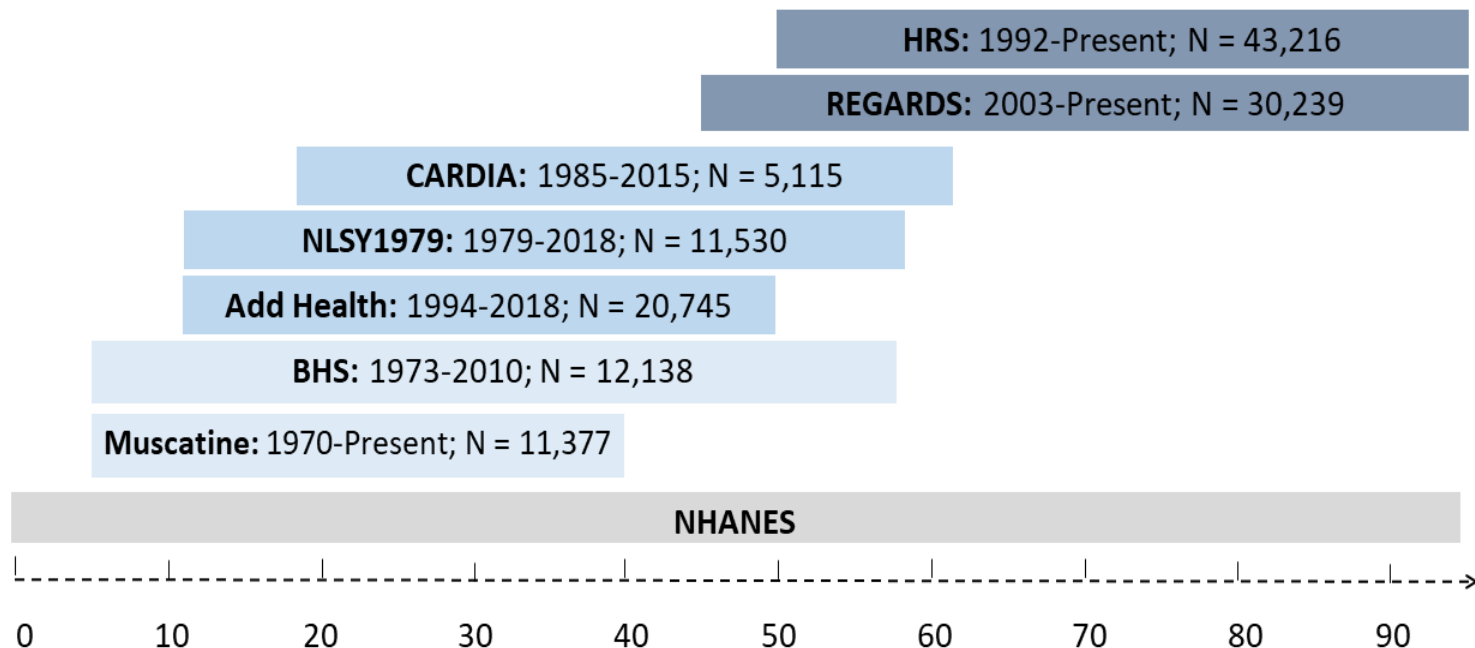
➤ Building an *unbiased* **life course synthetic cohort** for the study of ADRD risk factors and disparities – SYNBAD
➤ Quantifies and corrects bias from differential survival and attrition
➤ Corrects for reverse causation

Helps address small samples: data sources often lack sufficiently well-numbered strata defined by race/ethnicity and sex to conduct robust intersectional analysis

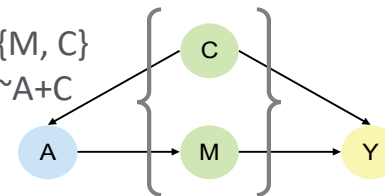# Simulation study

Simulation setting
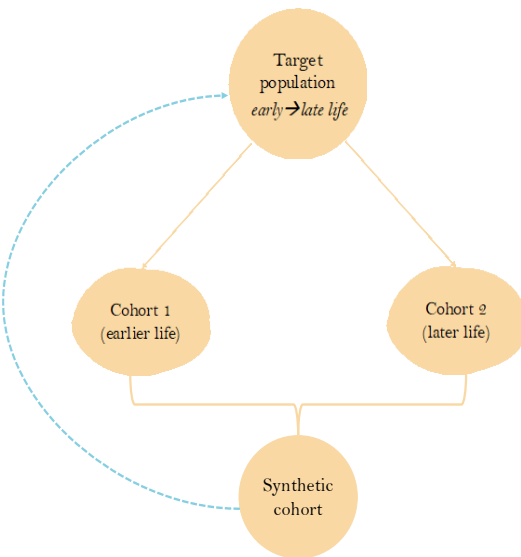
DAG 1
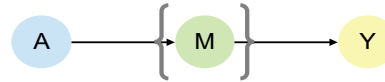
DAG 2
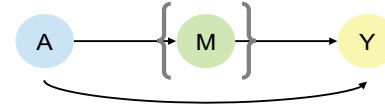
DAG 3
- Matching: {M}
- Analysis: Y~A
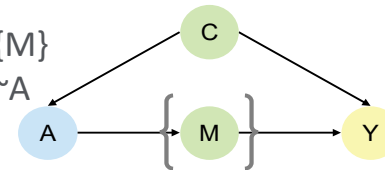
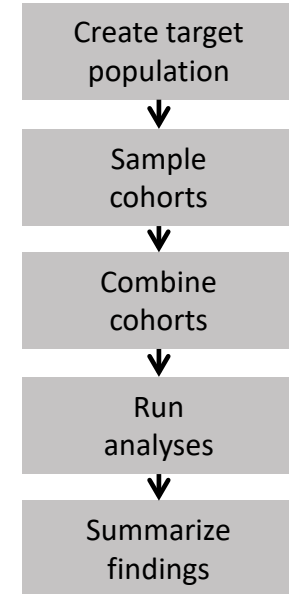**DAG 3**
- Matching: {M, C}
- Analysis: Y~A+C

Simulation overview

In early-life cohort   In both cohorts   In later-life cohort

Kezios K,,,,Zeki Al Hazzouri, M Glymour. Epidemiology 2024; 35(5): 610-617.

Challenge # 2: Data reporting and accuracy

➢ Subjective vs. objective measures of financial well-being

➢ Data accuracy: often rely on self-reported measures

  ➢ Triangulate and validate evidence from multiple data sources: including linkages such as social security administration (R01AG072681-S1)

  ➢ Debt as a SDoH: credit card report linkages (e.g., Education Studies for Healthy Aging Research (EdSHARe)).

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Challenge # 3: Building causal evidence

Very commonly, we wish to know about causal relations…

   If we increased X (wages), would cognitive function also improve?

But instead, we derive statistical associations…

Challenge # 3- Building causal evidence

- ➢ Confounder adjustment
- ➢ Inverse probability weighting
- ➢ Trial emulation and quasi-experimental (e.g., IV, DID, RDD)

Quasi-Experimental designs bridge the gap between observational and experimental studies
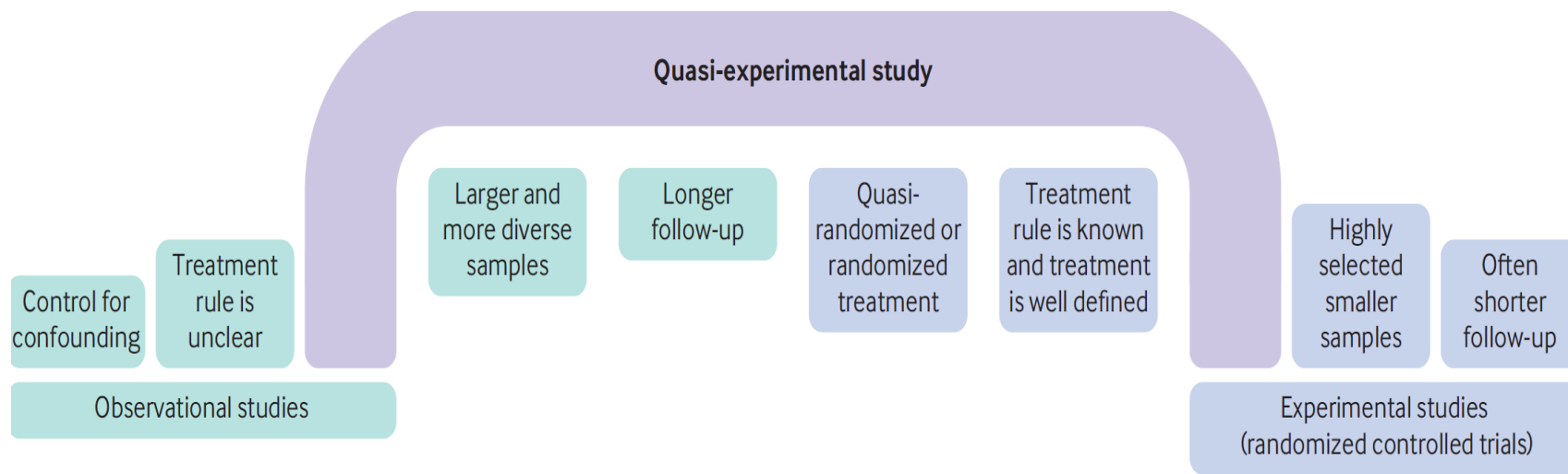
- Joins the strengths of (observational) sample size and follow up length with (experimental) random or quasi-random assignment, and well known/transparent treatment rules

- Transparent statistical approach that provides "real-world" effects of treatments and policies and has distinct advantages over traditional RCTs

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Adopt a structural lens

Racial/ethnic and other social inequities in dementia are attributable to historical and social processes (e.g., immigration, wealth generating mechanisms) that shape access to health-promoting resources and to major underlying pathways.

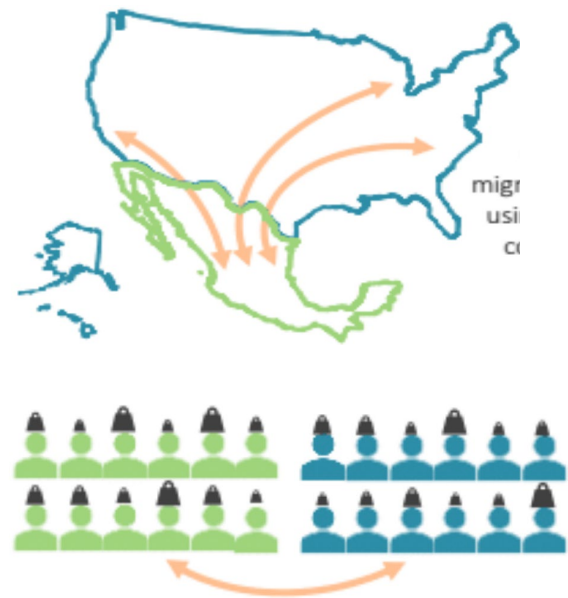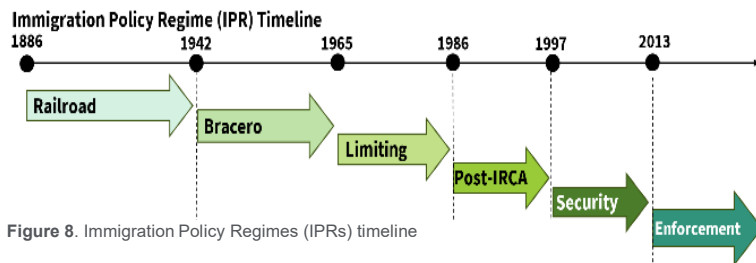# Racial residential segregation & cognition, CARDIA
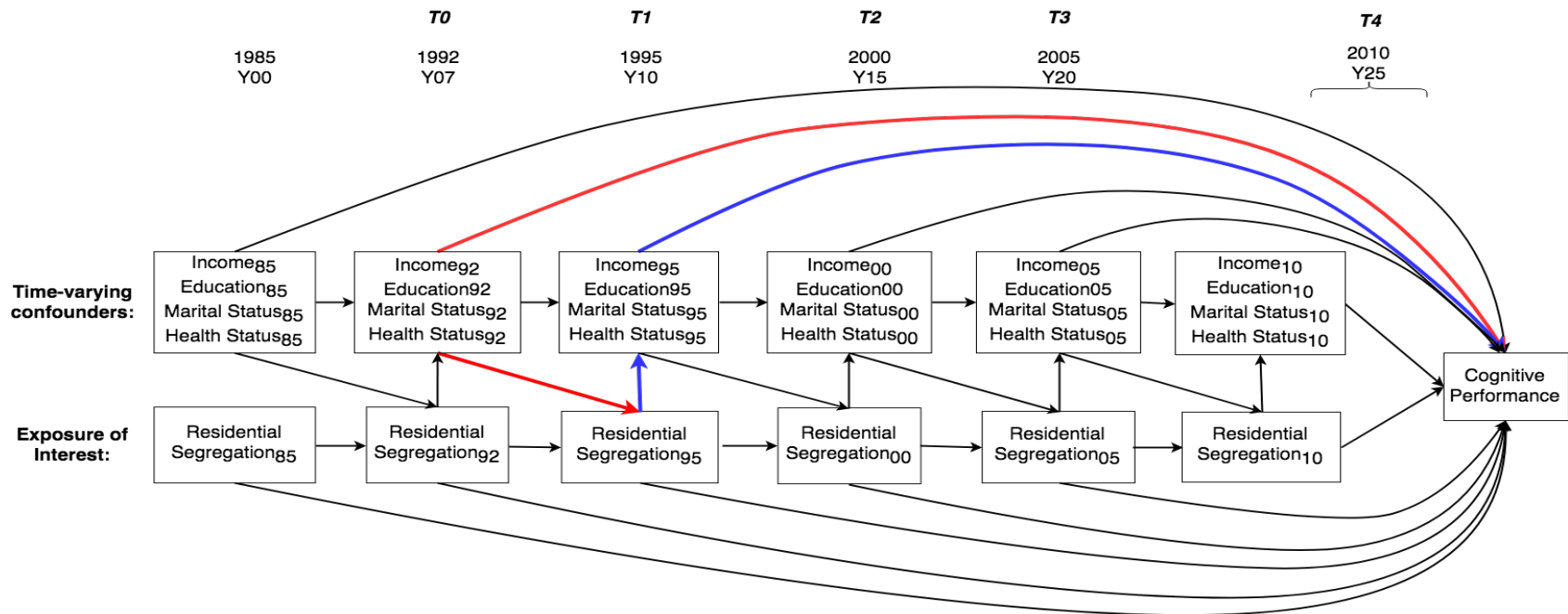
Longitudinal marginal structural models: Segregation impacts income, marital status, health, and education, and these factors also impact residential mobility.

Bringing a Structural Lens to Immigration & Cognitive Health (R01AG089174)

Use immigration policy regimes and neighborhood-level migration flows to address socio-political contexts beyond SES

Immigration Policy Regime (IPR) Timeline
1886   1942   1965   1986   1997   2013

Railroad
Bracero
Limiting
Post-IRCA
Security
Enforcement

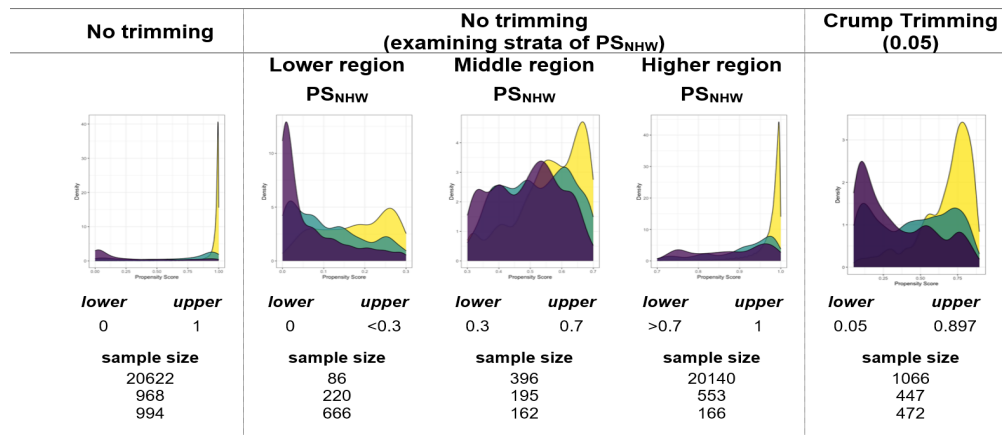**Figure 8**. Immigration Policy Regimes (IPRs) timeline

Better captures life course experience of immigration on health from various levels of influence and enhances knowledge of how these factors drive ADRD disparities

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Immigration & Cognition (RF1AG055486)

life course and social process
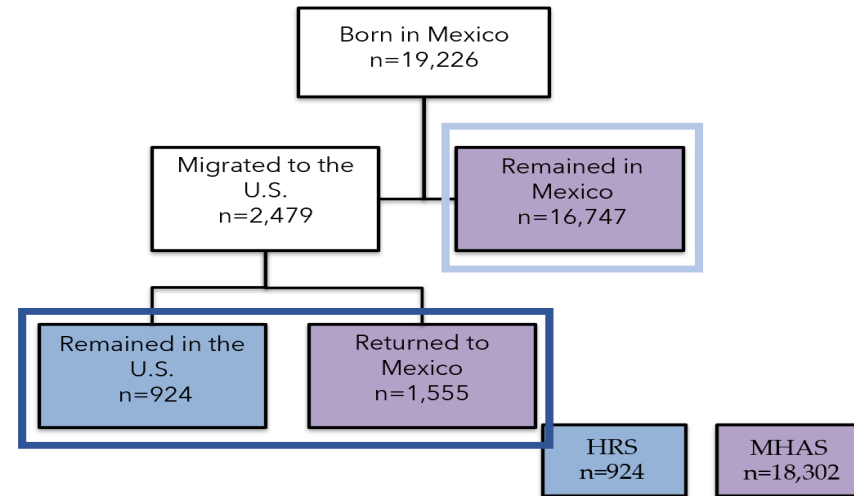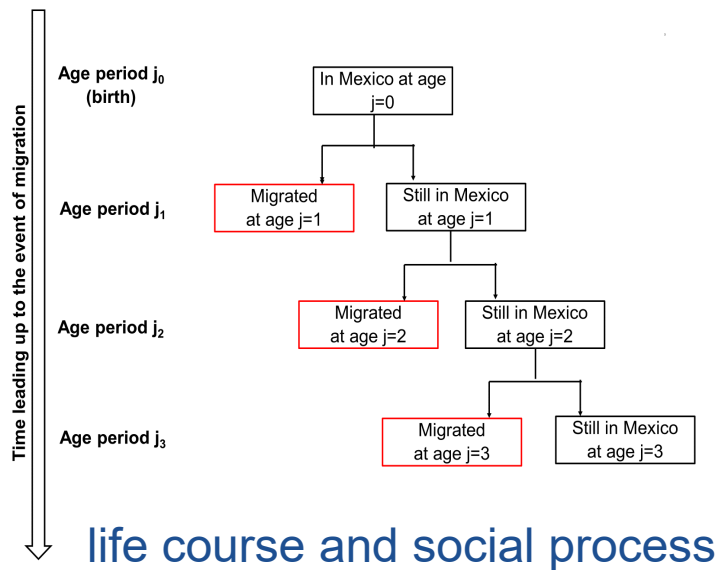
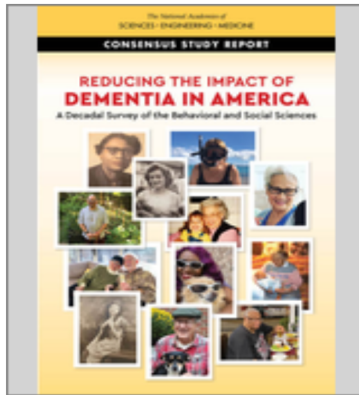What is the causal contrast?

Establishing risk factor overlap

Kezios K,,,M. Glymour, Zeki Al Hazzouri. Epidemiology 34(4): 495-504; 2023.

Zeki Al Hazzouri,,,M. Glymour. Epidemiology 32(1): 50-60; 2021

Future Directions

Reducing the Impact of Dementia in America
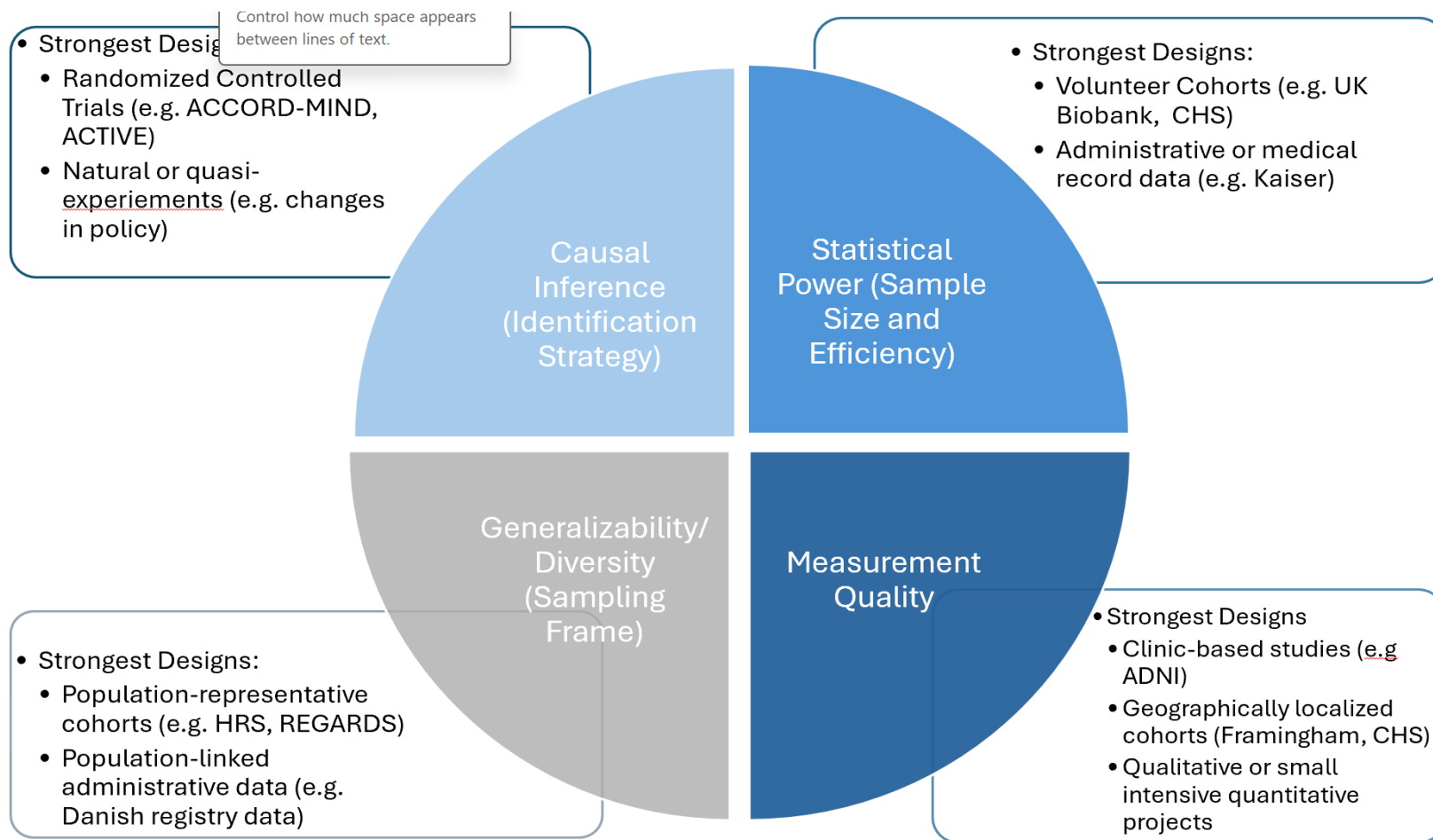
A Decadal Survey of the Behavioral and Social Sciences

Authors

National Academies of Sciences, Engineering, and Medicine; Division of Behavioral and Social Sciences and Education; Board on Behavioral, Cognitive, and Sensory Sciences; Committee on the Decadal Survey of Behavioral and Social Science Research on Alzheimer's Disease and Alzheimer's Disease-Related Dementias.

Washington (DC): National Academies Press (US); 2021 Jul 26.
The National Academies Collection: Reports funded by National Institutes of Health.

Future Directions

- Strongest Designs:
  - Randomized Controlled Trials (e.g. ACCORD-MIND, ACTIVE)
  - Natural or quasi-experiements (e.g. changes in policy)

Causal Inference (Identification Strategy)

- Strongest Designs:
  - Volunteer Cohorts (e.g. UK Biobank, CHS)
  - Administrative or medical record data (e.g. Kaiser)

Statistical Power (Sample Size and Efficiency)

Generalizability/ Diversity (Sampling Frame)

Measurement Quality

- Strongest Designs:
  - Population-representative cohorts (e.g. HRS, REGARDS)
  - Population-linked administrative data (e.g. Danish registry data)

- Strongest Designs
  - Clinic-based studies (e.g ADNI)
  - Geographically localized cohorts (Framingham, CHS)
  - Qualitative or small intensive quantitative projects

Future Directions and Pathways to Reducing the Impact of Dementia: Research and Teaching

Adapted From the book: Reducing the Impact of Dementia in America. *Chapter 8, p 246*

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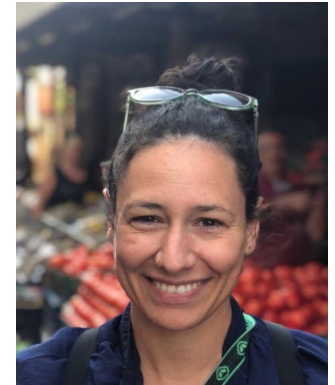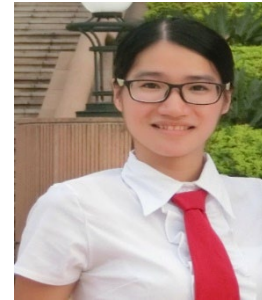
THANK YOU

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