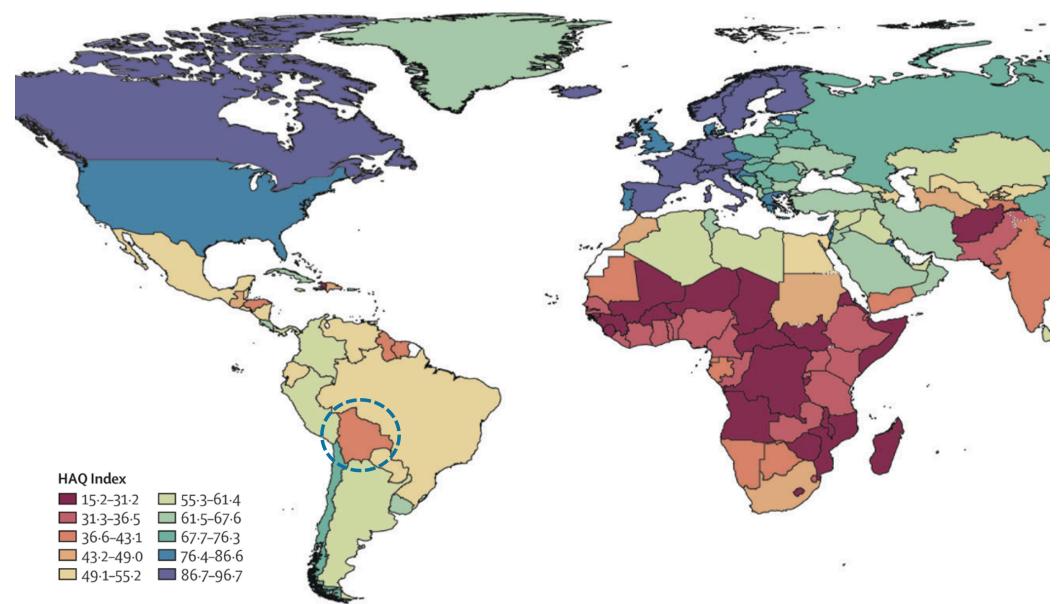


Advancing Health Equity in Aging Research through a Causal Inference Framework

L. Paloma Rojas-Saunero MD, PhD
Postdoctoral scholar
Department of Epidemiology, UCLA

Background

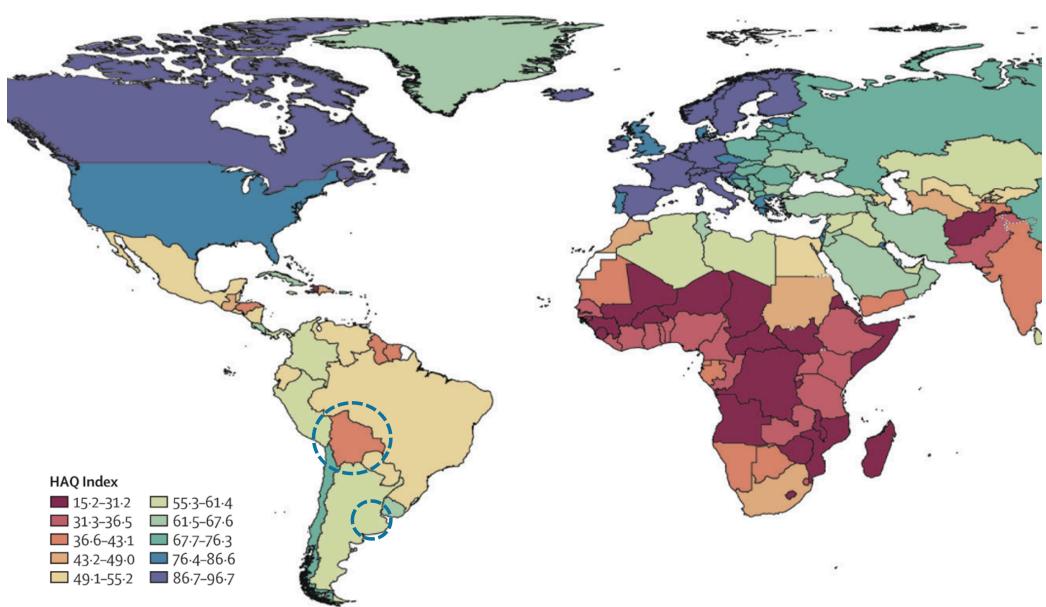
- **Bolivia**
 - Medicine
 - Undergraduate Research Assistant



Healthcare Access and Quality Index, Lancet Global Health, 2022

Background

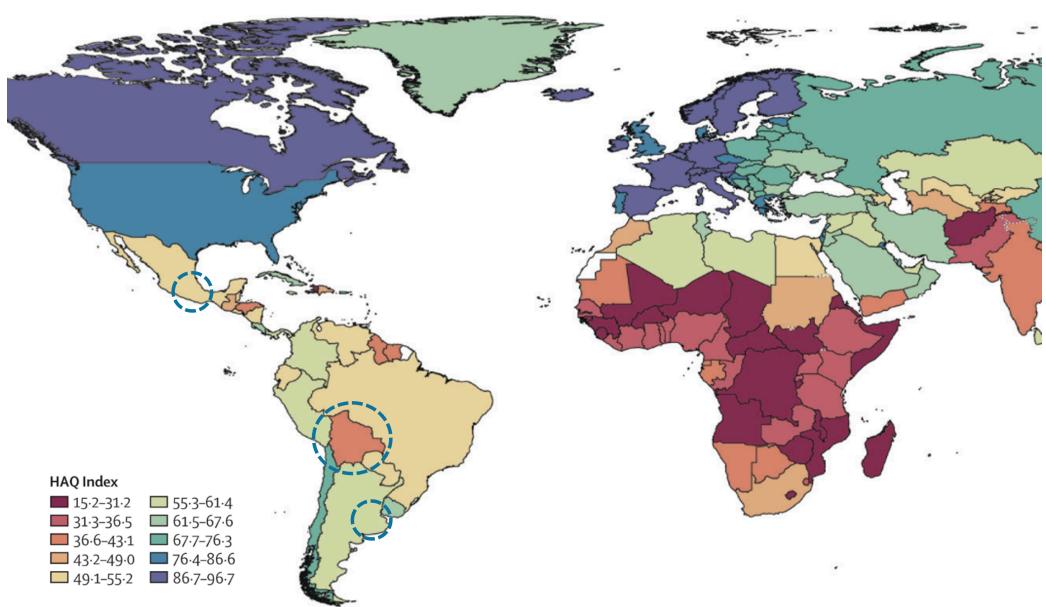
- **Bolivia**
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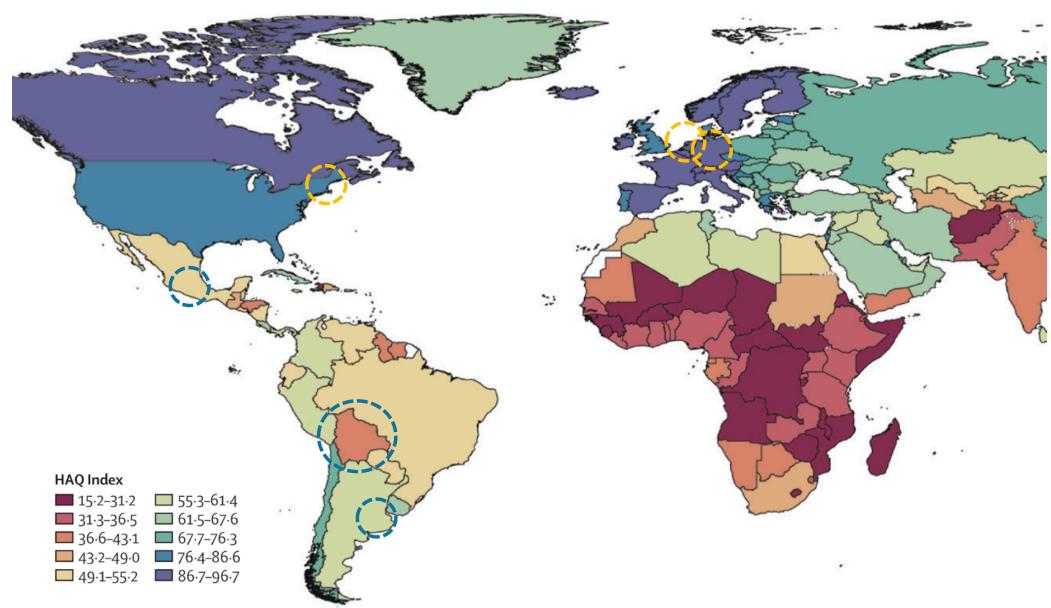
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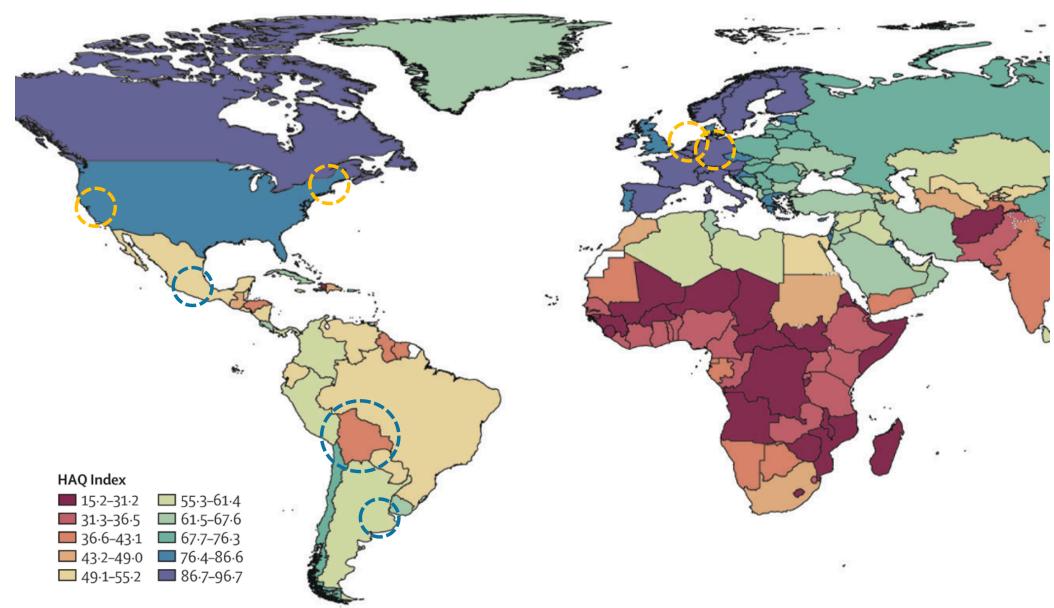
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 - PhD. in Epidemiology, Erasmus MC
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 - Visiting Scholar CAUSALab
- **Germany**
 - Visiting Scholar, Leibniz Inst



Healthcare Access and Quality Index, Lancet Global Health, 2022

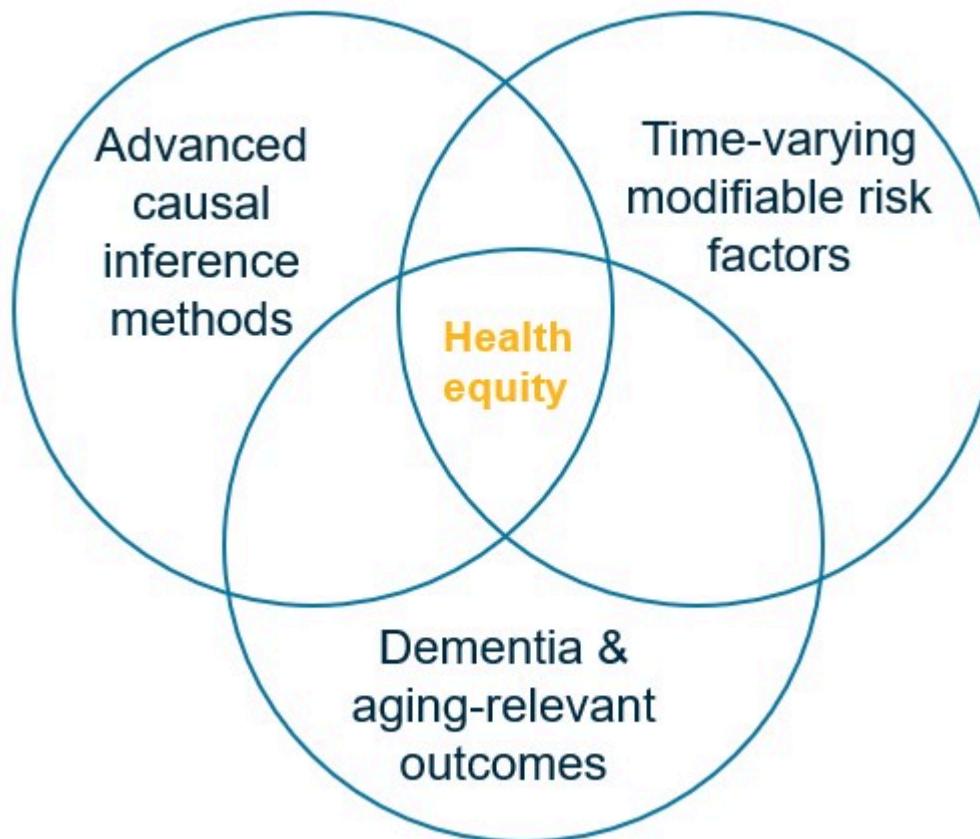
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- **United States**
 - Postdoctoral Scholar, FSPH, UCLA



Healthcare Access and Quality Index, Lancet Global Health, 2022

Research Focus



Research Outline

- **Estimands for competing and truncation events on aging-related outcomes**
 - Smoking and dementia risk
 - Social isolation and functional impairment trajectories

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- **Future work**
 - Occupational determinants of cognitive and brain health

Estimands for Competing and Truncation Events on Aging-related Outcomes

Considering Questions Before Methods in Dementia Research With Competing Events and Causal Goals

Rojas-Saunero LP, Young JG, Didelez V, Ikram A, Swanson SA

American Journal of Epidemiology, 2023

Why smoking may prevent dementia, according to researchers

NICOTINE has been found to protect the brain as it ages so smoking could help prevent dementia, researchers claimed.

By [JOHN FITZPATRICK](#)

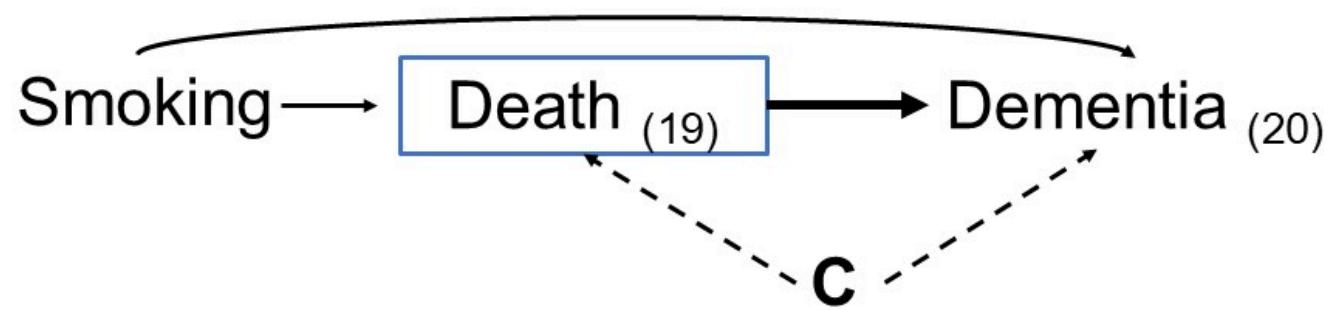
PUBLISHED: 16:25, Sun, Oct 2, 2016 | UPDATED: 18:09, Sun, Oct 2, 2016

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0 



Quitting smoking and 20-year dementia risk

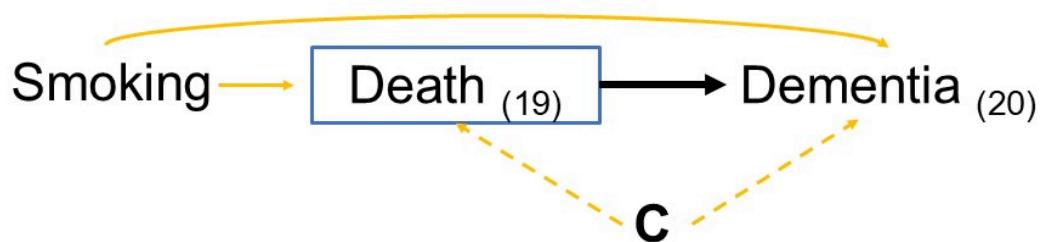


C: Shared risk factors

Questions before methods

Total effect

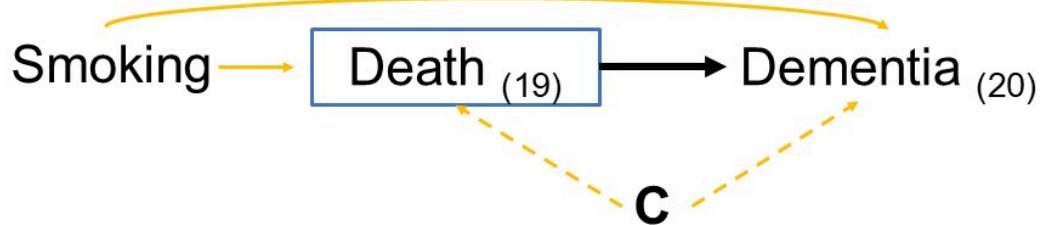
What is the risk of dementia at 20 years of follow-up had all individuals stopped smoking, compared to had all individuals continued smoking?



Questions before methods

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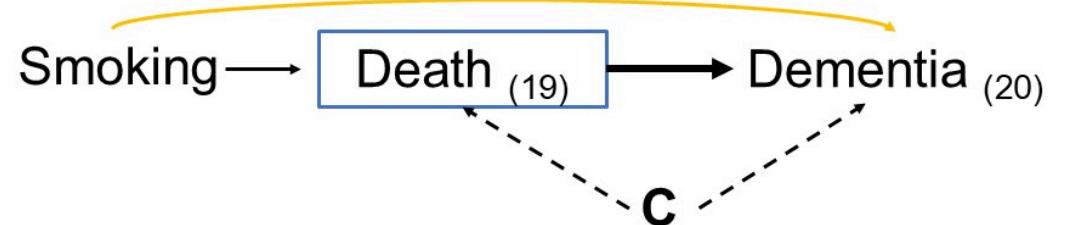
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C: Shared risk factors

Controlled direct effect

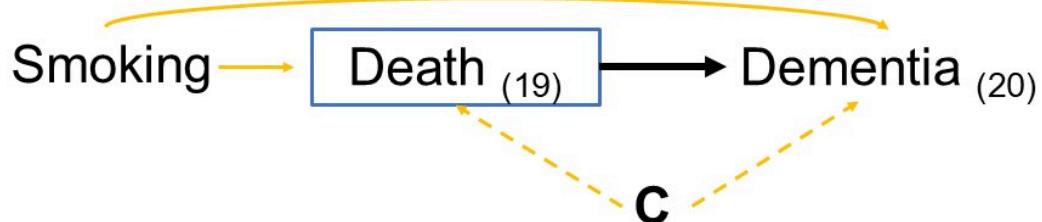
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Questions before methods

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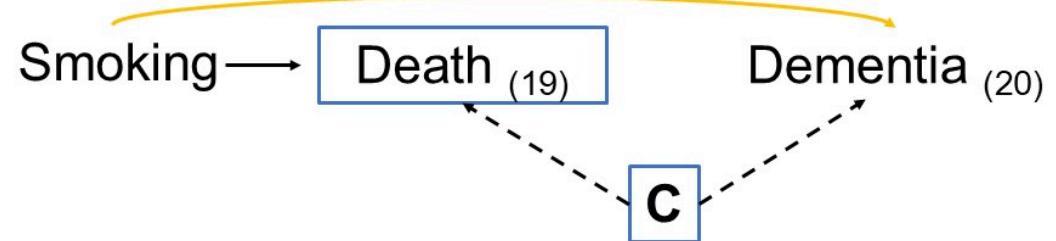
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What is the risk of dementia at 20 years of follow-up had all individuals stopped smoking **and not died** during the study period, compared to had all individuals continued smoking **and not died** ?



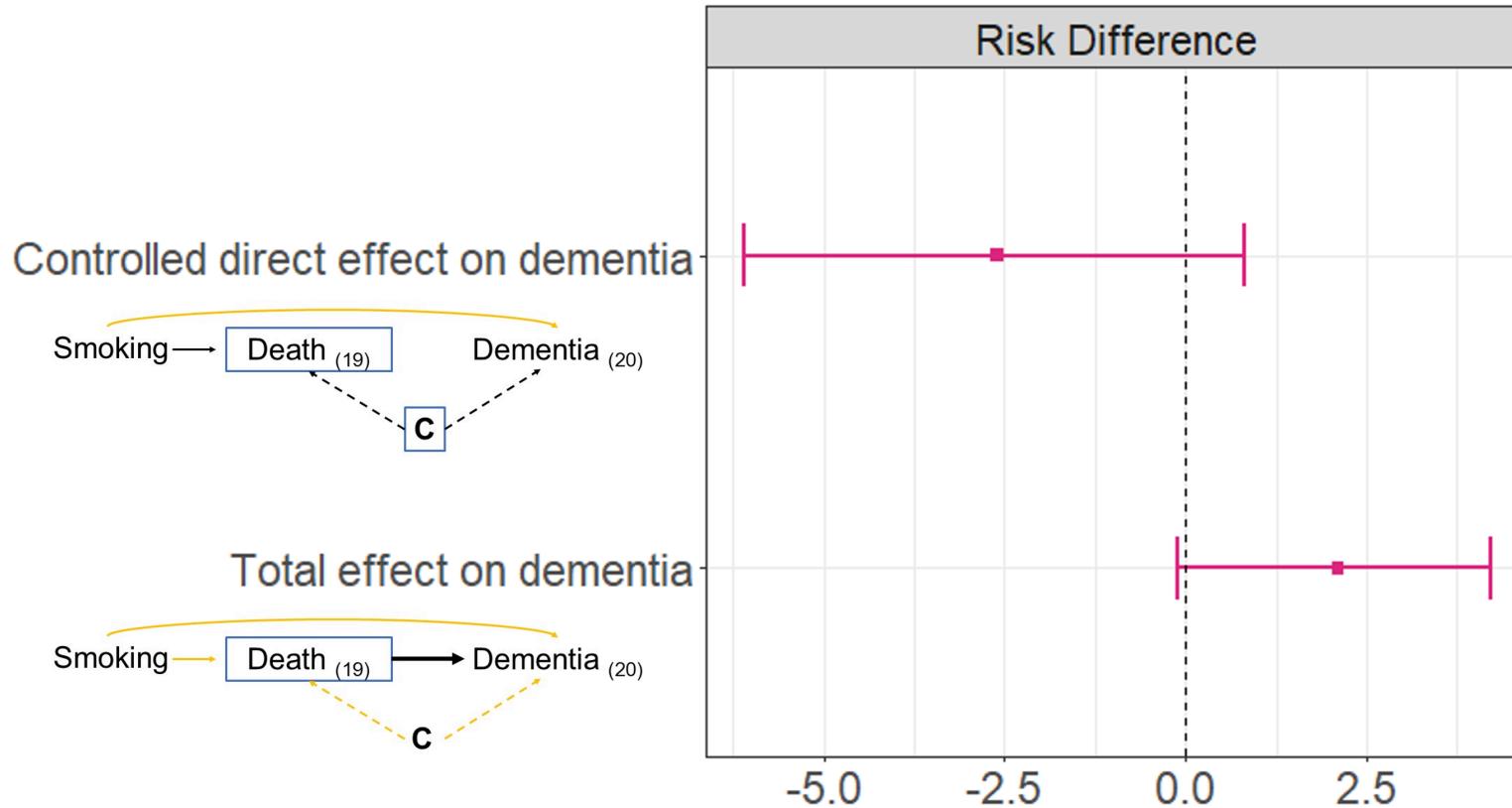
Identifiability assumptions for death

Assumption	Total Effect	Controlled direct effect
Exchangeability	Not needed	Death is independent of future outcomes had everyone followed A = a and death was eliminated, conditional on covariates
Positivity	Not needed	At every follow-up time, there are individuals with any possibly observed level A = a and covariate history who remain alive and free of dementia diagnosis.
Consistency	Not needed	An intervention that “eliminates death” is well-defined.

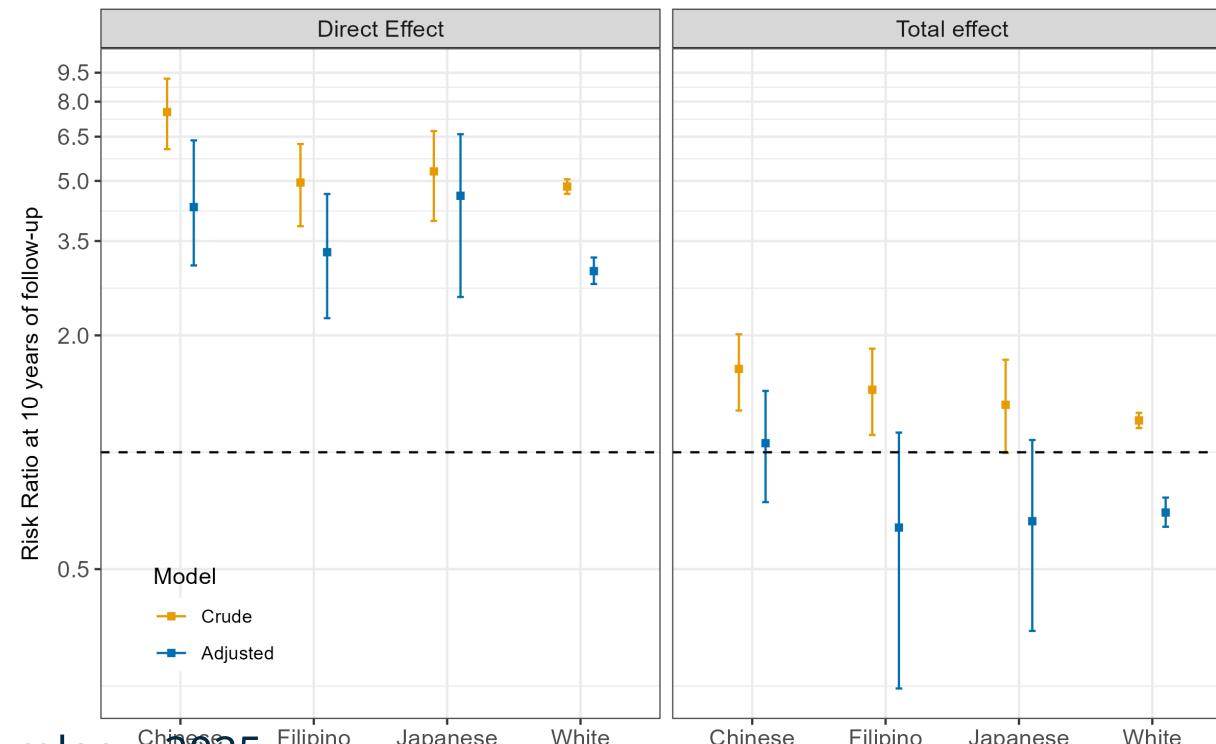
Estimators

Feature	Total Effect	Controlled Direct Effect
Estimator	Aalen–Johansen	Kaplan–Meier
Death handling	Competing event	Censoring event
Hazards needed	Dementia + death	Dementia only
Risks	Risk of dementia = conditional risk of dementia in year $t \times$ cumulative probability of surviving dementia-free and death-free up to $t-1$	Risk of dementia = conditional risk of dementia in year $t \times$ cumulative probability of surviving dementia-free up to $t-1$

Quitting smoking on dementia risk at 20 years



Incident stroke on dementia risk in Asian American and White population



Rojas-Saunero et al. Neurology. 2025



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Social isolation and functional impairment trajectories in a diverse cohort of middle-aged and older adults in Northern California

Rojas-Saunero LP, Ikesu R, Zhou Y, Hayes-Larson E, Fong J, Chen R, Posis AIB, Whitmer RA, Gilsanz P, Glymour MM, Torres JM, Kotwal AA, Mayeda ER

Currently under R&R at J Gerontol A Biol Sci Med Sci. 2025

Work supported by USC/UCLA Biodemography Center Pilot Project Award



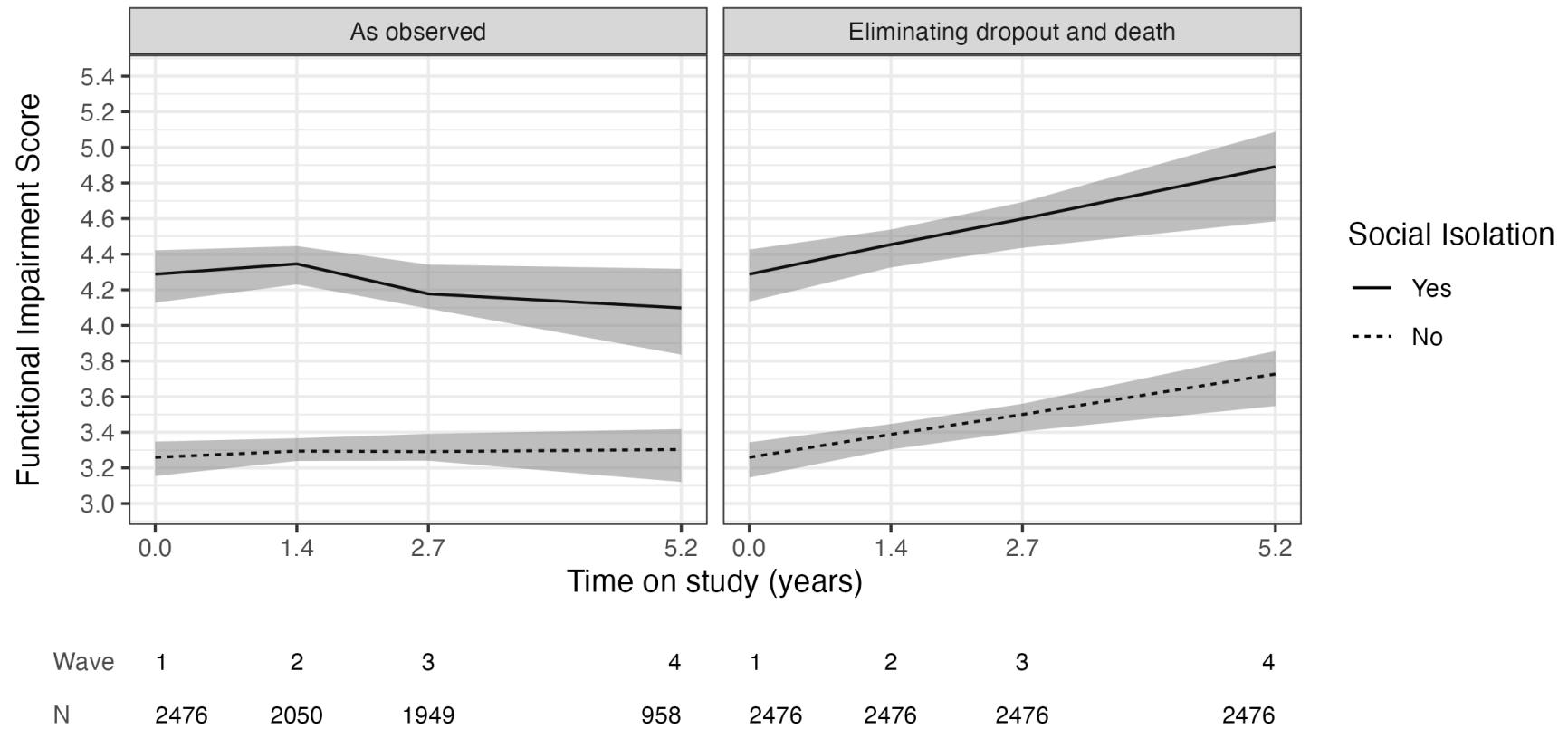
Motivation

- There is mixed evidence on the relationship between social isolation and functional impairment in older adults
- Most longitudinal studies consider disability as an absorbing state, and often restrict their analytic sample to those with measured outcome
- When death is present, the outcome at future time-points is unknown

Methods

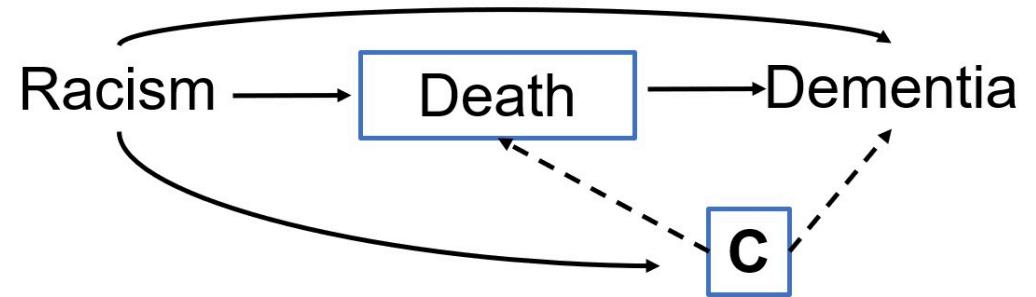
- **Data:** Kaiser Healthy Aging and Diverse Life Experiences (KHANDLE) and Study of Healthy Aging in African Americans (STAR)
- **Social Isolation:** Steptoe 5-item Social Isolation Index, binarized
- **Functional Impairment:** Sum of 12 items measuring basic activities of daily living (ADLs), instrumental ADLs, and mobility; range: 0-36
- **Descriptive estimands:**
 - **As observed:** Marginal trajectories based on outcome predictions for the full cohort and averaged within each wave among those participants who remained in the study.
 - **Under elimination of dropout and death:** Marginal trajectories based on outcome predictions for the full cohort at all waves

Social isolation and trajectories of functional impairment



Competing/truncation events in health equity research

Descriptive, predictive or causal contrasts comparing dementia risk or aging-relevant biomarkers between two groups (*disparity estimand*) will be impacted by differential mortality



Rojas-Saunero LP, Glymour MM, Mayeda ER. Selection Bias in Health Research: Quantifying, Eliminating, or Exacerbating Health Disparities?. *Current Epidemiology Reports*. 2024

Related work

- **Rojas-Saunero LP**, Wu Y, Gee GC, Brookmeyer R, Posis AIB, Whitmer RA, Gilsanz P, Mayeda ER. Sex/gender differences in the risk of dementia for Asian American ethnic subgroups and non-Latino White older adults in California. *npj Dementia*. 2025.
- **Rojas-Saunero LP**, van der Willik KD, Schagen SB, Ikram MA, Swanson SA. Towards a clearer causal question underlying the association between cancer and dementia. *Epidemiology*. 2024.
- **Rojas-Saunero LP**, Patino CM, Ferreira JC. Intercurrent events in clinical research: the norm, not the exception. *Jornal Brasileiro de Pneumologia*. 2022.
- Young J, Stensrud M, **Rojas-Saunero LP**. Society of Epidemiologic Research Pre-Conference Workshop: "**Causal inference with competing events**". 2022-2023.

Take away points

- When competing events are present there is more than one way to consider them as part of the primary research question

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- Let the question guide the most appropriate methods and estimators

Take away points

- When competing events are present there is more than one way to consider them as part of the primary research question
- Let the question guide the most appropriate methods and estimators
- We need to communicate that all these questions are possible with their trade-offs, rather than continuing a narrative that "One size fits all"

Causal Methods to Study Cardiovascular Risk Factors Related to Dementia

Racial and ethnic differences in the risk of dementia diagnosis under hypothetical blood pressure-lowering interventions: The Multi-Ethnic Study of Atherosclerosis

Rojas-Saunero LP, Hughes TM, Mayeda ER, Jimenez MP

Alzheimer's & Dementia, 2024



Motivation

- High blood pressure is considered a potential modifiable risk factor for dementia risk

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- Most observational studies have either used blood pressure measure at 1 one time-point in life, or have evaluated the association between blood pressure trajectories and dementia risk without accounting for time-varying confounders

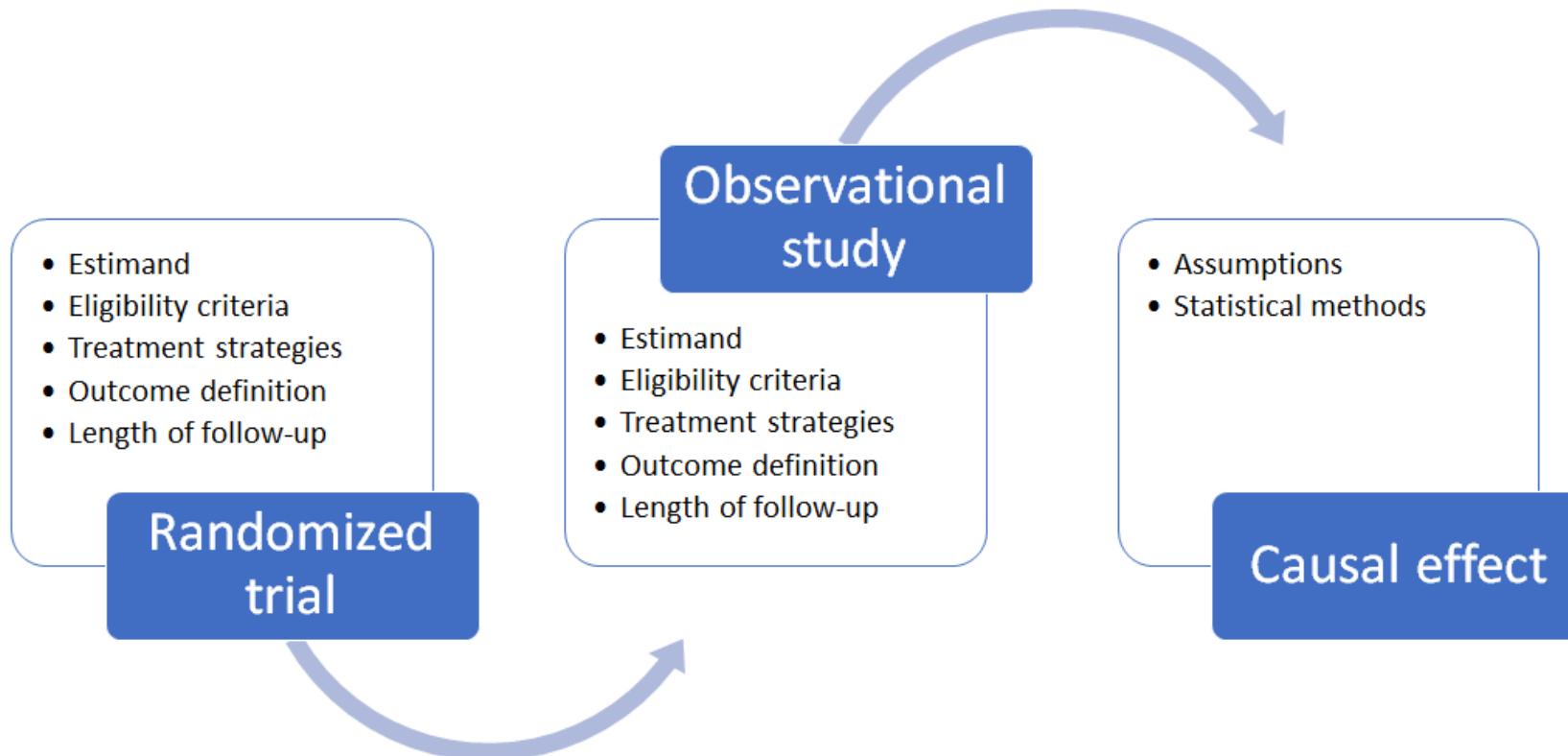
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Motivation

- High blood pressure is considered a potential modifiable risk factor for dementia risk
- Most observational studies have either used blood pressure measure at 1 one time-point in life, or have evaluated the association between blood pressure trajectories and dementia risk without accounting for time-varying confounders
- The SPRINT MIND trial is the first trial to assess the effect of **intensive SBP (<120 mmHg)** vs. **standard (<140 mmHg)** blood pressure control on probable dementia, but their study population was highly selected
- Limited evidence on effect heterogeneity

Target trial framework



Section	Target trial protocol	Emulation using observational data
Eligibility criteria	Chinese, Black, Latinx, White ‐ < 85 years old ‐ Free of cardiovascular disease ‐ No dementia diagnosis at baseline	Same
Treatment strategies	0. Natural course (comparison arm) 1. Keep SBP < 120 mmHg 2. Keep SBP < 140 mmHg	Same strategies during the first 10 years of follow-up
Follow-up	From year of first visit until 19 years of follow-up, or year of dementia or death, whichever happened first	Same
Outcome	Dementia (Death as a censoring event)	Same
Causal contrast	What would have been the risk of dementia if all individuals adhered to their assigned strategy and death was eliminated (Controlled direct per protocol effect)	Same

Statistical analysis

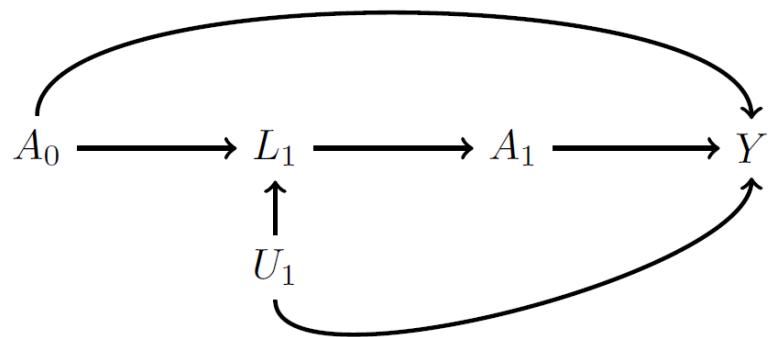
What would have happened had everyone was randomized and had adhered to each intervention (g)?

Parametric G-formula: Allows presence of time-varying confounding feedback

Statistical analysis

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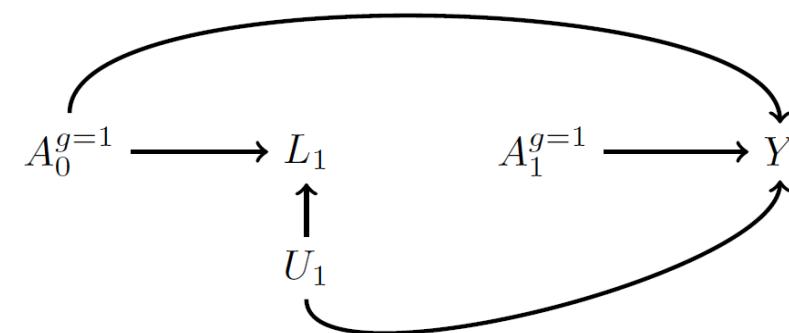
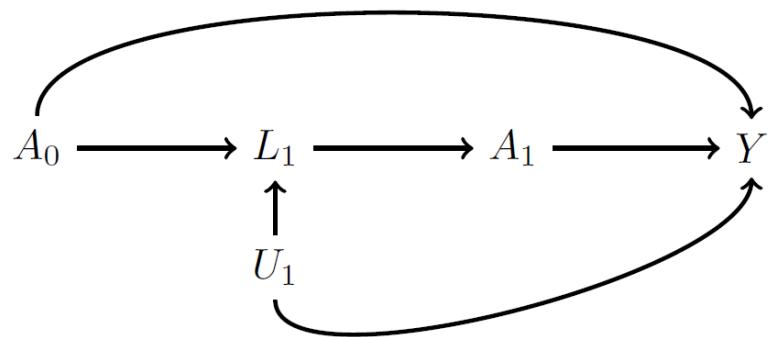
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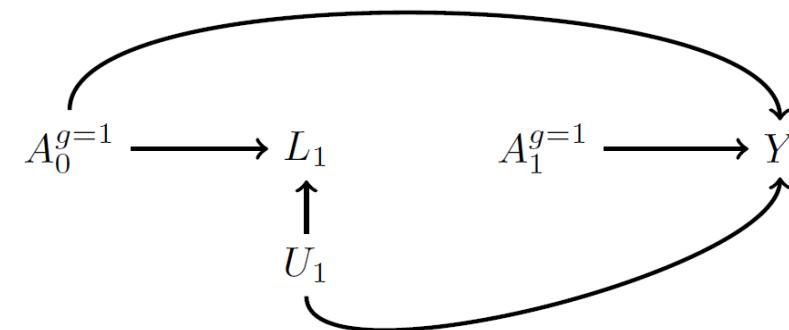
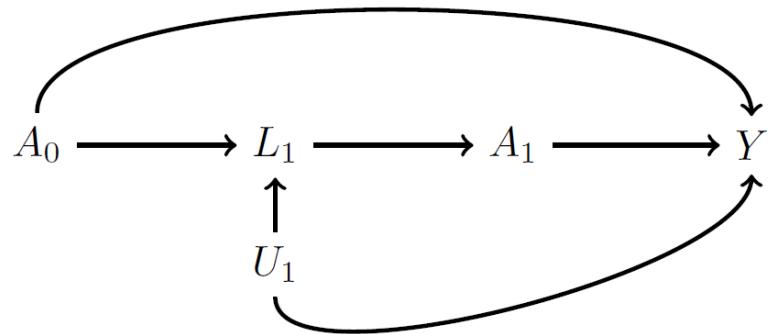
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Statistical analysis

What would have happened had everyone was randomized and had adhered to each intervention (g)?

Parametric G-formula: Allows presence of time-varying confounding feedback



A = SBP, **L** = *Fixed covariates*: age, sex, education, income, health insurance, marital status, APOE- $\epsilon 4$ genotype, history of diabetes. *Time-varying covariates*: SBP, cardiometabolic biomarkers, behavioral measurements, incident cardiovascular comorbidities **Y** = Dementia

Methods

1. Model each variable (A , L , Y , D) using the covariate history.

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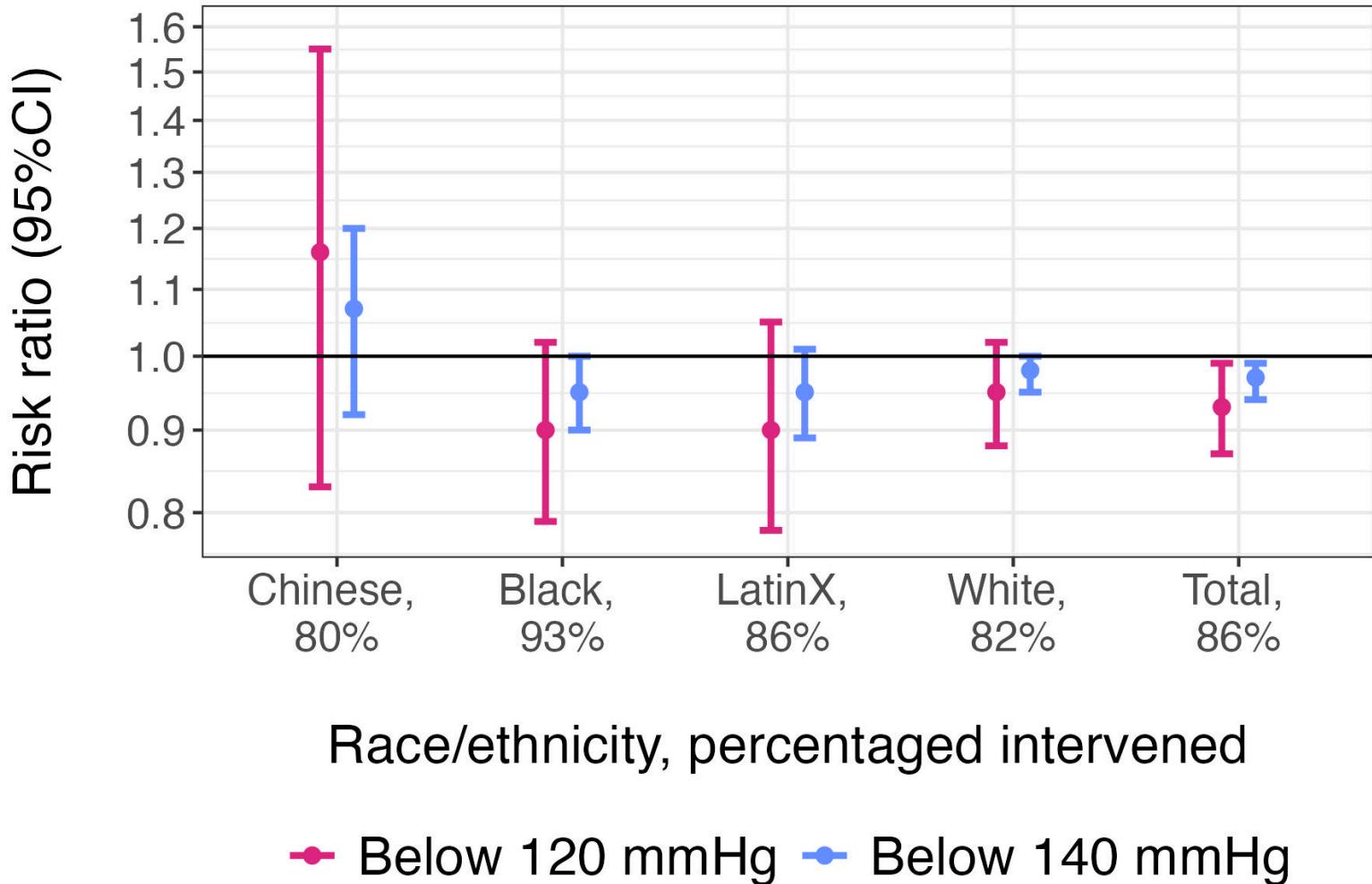
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6. Repeat steps 2-6 for each hypothetical intervention.

A (exposure), L (confounders), Y (outcome), D (competing event)

Results



Related work

- **Rojas-Saunero LP**, Hilal S, Murray EJ, Logan RW, Ikram MA, Swanson SA. Hypothetical blood-pressure-lowering interventions and risk of stroke and dementia. *European Journal of Epidemiology*. 2021.
- Caniglia EC, **Rojas-Saunero LP**, Hilal S, Licher S, Logan R, Stricker B, Ikram MA, Swanson SA. Emulating a target trial of statin use and risk of dementia using cohort data. *Neurology*. 2020.
- *Triangulation of Innovative Methods to End Alzheimer's Disease (TIME-AD)* grant, P01AG082653-01A1: Collaborator, currently writing guidelines on target trial emulation

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Target trial emulation in critical care

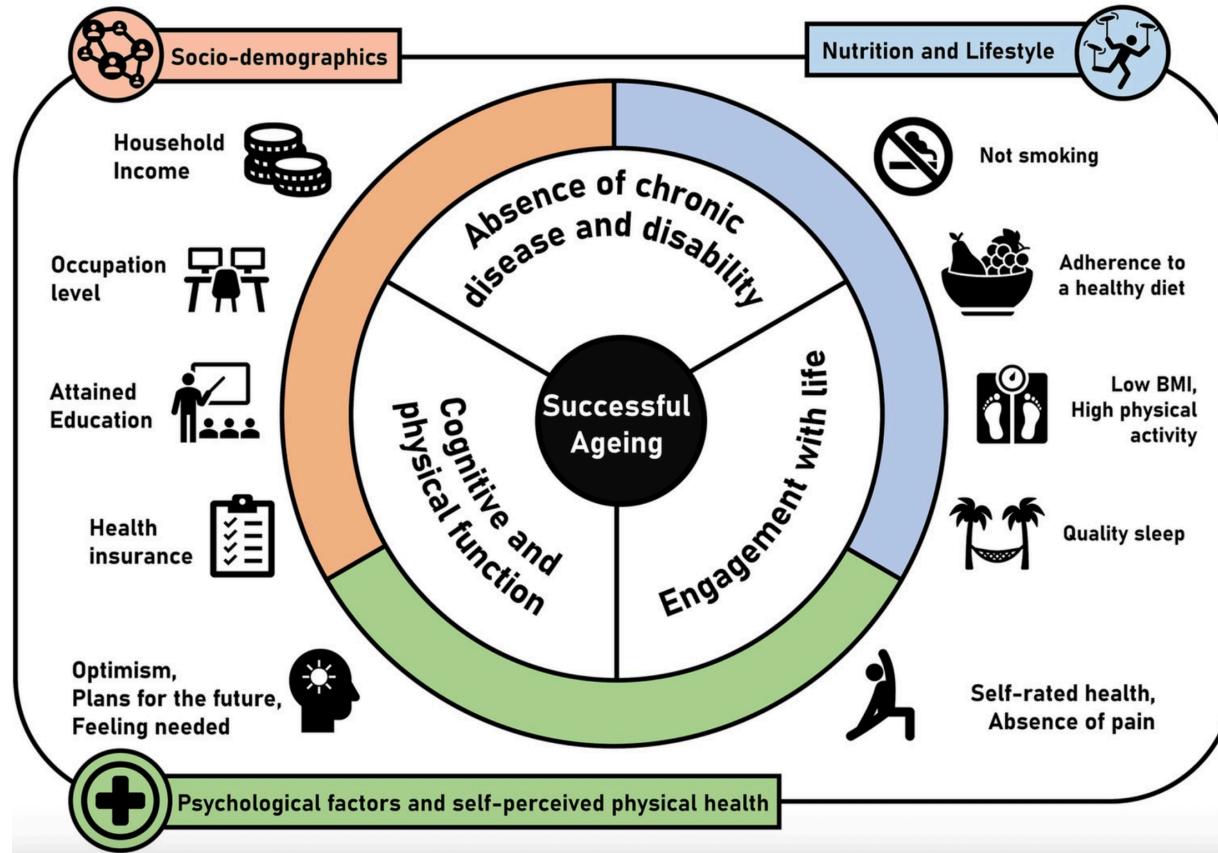
- Urner M, Jüni P, **Rojas-Saunero LP**, Hansen B, Brochard LJ, Ferguson ND, Fan E. Limiting Dynamic Driving Pressure in Patients Requiring Mechanical Ventilation. *Critical Care Medicine*. 2023.

Related work

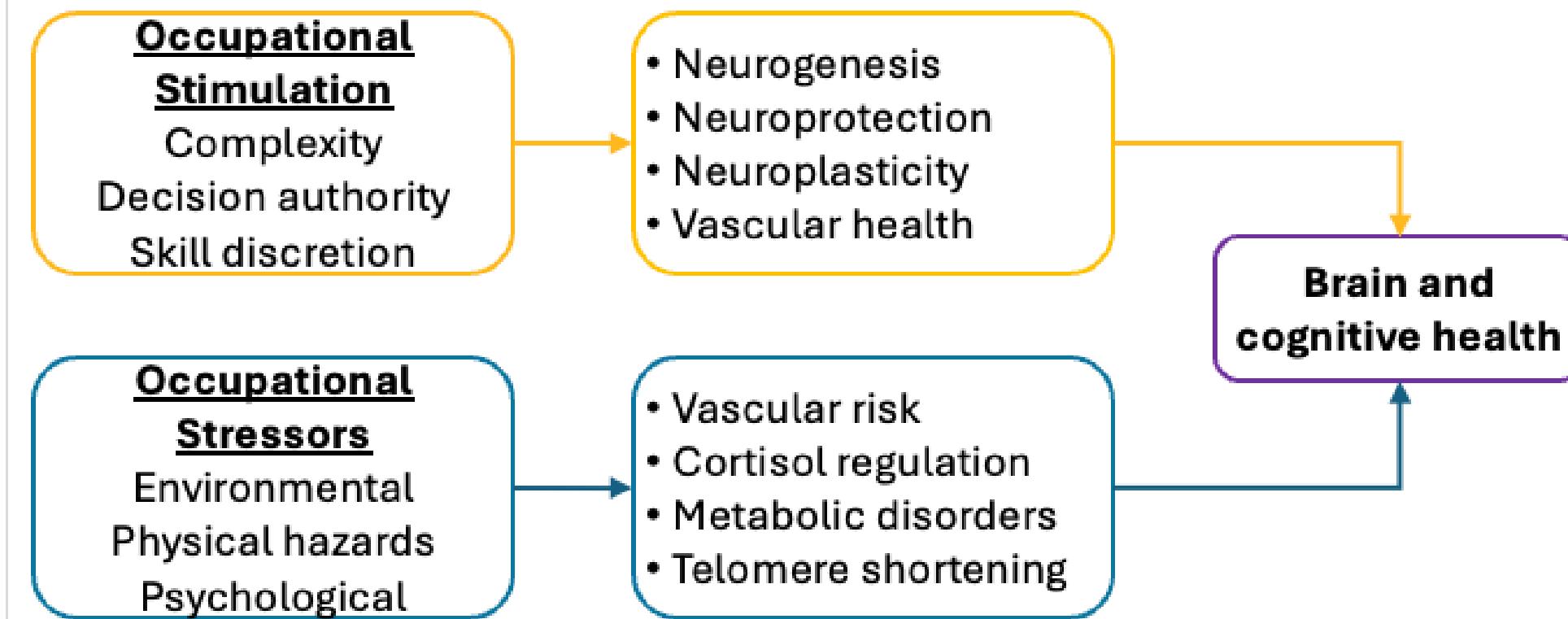
Target trial emulation for social determinants of health

- **Rojas-Saunero LP**, Labrecque JA, Swanson SA. Invited Commentary: Conducting and Emulating Trials to Study Effects of Social Interventions. *American Journal of Epidemiology*. 2022.
- Ikesu R, Wu Y, **Rojas-Saunero LP**, Nianogo R, Torres J, Kotwal A, Yusuke T, Ramirez C, Mayeda ER. Estimating the effects of hypothetical loneliness interventions on memory function among middle-aged and older adults in the United States. *Under review* 2025
- Wu Y, Zhou Y, **Rojas-Saunero LP**, Chen R, Gross AL, Nianogo R, Ritz BR, Mayeda ER. Effect of hypothetical education interventions on late-life memory function and decline among middle-aged and older adults in China. *Work in progress*.
- Wu Y, Ikesu R, **Rojas-Saunero LP**, Nianogo R, Gross AL, Ritz BR, Seamans MJ, Elser H, Mayeda ER. Emulating a target trial of sustained influenza vaccination and memory function and decline among middle-aged and older adults in the United States. *Work in progress*.

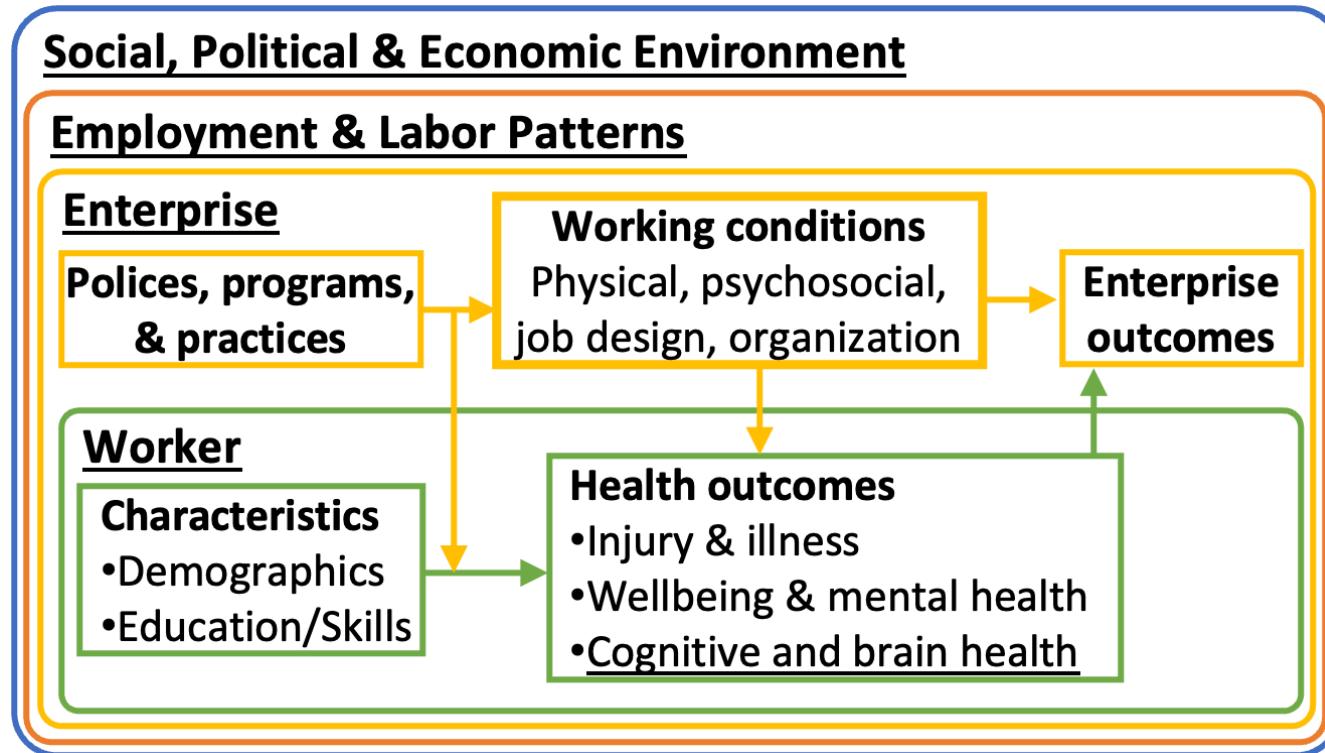
Future Directions



Occupational Determinants of Cognitive and Brain Health



Conceptual framework



Occupational Determinants of Cognitive and Brain Health Among Middle-Aged and Older Latinxs

- **Goal:** Understand how work-related exposures shape cognitive aging and ADRD risk in Latinx populations



Occupational Determinants of Cognitive and Brain Health Among Middle-Aged and Older Latinxs

- **Goal:** Understand how work-related exposures shape cognitive aging and ADRD risk in Latinx populations
- **Early life to midlife:** Do physical & mental job stressors shape cognitive function in Latina women from agricultural areas? (CHAMACOS)
- **Mid- and Late Life** How do job stressors & occupational complexity relate to neuroimaging biomarkers? (SOL-INCA)



Occupational Determinants of Cognitive and Brain Health Among Middle-Aged and Older Latinxs

- **Goal:** Understand how work-related exposures shape cognitive aging and ADRD risk in Latinx populations
- **Early life to midlife:** Do physical & mental job stressors shape cognitive function in Latina women from agricultural areas? (CHAMACOS)
- **Mid- and Late Life** How do job stressors & occupational complexity relate to neuroimaging biomarkers? (SOL-INCA)

Interventions: What much would cognitive decline change had we reduced job stressors and/or increased occupational complexity? Who benefits most? (SOL-INCA)

NIH | NIA K99/R00, Impact score: 16, *pending*



Potential collaborations

- Epidemiology Data Center
- Center for Social Dynamics and Community Health
- Center for Aging and Population Health
- Aging Institute
- T-32 Epidemiology of Aging Training Grant Program

Potential teaching

Core Epidemiology & Methods

- Intro to public health/epidemiology
- Advanced methods: Causal inference

Quantitative & Computational Tools

- Biostatistics for Public Health
- R Programming & Data Visualization
- Reproducibility and Open Science

Specialized Methods

- Causal Survival Analysis & Competing Risks
- Target Trial Emulation for Time-varying Exposures

Specialized Topics

- Epidemiology of Aging
- Lifestyle intervention for noncommunicable chronic diseases
- Social epidemiology
- Decolonizing Public Health

Mentors, students and collaborators

- Elizabeth Rose Mayeda, UCLA
(Postdoc Mentor)
- Sonja A. Swanson, Pitt (*PhD Mentor*)
- Alexander Ivan Posis, UC Davis
- Courtney S. Thomas Tobin, UCLA
- Dan Mungas, UC Davis
- Eleanor Hayes-Larson, USC
- Eleanor Murray, BU
- Ellen Caniglia, Penn
- Gilbert C. Gee, UCLA
- Hector Gonzalez, UCSD
- Hirám Beltrán Sánchez, UCLA
- Jian Li, UCLA
- Jessica G. Young, HSPH
- Joan Casey, UWashington
- Joey Fong, UCLA
- Lan Wen, U. Waterloo
- Laura Acion, Metadocencia
- M. Martha Tellez Rojo, INSP

- Marcia Pescador Jimenez, BU
- Maria M. Glymour, BU
- Mirella Díaz-Santos, UCLA
- Onyiebuchi A. Arah, UCLA
- Paola Gilsanz, KPNC
- Rachel Whitmer, UC Davis
- Roch A. Nianogo, UCLA
- Ron Brookmeyer, UCLA
- Ruijia Chen, BU
- Vanessa Didelez, Leibniz Inst.

Students

- Cecilia Curvale, Hosp. El Cruce
- Gina Nam, UCLA
- Kelly Guo, EMC
- Ryo Ikesu, UCLA
- Taylor Mobley, UCLA
- Yixuan Zhou, UCLA
- Yingyan Wu, UCLA

Academic communities

- Mayeda Research Group
- Practical Causal Inference Lab
- FSPH Rooted Academy
- MELODEM
- Equity for Latinx-Hispanic Healthy Aging (ELHA) Lab
- California Center for Population Research

Grant Support

- USC/UCLA Center on Biodemography and Population Health (PI)
- NIA R01AG074359 (Mayeda)
- NIA R01AG0603969 (Mayeda)
- NIA R01AG052132 (Mayeda)

Thank You, Gracias!

lp.rojassaunero@ucla.edu

Effect of Incident Stroke on Dementia Risk Over 10 Years in a Cohort of Asian American and Non-Latino White Older Adults in California

Rojas-Saunero LP, Zhou Y, Hayes-Larson E, Wu Y, Mobley T, Nianogo R, Elser H, Gee GC, Brookmeyer R, Whitmer R, Gilsanz P, Mayeda ER

Neurology, 2025



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Motivation

- Stroke can trigger pathological changes in the neurovascular unit, disrupting structural and functional connectivity and increasing dementia risk

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- Stroke can trigger pathological changes in the neurovascular unit, disrupting structural and functional connectivity and increasing dementia risk
- Previous work had major methodological limitations: immortal time bias, insufficient adjustment, did not handle competing events
- Studies on this topic have very selected samples with minimal (if any) representation of the Asian American population

Study population & Design

- Asian American and White members of Kaiser Permanente Northern California who participated in health surveys.
 - With no history of stroke
 - With no history of dementia
 - From 60 to 89 years old

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- Asian American and White members of Kaiser Permanente Northern California who participated in health surveys.
 - With no history of stroke
 - With no history of dementia
 - From 60 to 89 years old
- Study Design
 - Exposure: Incident stroke in EHR (ischemic stroke, hemorrhagic stroke)
 - Outcome: Incident dementia diagnosis in EHR
 - Time zero/Baseline: Time of survey
 - End of follow-up: Dementia diagnosis, death, or age 90

Methods

Time-updated inverse probability weights for stroke (IPTW):

To make participants who have a stroke and those who don't comparable at every time-point before stroke

Inverse probability weights for death over follow-up (IPCW):

To make participants who remain alive after stroke comparable to the no-stroke group over follow-up

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Inverse probability weights for death over follow-up (IPCW):

To make participants who remain alive after stroke comparable to the no-stroke group over follow-up

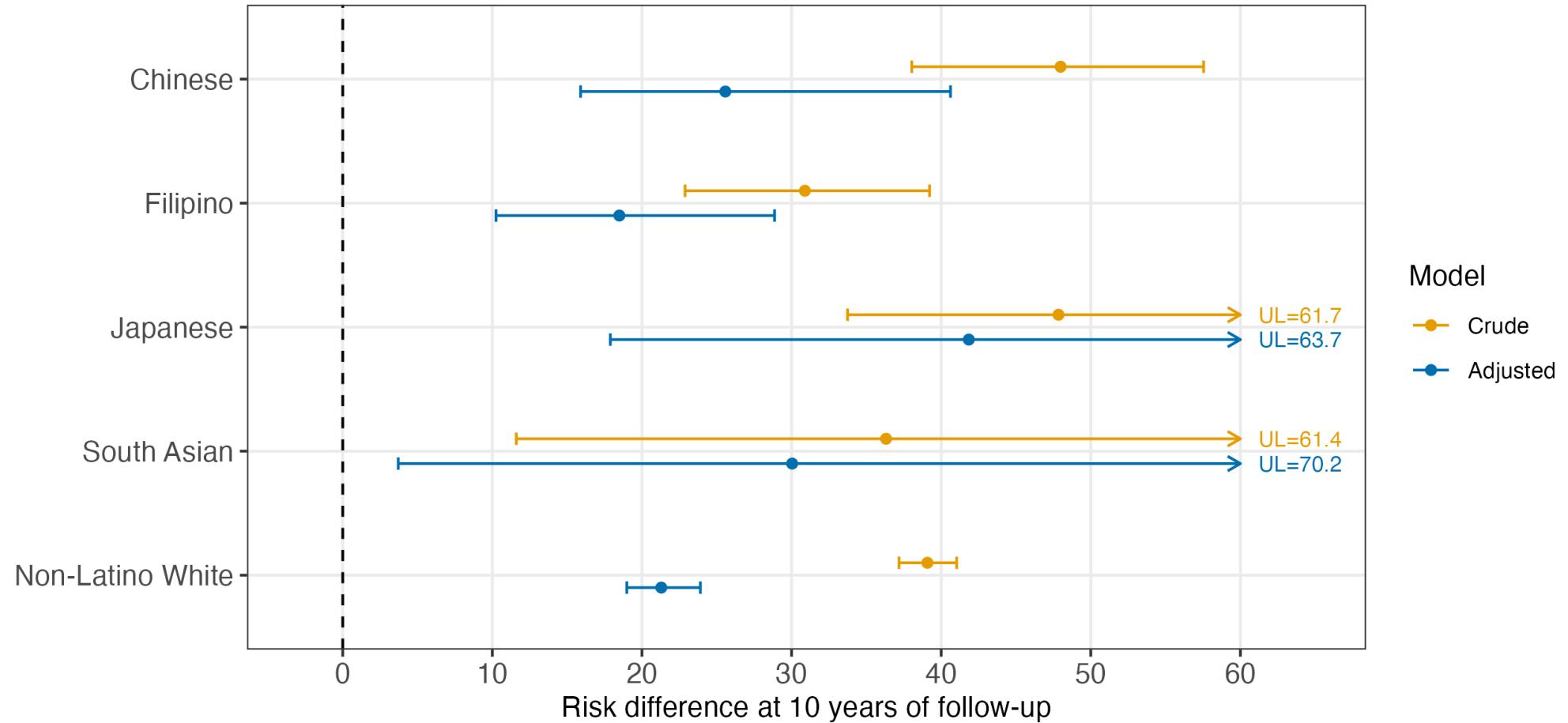
Time-fixed covariates

- Baseline age
- Sex/gender
- Nativity status
- Educational attainment
- Health status
- Smoking status

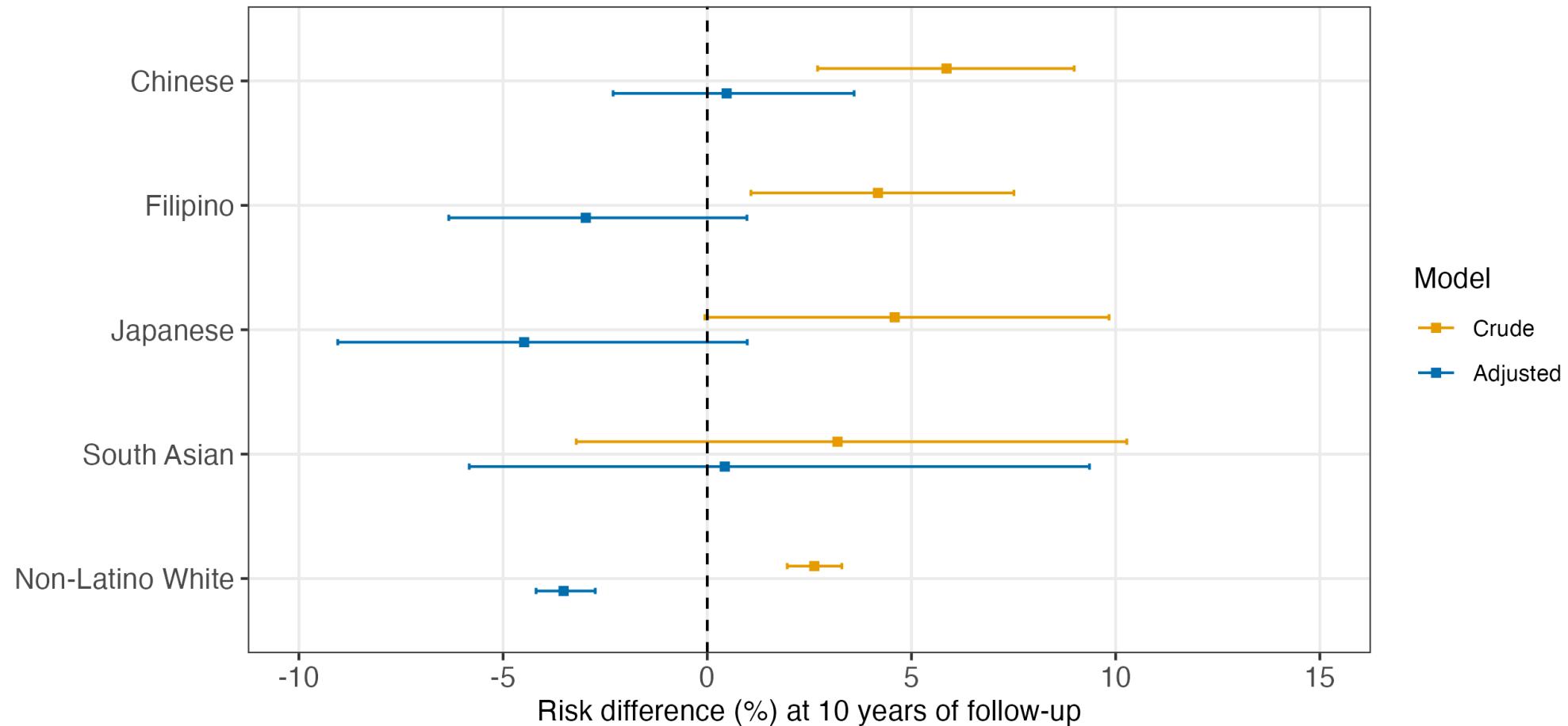
Time-varying covariates

- Systolic blood pressure (median value/year)
- BMI (median value/year)
- Cholesterol (median value/year)
- Incident comorbidities
 - Diabetes
 - Hypertension
 - Myocardial infarction
 - Congestive heart failure
 - Cancer

Controlled direct effect of stroke on dementia risk



Total effect of stroke on dementia risk



Quantitative bias analysis for differential dementia diagnosis

We set the sensitivity of dementia diagnosis in the stroke arm to 0.99 and considered a range of sensitivity values in the no-stroke arm, from 0.50 (worst case scenario) to 0.90.

