

Advancing Health Equity in Aging Research through a Causal Inference Framework

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Fielding
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Outline

Estimands for competing and truncation events on aging-related outcomes

- Smoking and dementia risk
- Stroke and dementia risk
- Social isolation and functional impairment trajectories

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Target trial framework to evaluate modifiable risk factors of dementia

- Intensive vs. standard management of systolic blood pressure across race/ethnic subgroups

Estimands for Competing and Truncation Events

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

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THE LANCET

Diabetes & Endocrinology

This journal Journals Publish Clinical Global health Multimedia Events About

CORRESPONDENCE · Volume 3, Issue 7, P499, July 2015

Does midlife obesity really lower dementia risk?

Helios Pareja-Galeano ^{a,b}✉ · Fabian Sanchis-Gomar ^b · Rafael Alis ^c · María Morán ^{b,d} · Alejandro Lucia ^{a,b}

Inverse Association Between Cancer and Dementia A Population-based Registry Study in Taiwan

Lin, Hsiu-Li MD^{*†}; Lin, Hsiu-Chen MD, PhD^{‡§}; Tseng, Yuan-Fu MD^{*}; Chen, Shih-Chang PhD[¶]; Hsu, Chien-Yeh PhD^{†||}

Author Information

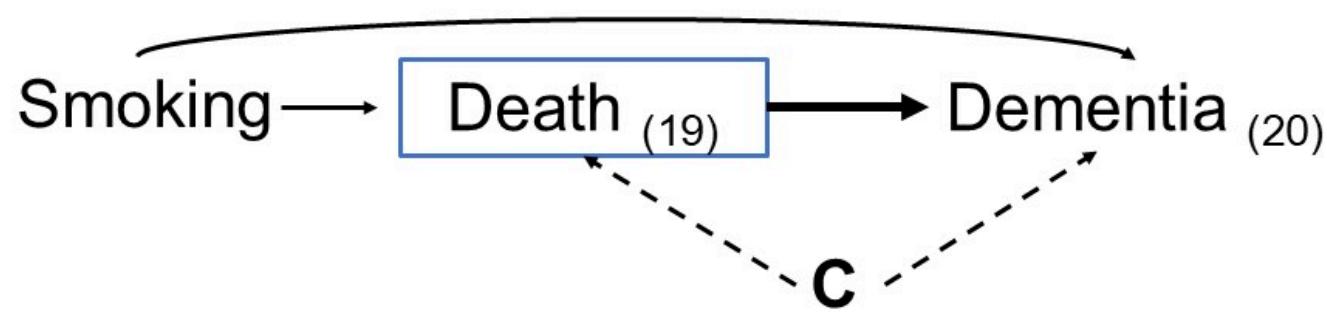
Alzheimer Disease & Associated Disorders 30(2):p 118-122, April–June 2016. | DOI: 10.1097/WAD.0000000000000116

The Association Between Blood Pressure and Incident Alzheimer Disease A Systematic Review and Meta-analysis

Power, Melinda C.^{a,b}; Weuve, Jennifer^{b,c}; Gagne, Joshua J.^{a,d}; McQueen, Matthew B.^e; Viswanathan, Anand^f; Blacker, Deborah^{a,g}

be a consistent pattern across studies. After stratifying on age at BP assessment, we found a suggestion of an inverse association between late-life hypertension and Alzheimer disease and a suggestion of an adverse association between midlife diastolic hypertension and Alzheimer disease.

Quitting smoking and 20-year dementia risk



C: Shared risk factors

Rojas-Saunero et al. *American Journal of Epidemiology*. 2023

Estimand



ESTIMAND

Ingredients

150g unsalted butter
150g chocolate pieces
150g all-purpose flour
1/2 tsp baking powder
1/2 tsp baking soda
200g brown sugar
2 large eggs



ESTIMATE

Directions

1. Heat oven to 160C. Grease 1 liter glass baking pan. Line a 450g loaf tin with baking paper.
2. Melt butter and chocolate in a saucepan over low heat.

Specific quantity that we want to estimate that answers our research question (*parameter of interest*).

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4. Summary measure: A population-level measure of frequency that is *interpretable* (e.g. risk difference: $Pr[Y_{20}^{a=1} = 1] - Pr[Y_{20}^{a=0} = 1]$)

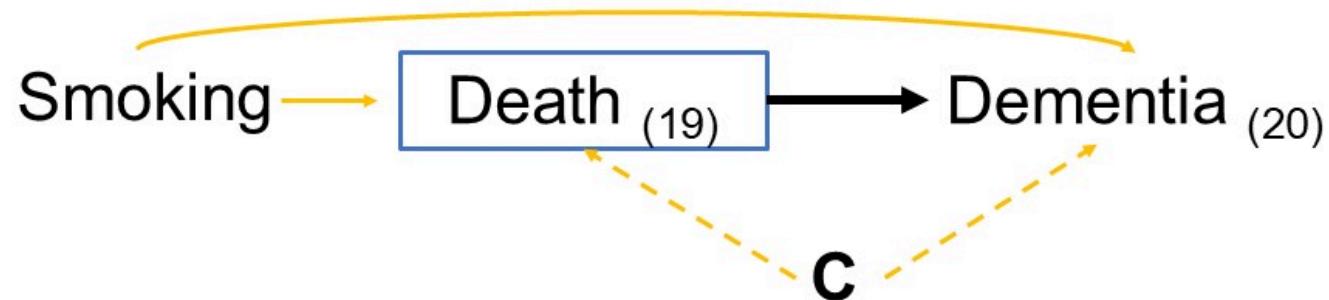
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4. Summary measure: A population-level measure of frequency that is *interpretable* (e.g. risk difference: $Pr[Y_{20}^{a=1} = 1] - Pr[Y_{20}^{a=0} = 1]$)
5. Intercurrent events: Events that prevent us from observing the exposure or outcome (e.g. death, loss to follow-up)

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?

$$Pr[Y_{20}^{a=1} = 1] - Pr[Y_{20}^{a=0} = 1]$$

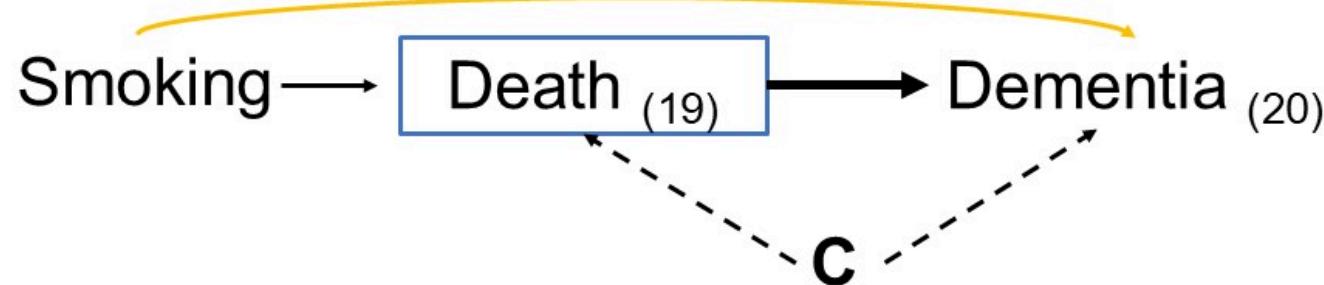


** Cause-specific cumulative incidence or crude risk

Controlled direct effect

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* ?

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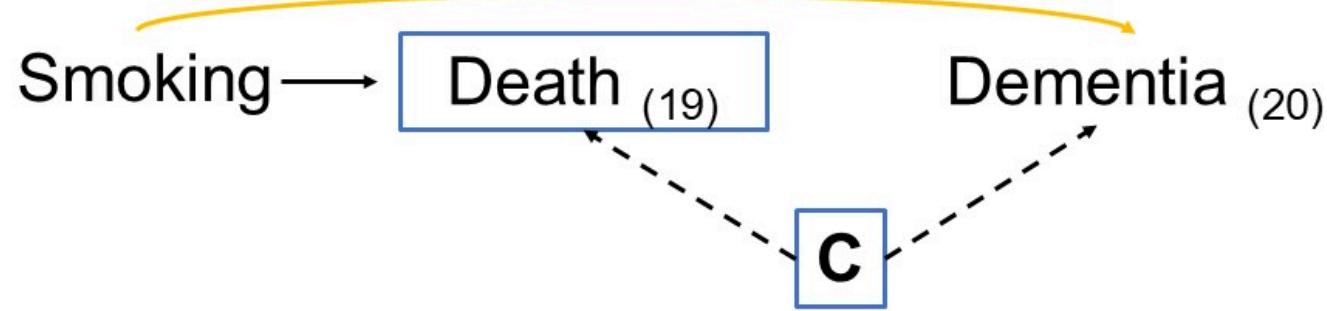


** Marginal or net risk

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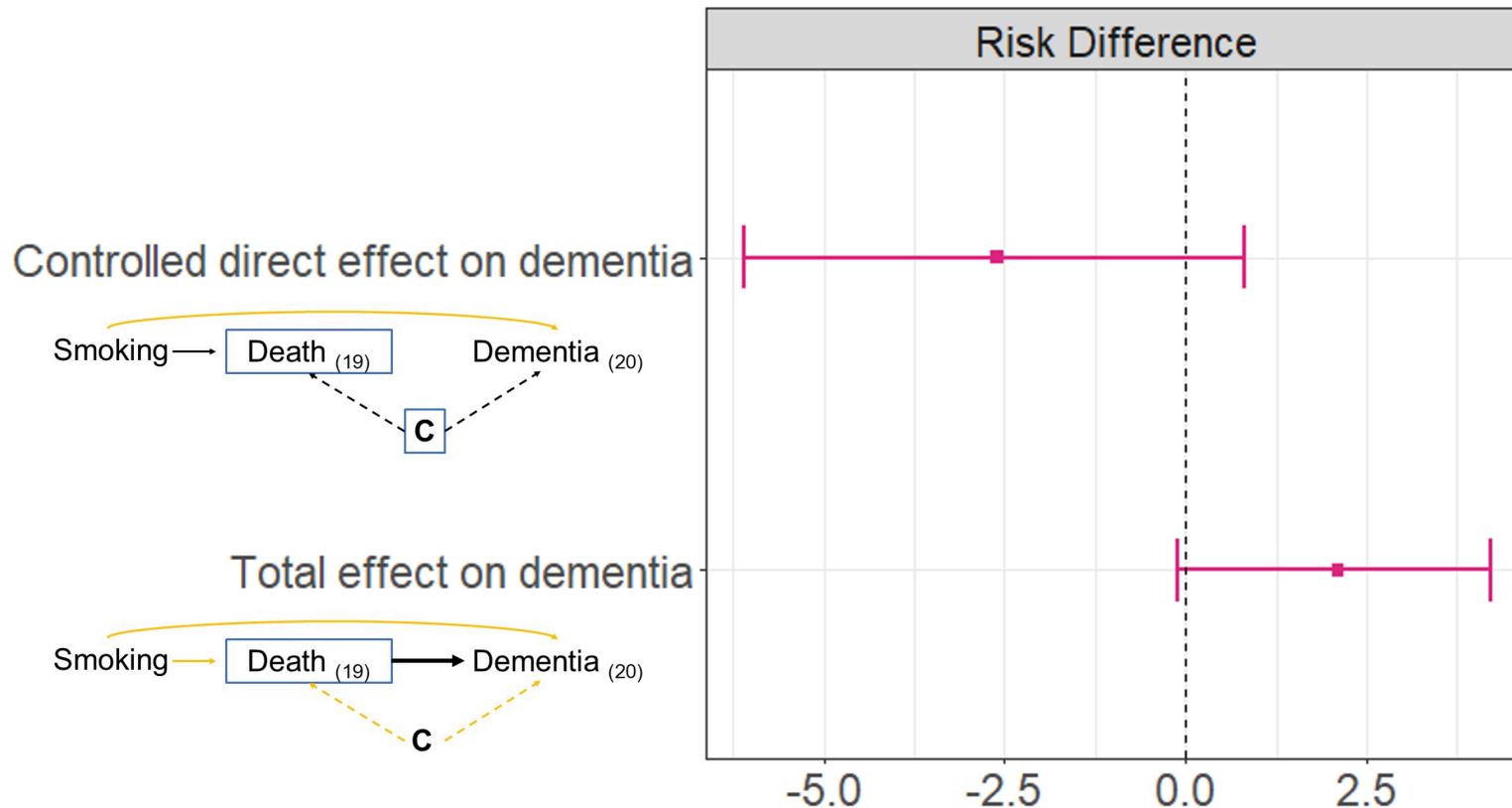
Identifiability assumptions for death

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 × cumulative probability of surviving dementia-free and death-free up to t-1	Risk of dementia = conditional risk of dementia in year t × cumulative probability of surviving dementia-free up to t-1

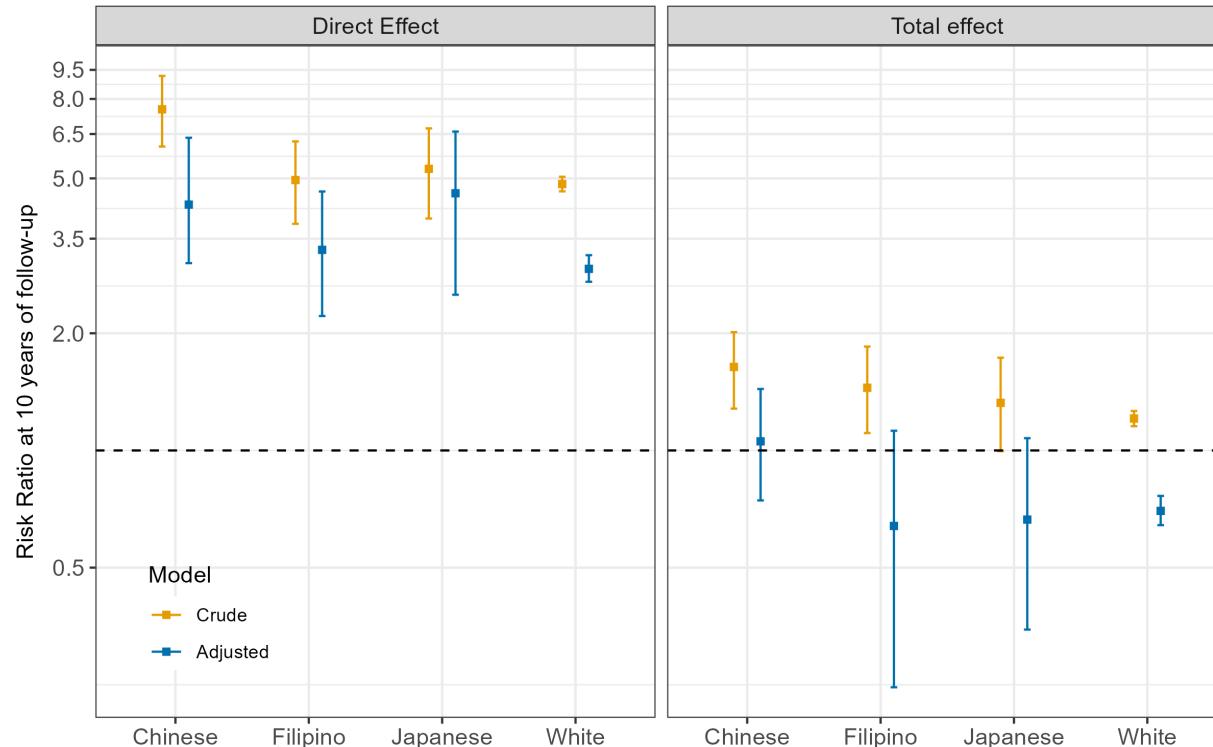
Quitting smoking on dementia risk at 20 years



Rojas-Saunero et al. *American Journal of Epidemiology*. 2023

ROTTERDAM
STUDY

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



- The evidence between social isolation and functional impairment is mixed
- Most studies have an analytic sample of only survivors
- Drop out and death act as truncation events, meaning that once they happen their future outcome is undefined

Methods

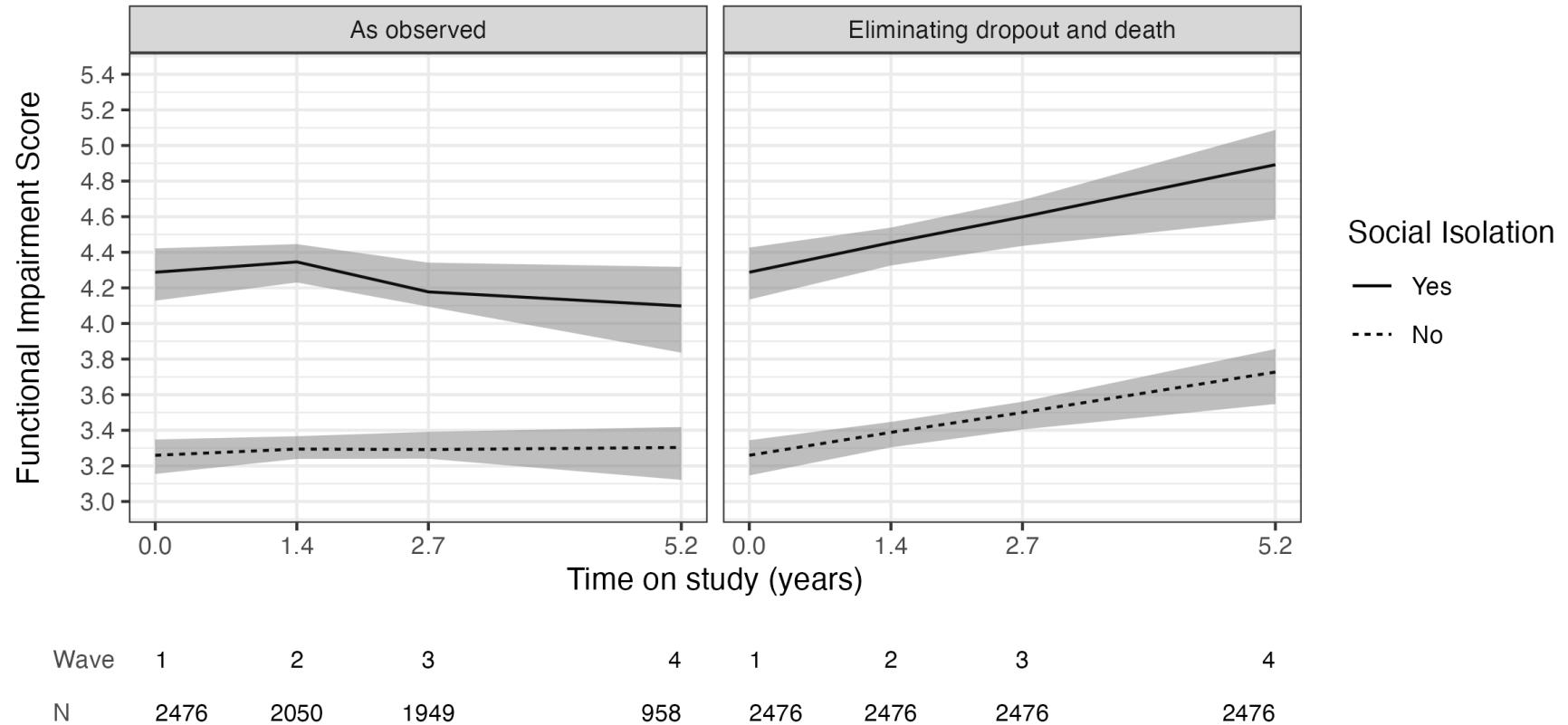
Social Isolation: Binarized 5-item Social Isolation Index

Functional Impairment: Functional impairment (ADLs + IADLs + mobility, 0-36) at 4 waves over 5 years

As observed estimand: among participants still alive and observed
 $E(Y_t|SI = 1, Death_t = 0)$ & $E(Y_t|SI = 0, Death_t = 0)$

Under elimination of dropout/death estimand predicts trajectories for all participants at all waves $E[\overline{Y_t^{\text{Death}=0}}|SI = 1]$ & $E[\overline{Y_t^{\text{Death}=0}}|SI = 0]$

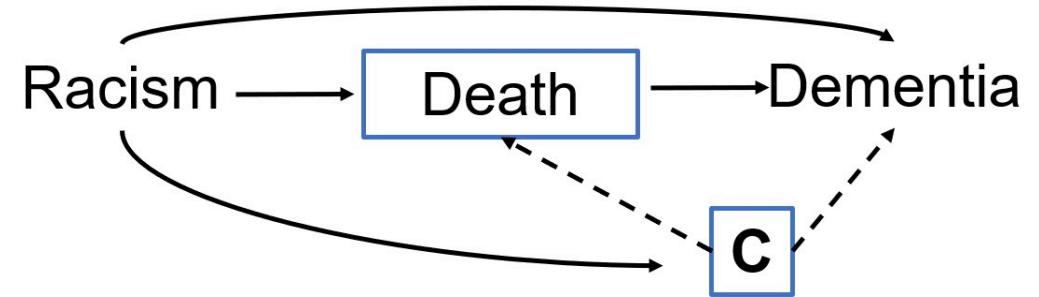
Social isolation and trajectories of functional impairment



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

Competing/truncation events in health equity research

- Differential mortality can bias descriptive, predictive, and causal comparisons across groups
- Accounting for death is critical when studying disparities in aging outcomes



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- Translating novel estimands into applied research requires acknowledging their importance first

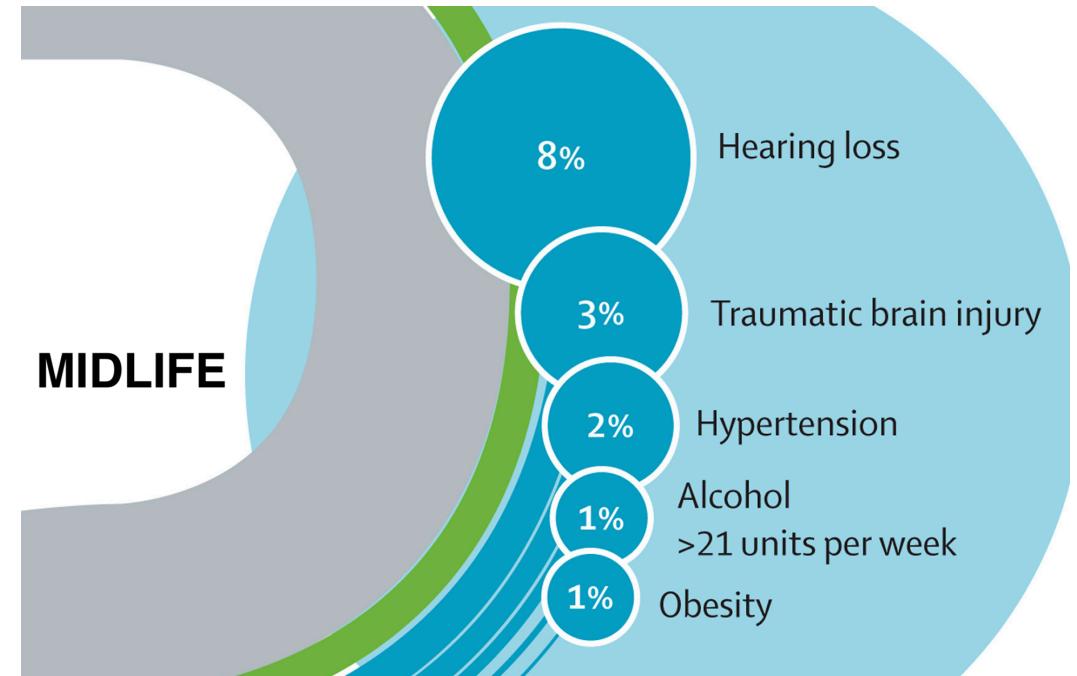
Discussion

- Competing events can be framed in different ways depending on the research question
- All approaches have trade-offs—there is no "one size fits all"
- Translating novel estimands into applied research requires acknowledging their importance first
- Progress needs collaboration across statisticians, epidemiologists, applied researchers, and stakeholders

Target trial emulation to study modifiable risk factors of dementia

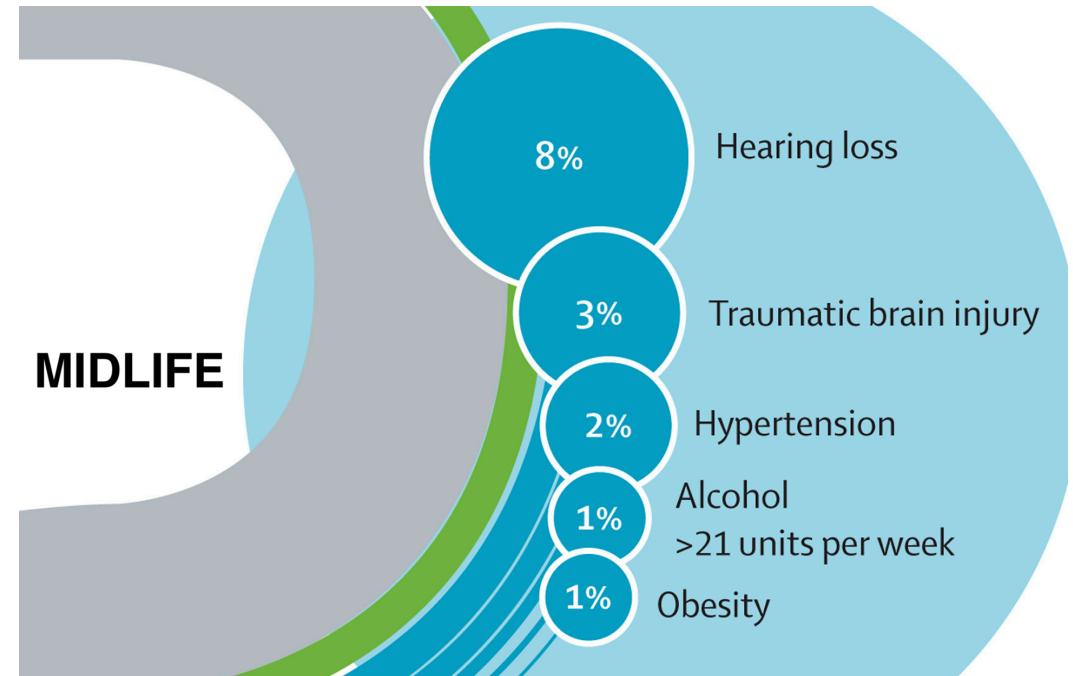
Motivation

- There is a need to identify modifiable risk factors across the life course, and we rely on observational data



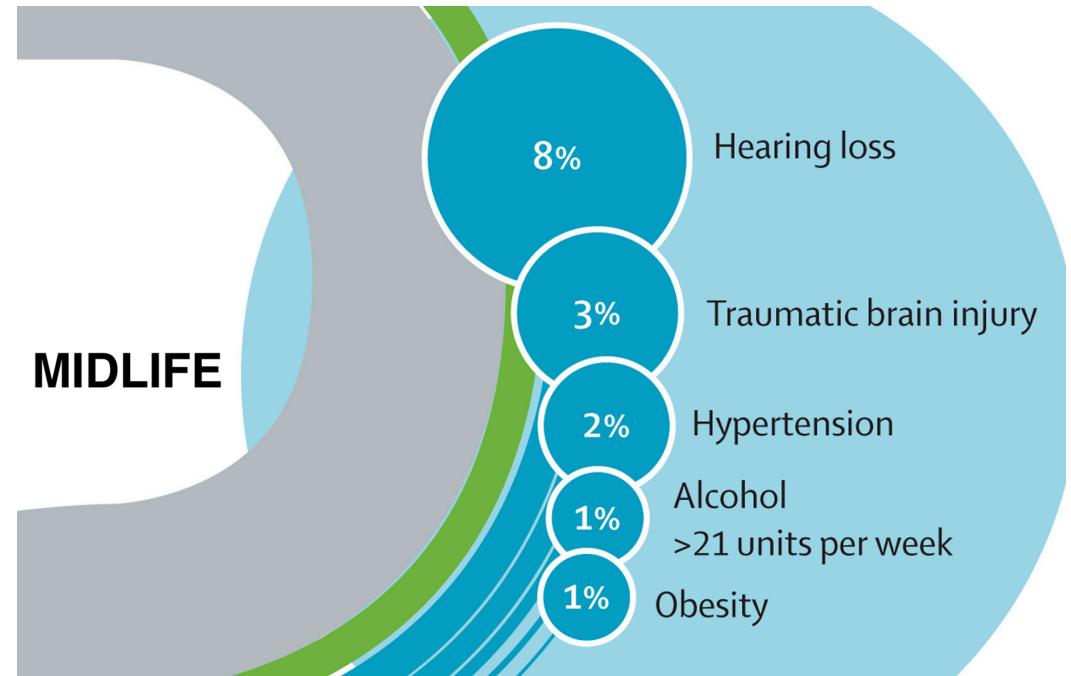
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- There is a need to identify modifiable risk factors across the life course, and we rely on observational data
- Studies focus on single time-point exposure assessment rather than the longitudinal effects
- We need causal methods to guide prevention strategies



Hypertension and Blood Pressure

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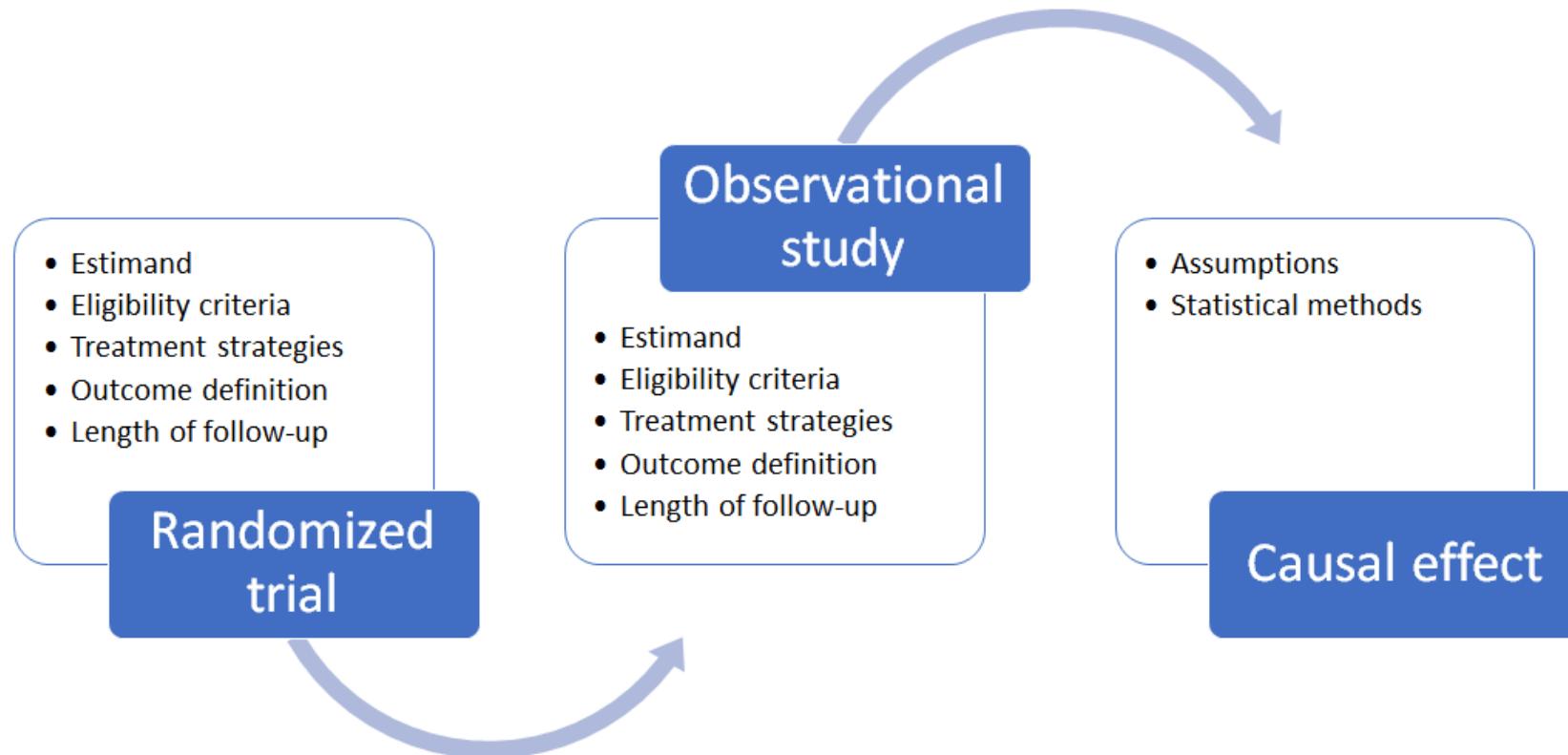
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- Hypertension burden is higher in Black and Latinx adults
- We need evidence on whether intensive blood pressure control could reduce disparities

Target Trial Framework



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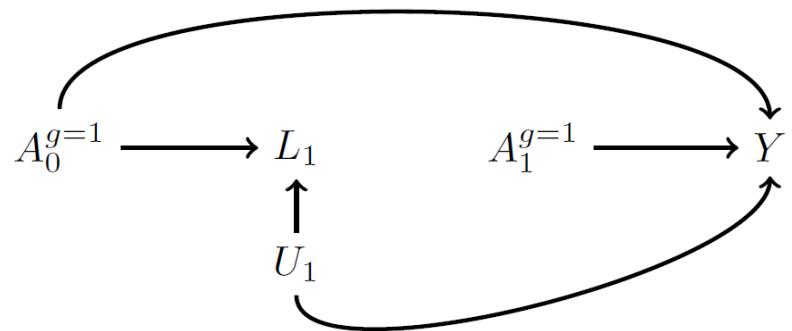
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Causal contrast	Controlled direct, per protocol effect	Same

Parametric G-formula

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

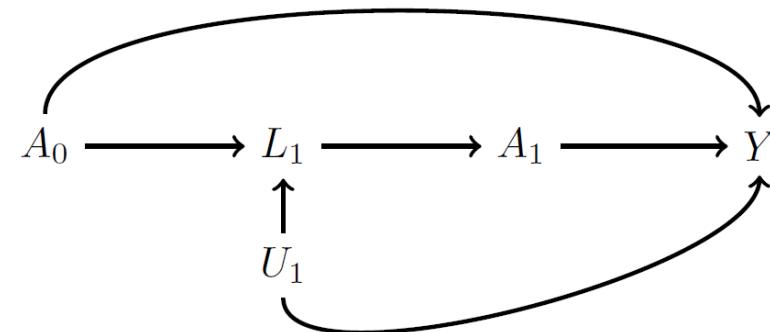
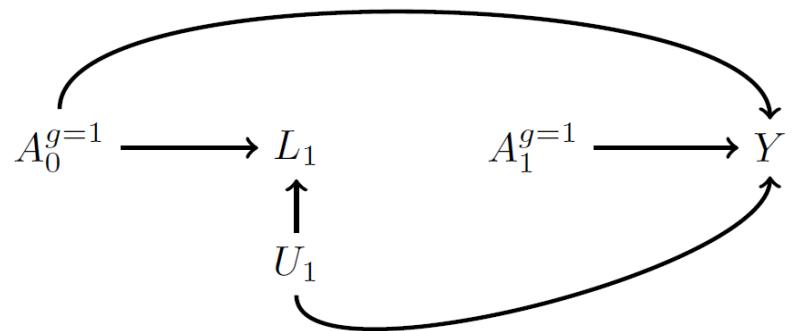
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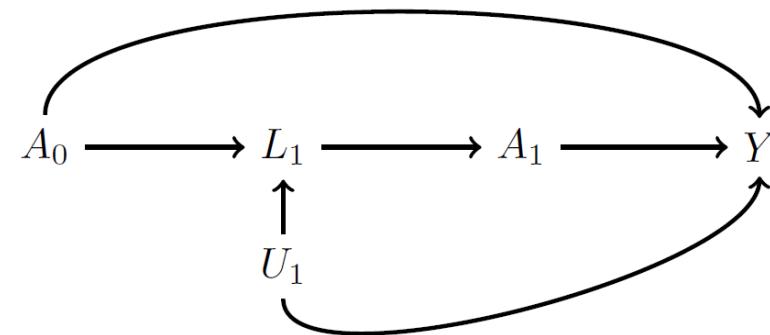
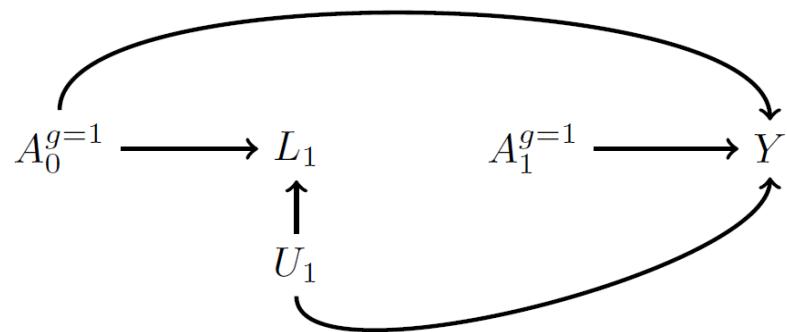
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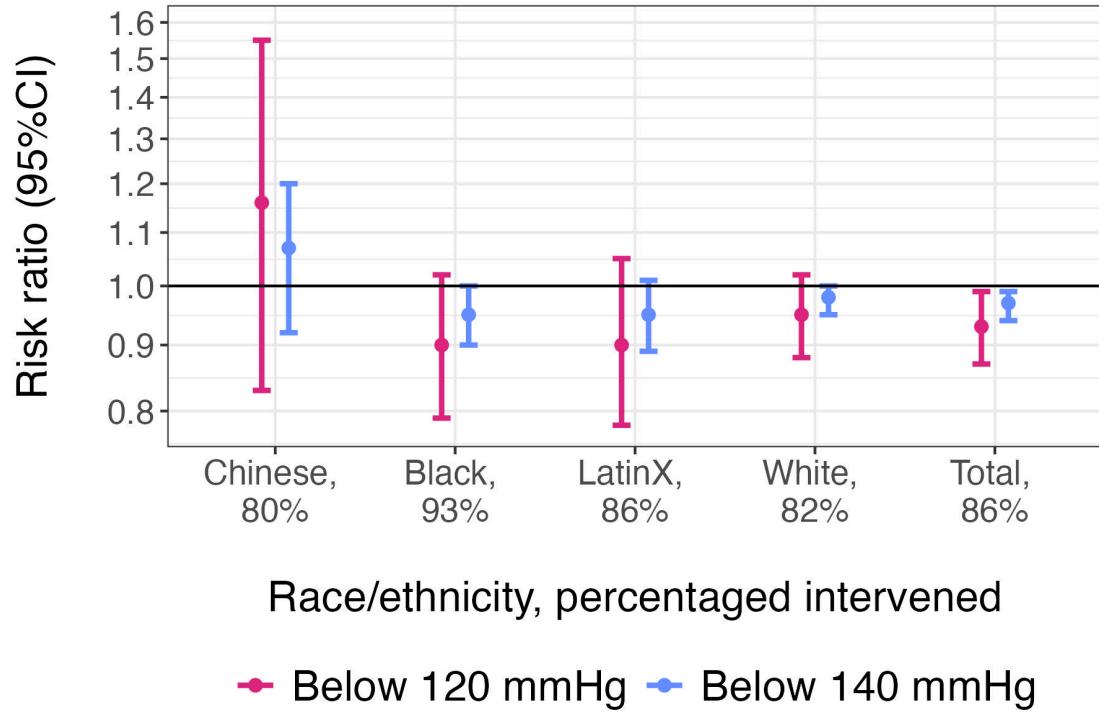
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A = SBP, **L** = *Fixed covariates*: age, sex, education, income, health insurance, marital status, APOE- ϵ 4 genotype, history of diabetes. *Time-varying covariates*: SBP, cardiometabolic biomarkers, behavioral measurements, incident cardiovascular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

Results



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- The target trial framework helps us refine research questions (i.e. estimands) to estimate the impact of potentially implementable and equitable interventions
- It promotes transparency on the assumptions needed to estimate causal effects from observational data

Future Directions

**Occupational determinants of
cognitive and brain health among
middle-aged and older Latinxs**

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



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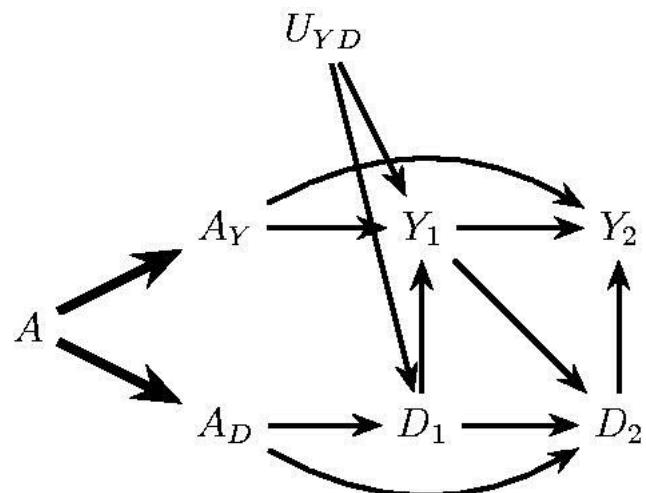
Occupational determinants of cognitive and brain health among middle-aged and older Latinxs

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Causal estimands for cognitive decline with truncation due to death

Separable effects:



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- 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

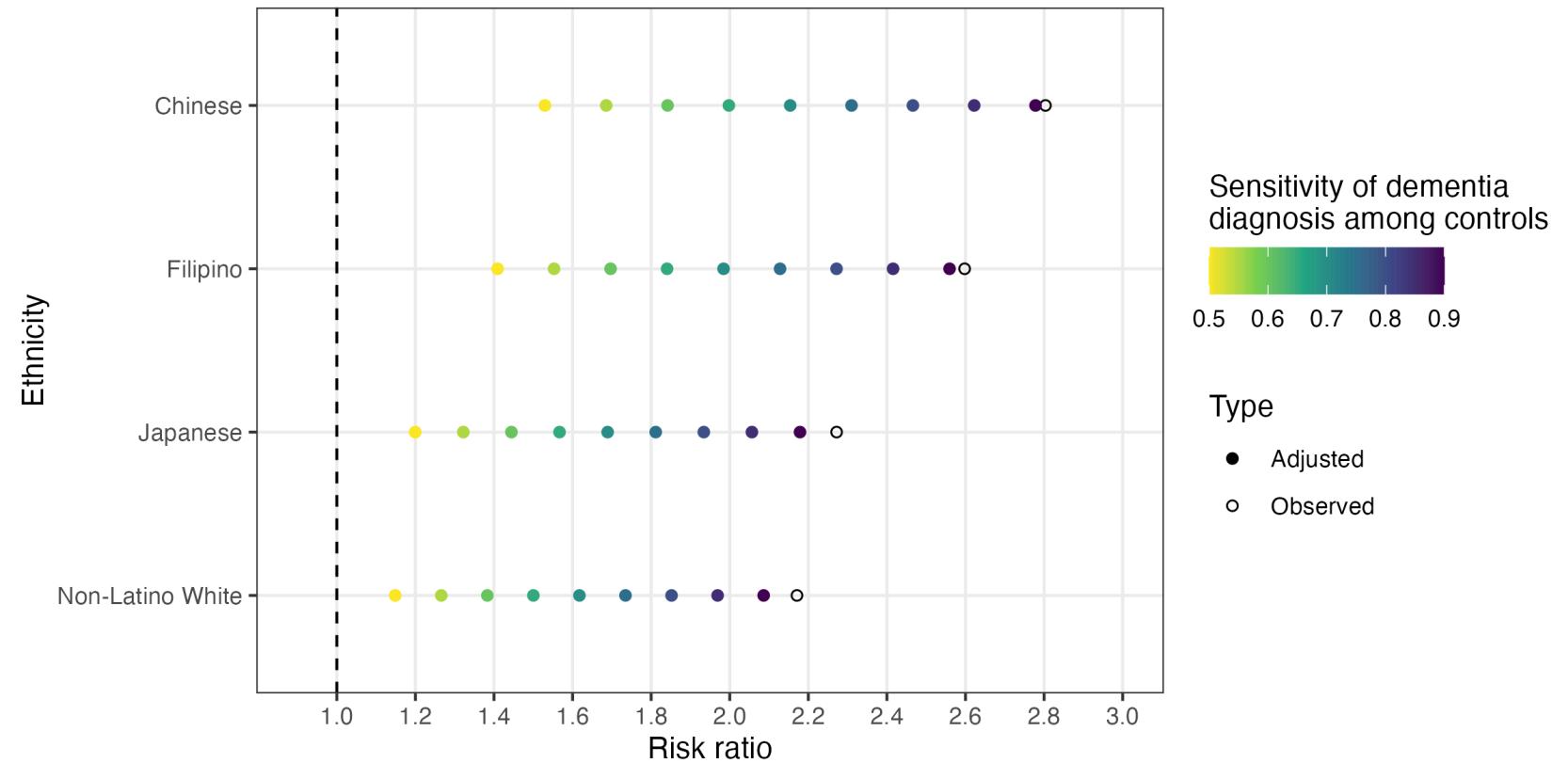
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Thank You, Gracias!

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Quantitative bias analysis for differential dementia diagnosis

We set the sensitivity of dementia diagnosis in the stroke group to 0.99 and considered a range (0.5 - 0.9) of sensitivity values in the no-stroke group



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6. Repeat steps 2-6 for each hypothetical intervention