

Advancing **Health Equity** in **Aging Research** through a **Causal Inference** Framework

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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](#)

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

THE LANCET Diabetes & Endocrinology

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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

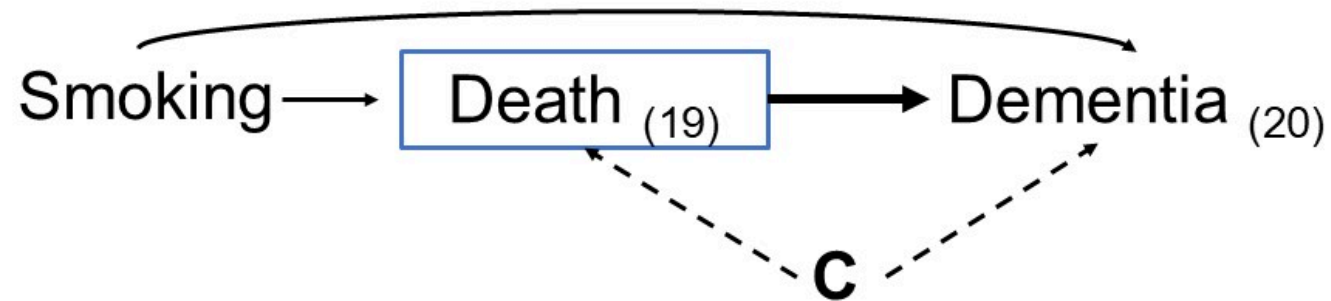
The Association Between Blood Pressure and Incident Alzheimer Disease

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	ESTIMATOR	ESTIMATE
	<p>Ingredients</p> <ul style="list-style-type: none">150g unsalted butter150g chocolate pieces150g all-purpose flour1/2 tsp baking powder1/2 tsp baking soda200g brown sugar2 large eggs <p>Directions</p> <ol style="list-style-type: none">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*).

Causal estimands have 5 elements

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

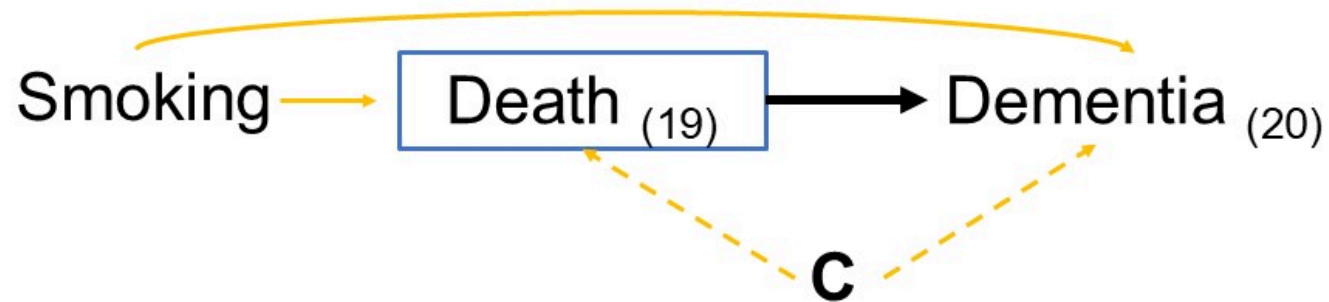
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4. Summary measure: A population-level measure of frequency that is *interpretable* (e.g. risk difference: $Pr[Y_{20}^{a=1} = 1] - Pr[Y_{20}^{a=0} = 1]$)
5. Intercurrent events: Events that prevent us from observing the exposure or outcome (e.g. death,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

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

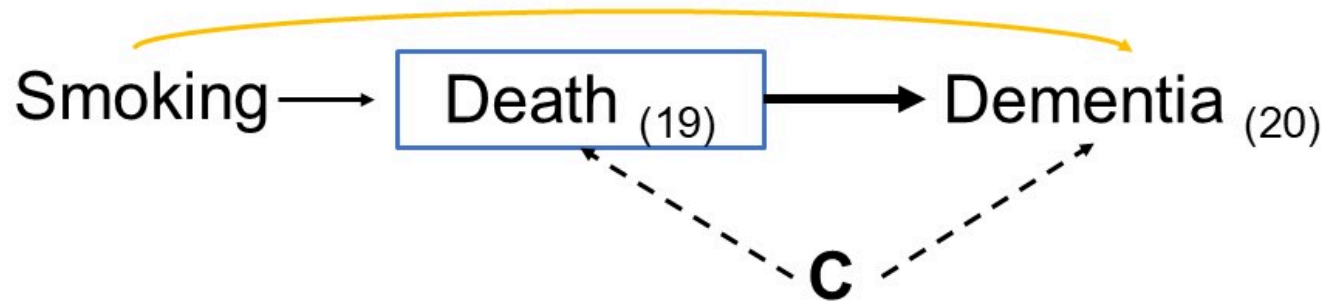


** *Cause-specific cumulative incidence or crude risk*

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*?

$$Pr[Y_{20}^{a=1, d_{19}=0} = 1] - Pr[Y_{20}^{a=0, d_{19}=0} = 1]$$

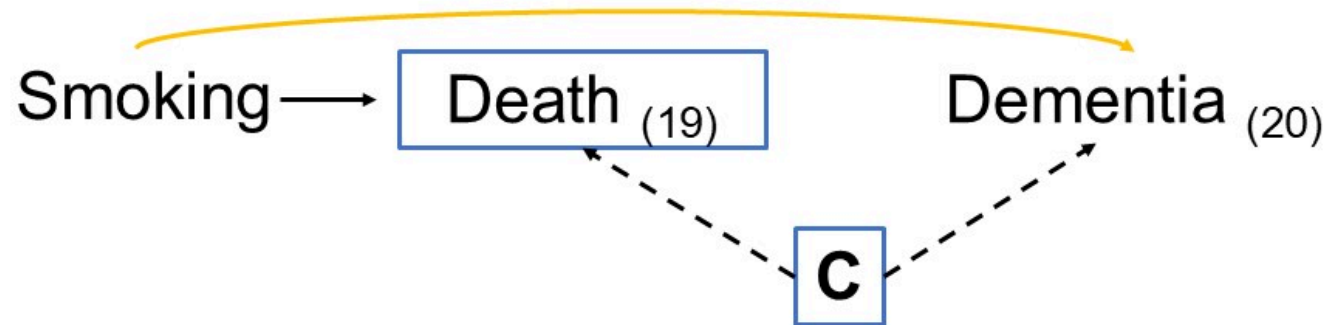


** *Marginal or net risk*

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** *Marginal or net risk*

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.

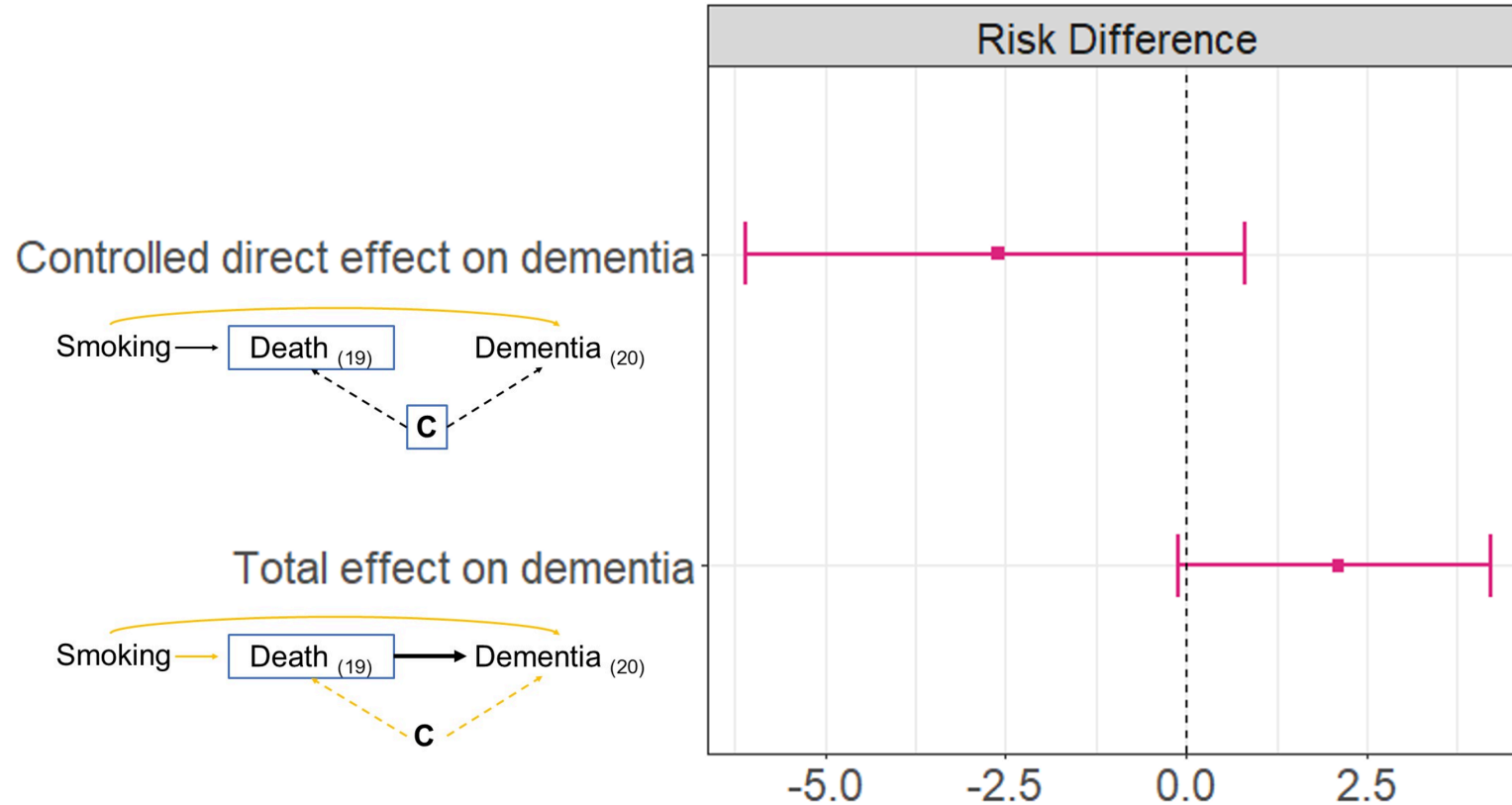
Rojas-Saunero et al. *American Journal of Epidemiology*. 2023

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 $t-1$

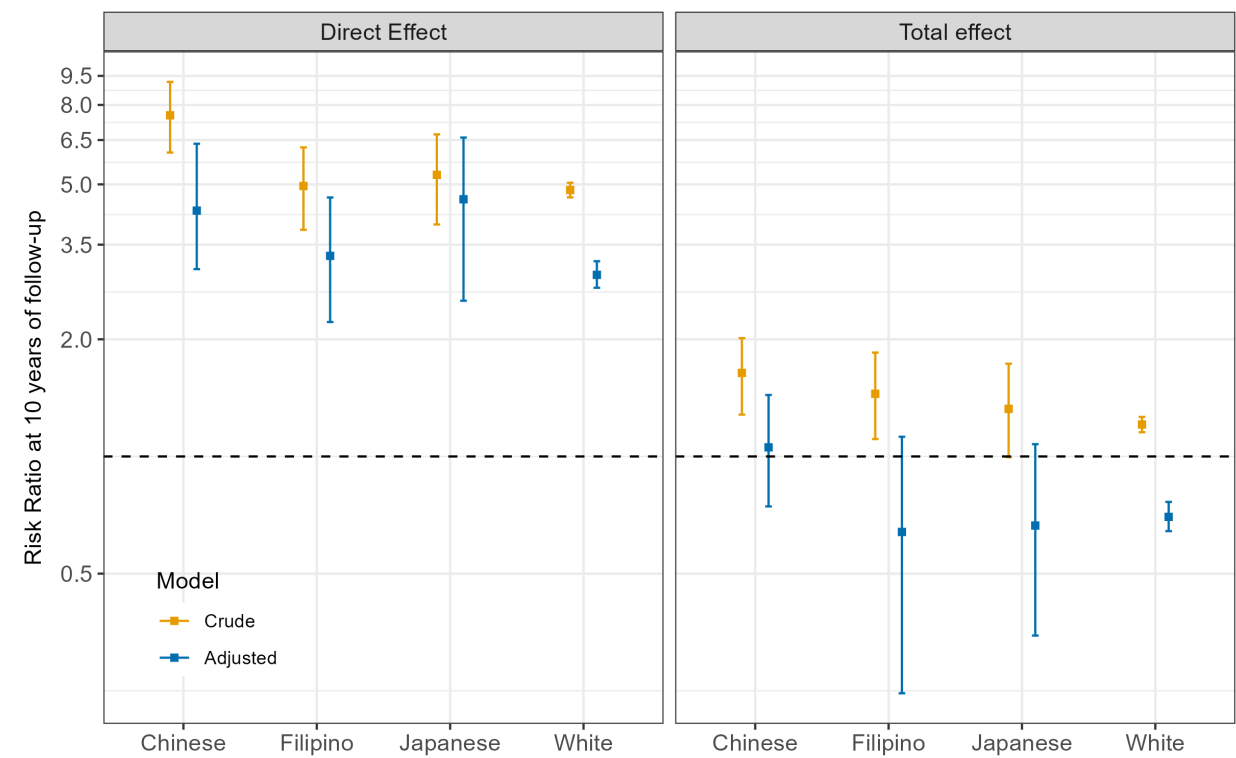
Rojas-Saunero et al. *American Journal of Epidemiology*. 2023

Quitting smoking on dementia risk at 20 years



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

Incident stroke on dementia risk in Asian American and White population



Rojas-Saunero et al. *Neurology*. 2025

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

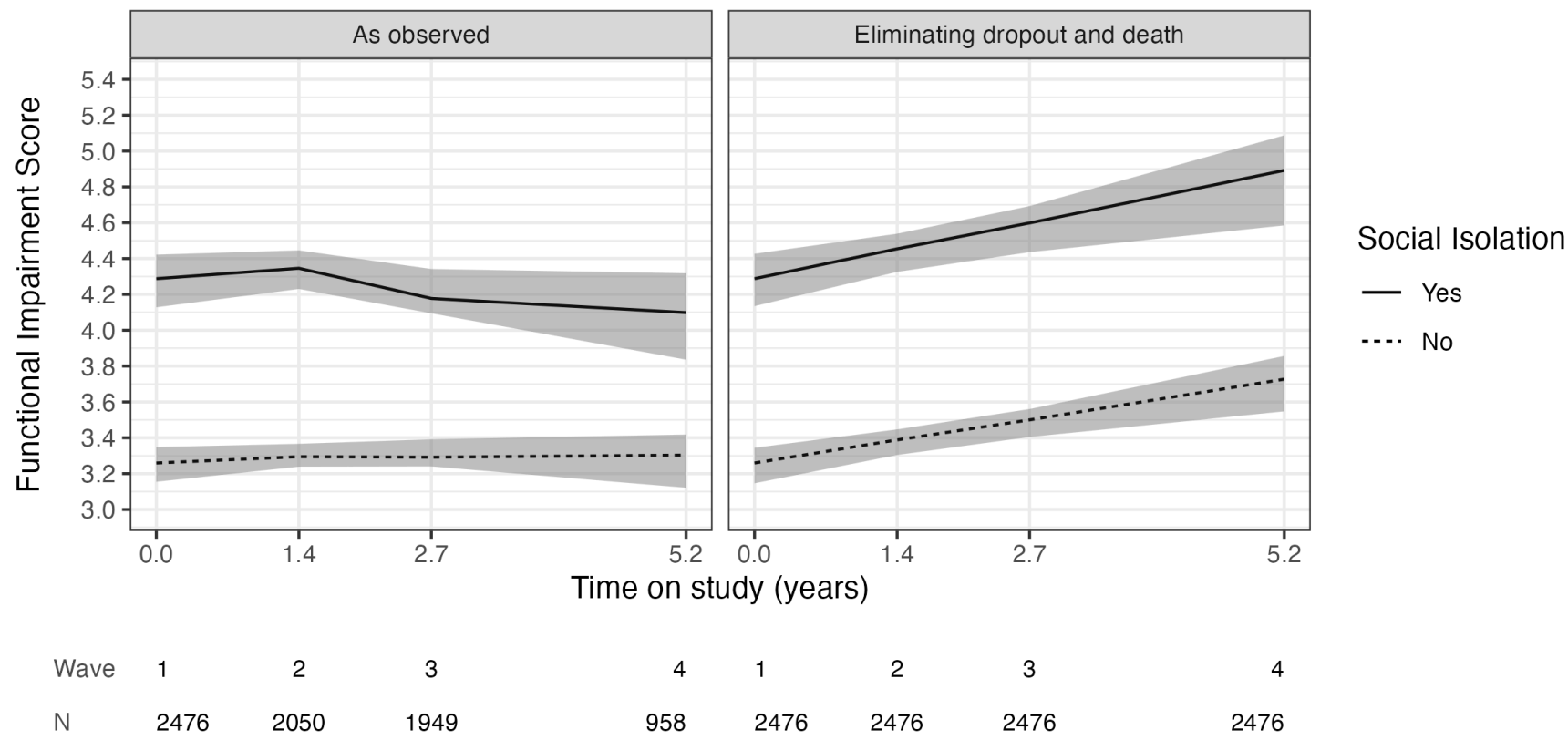
Social Isolation: Binarized 5-item Social Isolation Index

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 $E[Y_t^{\overline{Death=0}} | SI = 1] \& E[Y_t^{\overline{Death=0}} | SI = 0]$

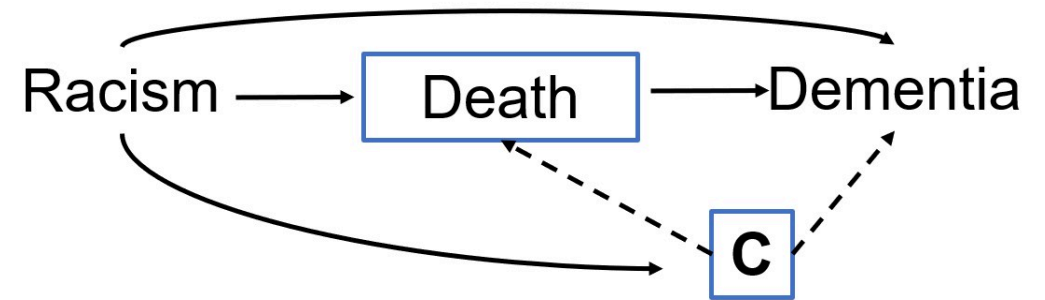
Social isolation and trajectories of functional impairment



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



Rojas-Saunero LP, Glymour MM, Mayeda ER. *Current Epidemiology Reports*. 2024

Discussion

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

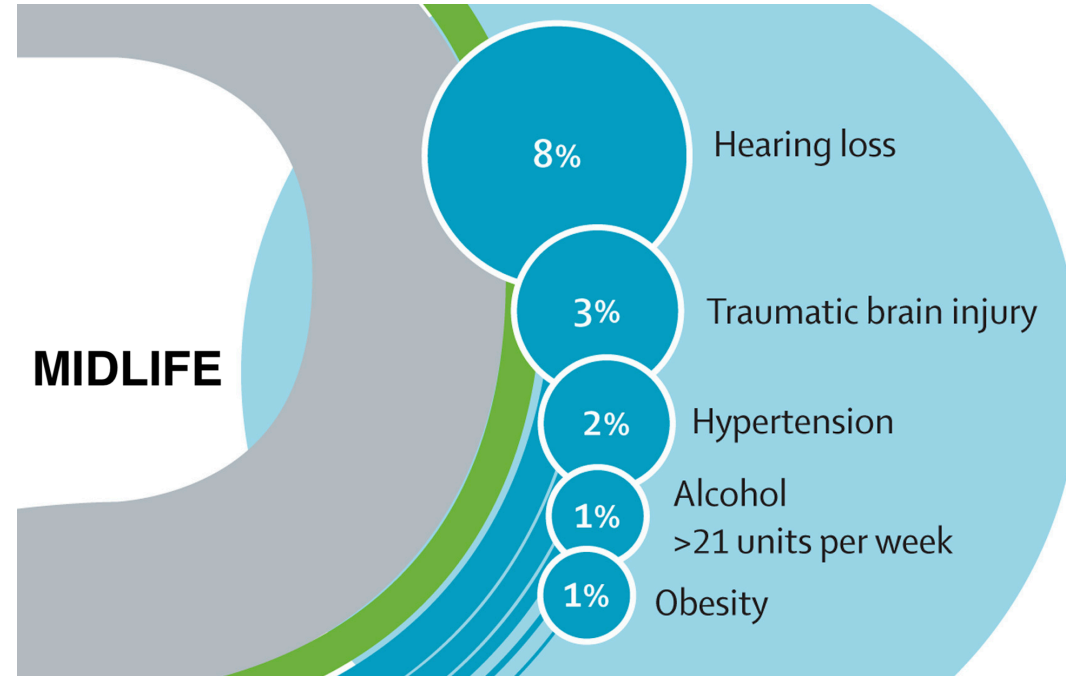
Discussion

- 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

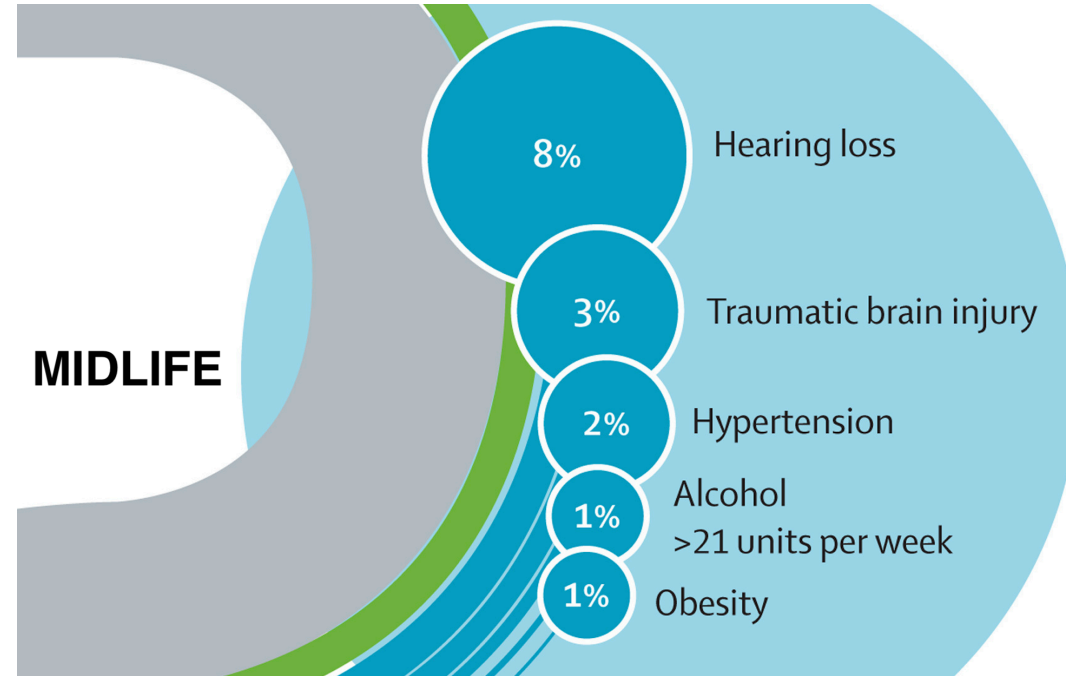
Motivation

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



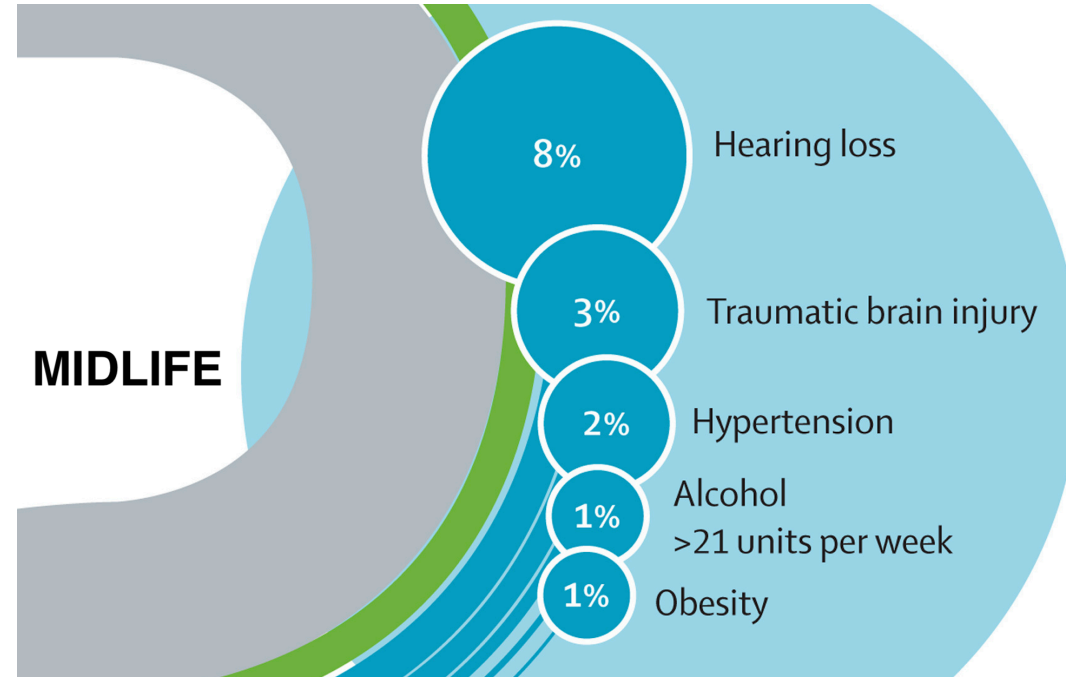
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- There is a need to identify modifiable risk factors across the life course, and we rely on observational data
- Studies focus on single time-point exposure assessment rather than the longitudinal effects
- We need causal methods to guide prevention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



Hypertension and Blood Pressure

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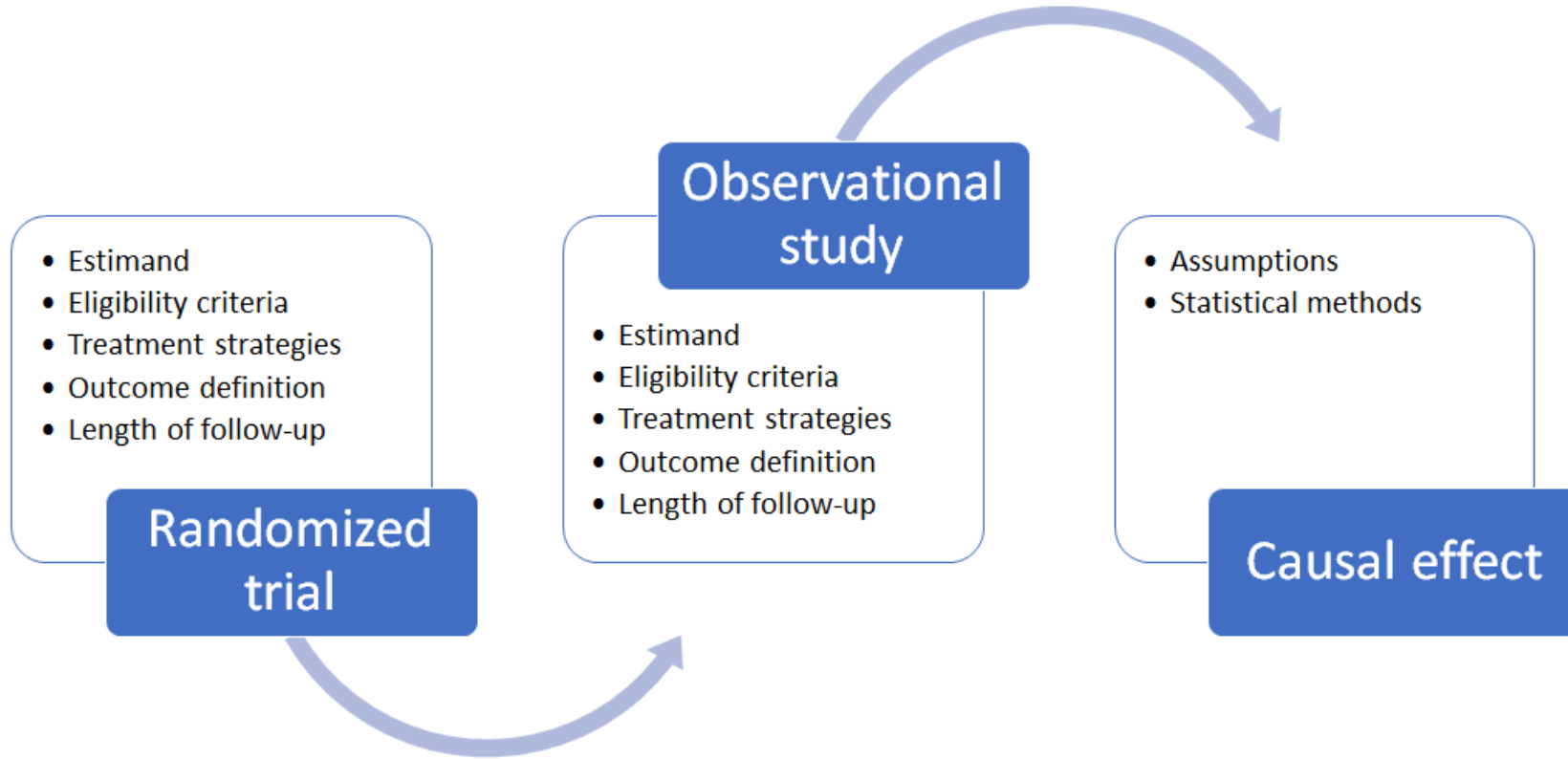
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- Highly selected population → limited generalizability
- Hypertension burden is higher in Black and Latinx adults
- We need evidence on whether intensive blood pressure control could reduce disparities

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

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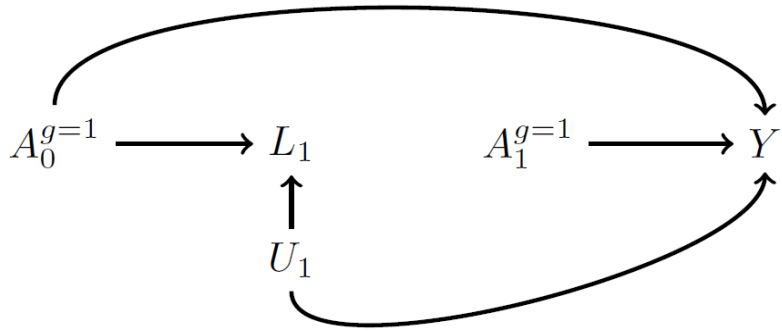
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Causal contrast	Controlled direct, per protocol effect	Same

Parametric G-formula

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

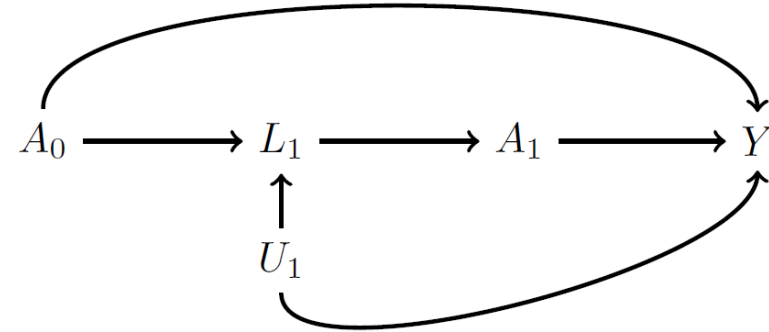
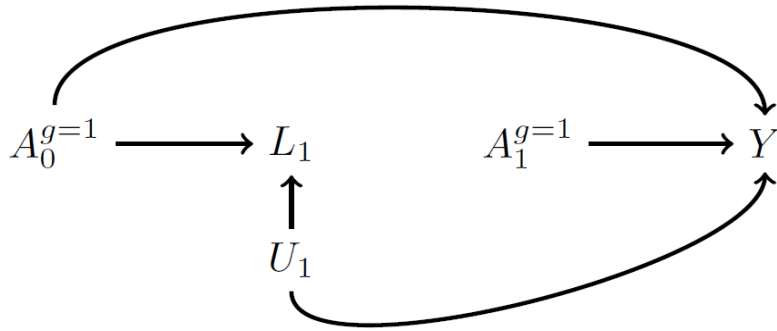
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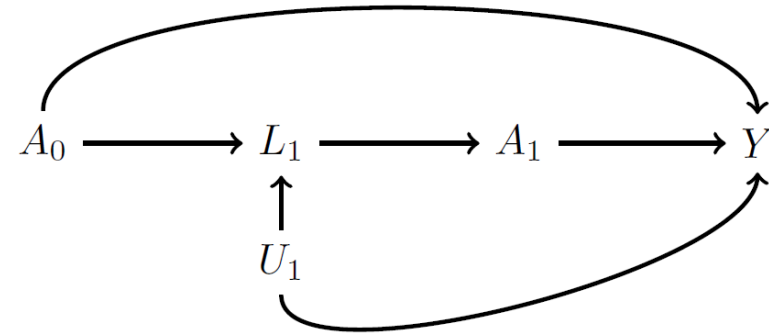
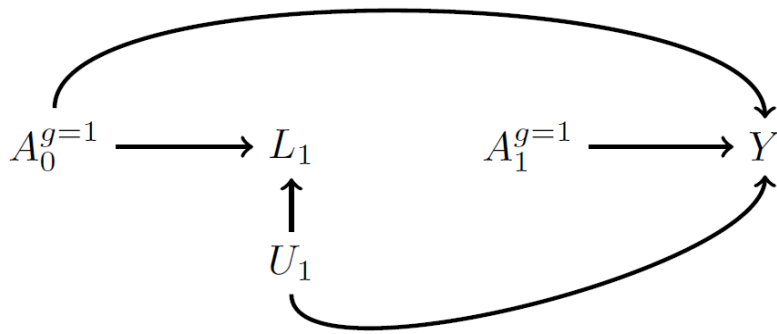
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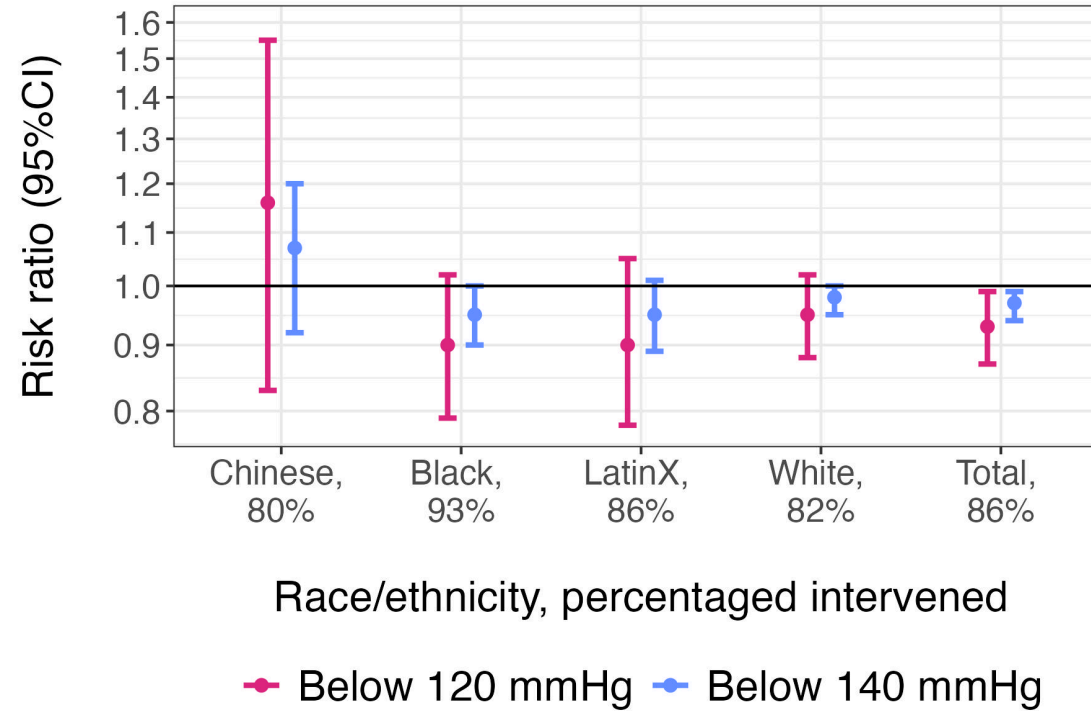
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A = SBP, **L** = *Fixed covariates*: age, sex, education, income, health insurance, marital status, APOE-ε4 genotype, history of diabetes. *Time-varying covariates*: SBP, cardiometabolic biomarkers, behavioral measurements, incident cardiovascular comorbidities **Y** = Dementia

Results



Discussion

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- Findings suggest that Black and Latinx adults may require greater support to sustain intensive control
- 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



Future Directions

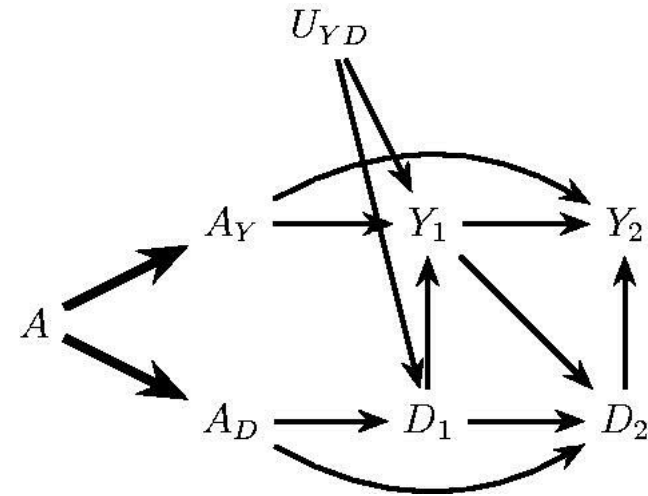
Occupational determinants of cognitive and brain health among middle-aged and older Latinxs

NIH | NIA K99/R00, Impact score: 16,
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Causal estimands for cognitive decline with truncation due to death

Separable effects:



Acknowledgements

- 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
- Hírám 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!

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References

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- Workshop on competing events for causal questions
https://github.com/palolili23/SER_competing_events_workshop