Causal estimands for Aging-Relevant Outcomes in the Presence of Death as a Competing or Truncation Event

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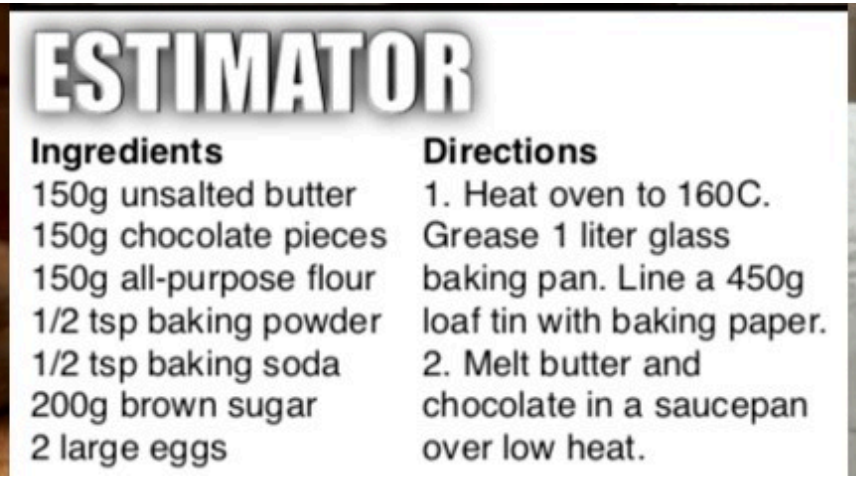
Estimand



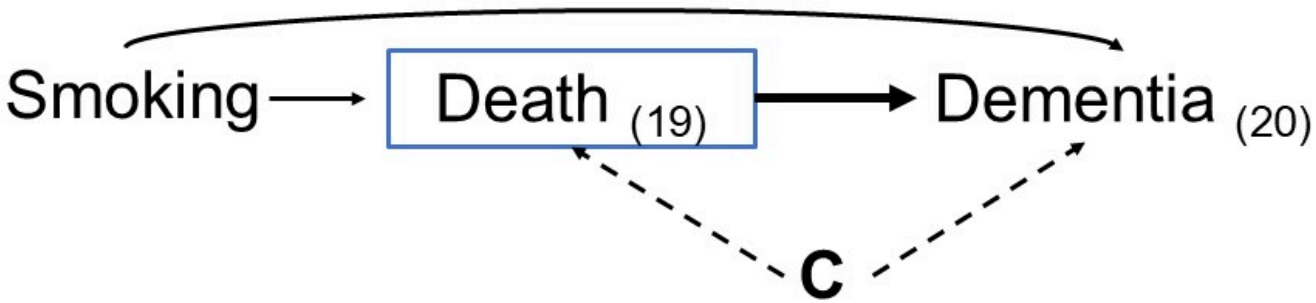
Specific quantity that we want to estimate that answers our research question.

Causal estimands have 5 elements

1. Target population
2. Exposure/treatment arms
3. Outcome defined within a time frame
4. Interpretable effect measure (e.g. mean difference, risk difference, risk ratio)
5. **Intercurrent events:** Events that will prevent us from observing the outcome (e.g. adverse reactions, death, loss to follow-up)

How can we incorporate death as part of incident dementia analysis?

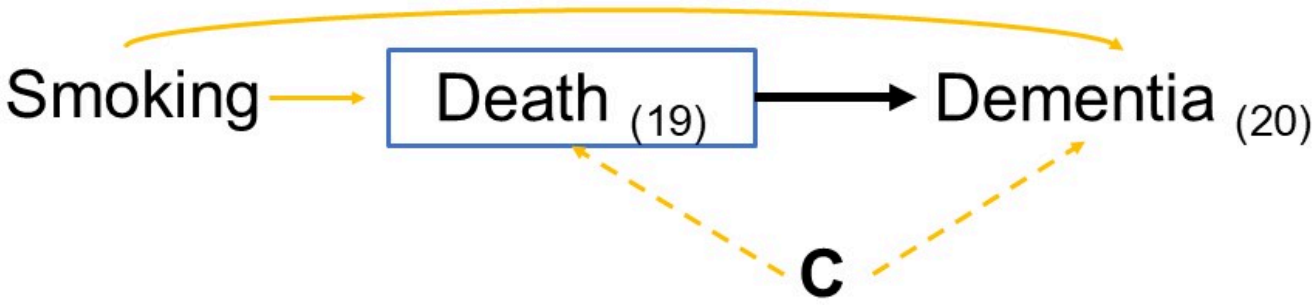
Quitting smoking and 20-year dementia risk



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?

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

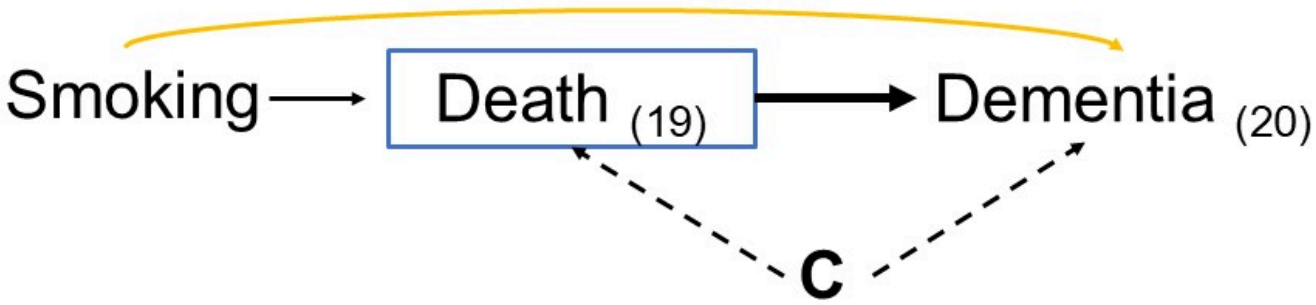


** *Cause-specific cumulative incidence* or *crude* risk

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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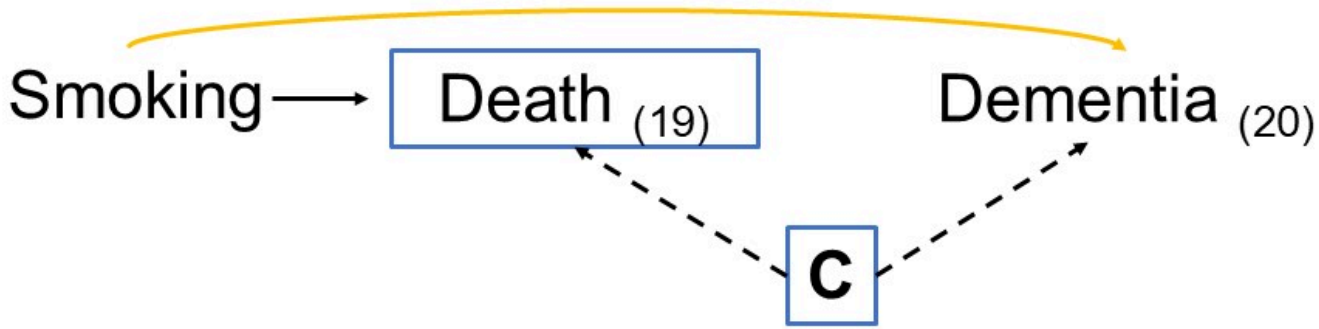
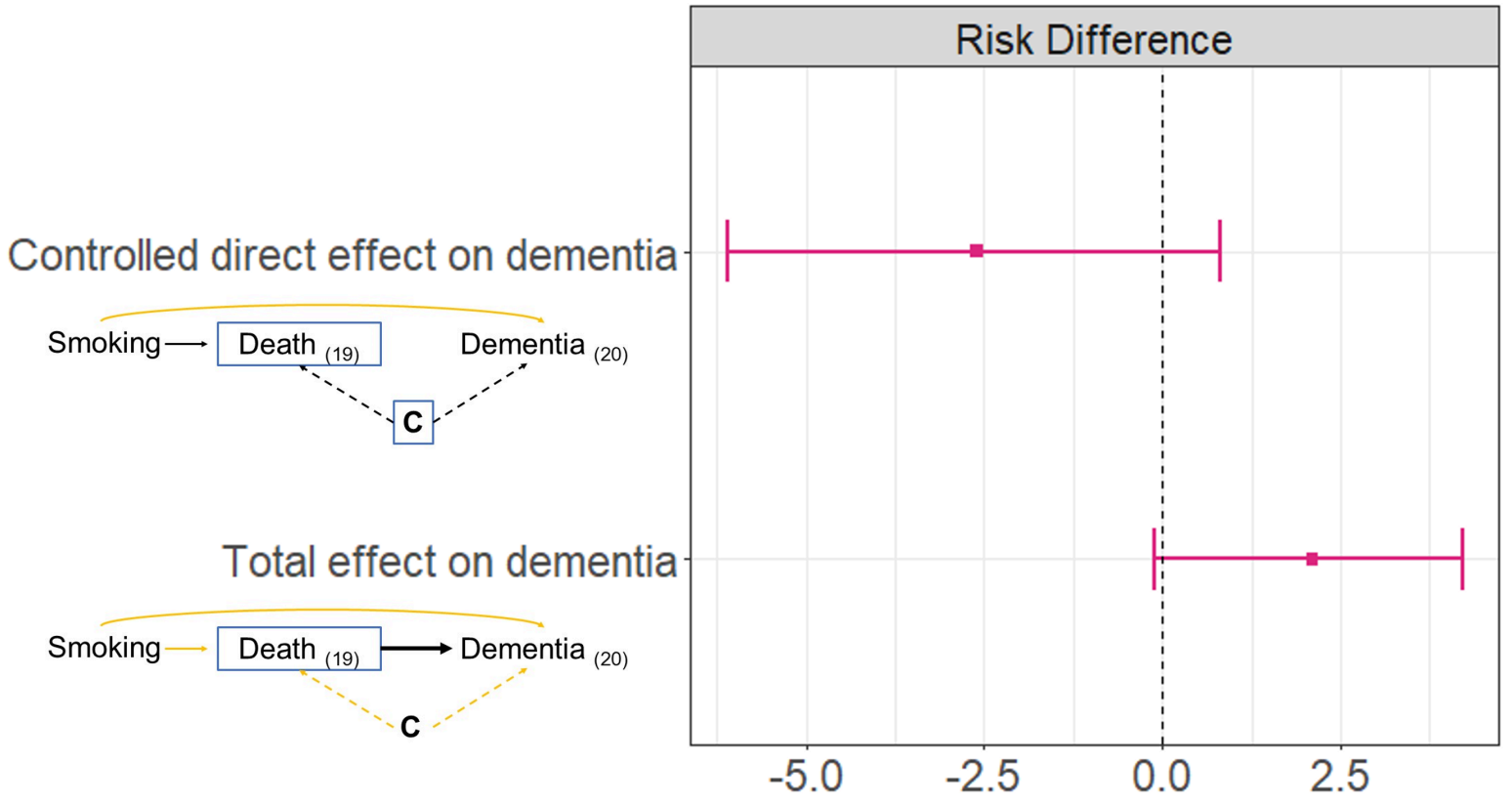


** *Marginal* or *net* risk

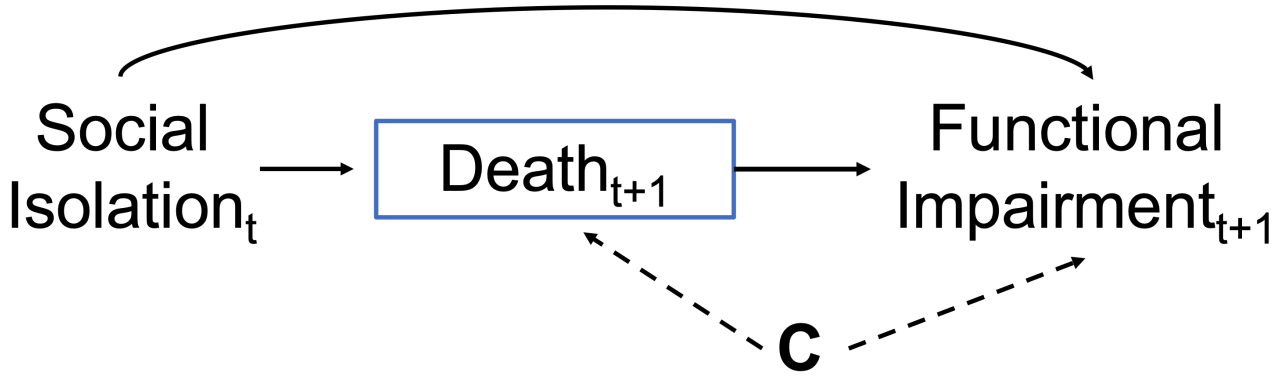
Quitting smoking on dementia risk at 20 years



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

How can we incorporate death as part of trajectories of a continuous outcome?

Social isolation and functional impairment trajectories



Social isolation and functional impairment trajectories

Social Isolation (SI): Binarized 5-item Social Isolation Index

Functional Impairment (Y): (I)ADLs + mobility items (0–36), 4 waves over 5 years

KHANDLE STUDY
Kaiser Healthy Aging and Diverse Life Experiences

STAR Study of Healthy Aging in African Americans

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As observed estimand

Trajectories for participants still alive and observed

$E(Y_t|SI = 1, Death_t = 0)$ &
$E(Y_t|SI = 0, Death_t = 0)$

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As observed estimand

Trajectories for 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

Trajectories for all participants at all waves

$E[Y_t^{\bar{d}=0}|SI = 1]$ & $E[Y_t^{\bar{d}=0}|SI = 0]$

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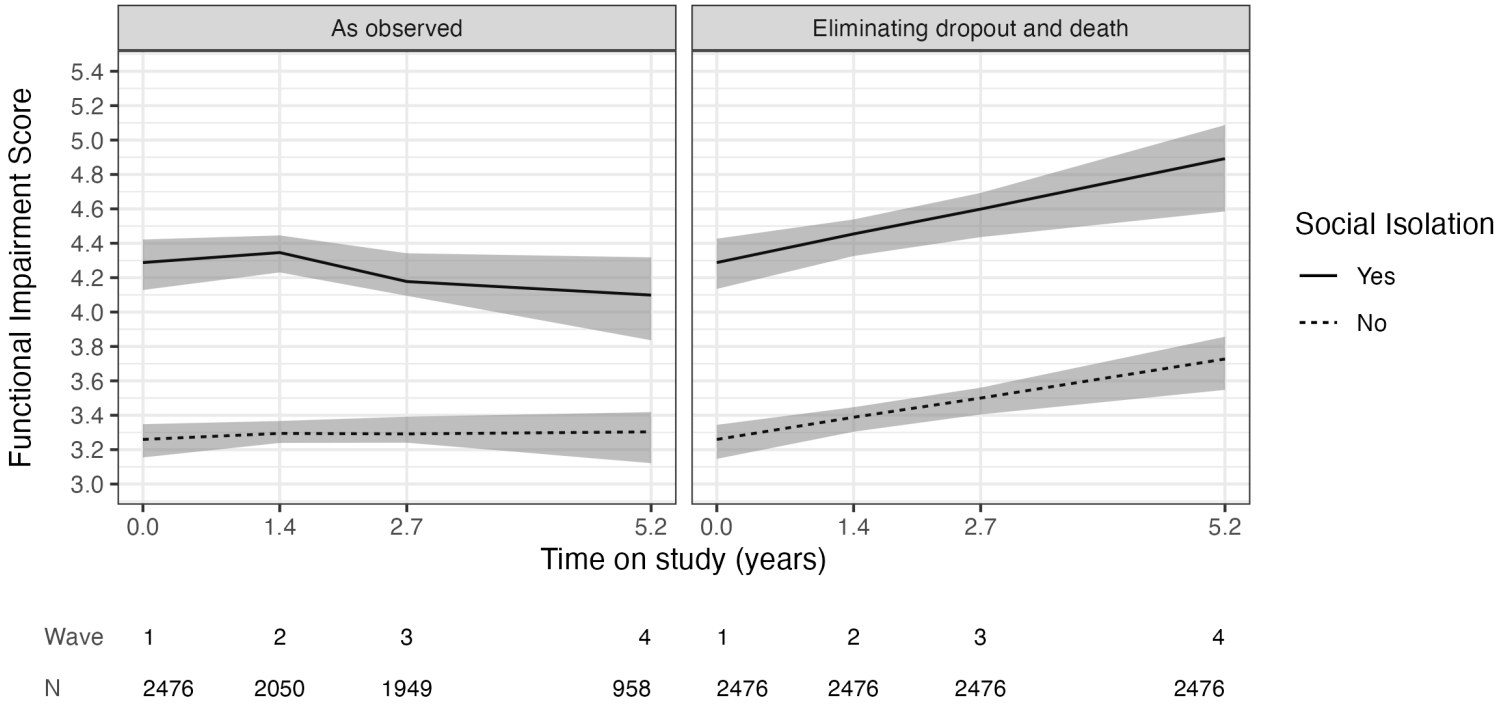
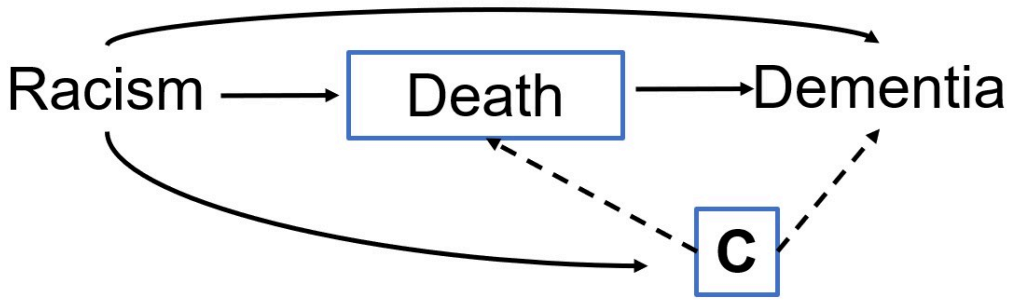


Currently under R&R at *J. Gerontol. A Biol. Sci. Med. Sci.*

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

Take aways

- Different questions (*estimands*) can lead to different (even opposite) results, with very different interprations, and no "one size fits all"

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- Different questions (*estimands*) can lead to different (even opposite) results, with very different interprations, and no "one size fits all"
- We can only understand bias relative to an specific estimand, as the all rely in different assumptions
- Progress needs collaboration across statisticians, epidemiologists, applied researchers, and stakeholders

Thank you, Gracias!

Mayeda Research Group

- Elizabeth Rose Mayeda
- Sonja Swanson
- Rachel Whitmer
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- Ryo Ikesu
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Other estimands

- Survival Average Causal Effect

$$E[Y_t^{a=1} | D_t^{a=1} = D_t^{a=0} = 0] - E[Y_t^{a=0} | D_t^{a=1} = D_t^{a=0} = 0]$$

- Composite Outcome

$E[Y_t^{a=1} \text{ or } Y | D_t^{a=1} = x] - E[Y_t^{a=0} \text{ or } Y | D_t^{a=0} = x]$, where x is a value for memory function after death