Mediation Considerations

BHET Meeting

Sam Harper
McGill University

2023-12-21

McGill | Department of Epidemiology, Biostatistics and Occupational Health

HEI study objectives

Aim 1.

Estimate the total effect of the intervention.

Aim 2.

Estimate the contribution of changes in the chemical composition of $PM_{2.5}$ to the overall effect on health outcomes.

Aim 3. 👈

Examine alternative pathways and mechanisms that may contribute to the intervention’s impact.

Basic idea for mediation study

To understand the pathways, mechanisms, and intermediates through which a treatment affects an outcome.

How much of the policy effect is through:

- Reduced exposure to $PM_{2.5}$
- Other pathways (behavioral changes?)
- Also consider multiple mediators

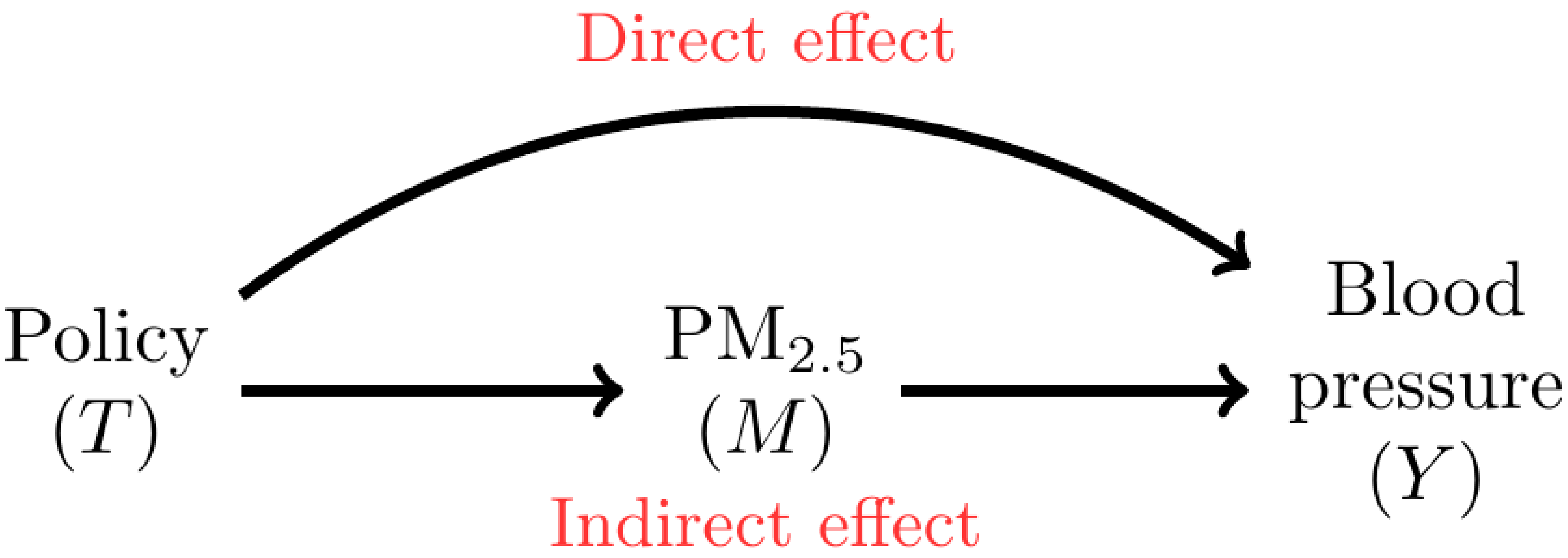
First part of mediation: total effect

Step 1: Estimate the total effect of T.

Second part of mediation: decomposition

Basic idea: understand pathways of effects

Step 2: Estimate how much of the total effect is due to $PM_{2.5}$ vs. other pathways?



Basic DAG for Mediation

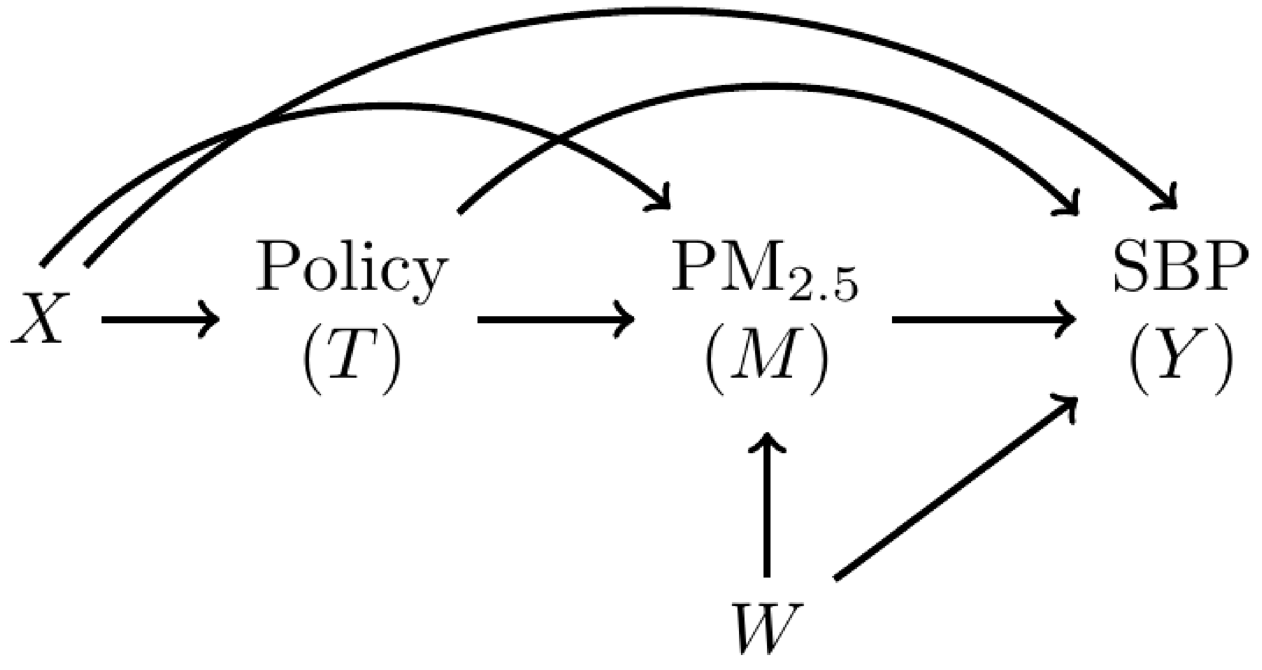
X = pre-treatment covariates

T = exposure

M = mediator

W = confounders

Y = outcome



Basic DAG for Mediation

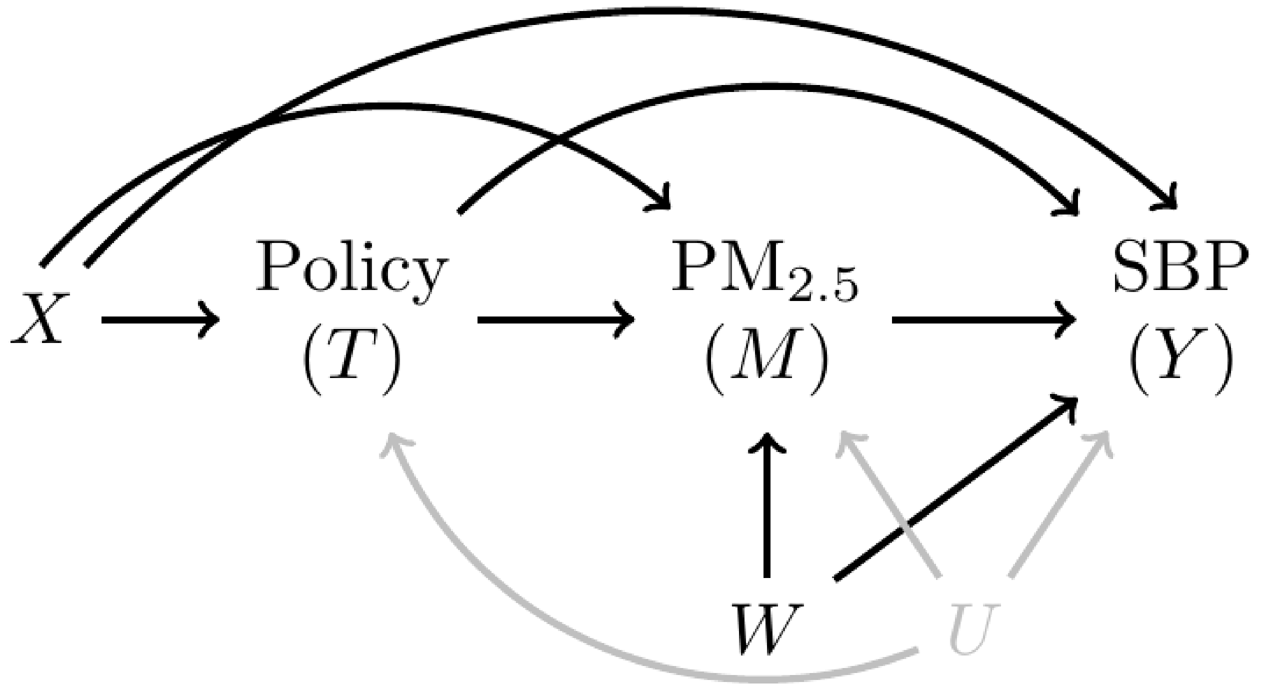
X = pre-treatment covariates

T = exposure

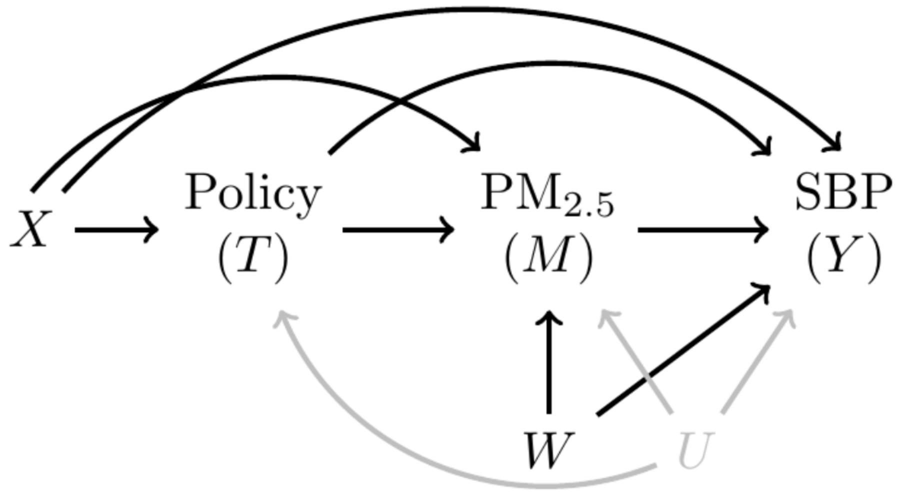
M = mediator

W = confounders

Y = outcome



Quantities of interest



Total effect:

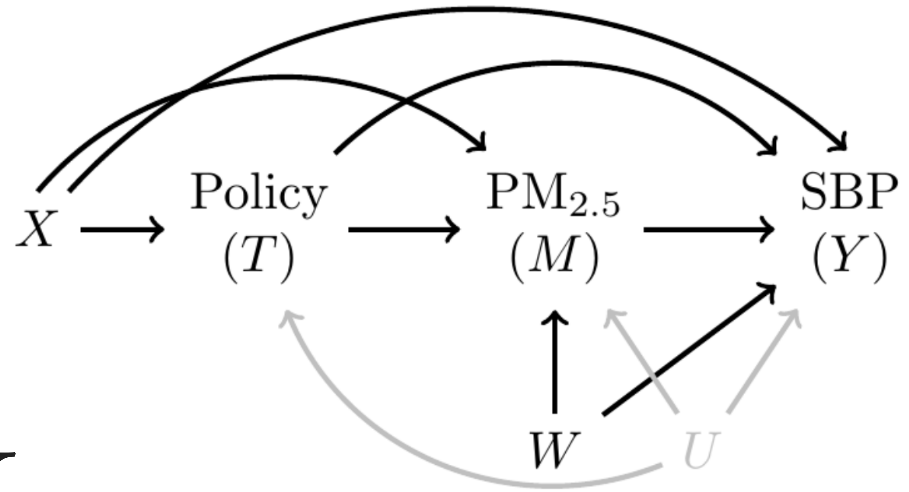
$$E[Y|T, X] = \beta_0 + \beta_1 T + \beta_2 X$$

This equation estimates the total effect of the ban:

$$TE = \beta_1(T^* - T)$$

where T^* is exposure to ban and T is no exposure.

Mediation model



Estimate two regressions:[1]

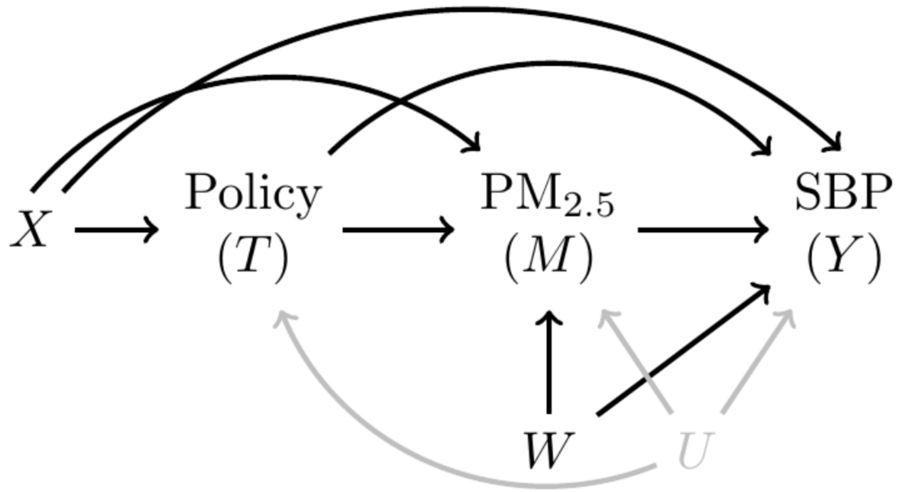
$$E[M|T,X] = \beta_0 + \beta_1 T + \beta_2 X$$

$$E[Y|T,X,M] = \theta_0 + \theta_1 T + \theta_2 M + \theta_3 TM + \theta_4 X + \theta_5 W$$

Second equation estimates the "Controlled Direct Effect":

$$CDE = \theta_1 + \theta_3 TM$$

Key assumptions



Assumptions for valid CDE:

- No confounding of the total effect.
- No confounding of the mediator-outcome effect.

Valid NDE and NIE also require:

- No confounding of the exposure-mediator effect.
- No mediator–outcome confounder affected by treatment.

What the hell is the CDE?

Interpretation

This effect is the contrast between the counterfactual outcome if the individual were exposed at $T = t$ *and the counterfactual outcome if the same individual were exposed at* $T = t*$*, with the mediator set to a fixed level* $M = m$.

English:

“By how much would blood pressure change if the policy were implemented and we held $PM_{2.5}$ *fixed at* m *?“*

Ex: Respiratory symptoms, Sleep

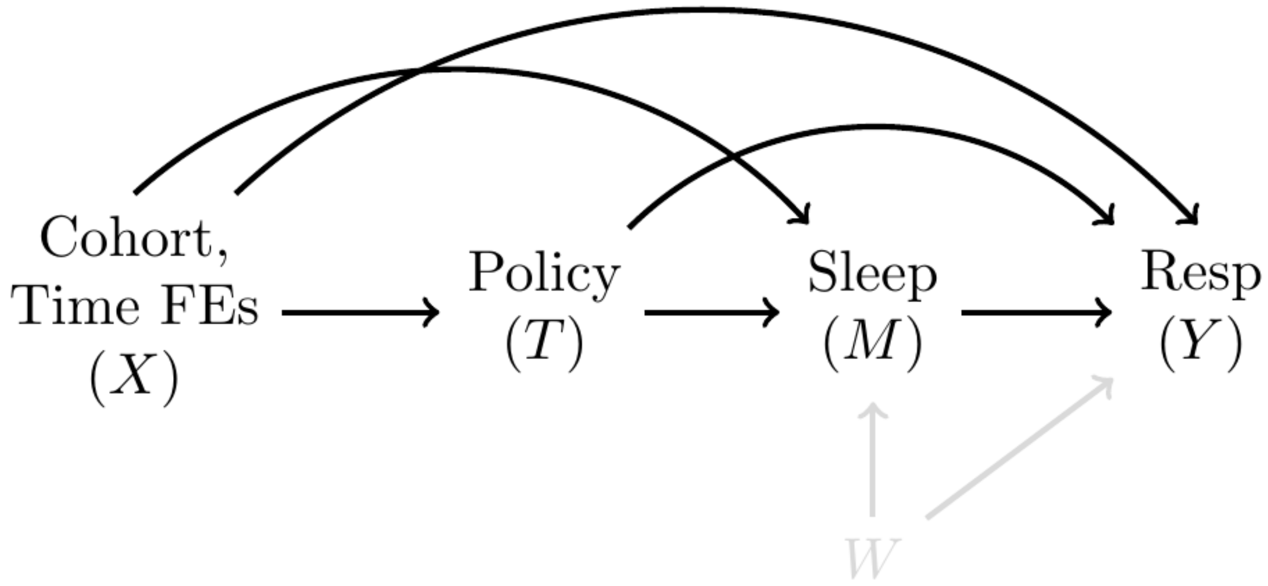
X = cohort, time FEs

T = policy

M = hours of sleep

W = {empty}

Y = Poor respiratory symptoms



'Poor respiratory symptoms' = 1 if frequency of any coughing, wheezing, etc. were "most" or "several" days a week.

Data

- 3 waves, complete data on outcome and mediator

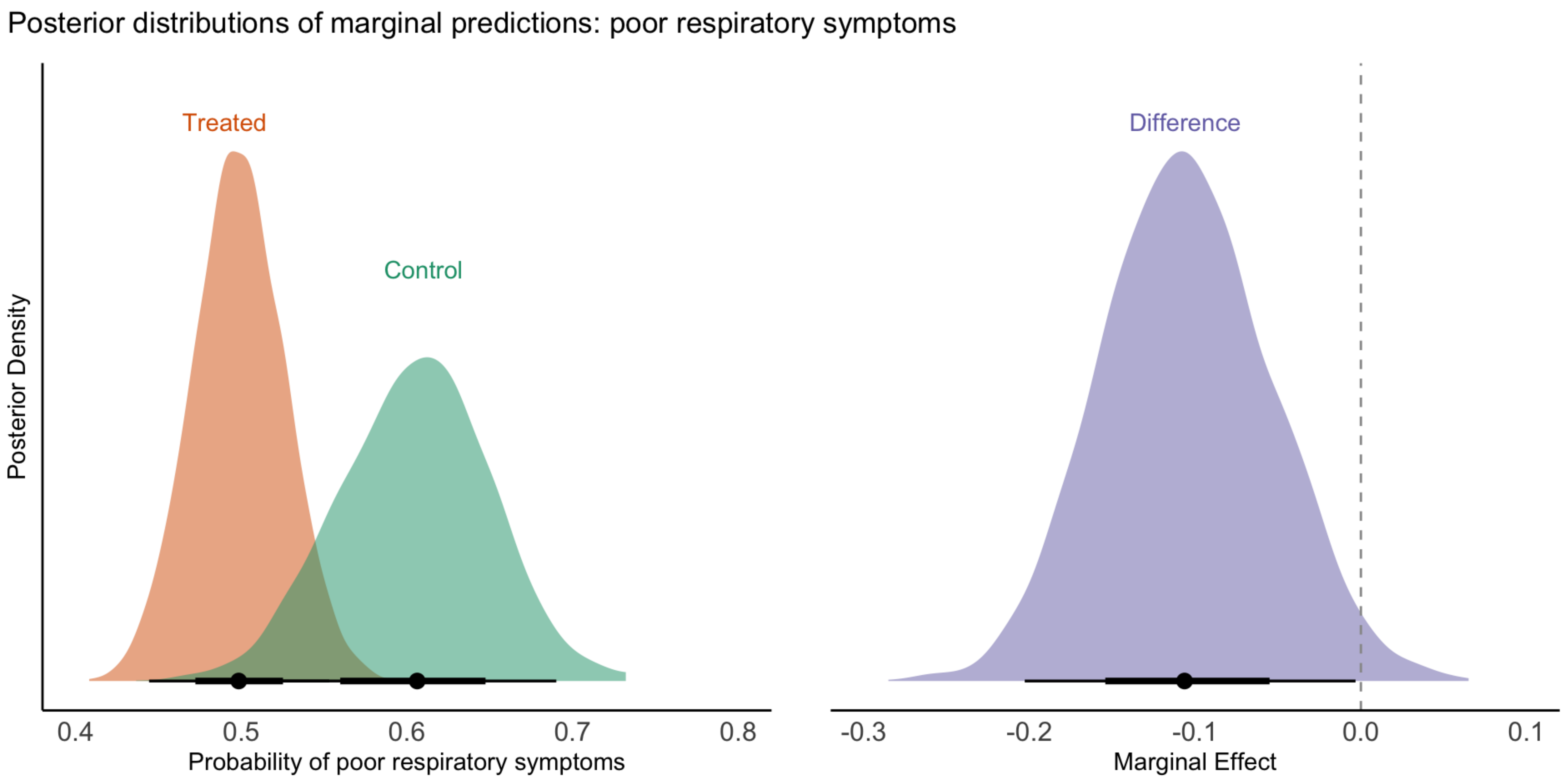
	Unique (#)	Missing (%)	Mean	SD	Min	Median	Max
v_id	50	0	25.3	14.2	1.0	25.0	50.0
year	3	0	2019.4	1.2	2018.0	2019.0	2021.0
cohort_year	4	0	2018.6	0.9	2018.0	2018.0	2021.0
treat	2	0	0.2	0.4	0.0	0.0	1.0
resp	2	0	0.5	0.5	0.0	1.0	1.0
hsleep	30	0	7.7	2.0	1.0	8.0	20.0

Total Effect

$$logit(Y_{it}) = \alpha_{v[i]}^{village} + \sum_{r=q}^{T} \beta_r d_r + \sum_{s=r}^{T} \gamma_s fs_t + \sum_{r=q}^{T} \sum_{s=r}^{T} \tau_{rt}(d_r \times fs_t)$$

- $\alpha_{v[i]}^{village}$ = village-level random intercept
- d_r = treatment cohort fixed effects
- fs_t = time fixed effects
- τ_{rt} = cohort-time *ATTs*[1]

Marginal effects



Cohort-specific ATTs

	Simple Average			
	Est.	**(S.E.)**	**2.5 %**	**97.5 %**
Avg ATT	−0.106	(0.051)	−0.203	−0.003

	Cohort Averages			
	Est.	**(S.E.)**	**2.5 %**	**97.5 %**
ATT(g2019)	−0.158	(0.067)	−0.284	−0.023
ATT(g2020)	0.013	(0.075)	−0.137	0.158
ATT(g2021)	−0.017	(0.111)	−0.241	0.194

Mediation model

$$logit(Y_{it}) = \alpha_{v[i]}^{village} + \sum_{r=q}^{T} \beta_r d_r + \sum_{s=r}^{T} \gamma_s fs_t + \sum_{r=q}^{T} \sum_{s=r}^{T} \tau_{rt}(d_r \times fs_t)$$
$$+\delta M_{it} + \sum_{r=q}^{T} \sum_{s=r}^{T} \eta_{rt}(d_r \times fs_t \times M_{it})$$

where now we have added:

- δ = conditional effect of mediator
- η_{rt} = treatment-mediator product terms

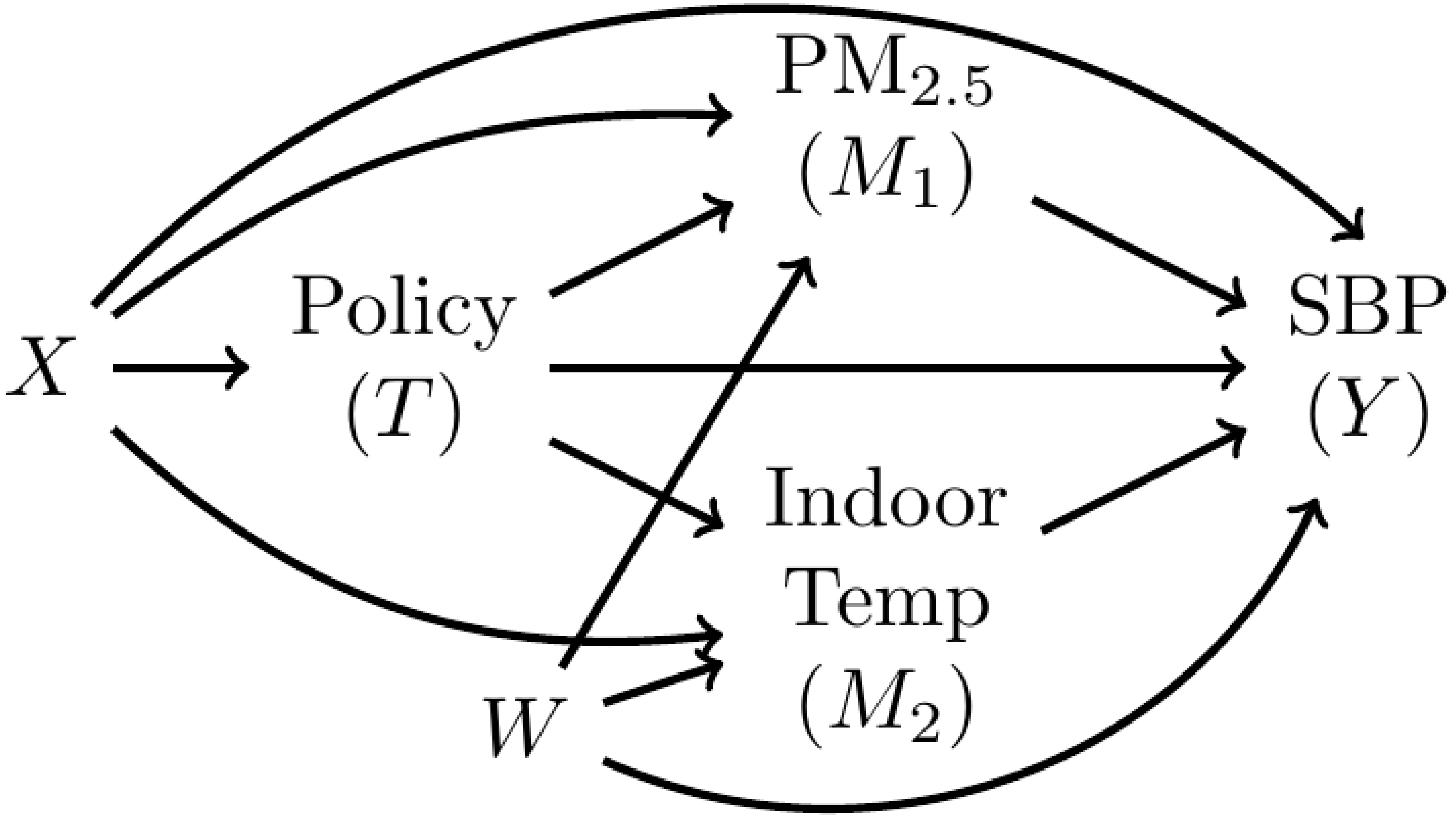
Estimates

	Total Effect			CDE		
	Est.	2.5 %	97.5 %	Est.	2.5 %	97.5 %
Untreated	0.606	0.514	0.690	0.599	0.505	0.688
Treated	0.498	0.444	0.553	0.500	0.447	0.554
Difference	–0.106	–0.203	–0.003	–0.098	–0.202	0.008

- Minimal evidence of mediation.
- Proportion explained: $PE = \frac{TE - CDE}{TE} = 0.08$

Extensions to multiple mediators

- More complicated
- Sequential mediators?
- Interactions between mediators?



Summary

- Mediation analysis aims are part of HEI project.
- Likely to focus mostly on CDEs.
- Tutorials, packages and macros in R, SAS, Stata available.[1]
- Recent *R* package `regmedint` from Yoshida and Li (2022)
- Implementation with staggered DiD more likely to require manual implementation rather than 'default' R packages.

References

Arel-Bundock V. Marginaleffects: Predictions, comparisons, slopes, marginal means, and hypothesis tests [Internet]. 2023. Available from: https://marginaleffects.com/

Bürkner PC. Brms: An R package for bayesian multilevel models using Stan. Journal of statistical software. 2017;80:1–28.

VanderWeele T. Explanation in causal inference: Methods for mediation and interaction. Oxford University Press; 2015.

Yoshida K, Li Y. Regmedint: Regression-based causal mediation analysis with interaction and effect modification terms [Internet]. 2022. Available from: https://kaz-yos.github.io/regmedint/