

Supplemental Methods:

Our effect estimates will have causal mediation interpretations if the following untestable assumptions hold: (1) there are no unmeasured confounders of the exposure-outcome relationship, (2) there are no unmeasured confounders of the mediator-outcome relationship, (3) there are no unmeasured confounders of the exposure-mediator relationship, and (4) no confounders of the mediator-outcome relationship are affected by the exposure. Our effect estimates are based on a multivariable regression model for the outcome including all baseline variables (except for the maternal heart disease covariate in the prematurity analyses), exposure, mediator, and exposure-mediator interaction and a logistic regression model for the mediator including all baseline variables (except for the maternal heart disease covariate in the prematurity analyses), and the exposure. The effect estimates given by CAUSALMED take these fitted models and apply to them the formulas for mediated effects with binary mediator and continuous outcome given in Valeri and VanderWeele (2013).¹