APPENDIX A. Parametric g-computation and total effect decomposition.

G-formula for causal mediation analysis

Conventional regression, controlling for time-varying characteristics, assumes that there exists no exposure-induced mediator-outcome confounding (Vanderweele 2014; Wodtke and Zhou 2020). The counterfactual comparison is between two populations that vary on exposure status (in this case, being racialized as Black or white in a system of racism), assuming *nothing else* changes across the two populations over time. As described above, previous research has demonstrated this assumption is untenable in the quantitative study of racism as a social process, where being racialized within a system of racism affects virtually all other observed variables over time (Sen and Wasow 2016).

The "g-formula" or "g-computation" is a generalization of standardization that allows for the estimation of unconfounded summary effects in the presence of observed post-treatment confounding. The g-formula was developed in the formal quantitative causal inference literature and is flexible for estimating any counterfactual contrast (A. Naimi, Cole, and Kennedy 2016; Robins 1986; Wang and Arah 2015). Equation 1 illustrates the population mean health outcome, $E[Y]$, standardized across all values of an exposure variable, X (e.g., being racialized as Black within the system of racism governing the distribution of Y).

$$E[Y] = \sum_{x} P(Y = y|X = x)\, P(X = x) \tag{1}$$

This generalized formula, or "g-formula," for the mean outcome at a given age can be extended over all stratifying variables, $\boldsymbol{V}$, which confound the association between X and Y, as well as variables which mediate the association, $\boldsymbol{M}$ (i.e., fall along the causal pathway). We use $P(y|x)$

as shorthand for $P(Y = y|X = x)$, $P(\boldsymbol{v})$ as shorthand for $P(\boldsymbol{V} = \boldsymbol{v})$, etc. In Equation 2, we illustrate the g-formula for the expectation of Y given exposure level $X = x$.

$$E[Y^x] = \sum_m P(Y|x, m, \boldsymbol{v})\, P(m|x, \boldsymbol{v})\, P(\boldsymbol{v}) \tag{2}$$

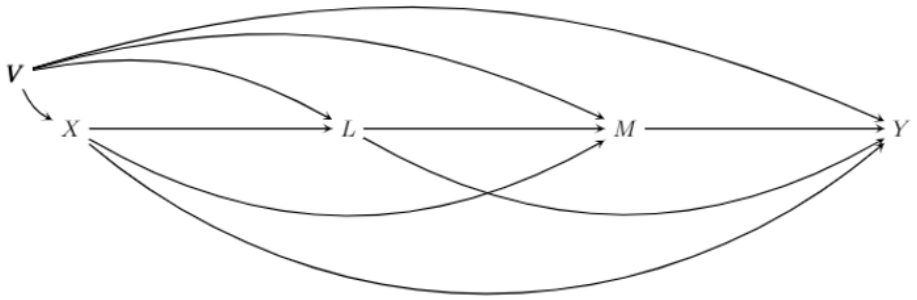
We extend Equation 2 to consider a simple two-mediator scenario: a mediator M which is dependent on a previous mediator L:

$$E[Y^x] = \sum_m \sum_l P(Y|x, m, l, \boldsymbol{v})\, P(m|x, l, \boldsymbol{v})\, P(l|x, \boldsymbol{v})\, P(\boldsymbol{v}) \tag{3}$$

Where:

- $Y =$ normalized z-score on cardio-metabolic risk index (continuous).
- $X =$ self-identified race (x = white, x^* = Black).
- $M =$ second mediator (e.g., college attainment) (m = index value, m^* = reference value).
- $L =$ first mediator (e.g., parent college attainment) (l = index value, l^* = reference value).
- $\boldsymbol{V} =$ vector of 1) exposure-outcome confounders and 2) mediator-outcome confounders not influenced by exposure.

The g-formula in Equation 3 can also be usefully illustrated with the following DAG:



When considering the effect on Y of changes to X via a specific mediator M, variables such as L are often referred to as "exposure-induced mediator-outcome confounders" because they are affected by the exposure and confound the relationship between M and Y (A. Naimi et al. 2016; Wang and Arah 2015). First, the presence of such confounding means that we cannot estimate the counterfactual associated with a given value of X while holding L constant (as in conventional regression or matching estimators, e.g., Baron-Kenny mediation), because such a world would be impossible to observe. In terms of our theoretical framework, this reflects on the critiques discussed above: what would it mean to consider the effect of being racialized one way vs. another *without* anything else changing? At best, this conventional approach involves describing a marginal counterfactual that is difficult to interpret because changing this exposure requires considering changes in everything else that is influenced by and acts on racialized status. At worst, this approach reifies the notion that race is a construct that can be considered separately and independently from other factors such as socioeconomic status (Kohler-Hausmann 2019; Sen and Wasow 2016; Zuberi and Bonilla-Silva 2008). Second, we agree with Zhou & Yamamoto (2022) that *L* is typically itself a mediator of interest, rather than simply a nuisance parameter in estimating the mediating effect of *M.* As Zhou & Yamamoto (2022) discuss, in considering complex social exposures, it is typically difficult to conceptualize any post-treatment variable that is not itself a mediator.

The generalization of the entire conditional probability space in Equation 3 is the critical contribution of the g-formula standardization because it has important implications for estimating population-level counterfactuals without requiring that all variables be fixed at their means or reference values. Rather, in decomposing any population disparity in Y by exposure X (or the total "average treatment effect" of X on Y conditioning on pre-treatment confounders),

specific mediating effects can be considered while other variables that are in any way dependent on the exposure take on the values they *would have had* under that particular counterfactual exposure history (Daniel et al. 2015; A. I. Naimi et al. 2016; Naimi 2016; Robins 1986; Wang and Arah 2015). In conventional regression models (e.g., Baron-Kenny mediation) or demographic decomposition (e.g., Das Gupta or Kitagawa decomposition), estimates of counterfactual change are calculated under the assumption that no other conditional probabilities change as a result of the exposure changing (Jackson and VanderWeele 2018; Sudharsanan and Bijlsma 2022). In contrast, g-formula standardization makes explicit the sum of all *cascades* of conditional probabilities for all variables as the cohort ages through that time and space. The conditional probabilities of all mediators (M, L) in Equation 3 can be expanded to include the specific dependence structure for each variable as described by a given causal model (in this analysis, the DAG in Figure 2).

Total effects calculated via g-computation are generally analogous to effects obtained by marginal structural models (MSM) with inverse-probability-of-treatment weighting (Lee and Jackson 2017; Lin et al. 2017; Robins, Hernán, and Brumback 2000; Wodtke, Harding, and Elwert 2011). In high-dimensional settings, especially with continuous mediators and/or exposure, MSM can also perform more poorly than the parametric g-formula approach (Lin SH et al. 2017). Further, the g-formula provides an intuitive method for decomposing this total effect or disparity into additive direct, interactive, and indirect pathways by predicting and differencing counterfactual quantities rather than relying on often complex weighting schemes. In the simplest case of a single mediator *M* (treating the first mediator in Equation 3, *L*, as a post-treatment confounder) the difference between $E[Y|x]$ and $E[Y|x^*]$ can be decomposed into the controlled direct effect (CDE; *racism via unobserved mediating pathways*), the proportion

attributable to interaction via each mediator M (PAI; *racial discrimination in the underlying system connecting M to Y*), and the pure indirect effect via each mediator M (PIE; *emergent discrimination*) (Reskin 2012; VanderWeele 2014; Wang and Arah 2015).

- $\text{CDE}_{M=m^*} = E[Y_{xm^*}] - E[Y_{x^*m^*}]$
- $\text{PAI}^{(M)} = E[(Y_{xm} - Y_{x^*m} - Y_{xm^*} + Y_{x^*m^*})(M_x)]$
- $\text{PIE}^{(M)} = E[Y_{x^*M_x}] - E[Y_{x^*M_{x^*}}]$

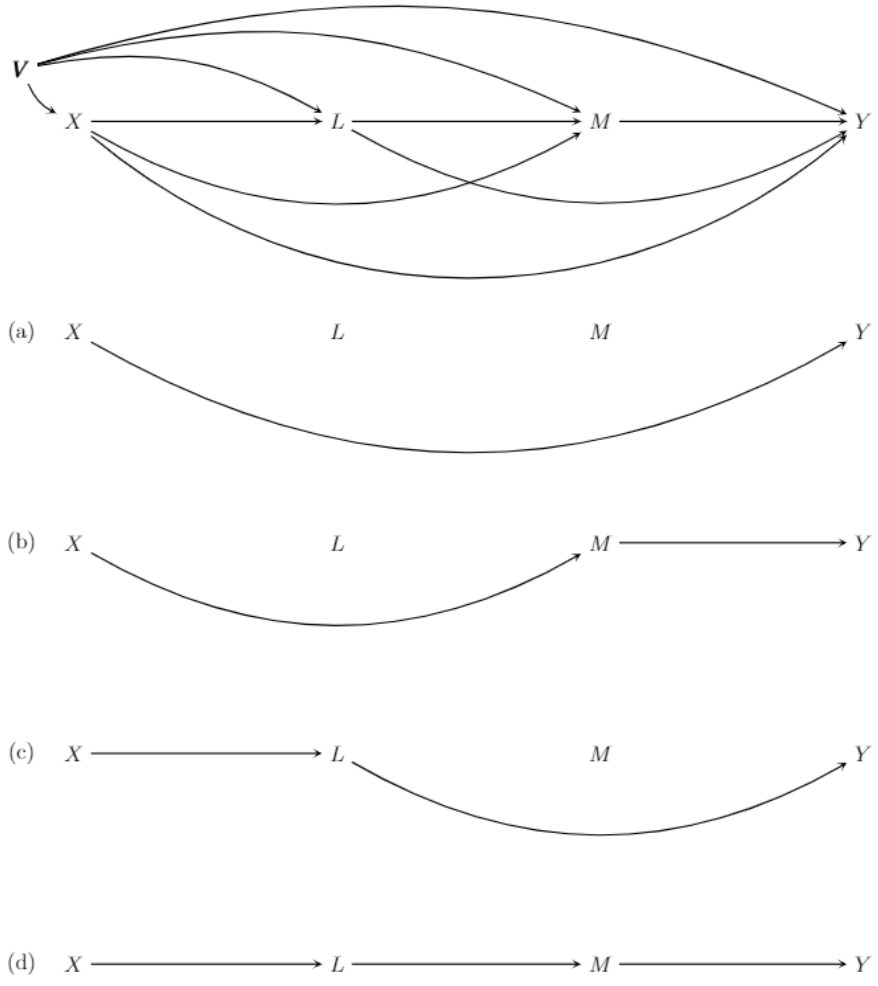
The case of multiple sequential mediators

Wang & Arah (2015) describe the general application of g-computation to causal mediation and effect decomposition considering *one mediator* with an exposure interaction. There have been many useful extensions developed in the context of *multiple dependent mediators*, for example: Daniel et al. (2015) (considering multiple dependent mediators, but not separately estimating effects due to exposure-mediator interactions), Shi et al. (2021) (considering a single PAI/PIE via a joint set of multiple dependent mediators), and Zhou & Yamamoto (2020) (considering path-specific effects via multiple dependent mediators, but not separately estimating effects due to exposure-mediator interactions) (Daniel et al. 2015; Shi, Choirat, and Valeri 2021; Zhou and Yamamoto 2020).

In the present study, we use a relatively straightforward extension of the decomposition in Wang & Arah (2015) to describe *separate mediated effects (PAI, PIE) via multiple sequential mediators*. As a simple example of two mediators as described in Equation 3 (L = parent college attainment, M = college attainment), we decompose the average treatment effect into the following:

- $\text{CDE}_{L=l^*,M=m^*} = E[Y_{xl^*m^*}] - E[Y_{x^*l^*m^*}]$
- $\text{PAI}^{(L)} = E[(Y_{xlm^*} - Y_{x^*lm^*} - Y_{xl^*m^*} + Y_{x^*l^*m^*})(L_x)]$
- $\text{PIE}^{(L)} = E[Y_{x^*L_xM_{x^*l^*}}] - E[Y_{x^*L_{x^*}M_{x^*l^*}}]$
- $\text{PAI}^{(M)} = E[(Y_{xl^*m} - Y_{x^*l^*m} - Y_{xl^*m^*} + Y_{x^*l^*m^*})(M_{xl})]$
- $\text{PIE}^{(M)} = E[Y_{x^*L_{x^*}M_{xl}}] - E[Y_{x^*L_{x^*}M_{x^*l^*}}]$

We note several differences in this decomposition compared to the single-mediator case. In discussing these differences and comparing this effect decomposition with other estimands and methods, consider the plot below for the two-mediator case, adapted from Figure 1 in Zhou & Yamamoto (2022):



First, the CDE in the two-mediator case is evaluated at the reference value for both mediators (e.g., no college degree *and* parent with no college degree); pathway (a) above.

Second, pathway (d) is now removed from the PAI/PIE of the most "upstream" mediator, *L*. In removing pathway (d) from these effects and only focusing on pathway (c), calculation of the PAI/PIE via *L* does not change depending on the distribution of *M*; using the reference value in the equations above is a convenient way to avoid picking up the PAI via *M* within these effects via *L*, as this calculation includes counterfactual values under different levels of the exposure. In other words, we are attempting to isolate change in *Y* that can be attributed to the *racialized returns of a particular mediator* along its direct path to *Y* ($A \rightsquigarrow M \rightarrow Y$). In this example, the PAI via *L* thus refers to the change in *Y* that would be expected if individuals were *racialized as Black by the system governing the distribution of* ***parental education*** *and its* ***relation*** *to cardiometabolic risk* but racialized as white by the system governing the relation between their own education and cardiometabolic risk. Conversely, the PAI via *M* refers to the change in *Y* that would be expected if individuals were *racialized as Black by the system governing the distribution of their* ***own education*** *and its* ***relation*** *to cardiometabolic risk* but racialized as white by the system governing the relation between parental education and cardiometabolic risk. Note that this is a different arrangement of specific exposure-mediator interactions from the path-specific effects (PSEs) described by Zhou & Yamamoto (2022). Zhou & Yamamoto (2022) flexibly account for exposure-mediator interactions, but many "downstream" interactions are attributed to the PSE via an "upstream" mediator. For example, if parent education influenced own education and then own education had a *racialized* (interactive) effect on the outcome, this interaction pathway is attributed to the PSE via parent education (to the extent that the distribution of own education is influenced by parent education). In our

mediation estimands defined above, this interactive pathway is attributed to the PAI via own education (L).

Third, in calculating the PAI/PIE via *M*, the distribution of *M* is equal to its counterfactual distribution under treatment (M_{xl}), which includes the ways in exposure influences *L* which in turn influences *M;* pathways (b) and (d) illustrated above. In other words, our decomposition somewhat preferences "downstream" mediators to the extent that the PIEs are relatively important in the effect decomposition. While this may be conceptually undesirable for the PIE, this is a tradeoff – as described above – in order to effectively locate all *exposure-mediator interactions* in the PAI along the direct path between the specific mediator and the outcome ($A \rightsquigarrow M \rightarrow Y$).

To summarize, the conceptual ambiguity in mapping separated mediation effects given multiple mediators to meaningful theoretical contrasts is in large part 1) how to handle pathway (d) above and 2) where to locate "downstream" exposure-mediator interactions. Our decomposition is effectively putting pathway (d) into the *mediated effects via M*; all separate mediated effects (PIE/PAI via *L*, PIE/PAI via *M*) then add up to the joint mediated effects via *L,M* (as in the R package *CMAverse*; Shi et al. 2021). Our particular decomposition, which can be extended to any number of sequential mediators, might be more or less theoretically justified depending on the specific research question and target counterfactual contrasts – here, we were very interested in separating the relative importance of exposure-mediator interaction effects (PAI). Users seeking to do their own analyses with multiple sequential mediators should consider whether our implementation is aligned to their specific theoretical estimand(s) (Lundberg, Johnson, and Stewart 2021), compared to the joint mediated effect of the set of multiple sequential mediators (*CMAverse* R package) or path-specific effects (*paths* R package); see Zhou

& Yamamoto (2022) for a comprehensive discussion on this topic, as well as considerations for sensitivity analyses concerning unobserved confounding.

Estimation

G-computation requires estimating multiple counterfactual values for Y using the relevant g-formula (Wang and Arah 2015). This is achieved via simulation/imputation, which involves the following general steps (Lin SH et al. 2017; Shi et al. 2021). For simplicity, consider the two-mediator case above (Equation 3). First, we fit a survey-weighted generalized linear model for each mediator (e.g., *L* and *M*) and the outcome (*Y*) using the *survey* package in R. These models take the following general form indexed by individual (*i*):

$$L_i = \beta_0 + \beta_1(X_i) + \boldsymbol{\beta_2}(\boldsymbol{V}_i) + \varepsilon_i$$

$$M_i = \beta_0 + \beta_1(L_i * X_i) + \boldsymbol{\beta_2}(\boldsymbol{V}_i) + \varepsilon_i$$

$$Y_i = \beta_0 + \beta_1(L_i * X_i) + \beta_2(M_i * X_i) + \boldsymbol{\beta_3}(\boldsymbol{V}_i) + \varepsilon_i$$

Models are parameterized with appropriate likelihoods (normal, binomial) and link functions (identity, logit) given the structure of each dependent variable. All models include age and gender ($\boldsymbol{V}_i$), account for the survey design of Add Health by including longitudinal survey weights, and standard errors are clustered by individual using the *survey* R package (Lumley 2010, 2018). Coefficient estimates from all generalized linear models are reported in Appendix Table A.1.

Given these fitted models, we then repeat the decomposition below 1000 times to propagate uncertainty to final effect estimates, which are summarized by the means and 95% intervals of those 1000 estimates:

1. Draw a random multivariate-normal sample of parameters from all survey-weighted models using fitted coefficients and variance-covariance matrices.
2. Create 30 replicates of the dataset to remove Monte Carlo error arising from stochastic individual-level response prediction in imputing counterfactuals.
3. Simulate two counterfactual datasets (one under exposure x and one under exposure x^*) by predicting forward with the sample of parameter estimates (i.e., "What if this cohort had all been racialized as white by the observed mediating systems?").
4. Use values drawn from these simulations to calculate all necessary population-average counterfactual quantities for effect decomposition (e.g., $E[Y_{x^*L_xM_{x^*l^*}}]$). Calculate the CDE and the PAI/PIE for each mediator by differencing these quantities as in the equations described above:
    i. $\text{CDE}_{L=l^*,M=m^*} = E[Y_{xl^*m^*}] - E[Y_{x^*l^*m^*}]$
    ii. $\text{PAI}^{(L)} = E[(Y_{xlm^*} - Y_{x^*lm^*} - Y_{xl^*m^*} + Y_{x^*l^*m^*})(L_x)]$
    iii. $\text{PIE}^{(L)} = E\left[Y_{x^*L_xM_{x^*l^*}}\right] - E\left[Y_{x^*L_{x^*}M_{x^*l^*}}\right]$
    iv. $\text{PAI}^{(M)} = E[(Y_{xl^*m} - Y_{x^*l^*m} - Y_{xl^*m^*} + Y_{x^*l^*m^*})(M_{xl})]$
    v. $\text{PIE}^{(M)} = E[Y_{x^*L_{x^*}M_{xl}}] - E[Y_{x^*L_{x^*}M_{x^*l^*}}]$

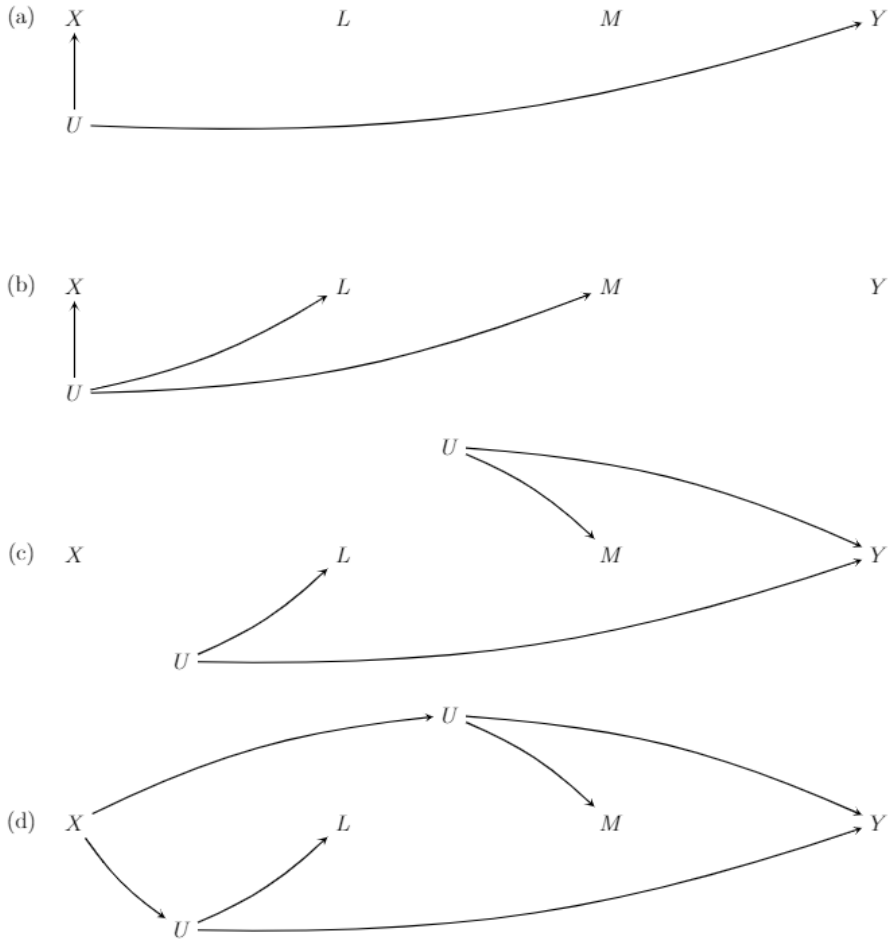
Two types of non-random missing data may result in biased effect estimates: item-nonresponse and censoring of observations. To avoid bias resulting from item-nonresponse, we create 30 multiply imputed datasets using chained equations to account for missing observations (Buuren and Groothuis-Oudshoorn 2011). To avoid bias resulting from the censoring of observations, the g-computation simulations begin with the full sample in the first wave and every individual is simulated through all subsequent waves. In effect calculations, we are then including all

simulated person-years that were censored in the survey sample, assuming these individuals would have responded the same in subsequent waves, on average, to those individuals observed.

Implementation

All analysis is conducted using R 4.0.2. The data used in this study come from the restricted Add Health survey and are not made available, but code and an analogous example is available at https://github.com/ngraetz/multmed_gcomp. Alternatively, the highly accessible *CMAverse* R package (Shi et al. 2021) provides similar g-formula estimators for the CDE and joint mediated effects (PIE/PAI).

Causal mediation assumptions



The effects above can only be identified under a set of potentially strong assumptions: (a) no unobserved treatment-outcome confounding, (b) no unobserved treatment-mediator confounding, (c) no unobserved mediator-outcome confounding, and (d) no unobserved treatment-induced mediator-outcome confounding. Further, a strict interpretation of the cross-world independence assumption posits that the PIE/PAI cannot be identified with *any* treatment-induced mediator-outcome confounding, even if observed (Andrews and Didelez 2021) – though it is possible to identify "randomized interventional analogues" of these estimands (VanderWeele and Tchetgen Tchetgen 2017; Wodtke and Zhou 2020). Still, causal inference methods and counterfactual reasoning represent a very useful quantitative framework for being explicit about the target counterfactual contrast(s) that relate to our complex social theories, describing assumptions around confounding/mediation and threats to validity, and ruling out alternative explanations (Hafeman and Schwartz 2009; Lundberg et al. 2021; Schwartz, Gatto, and Campbell 2016, 2017). As we argue in this paper, while these methods are not without important limitations (highlighting the need for causal triangulation), they help to describe issues related to post-treatment confounding inherent to Baron-Kenny mediation and demographic decomposition (Das Gupta, Blinder-Oaxaca), which remain very commonly used quantitative methods across a variety of disciplines for examining mechanisms and explaining population disparities.