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Evaluating the Population Impact on Racial/Ethnic Disparities in HIV in Adulthood of Intervening on Specific Targets: A Conceptual and Methodological Framework

Chanelle J. Howe*, Akilah Dulin-Keita, Stephen R. Cole, Joseph W. Hogan, Bryan Lau, Richard D. Moore, W. Christopher Mathews, Heidi M. Crane, Daniel R. Drozd, Elvin Geng, Stephen L. Boswell, Sonia Napravnik, Joseph J. Eron, Jr., and Michael J. Mugavero, for the CFAR Network of Integrated Clinical Systems

* Correspondence to Dr. Chanelle J. Howe, Centers for Epidemiology and Environmental Health, Department of Epidemiology, School of Public Health, Brown University, 121 South Main Street, Providence, RI 02912 (e-mail: chanelle_howe@brown.edu).

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Reducing racial/ethnic disparities in human immunodeficiency virus (HIV) disease is a high priority. Reductions in HIV racial/ethnic disparities can potentially be achieved by intervening on important intermediate factors. The potential population impact of intervening on intermediates can be evaluated using observational data when certain conditions are met. However, using standard stratification-based approaches commonly employed in the observational HIV literature to estimate the potential population impact in this setting may yield results that do not accurately estimate quantities of interest. Here we describe a useful conceptual and methodological framework for using observational data to appropriately evaluate the impact on HIV racial/ethnic disparities of interventions. This framework reframes relevant scientific questions in terms of a controlled direct effect and estimates a corresponding proportion eliminated. We review methods and conditions sufficient for accurate estimation within the proposed framework. We use the framework to analyze data on 2,329 participants in the CFAR [Centers for AIDS Research] Network of Integrated Clinical Systems (2008–2014) to evaluate the potential impact of universal prescription of and ≥95% adherence to antiretroviral therapy on racial disparities in HIV virological suppression. We encourage the use of the described framework to appropriately evaluate the potential impact of targeted interventions in addressing HIV racial/ethnic disparities using observational data.

health status disparities; HIV

Abbreviations: AA, African-American; ART, antiretroviral therapy; CDE, controlled direct effect; CI, confidence interval; CNICS, CFAR Network of Integrated Clinical Systems; HIV, human immunodeficiency virus; PE, proportion eliminated; PROs, patient reported data or outcomes; SD, standard deviation; TE, total effect.

In the United States, African Americans (AAs) are the racial/ethnic group most affected by the human immunodeficiency virus (HIV) epidemic, disproportionately experiencing adverse HIV-related outcomes (1–7). Reducing such health disparities is a key component of the US National HIV/AIDS Strategy (8–10). Racial/ethnic disparities in HIV can potentially be reduced by intervening on important intermediate factors that contribute to the disparity. The potential population impact of intervening on intermediates can be validly evaluated using observational data when certain conditions are met. However, using standard stratification-based approaches commonly employed in the observational HIV literature to estimate the potential population impact may yield results that do not accurately estimate quantities of interest.

Suppose a researcher has hypothesized that prescription of antiretroviral therapy (ART) is an important intermediate factor in racial/ethnic disparities in virological suppression, as captured in the Figure 1 causal diagram. Furthermore, suppose that the researcher is interested in the potential impact on the aforementioned disparity of intervening on ART prescription. Standard stratification-based approaches to estimate the potential impact would probably entail examining the racial/ethnic disparity after controlling for ART prescription via restricting the analytical sample to persons who have been prescribed ART or performing

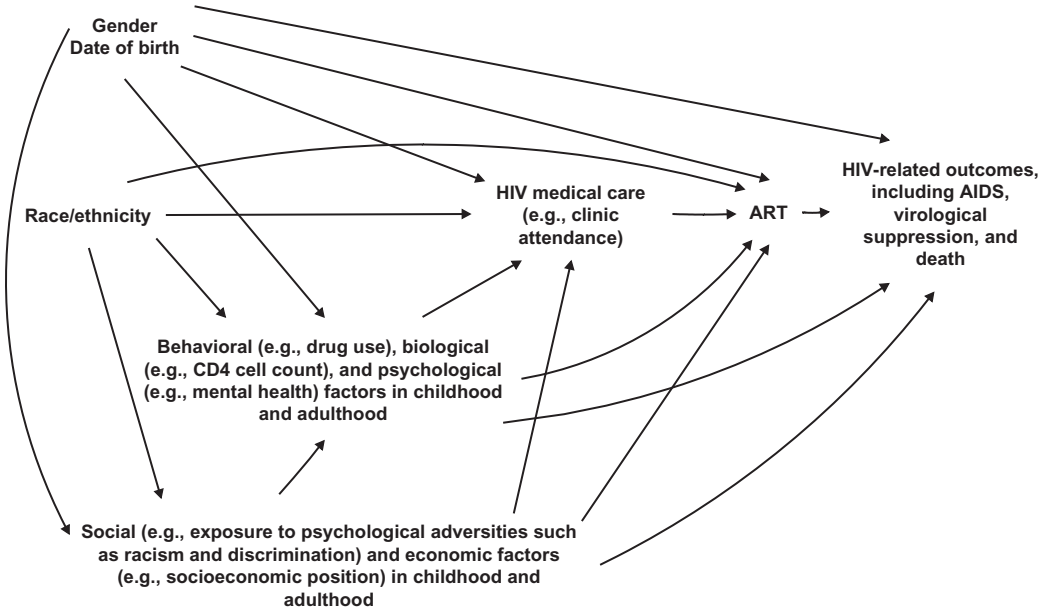

Figure 1. Causal diagram depicting receipt of human immunodeficiency virus (HIV) medical care and use of antiretroviral therapy (ART) as the main mediators of the influence of race/ethnicity on HIV-related outcomes in adulthood. AIDS, acquired immunodeficiency syndrome.

standard regression adjustment for ART prescription (6, 11–14). However, as depicted in Figure 1, the aforementioned restriction or standard regression adjustment may overestimate or underestimate the potential impact by introducing selection bias due to the presence of common causes (e.g., behavioral factors) of ART prescription and virological suppression that results in collider-stratification bias when ART prescription is controlled for via restriction or standard regression adjustment (15–19).

Collider-stratification bias occurs via the path from race/ethnicity to ART prescription to the common causes (e.g., behavioral factors) to virological suppression (15–19). Based on the Figure 1 causal diagram, this collider-stratification bias can only be minimized via standard stratification-based approaches if all of the common causes of ART prescription and virological suppression in Figure 1 are measured. However, even if all of the common causes have been measured, because several of the previously-referred-to common causes are influenced by race/ethnicity, the impact of intervening on ART prescription may still be overestimated. This overestimation may occur because controlling for common causes that are influenced by race/ethnicity via restriction or standard regression adjustment blocks the effect that race/ethnicity has on virological suppression through the common causes determined by race/ethnicity but not operating through ART prescription (15–19). Further detail regarding how causal diagrams can be used to identify selection bias or blocked pathways is included in the appendix of Hernán et al. (20).

Informed by prior work (16, 21–24), here we describe a conceptual and methodological framework for appropriately evaluating the potential population impact on HIV-related racial/ethnic disparities in adulthood of intervening on specific targets. We reframe relevant scientific questions as a controlled direct effect (CDE) and apply more modern approaches for estimation that minimize selection bias without blocking pathways of interest (16, 25–28). To aid our description, we use this framework to analyze longitudinal data on 2,329 participants enrolled in the CFAR [Centers for AIDS Research] Network of Integrated Clinical Systems (CNICS).

CONCEPTUAL AND METHODOLOGICAL FRAMEWORK

Definition of the CDE and the PE

The total effect (TE) captures the effect of a given exposure on an outcome that operates through all intermediate pathways. The CDE represents the effect that the exposure has on the outcome if everyone in a given population were uniformly assigned to have a specific level for the mediator of interest or the distribution of the mediator of interest were intervened upon (16, 21, 24, 29). The TE and CDE can be used to estimate the proportion eliminated (PE) (i.e., the proportion of the TE that could be eliminated through the aforementioned uniform assignment) (24).

The CDE and PE are particularly useful for evaluating the potential population impact on HIV racial/ethnic disparities of interventions, given that the CDE and PE quantify the impact of interventions targeted at the intermediate factor rather than solely the exposure. Such interventions are necessary in this context because the intermediates that most likely contribute to HIV racial/ethnic disparities tend to be more amenable to intervention than race/ethnicity (5, 6, 11, 12, 30–37). Thus, the CDE and PE provide quantities that capture the potential impact of real-world policy interventions. Although it is not realistic to assign the level or distribution of the intermediate to be the same for the entire population, the PE obtained from such an

intervention can provide an upper bound regarding the impact of the intervention. However, approaches within the framework can be pursued if more than an upper bound is preferred (25). We focus on estimating the upper bound via assigning everyone to have the same level of the intermediate.

Even if a potential intermediate turns out not to mediate HIV racial/ethnic disparities because race/ethnicity does not influence the potential intermediate, if there is an interaction between race/ethnicity and the potential intermediate in their impact on the outcome, interventions targeted at the potential intermediate can still affect HIV racial/ethnic disparities as quantified by the CDE and PE (24). Therefore, we refer to the nonexposure variable under consideration for intervention as a *potential* intermediate/mediator rather than an intermediate/mediator to allow for the evaluation of interventions focused on mediators as well as hypothesized mediators that do not mediate the disparity but still affect the outcome.

Estimation of the CDE and the PE

VanderWeele (16) outlined methods for estimating the CDE while accounting for potential interactions between the exposure and the potential intermediate using the g-method, inverse probability weighted marginal structural models. Formulas for calculating the PE when the measure of effect was a difference in the mean outcome (e.g., risk difference) or another function (e.g., risk ratio) were later provided (16, 23, 38). Highlighted in this prior work (23) was the fact that despite being referred to as a "proportion," the PE will not necessarily fall between 0 and 1 when an interaction between the exposure and a potential intermediate is present.

VanderWeele (16) also emphasized that standard stratification-based approaches (e.g., standard regression adjustment) should not be used to estimate the CDE and PE in settings that are the focus of this paper due to the likely presence of a common cause of the potential mediator and outcome that is influenced by the exposure, as in Figure 1 (e.g., behavioral factors). As previously described, the presence of the aforementioned common cause can result in selection bias that cannot be minimized via standard stratification-based approaches without potentially blocking pathways of interest. The aforementioned common cause may also be related to selection (e.g., censoring), as illustrated in the later CNICS example, which further limits the utility of standard stratification-based approaches in this setting because standard approaches cannot be used to minimize bias stemming from the selection mechanism without potentially also blocking pathways of interest (18, 39). However, more modern techniques (e.g., inverse probability-of-censoring-and-potential-mediator weighted marginal structural models) can still be used for appropriate estimation and have been previously summarized (18, 25, 39, 40).

Moreover, even if the data do not provide evidence of a statistically significant association between race/ethnicity and the potential mediator, we caution against assuming the absence of mediation and using standard stratification-based approaches given the prior evidence. We caution because the lack of a statistically significant association between race/ethnicity and the potential mediator may be due to a lack of adequate power to detect a statistically significant association rather than the absence of mediation because race/ethnicity does not influence the potential mediator. Instead, we recommend that the conceptual model be used to determine whether more modern approaches are necessary and then use the relationships observed in the data to aid in explaining the estimated CDE and PE.

Conditions sufficient for estimation of the CDE and the PE

The CDE and PE can be appropriately estimated when 1) the assumptions of exchangeability and positivity hold for the exposure, the potential intermediate, and the selection mechanism that generated the analytical sample; 2) all fitted regression models have been correctly specified; 3) measurement error is absent; and 4) the exposure, potential intermediate, and selection mechanism are well-defined (15, 16, 41). To achieve exchangeability, there must be no unmeasured confounding of the exposure-outcome relationship or the potential mediator-outcome relationship. Furthermore, there must be no unmeasured sources of selection bias. To achieve positivity, there must be a nonzero probability of each level of the exposure within every observed combination of the confounders. Similarly, there must be a nonzero probability of each level of the potential intermediate within every observed combination of the relevant confounders and the exposure. There must also be a nonzero probability of being selected within every observed combination of relevant determinants of selection, including the exposure and potential intermediate.

Correct model specification means that the model choice, including functional forms, is correct in all fitted regression models. Well-defined exposures, potential intermediates, and selection mechanisms do not suffer from interference (42) and correspond to a single well-defined intervention or have version irrelevance when more than one well-defined intervention exists (43). Given that race/ethnicity is not a well-defined exposure because it does not correspond to a well-defined intervention and is less amenable to intervention, race/ethnicity does not represent a point of intervention in the framework. However, because the traditional definitions of the TE, CDE, and PE imply an intervention on the exposure and potential intermediate, we refrain from referring to the aforementioned quantities as the TE, CDE, and PE in the framework. Instead, and consistent with prior work (21, 22), in the framework we refer to the TE as the racial/ethnic disparity that exists before an intervention on the potential intermediate; to the CDE as the racial/ethnic disparity that exists after an intervention on the potential intermediate; and to the PE as the proportion of the racial/ethnic disparity that is eliminated due to an intervention on the potential intermediate.

Conceptual model

Next we present a conceptual model for evaluating interventions upon potential intermediates on racial/ethnic disparities in outcomes (e.g., virological suppression) among HIV-infected adults. Such a conceptual model is necessary to appropriately evaluate interventions. The model we offer can be easily modified to explore other endpoints (e.g., HIV infection). Figure 1 is a causal diagram that presents a conceptual model for the influence of race/ethnicity on outcomes among HIV-infected adults, where receipt of HIV medical care and ART use (i.e., prescription, modification, and adherence) are the main potential mediators of racial/ethnic disparities in outcomes among HIV-infected adults (5, 6, 11, 12, 30–36).

In Figure 1 as well as in the framework, race is considered to be a socially constructed classification based on phenotype that measures a combination of factors, including genes, socioeconomic position, heritage, culture, and historical factors such as structural racism and discrimination prior to or at birth (21, 22, 44). Race/ethnicity may influence the likelihood of receipt of HIV medical care, ART use, and HIV-related outcomes in adulthood through several pathways, including behavioral, biological, psychological, and social pathways, as well as economic factors in childhood and adulthood (45–56). In prior work (21, 22), some of the above-mentioned factors present prior to or at birth have been considered to be confounders of the relationship between race/ethnicity and a given outcome of interest. However, because 1) researchers will often not have the data required to differentiate among the components of the framework's definition of race/ethnicity and 2) race/ethnicity is not a point of intervention, for simplification we have included confounding factors in the framework's definition of race/ethnicity. But, as in prior work (21, 22, 44), if relevant data are available, the framework can be modified to examine certain aspects of race/ethnicity (e.g., culture). Such relevant data include data on components not of interest that the investigator considers to be potential confounders.

APPLICATION

Research question

A policy-relevant research question that could be answered using the framework is, "Would racial disparities in HIV virological suppression in adulthood remain between AAs and Caucasians had both groups been universally prescribed ART and were ≥95% adherent to their prescribed ART regimens after entering HIV care?"

Study population, design, and measures

We used the framework to analyze modified data on adult HIV-infected patients enrolled in 7 US HIV clinics in CNICS. Data modifications are briefly described below. The secondary data analysis presented below was approved by the institutional review boards at Brown University and the 7 clinic sites. Additional details concerning CNICS are provided elsewhere (57).

CNICS collects relevant information from medical records and through clinical assessments of patient reported data or outcomes (PROs) (58) captured every 4–6 months. We used data from 2,329 male and female AA and Caucasian adults who had necessary data available (e.g., attendance at 1 or more HIV primary-care appointments during the study period (January 1, 2008–July 30, 2014)) and were ART prescription-naive at the start of the study period. We assumed that any potential selection bias due to restricting the sample to patients with the necessary data available was negligible, to focus on minimizing potential sources of selection bias induced when trying to estimate the racial disparity in virological suppression after intervening on ART prescription and adherence in the analytical sample. However, beyond this demonstration, the potential sources of selection bias that we assumed to be negligible should be more thoroughly considered, potentially in sensitivity analyses (15, 21, 59). To avoid selection bias due to pattern of care (60), we modified the data to correspond to an interval cohort (61), where all clinical and PROs data are collected and updated once every 6 months subsequent to the first PROs assessment in the study period.

Simple methods (e.g., last observation carried forward) were used to complete clinical and PROs data that were unavailable. Completed values were assumed to represent the truth. However, beyond this demonstration, other, more sophisticated approaches for addressing missing data should be considered, potentially in sensitivity analyses (59, 62).

Race was a time-fixed binary indicator of AA race. The potential mediator was a time-updated binary indicator of meeting conditions A and B below or meeting conditions A and C below. Condition A was earliest ART prescription occurring before a given PROs assessment. Condition B was ≥95% ART adherence during the time between the earliest ART prescription and the first subsequent PROs assessment. Condition C was ≥95% ART adherence during the 6 months prior to a given PROs assessment subsequent to the first ART prescription and the earliest PROs assessment.

The outcome was a repeated binary indicator of achieving virological suppression (i.e., ≤200 copies/mL) at the first HIV-1 RNA assessment in the 6 months after the PROs assessment. Birth year, gender, CD4 cell count, mental illnesses, HIV-1 RNA, at-risk alcohol and drug use, and ART prescription and adherence were covariates. Patients were followed until their death (if applicable), July 30, 2014, or 1 year after their last PROs assessment (i.e., dropout), whichever occurred first.

Conceptual model, notation, and statistical analysis

Figure 2 depicts the specific conceptual model that guided the subsequently detailed notation and employed statistical analysis based on the data available in CNICS. Regarding notation, capital letters represent random variables, while lowercase letters or numbers represent particular values of random variables. In the CNICS cohort of $i = 1, 2, \ldots, 2{,}329$ AA and Caucasian individuals, for patient i, let $X_i = 0{,}1$ correspond to a binary indicator of AA race. Next, $M_i(t) = 0{,}1$ is a binary indicator of meeting above-described conditions A and B or above-described conditions A and C at a PROs assessment at time t. Additionally, $Y_i(t+1) = 0{,}1$ is a binary indicator of achieving virological suppression at time $t+1$ that was observed.

Next, $\mathbf{L}_{1,i}$ is a vector denoting the levels of the measured covariates at or during the year prior to the first attended HIV primary-care appointment during the study period, excluding gender and year of birth; $\mathbf{L}_{2,i}(t)$ is a vector denoting the levels of the measured covariates at or during the year prior to time t, excluding gender and year of birth; and $\mathbf{Z}_i$ is a vector denoting the levels of gender and year of birth. Furthermore, $C_i(t) = 0{,}1$ is a binary indicator of being censored due to dropout or death at time t. Lastly, $t = 0, 1, \ldots, 13$ is time (in 6-month periods) since the first PROs assessment, while a bar over a random variable represents the history of that variable from the first PROs assessment through time t. Therefore, $Y_i^{\bar{m}(t)}(t+1) = 0{,}1$ is a binary indicator of achieving virological suppression at time $t+1$ had patient i's ART prescription and adherence history at time t been set to $\bar{m}(t)$, possibly contrary to fact. The subscript i will henceforth be suppressed wherever possible.

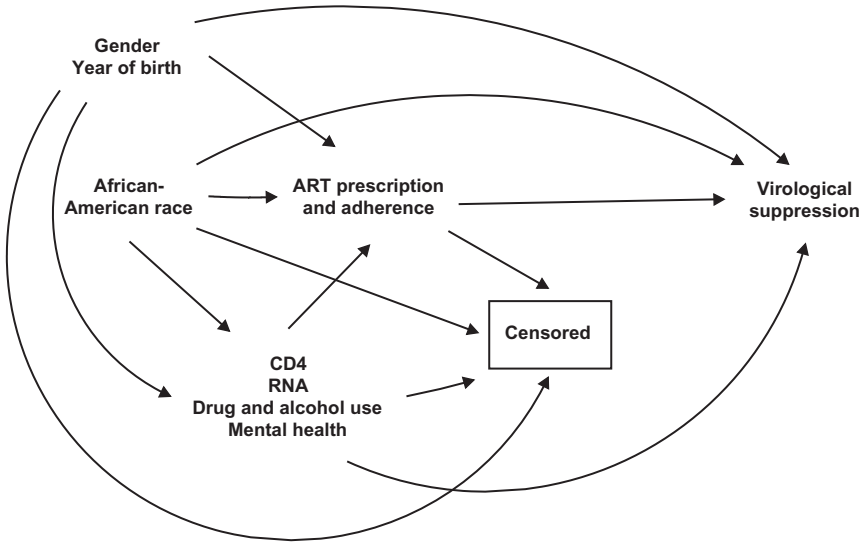

Figure 2. Causal diagram depicting the relationship between African-American race and virological suppression in the unweighted data among 2,329 human immunodeficiency virus–infected African-American and Caucasian adults, CFAR Network of Integrated Clinical Systems, 2008–2014. Unmeasured variables have been omitted for simplicity. A box appears around "Censored" because the analysis is restricted to those participants who remain not censored due to dropout or death. ART, antiretroviral therapy.

The racial disparity in virological suppression that exists prior to intervening on ART was estimated on the risk difference scale from α_2 in the following modified Poisson regression model (63):

$$E[Y(t+1) \mid X, Z] = \alpha_0 + \alpha_1 f(t) + \alpha_2 X + \alpha_3 Z, \quad \text{(Model 1)}$$

where $f(\cdot)$ is a function of time. Model 1 was fitted using participant-specific inverse probability-of-censoring weights estimated from the following equation:

$$W(t)_1 = \prod_{k=0}^{k=t} \frac{P[C(k+1) = 0 \mid X, Z, \bar{C}(k) = 0]}{P[C(k+1) = 0 \mid X, \bar{M}(k), Z, L_1, \bar{L}_2(k), \bar{C}(k) = 0]}. \quad (1)$$

Inverse probability-of-censoring weights were used to minimize the potential for selection bias because of censoring due to dropout or death related to certain measured covariates. For comparison, an unadjusted version of model 1 was also fitted based on the unweighted data that solely included time and race as independent variables. An adjusted version of model 1 was also fitted based on the unweighted data that included time and race as well as all of the measured covariates that were used to predict censoring in equation 1 (excluding ART prescription and adherence) as independent variables.

The racial disparity that would have existed had all AAs and Caucasians been prescribed ART and been ≥95% ART-adherent during the prior 6 months or the period between the first ART prescription and the earliest PROs assessment was estimated from $\beta_2 + \beta_4$ in the following modified Poisson regression model (63):

$$E[Y^{\bar{m}(t)}(t+1) \mid X, Z] = \beta_0 + \beta_1 f(t) + \beta_2 X + \beta_3 m(t) + \beta_4 X \times m(t) + \beta_5 Z. \quad \text{(Model 2)}$$

For simplicity, model 2 assumed that virological suppression depended only on ART prescription and adherence reported at the most recent prior PROs assessment, but other specifications are possible (60). Model 2 was fitted using participant-specific inverse probability-of-censoring-and-potential-mediator weights estimated from the product of equation 1 and equation 2,

$$W(t)_2 = \prod_{k=0}^{k=t} \frac{P[M(k) = m \mid \bar{M}(k-1), X, Z, \bar{C}(k) = 0]}{P[M(k) = m \mid \bar{M}(k-1), X, Z, L_1, \bar{L}_2(k), \bar{C}(k) = 0]}. \quad (2)$$

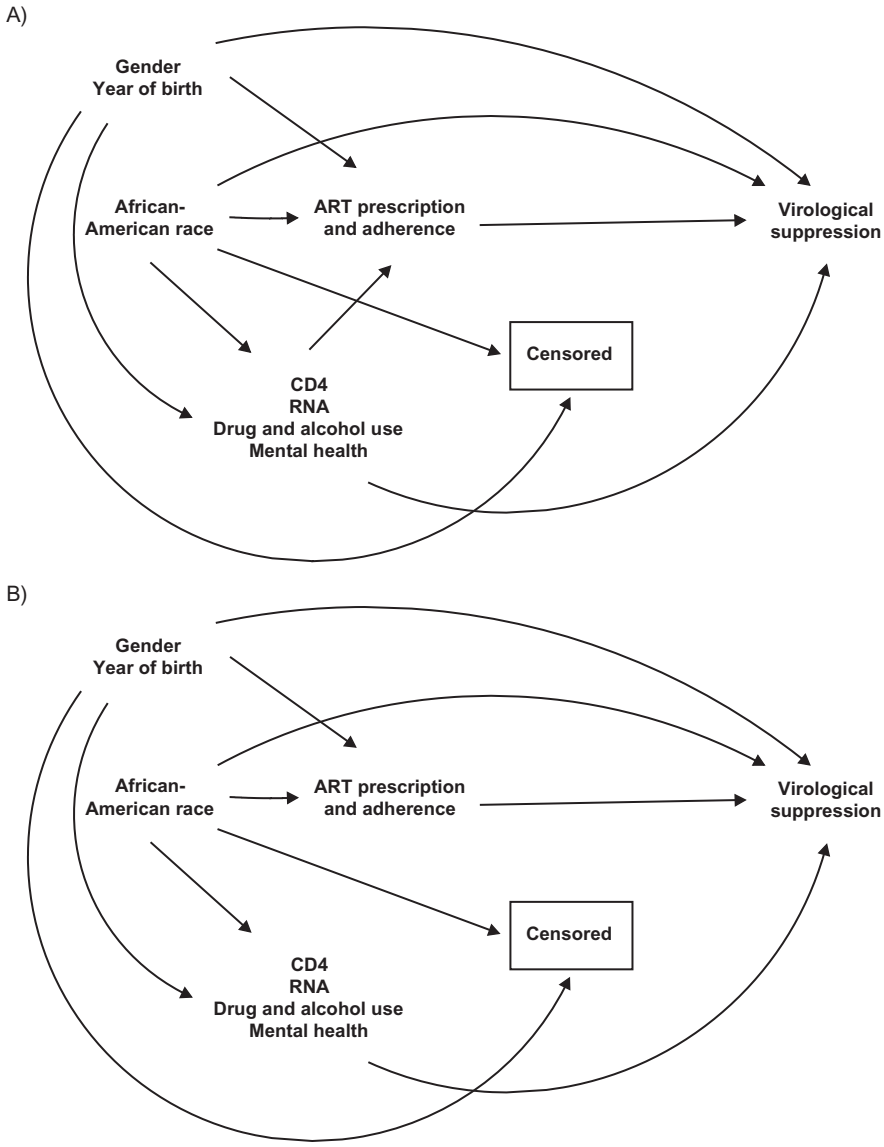

Figure 3. Causal diagrams depicting the relationship between African-American (AA) race and virological suppression in the weighted data among 2,329 human immunodeficiency virus (HIV)–infected AA and Caucasian adults, CFAR Network of Integrated Clinical Systems, 2008–2014. In diagram A, potential selection bias because of censoring due to dropout or death related to certain measured covariates is accounted for. In diagram B, potential selection bias because of censoring due to dropout or death and potential confounding of the relationship between antiretroviral therapy (ART) prescription and adherence and virological suppression related to certain measured covariates is accounted for. Unmeasured variables have been omitted for simplicity. A box appears around "Censored" because the analysis is restricted to those participants who remain not censored due to dropout or death. The arrows from gender, year of birth, and AA race to "Censored" and "ART prescription and adherence" remain because gender, year of birth, and AA race were used to stabilize the weights.

Inverse probability-of-censoring-and-potential-mediator weights were used to minimize the potential for selection bias because of censoring due to dropout or death related to certain measured covariates, as well as to control for confounding of the potential mediator-outcome relationship. For comparison, an unadjusted version of model 2 was also fitted using the unweighted data that solely included time, race, and the potential mediator as independent variables. An adjusted version of model 2 was also fitted based on the unweighted data that included time, race, the potential mediator, and all of the measured covariates that were used to predict censoring or ART prescription and adherence in equations 1 and 2 as independent variables.

The proportion of the racial disparity that was eliminated on the risk difference scale was estimated based on equation 3,

$$\frac{\alpha_2 - (\beta_2 + \beta_4)}{\alpha_2}, \quad (3)$$

Table 1. Racial Disparity (African Americans vs. Caucasians) in Virological Suppression Among 2,329 Adult Male and Female Participants in the CFAR Network of Integrated Clinical Systems, 2008–2014

Racial Disparity	Risk Difference	95% CI	Proportion of Disparity Eliminated[a]	95% CI
Unadjusted racial disparity	−0.10	−0.14, −0.07		
Adjusted[b] racial disparity	−0.06	−0.09, −0.02		
Weighted[c] racial disparity	−0.09	−0.12, −0.05		
Unadjusted racial disparity given universal prescription of and ≥95% adherence to ART	−0.05	−0.08, −0.02	0.52	0.19, 0.81
Adjusted[b] racial disparity given universal prescription of and ≥95% adherence to ART	−0.04	−0.08, 0.00	0.33	−0.53, 1.04
Weighted[c] racial disparity given universal prescription of and ≥95% adherence to ART	−0.05	−0.10, −0.01	0.38	−0.25, 0.89

Abbreviations: ART, antiretroviral therapy; CI, confidence interval.

[a] Difference between the proportion eliminated presented in the table and the proportion eliminated calculated on the basis of risk differences included in the table due to rounding.

[b] Accounts for year of birth, gender, CD4 cell count, HIV-1 RNA level, mental illness, and at-risk alcohol and drug use as covariates.

[c] Accounts for year of birth, gender, CD4 cell count, HIV-1 RNA level, mental illness, at-risk alcohol and drug use, and ART use as covariates.

or an equivalent equation derived from the unadjusted or adjusted analysis. Other representations of the aforementioned proportion may be considered (38). To aid in explaining whether the equation 3 estimate was due to mediation, interaction, both, or neither, an additional modified Poisson regression model, model 3, was fitted using the equation 1 weights with ART prescription and adherence as a repeated outcome and time, birth year, race, and gender as predictors.

Logistic regression models were used to estimate weights. In all modified Poisson and logistic regression models, linear and quadratic terms were used to fit continuous predictors, while indicators were used to fit categorical predictors. Generalized estimating equations (64, 65) were used to fit all modified Poisson regression models. Analyses were performed in SAS, version 9.4 (SAS Institute, Inc., Cary, North Carolina). The SAS code used to perform analyses is included in the Web Appendix (available at https://academic.oup.com/aje).

RESULTS

The weights that were estimated to fit models 1–3 had mean values of 1.04 (standard deviation (SD), 0.42) and 1.05 (SD, 0.70) with ranges of 0.11–7.15 and 0.02–27.34, respectively. Thus, the weights estimated for models 1 and 3 were well-behaved and used to fit models 1 and 3. However, the weights estimated for model 2 were extreme (e.g., 1/0.02 = 50) and indicated potential nonpositivity or model misspecification (66). Therefore, the weights estimated for model 2 were truncated at the first and 99th percentiles (66, 67) prior to using them to fit model 2. The aforementioned truncation yielded a mean value of 1.03 (SD, 0.47) with a range of 0.09–3.48.

Assuming that all sufficient conditions hold, parts A and B of Figure 3 depict the weighted populations used to fit models 1 and 2, respectively. Table 1 provides the racial disparities derived from models 1 and 2 or their equivalent unadjusted and adjusted versions. Compared with Caucasians, the weighted risk difference for achieving virological suppression for AAs was −0.09 (95% confidence interval (CI): −0.12, −0.05). After universal prescription of and ≥95% adherence to ART, the aforementioned risk difference was reduced by 38% (95% CI: −25, 89), thus indicating that universal ART prescription and adherence after entering HIV care could considerably reduce racial disparities in virological suppression in adulthood. However, the confidence interval for the aforementioned reduction was imprecise. Furthermore, the estimated values for β_3 and β_4 (i.e., 0.20 (95% CI: 0.17, 0.22) and 0.05 (95% CI: −0.01, 0.10), respectively) in model 2, along with the point estimate (i.e., 0.02, 95% CI: 0.00, 0.04) for race in model 3, indicate that the aforementioned 38% reduction may be due to mediation and interaction because of the nonnull (i.e., nonzero) estimated values for β_3 and β_4 and the race point estimate in model 3. The corresponding reduction in the risk difference in the adjusted analysis was smaller (i.e., 33%, 95% CI: −53, 104) than the estimated reduction based on the weighted approach.

DISCUSSION

Compared with standard approaches, the framework described here provides potentially more accurate techniques for using observational data to evaluate the potential population impact on HIV racial/ethnic disparities in adulthood of intervening upon specific targets. The gain in accuracy is due to better minimizing the potential for selection bias while avoiding pathways of interest from being blocked. For the CNICS example, the proportion of the racial disparity that was eliminated based on the standard regression approach quantitatively differed from the corresponding proportion estimated based on the inverse probability weighted analysis. This difference may have been due to the described framework better minimizing the potential for selection bias and not blocking pathways of interest. However, the above-mentioned difference was small, and the confidence intervals for the proportions estimated from the adjusted

and inverse probability weighted analyses were both imprecise and included a value of 0.

Regardless, employing the framework may lead to new inferences or the refinement of prior inferences (12, 13) based on standard approaches regarding the potential impact on HIV racial/ethnic disparities in adulthood of intervening upon specific targets. Employing the framework may also provide evidence regarding whether an observed impact is likely to be due to interaction, mediation, or both. Although evidence regarding whether a reduction in a racial/ethnic disparity is due to interaction, mediation, or both may not have policy implications, because a considerable reduction may warrant an intervention regardless of the source, learning whether an observed reduction is due to interaction, mediation, or both will probably enhance the conceptual models that are used to explain and identify the best targets to reduce racial/ethnic disparities. Enhanced conceptual models will help ensure that the most appropriate methodological approaches are used in future analyses when studying racial/ethnic disparities. Note that to accurately quantify how much of a reduction is due to interaction, mediation, or both, other techniques than those used to analyze the CNICS data are needed (68).

In closing, we encourage researchers studying HIV and non-HIV racial/ethnic disparities, as well as other health disparities with a causal structure similar to the structure included in Figure 1 and an exposure that is difficult to intervene on (e.g., socioeconomic position), to readily adapt and apply the framework. Because factors relevant to studying health disparities may often not be measured (69), as in the CNICS example, conditions sufficient for accurate estimation (e.g., exchangeability) may frequently not hold. Thus, beyond our simplified demonstration, which focused on illustrating how to apply the framework using the CNICS data in as straightforward a manner as possible, when feasible the framework should be applied in combination with sensitivity analyses (59, 62, 70) when sufficient conditions probably do not hold.

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Author affiliations: Centers for Epidemiology and Environmental Health, Department of Epidemiology, School of Public Health, Brown University, Providence, Rhode Island (Chanelle J. Howe); Center for Health Equity Research, Department of Behavioral and Social Sciences, School of Public Health, Brown University, Providence, Rhode Island (Akilah Dulin-Keita); Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina (Stephen R. Cole, Sonia Napravnik); Center for Statistical Sciences, Department of Biostatistics, School of Public Health, Brown University, Providence, Rhode Island (Joseph W. Hogan); Department of Epidemiology, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, Maryland (Bryan Lau, Richard D. Moore); University of California San Diego Medical Center, San Diego, California (W. Christopher Mathews); Department of Medicine, School of Medicine, University of Washington, Seattle, Washington (Heidi M. Crane, Daniel R. Drozd), Division of HIV, ID, and Global Medicine, Department of Medicine, School of Medicine, University of California, San Francisco, San Francisco, California (Elvin Geng); The Fenway Institute, Fenway Health, Boston, Massachusetts (Stephen L. Boswell); Division of Infectious Diseases, Department of Medicine, School of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina (Sonia Napravnik, Joseph J. Eron, Jr.); and Division of Infectious Diseases, Department of Medicine, School of Medicine, University of Alabama at Birmingham, Birmingham, Alabama (Michael J. Mugavero).

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