Annals of Epidemiology 29 (2019) 1–7

Contents lists available at ScienceDirect

Annals of Epidemiology

Commentary

How do we assess a racial disparity in health? Distribution, interaction, and interpretation in epidemiological studies

Julia B. Ward, PhD, MPH [a,b,c], Danielle R. Gartner, MS [a,b], Katherine M. Keyes, PhD, MPH [d,e], Mike D. Fliss, MSW [a], Elizabeth S. McClure, MS [a,b], Whitney R. Robinson, PhD, MSPH [a,b,f,*]

[a] Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina, Chapel Hill
[b] Carolina Population Center, University of North Carolina, Chapel Hill
[c] Social and Scientific Systems, Inc., Durham, NC
[d] Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY
[e] Center for Research on Society and Health, Universidad Mayor, Providencia, Santiago, Chile
[f] Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill

ARTICLE INFO

Article history:
Received 24 November 2017
Accepted 25 September 2018
Available online 29 September 2018

Keywords:
Health disparities
Interaction
Interpretation
Modification
Race
Regression

ABSTRACT

Identifying the exposures or interventions that exacerbate or ameliorate racial health disparities is one of the fundamental goals of social epidemiology. Introducing an interaction term between race and an exposure into a statistical model is commonly used in the epidemiologic literature to assess racial health disparities and the potential viability of a targeted health intervention. However, researchers may attribute too much authority to the interaction term and inadvertently ignore other salient information regarding the health disparity. In this article, we highlight empirical examples from the literature demonstrating limitations of overreliance on interaction terms in health disparities research; we further suggest approaches for moving beyond interaction terms when assessing these disparities. We promote a comprehensive framework of three guiding questions for disparity investigation, suggesting examination of the group-specific differences in (1) outcome prevalence, (2) exposure prevalence, and (3) effect size. Our framework allows for better assessment of meaningful differences in population health and the resulting implications for interventions, demonstrating that interaction terms alone do not provide sufficient means for determining how disparities arise. The widespread adoption of this more comprehensive approach has the potential to dramatically enhance understanding of the patterning of health and disease and the drivers of health disparities.

Introduction

A growing body of literature documents consistent and widening racial and ethnic disparities in health [1]. Health disparities have been defined by the Centers for Disease Control and Prevention as "preventable differences in the burden of disease, injury, violence, or opportunities to achieve optimal health that are experienced by socially disadvantaged populations [2]." Health disparities in this context do not refer to all differences in health but rather to a particular type of difference in which groups that have persistently experienced social disadvantage or discrimination systematically experience worse health compared with more advantaged social groups [3]. The term "health inequities" has also increased in usage to emphasize the implication of injustice in differences in health status between groups [4]. In this article, for the purpose of consistency, we will focus on the term "health disparity" to denote differences characterized by some form of injustice.

The United States (US) is increasing in racial and ethnic diversity. At the same time, sizable racial health disparities persist [5]. The socially constructed concept of race is complex [6]. For our purposes, when we refer to race, we mean a classification system associated with one's physical phenotype (i.e., skin color), parental phenotype, social identity, genetic background, and cultural context, all of which are shaped by complex historical processes that give rise to the associations between self-identified race and ethnicity, socioeconomic disadvantage, and health outcomes [7–9]. Epidemiologic racial health disparities research

* Corresponding author. Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina, Chapel Hill, 2104B McGavran-Greenberg Hall CB #7435 Chapel Hill, NC 27599. Tel: +1 919 966 7940; fax: +1 919 966 2089.
E-mail address: whitney_robinson@unc.edu (W.R. Robinson).

https://doi.org/10.1016/j.annepidem.2018.09.007

seeks to understand the social, environmental, and biological processes that generate racial health disparities, with the ultimate goal of finding ways to ameliorate these disparities. Implementing interventions targeted at populations that are at the highest risk may be one approach for eliminating health disparities.

One common method used in the epidemiologic literature when assessing whether to target an intervention is to examine the statistical significance and magnitude of an interaction term between race and an exposure of interest. Indeed, a recent article in the International Journal of Epidemiology explicitly suggests that examining an interaction term on the additive scale can indicate "whether the effect of a risk factor would be greater in one subpopulation than in another" and would therefore be "useful in targeting specific populations and in resource allocation [10]."

However, health disparities research may require a more nuanced approach. In this article, we argue that evaluating interaction terms alone is not the best approach for prioritizing interventions to reduce health disparities. Instead, we present a more comprehensive framework for assessing health disparities, focusing on the distribution of the outcome and exposure across racial groups as a critical companion to assessment of interaction terms and stratum-specific effects. This article expands upon a long tradition in epidemiology of interaction assessment by adding a specific focus on *racial* health disparities, which is a central component for the investigation of health disparities [11] and an area of research in which there may remain an overreliance upon statistical significance testing [12–14]. We promote a framework of three guiding questions for disparity investigation by exploring the relationship of exposure, outcome, and interactions to assess meaningful differences in population health and the resulting implications for interventions.

Illustrative examples and three guiding questions

One goal of health disparities researchers may be to answer the question, "Would changing the prevalence of an exposure in specific racial groups reduce racial disparities in an outcome?", but the methods often used in epidemiologic literature operationalize this question as, "Is there an interaction between race and exposure? [10]" Such an approach may be problematic as the latter question (and its answer) may not fully address the former. We propose three guiding questions that researchers could use to gain a more comprehensive understanding of the most effective intervention targets to reduce a disparity:

Question 1 Is there a difference in the prevalence of the outcome between groups?
Question 2 Is there a difference in the prevalence of the exposure between groups?
Question 3 Does the relationship between the exposure and outcome differ between groups?

Note that the third guiding question is also asked when evaluating an interaction term, the approach that we are critiquing. We include this third question to emphasize that interaction terms and examination of between-group differences in exposure-outcome effects are not inconsequential in and of themselves. This approach can offer valuable information, but only if interaction is examined in the context of the other two guiding questions. We argue that the combination of the answers to all three guiding questions provides the investigator with the most reliable information about the causes of a given health disparity.

We use figures to illustrate the three guiding questions listed previously. For all provided examples, we assume a dichotomous adverse outcome and harmful exposure where presence of the outcome and exposure is coded as 1. For illustrative purposes, we also present a simplified, dichotomous race classification, with a black sample population (solid lines) coded as 1 and a white sample population (dashed lines) as the referent. In the figures, exposure is indicated on the x-axis and outcome along the y-axis. Strength and direction of the exposure-outcome relationship is indicated by the line's slope. For all examples, we assume no unmeasured confounding and sufficient power to detect group-specific prevalence differences and modification of the exposure-outcome association. Although we believe this framework applies on all scales, examples refer to modifications on the additive scale as this scale is supported in interaction literature because of its collapsibility and interpretability [12,14].

In Figure 1, the slopes of both the lines indicate a positive relationship between the exposure and outcome among both blacks and whites. An interaction term between race and exposure allows the estimated exposure-outcome association to vary by race; this is visually represented in Figure 1 by slopes that differ by group. Given the race-, exposure-, and outcome-coding schema assumed in our examples, a positive beta coefficient for the interaction term would indicate a stronger exposure-outcome association among the black population, and a negative interaction term beta would indicate a stronger association among the white population. Figure 1 also includes four density circles, representing the relative prevalence of exposure among blacks and whites. Among each race, the percent exposed and unexposed sums to 100%; smaller circles indicate that a smaller proportion of the sample population experiences the exposure, and equal-sized circles indicate equal exposure prevalence.

We use Figure 1 as a heuristic to demonstrate the application of the three guiding questions proposed previously. Our first guiding question asks, "Is there a difference in the prevalence of the outcome between groups?" We ask this guiding question first because establishment of a difference in the prevalence of a health outcome between racial groups is fundamental to the definition of a racial health disparity. In the scenario depicted in Figure 1, the outcome is more common among blacks than whites. Note that the overall outcome prevalence for each racial group is not directly observable in Figure 1 because the outcome prevalence for the racial groups has been stratified by exposure status, as described in the answer to the next guiding question. Examining Figure 1 to answer the second guiding question ("Is there a difference in the prevalence of the exposure between groups?") leads us to conclude that the exposure is evenly distributed among both blacks and whites (denoted by the equally sized density circles). Regarding the third guiding question ("Does the relationship between the exposure and outcome differ between groups?"), we see that both blacks and whites experience increased prevalence of the outcome when exposed (both lines have a positive slope) but that the strength of the exposure-outcome association is stronger among blacks than whites (the slope of the line is steeper among blacks).

Investigators might be tempted to interpret the presence of an interaction in this scenario as evidence of a disparity-producing exposure and therefore support for a targeted intervention. However, an exclusive focus on the interaction term overlooks other equally, if not more, important information: (1) stratum-specific exposure prevalence, (2) outcome prevalence, and (3) meaningfully different effects. Figure 1 depicts a relatively straightforward example of a disparity-producing scenario. However, as seen in subsequent examples, this is not the only scenario compatible with a disparity-producing exposure. In fact, Figure 1 represents an uncommon scenario in racial health disparities research. Exposures that are uniformly distributed by race are rare. We argue that, in the more complex scenarios that health disparities researchers routinely encounter, the presence of an interaction does not

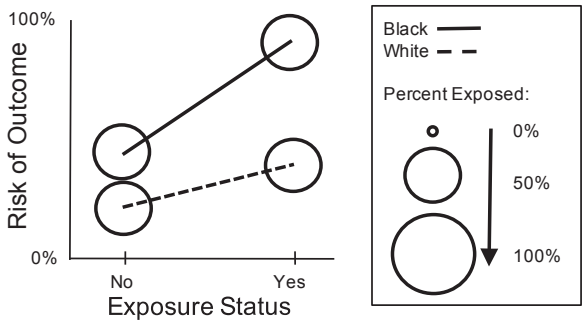

Fig. 1. A hypothetical scenario demonstrating an equal exposure distribution by racial group but different relationships between exposure and outcome for each racial group. The exposure is indicated along the x-axis and the outcome along the y-axis. The simplified, dichotomous race classification is denoted by a solid line for the black sample and a dashed line for the white sample. The circles represent the proportion of each racial group at each level of exposure so that equally sized circles indicate that equal proportions of the racial group are exposed and unexposed. Larger circles represent a larger proportion exposed (or unexposed).

provide sufficient evidence for whether an exposure contributes to a racial health disparity or whether that exposure should be targeted to reduce the disparity.

To illustrate the importance of a more holistic approach to evaluating the causes of health disparities, we will present several scenarios grounded in empirical examples and visually depicted in Figure 2. We observed the presence of an interaction in the two left-column scenarios (A and C) and no interaction in the right-column scenarios (B and D). In the top row (A and B), we illustrate two scenarios in which the exposure contributes to a health disparity. In the bottom row (C and D), the exposure does not contribute to a health disparity. We highlight these two dimensions in the rows and columns because the discordant scenarios (B: no interaction, but disparity-producing exposure, C: interaction present, but not a disparity-producing exposure) can, and do, exist.

In the next section, we discuss the four scenarios represented in Figure 2 to demonstrate that the significance of the interaction term should be interpreted with the use of additional information, particularly the distributions of the outcome and exposure. Although the examples described in the next section and illustrated in Figure 2 are based on real studies, the figures themselves are simplified, conceptual representations of the scenarios described in these studies.

Interaction present, with an exposure distribution that contributes to the disparity

We first address the upper left quadrant of our 2 × 2 table (Fig. 2A). An example of this scenario has been seen in the association between population-level unemployment and mortality [15]. The first of our three guiding questions asks whether there are between-group differences in the outcome; indeed, the literature indicates that mortality in late adulthood is greater among blacks than among whites [16]. In this example and in subsequent examples, the dashed and solid lines are separated at all levels of exposure; the causes of this separation are factors for which race acts as a proxy, including racism, socioeconomic position, and other historical and present-day experiences faced by marginalized populations that may also impact mortality [17].

Our second guiding question asks whether there is a difference in exposure prevalence between the racial groups. As demonstrated with the density circles, compared with whites who are equally likely to reside in areas of high and low unemployment, a larger proportion of blacks live in areas with high unemployment [18]. The third guiding question asks whether the exposure-outcome association differs by race. Examining the race-unemployment interaction term, an investigator may note that the association is stronger among blacks (depicted by the steeper solid line). Unemployment may be more strongly associated with black mortality than white mortality because of other factors connecting unemployment with being a member of a marginalized group, such as access to health care and availability of social safety nets.

Figure 2A illustrates a situation in which differences in exposure prevalence contribute to a racial disparity in the outcome, and we also observe an interaction between race and the exposure. The primary difference between this scenario and the hypothetical scenario in Fig. 1 is the difference in the exposure distributions between the racial groups. The scenario represented in Fig. 2A is likely more common in racial health disparities research than that depicted in Fig. 1.

No interaction, with an exposure distribution that contributes to the disparity

There are situations in which a race-exposure interaction is not present, but the differences in exposure prevalence produce disparities in the outcome. Such scenarios deserve particular attention because they may be overlooked in the literature when only the presence of an interaction is assessed. The second quadrant of our figure (Fig. 2B) demonstrates such a situation. Considering the association between poverty and mortality by race [19,20], we see from Figure 2B and outside literature that overall mortality is higher among the black population than the white population [16]; exposure to poverty is greater among blacks than among whites (denoted by the larger density circle for high-poverty among blacks vs. whites); and for this example, poverty is equally detrimental to the health of individuals from both the racial groups (denoted by the identical slopes of the two lines). Given that the slope of the association between poverty and mortality is similar between the groups, no race-poverty interaction would be detected.

Our responses to guiding questions 1 and 2, however, provide evidence that poverty might be an important contributing factor to the black-white mortality disparity despite the absence of interaction. As we see in the literature, the prevalence of individuals living below the poverty line is much higher among certain racial/ethnic groups, such as non-Hispanic Blacks, than among non-Hispanic Whites [19,20]. In this example, the between-group difference in exposure prevalence, not difference in the effect, contributes to the between-group outcome disparity. Concluding that the exposure does not contribute to disparate outcomes because of a lack of interaction assumes that the exposure burden is equal between the studied groups. In this case, examining crude outcome and exposure prevalence is more informative than modeled interaction.

Nevertheless, lack of interaction is often interpreted as evidence against a disparity-producing exposure. One such example in the literature occurred in a study of white and black differences in the association between 25-hydroxyvitamin D and coronary heart disease (CHD) [21]. It was hypothesized that low 25-hydroxyvitamin D would be associated with CHD incidence and that this association would vary by race. However, there was no evidence of an interaction between race and 25-hydroxyvitamin D levels, which the authors interpreted as evidence that 25-hydroxyvitamin D levels do not contribute to the racial disparity in CHD incidence. Yet, important information goes unacknowledged: in this study population, both low 25-hydroxyvitamin D prevalence and CHD incidence were higher in blacks than whites. Consequently (assuming that there is in fact a biological effect of

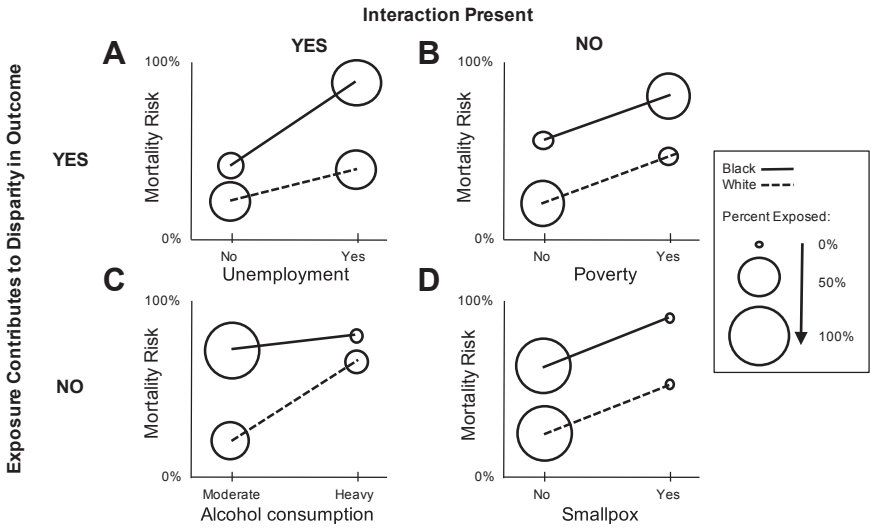

Fig. 2. Four example interaction analysis scenarios highlighting two important axes, namely, columns indicating the presence of an interaction (yes or no) and rows indicating whether the exposure contributes to a disparity in the outcome (yes or no). The four quadrants depict the following scenarios: (A) interaction is present, but the exposure does not contribute to the disparity; (B) interaction is not present with an exposure distribution that contributes to the disparity; (C) interaction is present, but the exposure does not contribute to the disparity; and (D) interaction is not present, and the exposure does not contribute to the disparity. The exposures are indicated along the x-axes and the outcomes along the y-axes. The simplified, dichotomous race classification is denoted by a solid line for the black sample and a dashed line for the white sample. The circles represent the proportion of each racial group at each level of exposure so that equally sized circles indicate that equal proportions of the racial group are exposed and unexposed. Larger circles represent a larger proportion exposed (or unexposed).

low 25-hydroxyvitamin D on CHD incidence), the higher concentration of low 25-hydroxyvitamin D among blacks may indeed contribute to the disparity in CHD incidence between black and white individuals in spite of lack of interaction [21]. The distributions of the outcome and exposure in the different groups being compared should factor into the interpretation of results, as these numbers provide essential information and may tell a different story than that afforded by the interaction alone.

Interaction present, but exposure does not contribute to the disparity

We now address the third quadrant of Figure 2 where the race-exposure interaction is present, but the exposure may not contribute to a health disparity in the outcome (Fig. 2C). One example of such a scenario occurs when examining racial/ethnic differences in mortality due to alcohol consumption [22]. Using outside literature and examining Figure 2C with our three guiding questions, we see that overall mortality is higher among blacks than whites, prevalence of heavy drinking is higher among whites than blacks, and the association between alcohol consumption and mortality differs by racial group.

There remains a great deal of controversy around the relationship between moderate alcohol consumption and mortality. Although observational studies consistently show a mortality benefit of moderate drinking [23], recent quasi experimental [24,25] and meta-analyses [26] suggest that most, if not all, of the "moderate-drinking benefit" is an artifact of confounding. One important subplot to this controversy is that the presence and magnitude of the "moderate-drinking benefit" vary across demographic groups; blacks, in particular, do not appear to greatly benefit from moderate alcohol consumption [22,27–29]. Furthermore, compared with whites, black individuals in the US have lower levels of total alcohol consumption; they are more likely to abstain, somewhat less likely to be moderate drinkers, and even less likely to be heavy drinkers [30]. This racial difference in the association between alcohol consumption and mortality is denoted in Figure 2C by the different slopes of the lines for the two racial groups. At moderate levels of alcohol consumption, mortality rates are much higher for blacks than for whites. At high levels of alcohol consumption, we see a convergence in mortality rates. These differences in slope indicate a stronger association between heavy drinking and mortality among whites, the socially advantaged group in this context.

The weak association among members of the high-mortality group may imply that they are protected against the adverse impact of heavy drinking on mortality [29]. However, there is no evidence that blacks are protected from heavy drinking's adverse impact. Despite the presence of an interaction, the positive slope of the solid line in Figure 2C indicates that heavy drinking does indeed adversely impact blacks. The literature further shows very low prevalence of heavy and binge drinking among blacks [30]; however, the interaction term alone would fail to indicate this. Despite the positive association between heavy drinking and mortality in both the groups, we argue that heavy drinking does not make a large contribution to the black-white mortality disparity. First, the additional mortality risk associated with heavy drinking among blacks is relatively small compared with the increase observed among whites. However, a relatively smaller mortality increase among blacks could still contribute to a disparity if a relatively large proportion of blacks were exposed to heavy drinking. However, in this example, heavy drinking was much less common among blacks than whites. Consequently, although a racial disparity in mortality rates certainly exists, alcohol consumption does not make a large contribution to this disparity. As such, interventions preventing this exposure would be unlikely to ameliorate the disparity in mortality due to the rarity of the exposure in the high-burden group.

No interaction, and exposure does not contribute to the disparity

Finally, we address the figure's lower right quadrant (Fig. 2D), a scenario represented by the relationship between smallpox and mortality in the US. Again, using our three questions as a guide, it is interpreted as follows: (1) overall mortality is higher among blacks

than among whites in the US; (2) blacks and whites have equal and identical prevalence of exposure (due to the eradication of smallpox in the US in 1949); and (3) while exposure to smallpox impacts mortality, the effect of the exposure on the outcome is the same among whites and blacks. Therefore, smallpox does not contribute to the excess mortality among blacks.

This scenario represents a situation in which the exposure does not contribute to a racial disparity in the outcome; there is no race-exposure interaction, and the exposure distribution is identical between racial groups. In their own right, such scenarios do not shed light on the causes of the health disparity in the outcome; however, it is worthwhile to compare this scenario to that represented in Figure 2B, where there is similarly no interaction, but the exposure distribution differs between racial groups. When the impact of the exposure on the outcome is the same across racial groups (denoted by the identical slopes of the lines), the exposure distribution alone determines whether or not exposure contributes to disparity in the outcome. This key insight is often overlooked when researchers rely on interaction terms alone to investigate racial disparities in health outcomes.

Case study: negative race-exposure interaction terms

The four examples provided in Figure 2 are not exhaustive of all possible race-exposure interaction scenarios. These relatively simplistic examples miss other nuances that health disparities researchers may encounter. Consequently, we will discuss a particular scenario we have observed in the literature that often confuses researchers investigating racial health disparities.

When the more socially advantaged group is the referent, presence of negative interaction indicates that a deleterious exposure-outcome relationship is stronger among the more advantaged group, as was the case in scenario C (interaction present, but exposure does not contribute to the disparity). However, the higher exposure and outcome burden may still be carried by the disadvantaged group. One such example of this has emerged from the cardiovascular health literature [31]. In a sample of 6134 individuals recruited from 50,844, Liu et al. aimed to evaluate the relationship between diabetes mellitus and uncontrolled blood pressure. Although this study contrasted Mexican Americans, blacks, and whites, for consistency with our previous examples, we will focus specifically on the black and white comparison. In this article, the authors introduced an interaction term between diabetes and race into their model and found a significant interaction; the association between diabetes and uncontrolled blood pressure was stronger among whites than among blacks. From these results, the authors concluded that “health providers need more efforts to weaken the association of diabetes with uncontrolled blood pressure outcomes by further improving care for diabetes and blood pressure in non-Hispanic whites [31].” In a health disparities context, such a suggestion should give one pause and warrants further investigation.

Using our initial guiding questions, Tables 1 and 2 provided by Liu et al., and outside literature regarding uncontrolled blood pressure, we see that uncontrolled blood pressure is more prevalent among blacks than whites, diabetes prevalence is higher among blacks than whites, and there is an overall association between diabetes and uncontrolled blood pressure that is positive in both race groups but varies in magnitude [32]. The information gained from asking these questions illustrates the scenario depicted in Figure 3. Although the presence of negative interaction indicates that the association may be stronger in non-Hispanic whites, blacks suffer the greater burden of both exposure and outcome. Thus, from a health disparities standpoint, the assertion that the white sample population should be targeted over the black sample population is troubling as it could lead to inappropriate redistribution of intervention resources and widening of racial disparities in uncontrolled blood pressure prevalence. This example further demonstrates the danger of drawing conclusions regarding health disparities based on interaction term significance alone and highlights the importance of additionally considering the exposure and outcome distributions in a health disparities context.

Conclusion

Racial health disparities in the US are large and pervasive [5]. Given the increasing diversity of the US, persistence of racial disparities will have important consequences for the overall health of the nation [33]. Understanding the causes of health disparities and working to eliminate them is one of the US government's primary health objectives [34], and many researchers are motivated by the same goals. Thus, the way in which we execute our analyses should reflect these objectives. We observe that it is common in the literature to evaluate an interaction between race and an exposure of interest as evidence (or lack thereof) that an exposure contributes to a racial health disparity. However, when using this method, researchers may attribute too much authority to the significance of this interaction term. Outside of health disparities literature, overreliance and misinterpretation of statistical significance has been well scrutinized [35,36]. Nevertheless, in health disparities research, important information regarding exposure and outcome prevalence is often overlooked in favor of discussion of interaction terms and their significance.

In this article, we proposed three guiding questions that researchers could use to gain a deeper understanding of the sources of racial health disparities: are there substantive between-group differences in (1) outcome prevalence, (2) exposure prevalence, and (3) the relationship between the exposure and outcome? As demonstrated previously with our discussion of Figure 2, the distribution of the exposure is of critical importance. If an exposure impacts the outcome, it is then the between-group distribution of this exposure that determines whether the exposure contributes to a racial disparity in the outcome and whether an intervention targeting the exposure could reduce this disparity, regardless of the presence of an interaction between race and exposure. As a result, the descriptive characteristics of the populations of interest contain enormously valuable information that deserves consideration, at the very least. However, this information is often inadvertently ignored. We encourage investigators to thoughtfully consider all of the information at their disposal before drawing conclusions and making policy recommendations regarding racial health disparities.

We acknowledge that our hypothetical examples require strong assumptions to make causal claims about the underlying etiology of health disparities. First, our examples are cross-sectional, and in most cases, use of these data precludes identification of the specific influence of a single exposure on an outcome. Indeed, there are often multiple, simultaneous effect pathways that generate an outcome. Consequently, use of the criteria that we suggest in the examples provided is only sufficient to identify potential determinants of health disparities. Nevertheless, our suggestions for a more comprehensive assessment are applicable to cross-sectional and longitudinal studies alike. Second, many of our examples include exposures that are proximate to the outcomes of interest. However, an exposure may be driven largely by one or more distal factors that health disparity researchers might also fruitfully pursue.

Furthermore, for illustrative purposes, we also present a simplified, dichotomous race classification, although we recommend more nuanced conceptualization and coding in practice. Our

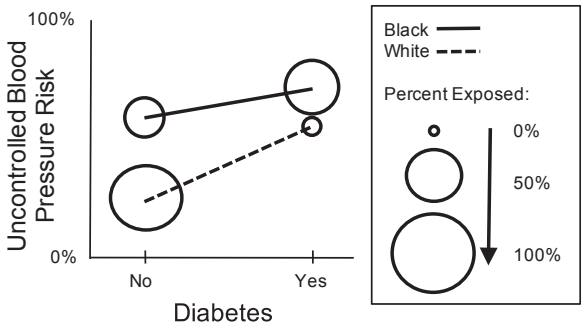

Fig. 3. Case study of a racial health disparity interaction analysis found in the literature, examining the relation between diabetes mellitus and uncontrolled blood pressure and whether this association varies by race. This represents a scenario where the interaction term indicates that the exposure-outcome relationship is stronger among the more advantaged group (captured by the steeper slope of the dashed line), yet the high exposure prevalence among the more disadvantaged group suggests that the exposure may be disparity-producing nonetheless. The exposure is indicated along the x-axis and the outcome along the y-axis. The simplified, dichotomous race classification is denoted by a solid line for the black sample and a dashed line for the white sample. The circles represent the proportion of each racial group at each level of exposure so that equally sized circles indicate that equal proportions of the racial group are exposed and unexposed. Larger circles represent a larger proportion exposed (or unexposed).

examples are also limited to discussions of racial health disparities and therefore address only one dimension of inequality separate from other dimensions. However, we recognize that multiple social categories (including race, ethnicity, gender, sexual orientation, and socioeconomic status) can intersect at the individual level to reflect multiple connected macro-level systems of privilege and oppression [37]. Consequently, although we simplified our inequality framework to only racial disparities for illustrative purposes, we suggest a more sophisticated approach that examines intersectional identities and how they influence health when carrying out actual studies of health disparities. For example, one could imagine multiple lines in Figure 2 to denote multiple intersecting social categories (e.g., race*gender*socioeconomic status). As our examples are limited to a two-way interaction between race and an exposure of interest, testing a three-way interaction could be as misleading as the traditional two-way interaction. Consequently, when samples are large enough to provide reliable estimates, the exposure prevalence, outcome prevalence, and exposure-outcome associations could be estimated for all combinations of these intersecting social categories.

For investigators interested in moving beyond isolated statistical testing of interaction terms when quantifying contributors to racial disparities, there are several alternative approaches. First, to address guiding questions 1 and 2 empirically, one could report, respectively, marginal race/ethnicity-specific outcome and exposure distributions. Similarly, to address question 3 empirically, one could create a contingency table that presents exposure-outcome risk differences or ratios and their confidence intervals for each combination of race/ethnicity and exposure level using a single reference category, most often the race-exposure stratum with the lowest risk of the outcome. Knol and VanderWeele have provided a practical overview of how to prepare and present such tables when examining interactions between two potentially causal influences on an outcome [10]. This method may inform a clearer assessment of question 3, how the exposure-outcome association differs across racial groups, than examining the interaction term alone.

Moreover, investigators interested in synthesizing the contribution of an exposure to a disparity in one or two empirical estimands may consider decomposition methods [38]. These methods dissect observed disparities (question 1) into contributions both from the unequal burden of the exposure between racial/ethnic groups (question 2) and different exposure-outcome effects between racial/ethnic groups (question 3). Such decomposition methods explicitly estimate the contribution of differences in exposure distributions to differences in between-group effect estimates. Many of these methods express the disparity as 0–100% attributable to the exposure and further divide that percentage into the percent attributable to differences in distribution of the exposure across groups and the differences in the exposure-outcome relationship across groups. For instance, in labor economics, the Oaxaca-Blinder decomposition method has been used to understand how the relationship between job characteristics and wages contributes to women's lower wages at the population level. These studies dissect the extent to which lower wages (question 1) are attributable to women's higher likelihood of entering lower-paying fields (question 2) versus women being paid less than male counterparts in the same field (question 3) [38–40].

However, making causal interpretations with these approaches requires very strong assumptions about confounding, linear relationships among variables, and other restrictions [41]. More recently, in epidemiology, the counterfactual causal inference community has proposed using weighting methods to overcome these barriers to interpretation of decomposition methods [41]. Furthermore, researchers have demonstrated that decomposition methods may be especially useful in epidemiology for identifying causes of racial/ethnic disparities in health [17,42–44]. However, the application of these methods is complex because each model form (e.g., dichotomous outcome vs. continuous outcome; multiple mediators vs. single mediator; causally dependent mediators vs. independent mediators; case-control data vs. cohort data) may require a distinct set of mathematical formulas [41]. Therefore, we recommend, before proceeding to conceptually and computationally intensive approaches such as counterfactual disparity measures, that researchers start with our guiding questions as a more accessible method for assessing the possibility that a factor may contribute to a health disparity.

Regardless of the final method chosen, studying health disparities in a rigorous and thoughtful manner is essential for a better understanding of the fundamental mechanisms that shape health. We believe that careful consideration of one's analysis and final interpretation and the implementation of a more comprehensive approach to the assessment of racial health disparities can powerfully inform policies and interventions that may reduce these disparities. An increasingly large quantity of data are collected and analyzed by epidemiologists, including data from population-based longitudinal studies, registries, surveillance efforts, and administrative databases. The vast majority of these data contain race/ethnicity information or some other measure of social stratification. Consequently, the widespread adoption of systematic approaches such as ours has the potential to dramatically enhance the understanding of the patterning of health and disease and the drivers of health disparities.

Acknowledgments

The authors thank Dr. Mike Griswold and Jonathan Tingle for helpful comments on early drafts of this manuscript.

Funding: This work was supported by the National Institute on Minority Health and Health Disparities (grant number: R01 MD011680), the National Institute of Child Health and Human Development at the National Institutes of Health (grant number: T32HD007168); the National Cancer Institute at the National Institutes of Health (grant number: K01CA172717); and the National Institute on Alcohol Abuse and Alcoholism at the National Institutes of Health (grant number: K01AA021511).

References

[1] Williams DR, Mohammed SA, Leavell J, Collins C. Race, socioeconomic status, and health: Complexities, ongoing challenges, and research opportunities. Ann N Y Acad Sci 2010;1186:69–101.
[2] CDC. Community Health and Program Services (CHAPS): Health Disparities Among Racial/Ethnic Populations. Atlanta, GA: Centers for Disease Control and Prevention; 2008.
[3] Braveman P. Health disparities and health equity: concepts and measurement. Annu Rev Public Health 2006;27:167–94.
[4] Adler NE, Stewart J. Health disparities across the lifespan: meaning, methods, and mechanisms. Ann N Y Acad Sci 2010;1186:5–23.
[5] Agency for Healthcare Research and Quality. 2015 National Healthcare Quality and Disparities Report and 5th Anniversary Update on the National Quality Strategy. Rockville, MD: Agency for Healthcare Research and Quality; 2016.
[6] Freeman HP. The meaning of race in science–considerations for cancer research: concerns of special populations in the National Cancer Program. Cancer 1998;82:219–25.
[7] Krieger N. Refiguring "race": epidemiology, racialized biology, and biological expressions of race relations. Int J Health Serv 2000;30:211–6.
[8] Williams DR, Lavizzo-Mourey R, Warren RC. The concept of race and health status in America. Public Health Rep 1994;109:26–41.
[9] LaVeist TA. On the study of race, racism, and health: a shift from description to explanation. Int J Heal Serv 2000;30:217–9.
[10] Knol MJ, VanderWeele TJ. Recommendations for presenting analyses of effect modification and interaction. Int J Epidemiol 2012;41:514–20.
[11] Phelan JC, Link BG. Is racism a fundamental cause of inequalities in health? Annu Rev Sociol 2015;41:311–30.
[12] Rothman KJ, Greenland S, Walker AM. Concepts of interaction. Am J Epidemiol 1980;112:467–70.
[13] Rothman KJ. Synergy and antagonism in cause-effect relationships. Am J Epidemiol 1974;99:385–8.
[14] Panagiotou OA, Wacholder S. Invited commentary: How big is that interaction (in my community)–and in which direction? Am J Epidemiol 2014;180:1150–8.
[15] Singh GK, Siahpush M. Inequalities in US life expectancy by area unemployment level, 1990-2010. Scientifica (Cairo) 2016;2016:8290435.
[16] Arias E, Heron M, Xu J. United States Life Tables, 2013. Natl Vital Stat Rep 2017;66:1–64.
[17] VanderWeele TJ, Robinson WR. On causal interpretation of race in regressions adjusting for confounding and mediating variables. Epidemiology 2014;25:473–84.
[18] Winkleby MA, Cubbin C. Influence of individual and neighbourhood socioeconomic status on mortality among black, Mexican-American, and white women and men in the United States. J Epidemiol Community Health 2003;57:444–52.
[19] Kimmel PL, Fwu C-W, Abbott KC, Ratner J, Eggers PW. Racial disparities in poverty account for mortality differences in US medicare beneficiaries. SSM Popul Health 2016;2:123–9.
[20] Zonderman AB, Mode NA, Ejiogu N, Evans MK. Race and poverty status as a risk for overall mortality in community-dwelling middle-aged adults. JAMA Intern Med 2016;176:1394–5.
[21] Michos ED, Misialek JR, Selvin E, Folsom AR, Pankow JS, Post WS, et al. 25-hydroxyvitamin D levels, vitamin D binding protein gene polymorphisms and incident coronary heart disease among whites and blacks: The ARIC study. Atherosclerosis 2015;241:12–7.
[22] Witbrodt J, Mulia N, Zemore SE, Kerr WC. Racial/ethnic disparities in alcohol-related problems: differences by gender and level of heavy drinking. Alcohol Clin Exp Res 2014;38:1662–70.
[23] Di Castelnuovo A, Costanzo S, Bagnardi V, Donati MB, Iacoviello L, de Gaetano G. Alcohol dosing and total mortality in men and women. Arch Intern Med 2006;166:2437.
[24] Holmes MV, Dale CE, Zuccolo L, Silverwood RJ, Guo Y, Ye Z, et al. Association between alcohol and cardiovascular disease: Mendelian randomisation analysis based on individual participant data. BMJ 2014;349:g4164.
[25] Taylor AE, Lu F, Carslake D, Hu Z, Qian Y, Liu S, et al. Exploring causal associations of alcohol with cardiovascular and metabolic risk factors in a Chinese population using Mendelian randomization analysis. Sci Rep 2015;5:14005.
[26] Stockwell T, Zhao J, Panwar S, Roemer A, Naimi T, Chikritzhs T. Do "moderate" drinkers have reduced mortality risk? a systematic review and meta-analysis of alcohol consumption and all-cause mortality. J Stud Alcohol Drugs 2016;77:185–98.
[27] Pletcher MJ, Varosy P, Kiefe CI, Lewis CE, Sidney S, Hulley SB. Alcohol consumption, binge drinking, and early coronary calcification: findings from the coronary artery risk development in young adults (CARDIA) study. Am J Epidemiol 2005;161:423–33.
[28] Jackson CL, Hu FB, Kawachi I, Williams DR, Mukamal KJ, Rimm EB. Black-White differences in the relationship between alcohol drinking patterns and mortality among US men and women. Am J Public Health 2015;105:S534–43.
[29] Kerr WC, Greenfield TK, Bond J, Ye Y, Rehm J. Racial and ethnic differences in all-cause mortality risk according to alcohol consumption patterns in the national alcohol surveys. Am J Epidemiol 2011;174:769–78.
[30] Zapolski TCB, Pedersen SL, McCarthy DM, Smith GT. Less drinking, yet more problems: understanding African American drinking and related problems. Psychol Bull 2014;140:188–223.
[31] Liu X, Song P. Is the association of diabetes with uncontrolled blood pressure stronger in Mexican Americans and blacks than in whites among diagnosed hypertensive patients? Am J Hypertens 2013;26:1328–34.
[32] Redmond N, Baer HJ, Hicks LS. Health behaviors and racial disparity in blood pressure control in the national health and nutrition examination survey. Hypertension 2011;57:383–9.
[33] Centers for Disease Control and Prevention. CDC Health Disparities and Inequalities Report — United States, 2013. MMWR Suppl 2013;62:1–2.
[34] Office of Disease Prevention and Health Promotion. Framework: The Vision, Mission, and Goals of Healthy People 2020. Washington, DC: Office of Disease Prevention and Health Promotion; 2017.
[35] Gelman A, Stern H. The difference between "significant" and "not significant" is not itself statistically significant. Am Stat 2006;60:328–31.
[36] Greenland S, Senn SJ, Rothman KJ, Carlin JB, Poole C, Goodman SN, et al. Statistical tests, P values, confidence intervals, and power: a guide to misinterpretations. Eur J Epidemiol 2016;31:337–50.
[37] Bowleg L. The problem with the phrase women and minorities: intersectionality-an important theoretical framework for public health. Am J Public Health 2012;102:1267–73.
[38] Jann B. The Blinder–Oaxaca decomposition for linear regression models. Stata J 2008;8:453–79.
[39] Blinder AS. Wage discrimination: reduced form and structural estimates. J Hum Resour 1973;8:436.
[40] Oaxaca RL. Male-female wage differentials in urban labor markets. Int Econ Rev (Philadelphia) 1973;14:693–709.
[41] VanderWeele TJ. Mediation analysis: a practitioner's guide. Annu Rev Public Health 2016;37:17–32.
[42] Naimi AI, Schnitzer ME, Moodie EEM, Bodnar LM. Mediation analysis for health disparities research. Am J Epidemiol 2016;184:315–24.
[43] Howe CJ, Napravnik S, Cole SR, Kaufman JS, Adimora AA, Elston B, et al. African American race and HIV virological suppression: beyond disparities in clinic attendance. Am J Epidemiol 2014;179:1484–92.
[44] Valeri L, Chen JT, Garcia-Albeniz X, Krieger N, VanderWeele TJ, Coull BA. The role of stage at diagnosis in colorectal cancer black-white survival disparities: a counterfactual causal inference approach. Cancer Epidemiol Biomarkers Prev 2016;25:83–9.