Minding the Competition: Racial Differences in Cardiovascular Risk

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While we have made great strides in reducing the burden of cardiovascular disease over the past 50 years, blacks in the United States still face increased cardiovascular mortality along with a disproportionate burden of risk factors\(^1\text{-}\text{3}\). However, if race-based comparisons become the basis for action, it is essential that they be measured and interpreted accurately. Blacks suffer from higher mortality rates of non-cardiovascular disease\(^2\). Some have argued that without accounting for non-CVD-related deaths amongst blacks, epidemiologists may be overestimating the true comparative rate of incident cardiovascular events among blacks. In other words, by failing to mind the competition, we may be overestimating the race-based gap in cardiovascular disease\(^4\text{-}\text{5}\).

Historically, researchers and the health care community have struggled to reduce the racial gap in cardiovascular risk and outcomes\(^6\text{-}\text{11}\). Moving disparities research from description to intervention will require discerning potentially mutable mediators of race-based differences. The ideal effort to reduce disparities, though, is to prevent them from ever occurring among all people, irrespective of race. Understanding the temporal order of events in a population will identify the seminal event on which to focus preventive efforts. In cardiovascular disease this strategy may be particularly appropriate since the first event is highly predictive of recurrent events. Additionally, the first event has the potential to be fatal or cause significant morbidity.

In this issue of Circulation, Feinstein and colleagues present a report on racial differences in incident cardiovascular events and deaths. In their sophisticated analyses, they focused on: 1) competing risks due to higher rates of non-cardiovascular disease deaths amongst blacks and 2) the order of events, non-CVD death versus the particular subtype of cardiovascular event\(^12\). The investigators followed the longitudinal course of black and white participants in three large multi-site cohort studies sponsored by the National Heart, Lung, and Blood Institute – Atherosclerosis Risk in Communities (ARIC), Cardiovascular Health Study (CHS), and Multi-
Ethnic Study of Atherosclerosis (MESA). The authors compared traditional Cox models to a competing risk framework to explore racial differences in first cardiovascular events and non-CVD death. They also accounted for socioeconomic factors (education and income) in addition to classic cardiovascular risk factors.

The authors found that cardiovascular events were more likely to precede non-CVD death in all age, sex, and race groups. However, the burden of cardiovascular events and non-CVD death affected blacks and whites differently. Blacks in ARIC were more likely to experience a cardiovascular event or non-CVD death as a first event. Among black men in ARIC, after adjustment for demographics and cardiovascular risk factors, cardiovascular events were no longer more likely than non-CVD death to be first events. Among black women in ARIC, cardiovascular events remained moderately more likely than non-CVD death to be first events even after adjustment for demographics and risk factors. Amongst individuals in CHS, there was no significant difference and in fact a trend toward fewer cardiovascular events among blacks. In both ARIC and CHS, analyses utilizing traditional Cox models that did not account for competing risks suggested that blacks were more likely to experience incident cardiovascular events. Traditional Cox models yielded disparate impressions from competing risk models for cardiovascular event subtypes. For example, black men in ARIC appeared to experience coronary heart disease as a first event. Competing risk models revealed that black men were less likely to experience coronary heart disease as a first event.

I commend the authors for their careful, thoughtful analyses, which nonetheless raise three key areas for caution in interpretation: outcomes being compared, differences among the cohorts, and generalizability.

**Outcomes being compared**
A competing risk model may be best suited in a comparison of outcomes that have similar implications for practice and policy. Non-CVD deaths may not have similar implications as a composite of fatal and non-fatal cardiovascular events. Furthermore, CVD death was parcelled among multiple different categories of outcomes, fatal and non-fatal cardiovascular event subtypes and other CVD death, precluding direct cause-of-death comparisons. We might surmise that despite some overlap, for the most part, preventive interventions may differ for cardiovascular and non-cardiovascular causes of death.

**Differences among the cohorts**

While the cohort studies the authors used offer several strengths – large numbers of well-characterized populations without cardiovascular disease at baseline – there are important differences, limiting comparisons across them.

The event rates for non-CVD death and cardiovascular events differ across the cohorts with lower rates being present in the younger MESA group (1.3% versus 4.7% respectively) and much higher rates in the older MESA group (4.8% and 12.1% respectively) and CHS cohort (15.7% versus 43.2% respectively). Additionally, length of follow-up was much shorter in MESA than in ARIC and CHS. Thus, perhaps the results represent three different analyses in three different populations.

Comparisons between the old and the young may not be valid as they come from different cohorts (except in MESA where the group is divided by age presumably for ease of comparison). When one examines the birth dates among the cohorts, the oldest and youngest participants in CHS were born in 1888 and 1944 respectively, in 1923 and 1942 for ARIC, and in 1916 and 1955 for MESA. There may be important, unaccounted for birth cohort effects that impacted the nature of the competing risks from non-CVD death. The older cohort in CHS
represents a population that has survived to 65 years of age, raising concerns about a survival bias that may affect blacks and whites differently. Blacks who survive to 65 years of age may have social, economic, and health characteristics that support their longevity as compared to blacks who die earlier in life.

There are other possible cohort-based effects, including differences in secular trends in risk factor management. Racial groups within a cohort could experience secular trends differently due to variations in access to care, location of care, achievement of treatment goals (e.g., hypertension control), and differential impact of emerging risk factors (such as obesity). Other explanatory factors beyond survival bias could account for the findings, particularly in CHS where there were no statistically significant differences by race in first events for this older cohort. The CHS observations may be confounded by the fact that the cohort was older at inception and likely experienced a different approach to risk factor management for the years preceding their enrollment in the cohort. If both blacks and whites experienced comparable less aggressive risk factor management than what is delivered today, racial differences may not have been apparent. On the other hand, higher risk factor burden amongst blacks with known less aggressive risk factor management could contribute to race-based differences seen in ARIC.

**Generalizability**

The relative small number of black participants in CHS and MESA limited the ability of the authors to produce precise and reliable estimates of the association between race and cardiovascular events. Furthermore, these black participants may not properly represent the greater black population of the United States. The cohort studies collected data from a small number of specific sites in the United States where competing non-CVD deaths could be either much higher (due to violence or accidents for example) or much lower than in communities
where most black Americans live.

Despite these limitations and the complexity of the report by Feinstein et al, I hope that one key message does not get lost in interpretation. While race per se was not a strong independent predictor of cardiovascular risk after accounting for competing risks, socioeconomic factors, and classical risk factors, the authors described important disparities that have important policy implications. Blacks suffered from higher burdens of baseline risk factors (particularly hypertension and diabetes) and greater socioeconomic disadvantage. Blacks, in particular black women, experienced greater comparative risks for non-CVD death and cardiovascular events. Classic risk factors, risk factors for which we have evidence-based preventive interventions, were stronger correlates for racial differences than socio-economic characteristics. Risk factor burdens appear particularly important for hypertension and diabetes, which occur at a younger age with longer duration among blacks. The authors’ analyses suggest that racial differences are a reflection of the differing pre-disposition to risk factors and, to a lesser extent, greater socioeconomic challenges. In these analyses, race may serve as a construct representing the confluence of these issues.

What is most compelling about a competing risk analysis is the idea that we may be able to identify events that occur earliest as specific targets for prevention. Thus, if we know that differences in cardiovascular outcomes exist by race, then understanding whether this difference accounts for the competing risk of non-CVD death could be less important if it does not offer an opportunity to alter an outcome. The strong relationship between risk factor burden and cardiovascular events creates actionable targets as aggressive action to control risk factors has the potential to alter mortality. If we want to close the gap in racial differences in cardiovascular events, then we need to focus our research, practice, and policy efforts on risk factor reduction.
and management.

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References:


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