A vexing observation among individuals with ESRD is the decreased mortality associated with attributes that, in healthy populations, confer increased risk of death. Examples include the apparent protective benefit of obesity, higher levels of LDL cholesterol, elevated systolic and diastolic BP, and increased levels of parathyroid hormone. Potential explanations for this survival paradox include unmeasured confounders, misspecification of exposures, selective survival with informative censoring, selection bias due to conditioning on a diseased population, and a true, unbiased protective benefit of the otherwise harmful attribute.

Self-reported black race is an interesting example of this conundrum. As summarized by Kimmel and colleagues in this issue of JASN, increased risk of mortality is consistently reported for black populations in the United States, a disadvantage that stands in stark contrast to their longer survival after the onset of hemodialysis. The authors sought to clarify this unexpected survival advantage by exploring the degree to which spatial measures of material disadvantage and racial segregation might mediate these survival differences. Material disadvantage was estimated using the Gini coefficient for a personal income in a county, which measures the degree of inequality of the income distribution in the population. It varies from 0, which represents perfect equality of income distribution, to 1, which represents maximal income inequality. The race-specific median income of an individual patient’s zip code of residence was used as a surrogate for individual income. A third measure, the dissimilarity index, was used to measure racial segregation in the county of residence. The index varies from 0, an equal distribution of blacks and whites in a county, to 1, indicative of a racially homogeneous population. The degree of racial segregation was used to assess perceived discrimination and related stress that an individual might experience in a community. It was hypothesized that these spatial measures would explain part of the observed excess mortality observed in white, compared with black, ESRD patients.

The results of this interesting article are provocative and instructive. First, neither measures of income inequality nor racial segregation attenuated the reduction in mortality among blacks compared with whites. After controlling for individual risk factors at the start of ESRD, including two surrogates for individual socioeconomic status (health insurance status and employment status), blacks were 73% less likely to die during follow-up (hazard ratio [HR], 0.73; 95% confidence interval [95% CI], 0.72, 0.75). Serial addition of income inequality and segregation measures actually accentuated the protective benefit of race, and after accounting for individual-level attributes and spatial characteristics, blacks were 30% less likely to die (HR, 0.70; 95% CI, 0.69, 0.71) during follow-up. Race-specific median income, income inequality, and segregation were independently associated with mortality after controlling for race and other covariates. Finally, in multivariable models stratified by race, there was a graded, inverse association between median zip code income and mortality such that HRs were lower as income level increased in both races. Taken together, these results lead to the conclusion that community measures of income, income inequality, and racial segregation as measured in this study cannot explain racial differences in survival among ESRD patients.

This interesting article raised important additional issues. Mortality in blacks and whites appears to be influenced differently by income inequality and racial segregation, because statistically significant interactions between race and both county income inequality and residential segregation were found. Kimmel et al. found that higher levels of income inequality were associated with higher mortality among whites but not blacks, whereas higher levels of racial segregation were associated with substantially higher mortality in blacks and not whites. Although such interaction may be artifactual, it may also signal modification of mortality risk among blacks and whites by unappreciated mechanisms that should be further studied.

The effect of income inequality on mortality in blacks is of similar magnitude as that reported by a recent meta-analysis. These meta-analytics support a posited threshold effect for income inequality, with Gini values <0.3 less likely to confer increased risk of adverse outcomes. It is interesting to speculate that this may be one mechanism through which race-specific income inequality may have increased mortality risk in whites, but not blacks, in this study. Because interactions may exist between individual and county measures of income inequality that could not be examined, it is possible
that black/white mortality differentials may be modified by individual incomes and these effects might differ by county income inequality.

Another consideration is the complexity inherent in measures of income inequality like the Gini index. The influence of income inequality on mortality may be mediated by either direct effects on an individual (e.g., impaired access to healthcare) or indirectly through community level, or contextual factors such as limited stores selling high-nutrition value foods.8,9 There were no data in this study to assess individual income inequality and the covariates used to estimate individual socioeconomic status, insurance, and employment status are, at best, weak surrogates.10 Consequently, we cannot infer that individual mortality risk in whites, but not blacks, varies directly with income inequality.

Furthermore, care should be taken when considering the effects of county income inequality in the race-specific results to reflect individual-level influences. In the presence of population subgroups (blacks and whites within counties), the overall Gini coefficient can be decomposed into three parts: the within-group inequality, the between-group inequality, and an interaction term.11 If the majority of variation in Gini coefficients between counties is due to within-group inequality of one subpopulation while the other components remain constant, only the subpopulation responsible for the variation will be affected by the change in the overall Gini coefficient. In this case, it could be that blacks experience high levels of inequality across all counties compared with whites, but this between-group inequality is overshadowed by the inequality between whites. This would lead to little variation in inequality blacks experience across the defined Gini quartiles and the apparent results that inequality does not exacerbate black mortality risk. Future studies of the association between inequality and higher mortality might also consider alternative inequality measures.12 A number of studies using these alternative measures showed no relationship between inequality and mortality, suggesting significant confounding effects.13 One potential confounder of the Gini measure, particularly at the county level, is population size, with smaller populations biasing the Gini measure downward; this should also be considered in subsequent studies.14

There are similar issues using racial segregation as a geospatial exposure. Counties are typically heterogeneous and a more discrete delineation of population-level exposures at the census tract or census block level is preferred.15 Again, inherent limitations to the available data necessitated using the county-level dissimilarity index rather than a more granular, census tract measure. It is possible that this might lead to some individuals being misclassified with respect to racial segregation. The dissimilarity index, although widely used as a segregation measure, also has limitations that should be weighed in future studies. Any differential movement of minorities between census block groups should increase a measure of segregation. However, the dissimilarity index is insensitive to re-distribution of minorities between block groups in which the minority population proportion is either above or below the county’s minority population proportion. That is, only transfers of minority members from areas where they are over-represented to areas where they are under-represented affect the value of the index.16 This notion could result in a downward bias in the measure, making these results a lower bound. Conversely, a small minority population in a low-density area will result in an upward bias in the dissimilarity index.17

Also of concern for both of these indices is the comparability of these measures across counties when the underlying distributions, defined by the Lorenz curve, cross one another. When one county’s distribution (Lorenz) curve always lies above another, it is unambiguously more equal than the one below it. However, if Lorenz curves cross, the ranking of the counties is subjective to the inequality measure used.18 Measures that address the shortcomings of the Gini and dissimilarity index have been derived and may offer opportunity for further work on the relationship between inequality and ESRD mortality risk.

Finally, it is noteworthy that the authors provide a testable theoretical framework within which to interpret their observations. They suggest that the association between inequality and mortality among blacks might reflect the cumulative stress, or allostatic load, generated by segregation. This attractive possibility is supported by studies that used National Health and Nutrition Examination Survey (NHANES) data to rank neighborhood socioeconomic status and a summary score of allostatic load. They found that allostatic load was higher in less favorable socioeconomic environments among blacks but not whites.19 A recent study of black and white NHANES adolescent participants reported similar findings.20–22 What is particularly intriguing, and worth further thought, is the possibility that similar mechanisms influence white mortality differentials associated with income inequality.

In conclusion, Kimmel et al.4 provide important perspectives on differences in mortality among ESRD patients. Their results serve to redirect our attention toward novel explanations for the survival advantage of black ESRD patients.

DISCLOSURES

None.

REFERENCES