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Black-White Differences in Breast Cancer Outcomes Among Older Medicare Beneficiaries Does Systemic Treatment Matter?

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Prior to the 1980s, there were minimal differences between blacks and whites in breast cancer mortality after adjustment for differences in incidence. There also were few available breast cancer treatments other than radical surgery. Black-white mortality differences in breast cancer mortality emerged in the United States in the late 1980s, with the advent of adjuvant systemic therapies and mammography, and they persist to the present.¹ These trends suggest that, unless the underlying biology of breast cancer has changed differentially by race over time, the majority of disparities are likely to be related to variations in the use and quality of screening and adjuvant treatment. Although a large body of research has sought the reasons for any such differences, most investigations have not included representative US population samples or could not quantify the separate and combined contributions of multiple factors to observed disparities.

In this issue of the *JAMA*, Silber and colleagues² attempt to fill this gap and identify potential leverage points for reducing disparities. The authors conducted a large, population-based study using Surveillance, Epidemiology and End Results (SEER)– Medicare data to investigate factors associated with black-white differences in breast cancer outcomes. What is notable about this study, compared with most prior research, is the use of rigorous matching methods to eliminate some of the biases that affect observational analyses. In particular, the authors examined black-white differences in 5-year breast cancer survival among women older than 65 years by sequentially matching black patients (n = 7375) to white patients (n = 7375) on demographics (age, year of diagnosis, and SEERsite), clinical presentation (comorbid conditions, tumor stage and other selected tumor factors), and treatment (details of surgery, radiation therapy, and chemotherapy).

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Silber et al report 3 major findings. First, despite some improvements in survival for both races, when matched on demographic characteristics, there was a 12.9% absolute difference in 5-year breast cancer survival by race (55.9% survival among black women, 68.8% survival among white women) that did not change appreciably from 1991 to 2005. Second, once blacks and whites were matched on demographic characteristics and clinical presentation, the survival difference declined to 4.4% (95% CI, 2.8%-5.8%). Third, the investigators concluded that, after matching on demographic characteristics and clinical presentation, local treatment and chemotherapy accounted for only a small portion (0.81%) of the remaining absolute race differences in survival.

The authors' conclusion that treatment is associated with a minimal fraction of the racial differences in breast cancer survival may be questioned for several reasons, some of which are related to limitations of the SEER data. First, even though blacks were matched to whites on chemotherapy use and general drug class, the study lacked information about doses, intensity, and completion of planned cycles. These factors have been shown to vary by race³⁻⁵ and to affect survival.^{4,6} An ongoing large prospective cohort study, the Breast Cancer Quality of Care Study (BQUAL), is collecting detailed information on doses and treatment cycles to address treatment quality by race.⁷ Silber et al also noted differences in primary care utilization prior to diagnosis and statistically significantly greater delays in treatment initiation by race (albeit clinically nonsignificant). These observations support the impression that there may be differences in processes of care that may be markers for suboptimal use of treatment, quality of treatment, or both, not captured in the SEER-Medicare database. In other settings, ratings of patient-physician communication and trust have been related to black women's, but not white women's, patterns of chemotherapy use,⁸ further reinforcing the idea that black women may have different cancer care experiences than white women.

Second, as the authors acknowledge, the analysis did not include information about use of hormone therapy. The majority of older women (77% of white women and 69% of black women) are estrogen receptor positive,¹ and a 5-year course of hormone therapy can lower breast cancer mortality by 30% in all groups.⁹ Therefore, differential patterns of hormone therapy use or adherence by race would lead to underestimation of the association between systemic treatment and survival differences. Although the studies cited by the authors did not report significant differences, other studies have reported black-white differences in initiation and adherence to completion of hormone regimens,¹⁰ or race differences related to socioeconomic variations.¹¹ Thus, assessment of the quality of hormone therapy will be critical to understanding the true contribution of breast cancer treatment to population-level race disparities in outcome.

Third, another factor that should be considered in placing the treatment results in context is that chemotherapy improves survival mainly for the subgroup of women with node-positive, nonmetastatic disease, at least up to age 70 years.¹² Thus, an additional analysis could have excluded women with metastatic cancer and been stratified by stage, rather than matched on this factor. Such analyses may have shown that treatment explains a meaningful portion of the race disparities among women with node-positive disease. Moreover, treatment has been shown in clinical trials to decrease mortality,^{9,12} whereas screening, which can make clinical

presentation appear more favorable, has not been shown in randomized trials to decrease mortality in women older than 74 years. Screening older women can result in detection and treatment of cancers that never would have been identified (overdiagnosis) or never would have harmed older women in their lifetimes (over-treatment). For these reasons, many argue that the most appropriate cancer outcome measure is mortality, rather than 5-year survival, as was used in the article by Silber et al.

Fourth, although the sequential matching approach in which treatment-related factors are added to demographic and clinical presentation factors is innovative, the inferences that can be drawn from these analyses should be more circumspect. After demographic matching, adding either presentation or treatment reduces the 5-year survival difference to a comparable extent (from 12.9% to 4.4% [95% CI, 2.8%-5.8%] or 3.6% [95% CI, 2.3% vs 4.9%], respectively). Thus, the order of the matching affects conclusions. Another interpretation of the results might be that either changing clinical presentation or improving treatment for blacks to be similar to that of whites could have important and equivalent contributions to reducing disparities. Because there is a synergy between presentation and treatment, it is difficult to disentangle their separate effects from this type of analysis.

Simulation modeling research has been useful to delineate the separate effects of screening and treatment and has been used to evaluate race differences in breast cancer mortality.¹³⁻¹⁵ In one study using 2 well-established Cancer Intervention and Surveillance Network (CISNET) models, higher breast cancer mortality for black women was found to be related primarily to differences in natural history (26%-44%) and use of adjuvant therapy (11%-19%). Screening, which affects stage (or tumor size) at presentation, accounted for only 7% to 8% of the black-white differences in breast cancer mortality.¹⁴ However, there remains much unknown about the biology of breast cancer. Future modeling research will benefit from a more refined understanding of disease natural history.

Overall, targeting standard-of-care treatment for women with breast cancer most likely to benefit by virtue of stage and tumor markers is a balanced public health approach for the increasing population of older women and may be the most efficient means of reducing black-white differences in the Medicare-aged population.¹³ Differing perspectives on the value of treatment illustrate the complexity of understanding racial disparities in cancer outcomes. This is underscored in the secondary analysis by Silber et al showing that after matching on dual eligibility for Medicare and Medicaid, the hazard ratio for black vs white differences in mortality was no longer significant. This result suggests that it is not black and white differences but rather socioeconomic status that most likely is a key driver of disparities in cancer outcomes, even among women with access to health care via the Medicare program.

The rigorous study by Silber et al provides additional clues to the black-white differences in breast cancer outcomes. Ultimately, for any cancer control strategy to succeed, improved care quality appears to be a necessary, but not sufficient, condition to eliminate race-based mortality differences in the United States.

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