Impact of Race and Area Deprivation on Triple-Negative Metastatic Breast Cancer Outcomes

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OBJECTIVES: To describe area deprivation, anxiety, depression, relative dose intensity of first-line metastatic breast cancer (MBC) treatment, and survival in Black and White women who had died from triple-negative MBC, including interaction analysis.

SAMPLE & SETTING: This cohort study drew from a database of women who had died from MBC (N = 53).

METHODS & VARIABLES: Descriptive statistics, independent t tests, analysis of variance, and Mann–Whitney U tests were used, and effect sizes were calculated.

RESULTS: Compared with White women, Black women reported higher anxiety and depression at MBC baseline. Black women living in areas of higher deprivation experienced shorter overall survival than White women living in similar areas (9.9 months versus 24.6 months). These results were not statistically significant, likely because of a small sample size, but were clinically meaningful.

IMPLICATIONS FOR NURSING: Black and low-income women with breast cancer experience inferior survival as compared with White and higher-income women. Newer explanatory models for racial disparity in cancer outcomes include the assessment of neighborhood deprivation. White women may be less affected by their neighborhood, even when living in areas of greater deprivation influencing cancer outcomes. This merits further exploration.

KEYWORDS metastatic breast cancer; survival; race; neighborhood; health disparity

***ONF, 50*(4), 449–457.**

DOI 10.1188/23.ONF.449-457

Dramatic disparities in cancer incidence, progression, therapy tolerance, and survival exist for patients with cancer who have low income and are from underrepresented groups (Zavala et al., 2021). The explanatory model for these disparities is no longer limited to late-stage diagnosis, absence of screening, and aggressive tumor subtypes. There is now evidence that through repeated experiences of lifetime trauma, poverty, and structural and interpersonal discrimination, patients of color and individuals with material and social disadvantage experience stress, which negatively affects health outcomes, including cancer outcomes (Penner et al., 2012; Singh & Jemal, 2017).

Metastatic Breast Cancer

Metastatic breast cancer (MBC) represents a model of chronic care that involves receiving aggressive cancer treatment while living with a progressive, life-ending illness (Drageset et al., 2021). Although MBC is challenging as a disease entity itself, non–older adult, non-Hispanic Black patients with MBC experience worse survival, with survival disparities persisting regardless of neighborhood socioeconomic status (Ren et al., 2019).

Social Determinants of Health

Late-stage presentation and more aggressive cancer etiology have often been implicated in racial survival disparity, yet the importance of measuring social determinants of health is becoming increasingly clear in the context of illness, including cancer (Coughlin, 2019, 2021). Individuals who reside in areas of high racial segregation and higher deprivation receive fewer cancer screenings (Buehler et al., 2019), undergo less intensive cancer therapy (Mora et al., 2021), and experience poorer overall survival

(Hufnagel et al., 2020; Mora et al., 2021; Poulson et al., 2021; Sadigh et al., 2022; Unger et al., 2021).

Neighborhood: The model outlined by Stafford and Marmot (2003) acknowledges that neighborhoods are important during illness because of the demands it makes on the individual and family. Tangible products and services such as prescription and over-the-counter medications, homecare services (paid or volunteer), home cleaning (paid or volunteer), health ministry provided by faith-based organizations, child care, and food delivery (paid or donated) are often needed. Communities with less wealth have fewer services to offer and have fewer residents who are able to donate time or funds (Stafford & Marmot, 2003).

Area deprivation index: Individuals residing in areas of higher deprivation experience worse health outcomes in multiple chronic medical conditions (Durfey et al., 2019). Residing in highly segregated Black neighborhoods is linked to poor cancer survivorship (Ellis et al., 2018; Kish et al., 2014). An area deprivation index (ADI) is an important measure of neighborhood socioeconomic disadvantage. ADI is estimated at the census block group level using key variables from 17 measures in the domains of income, education, employment, and housing quality (Kind & Buckingham, 2018). An analysis of one center's MBC cohort from the years 2000 through 2017 (N = 1,246) found that the high-deprivation neighborhood group had a higher proportion of African American individuals, but in multivariate analysis, deprivation index, not race, had a significant effect on overall MBC survival (Puthanmadhom Narayanan et al., 2022).

Stress and ADI: The mechanistic process by which ADI may indirectly influence cancer outcomes may be explained by a stress, or allostasis, model. There has been increasing interest in the concept of allostatic load, which is the accumulation of physiologic disturbances resulting from repeated or chronic stressors in daily life (Guidi et al., 2021). Allostatic load is an indirect measure of the body's response to external stressors (Kenrik Duru et al., 2012). Over time, these physiologic disturbances accumulate as stress, which can lead to premature morbidity and mortality from chronic diseases (Fagundes et al., 2017; Lee et al., 2018). In the United States, regardless of economic status, Black individuals have a higher allostatic load than White individuals (E. Obeng-Gyasi et al., 2022; S. Obeng-Gyasi et al., 2021). Specifically in patients with breast cancer, a higher baseline allostatic load is associated with poorer quality of life (E. Obeng-Gyasi et al., 2022; S. Obeng-Gyasi et al., 2021). However, the impact of allostatic load on MBC outcomes has not been studied. For this retrospective review in which allostatic load could not be fully measured, patient reports of stress and depression during MBC treatment, available through electronic health records, were measured and considered for possible linkage between deprived neighborhoods and poor cancer outcomes.

Objectives

The authors' team drew from a well-established database of women with MBC, all of whom had been diagnosed with triple-negative breast cancer. Examining only women with MBC and triple-negative disease essentially eliminates the two presumed causative etiologies for racial disparity in breast cancer survival: late-stage presentation (Poulson et al., 2021) and higher incidence of triple-negative breast cancer (Scott et al., 2019). Harmonizing these factors allows for a closer examination of area deprivation and its possible influence on MBC outcomes. In a cohort of women who had died from triple-negative MBC, the authors' aims were (a) aim 1, to describe area deprivation, baseline anxiety and depression, first-line MBC relative dose intensity (RDI), time to first progression (TTFP), and postmetastasis overall survival (PMOS) for the total sample as well as by race (among Black individuals versus White individuals) and ADI (low versus high), and (b) aim 2, to assess for an interaction effect between race and ADI on survival outcomes.

Methods

Theoretical Model

To consider MBC, the authors placed study variables into an adapted version of the Symptom Experience, Management, and Outcomes According to Race and Social Determinants (SEMOARS) model, which derives from the authors' previous exploration of disparity in early-stage breast cancer treatment (McCall et al., 2020). The SEMOARS model evaluates the deep multifactorial phenotype of the individual, with consideration of sociocultural and neighborhood factors as patients embark on cancer treatment. The distal outcomes of the model include RDI of treatment, TTFP, and PMOS.

Sample and Setting

Data for this study were gathered from an established database of women who had died from MBC and had been treated at a National Cancer Institute–designated medical oncology breast cancer clinic at the University of Pittsburgh Medical Center Magee-Womens Hospital. Women who had died from MBC

between November 1, 2016, and April 1, 2021, were included in the database. Data collection was performed by two RNs. To ensure accuracy, 10% of the sample was randomly selected and data were verified by another study staff member. Any data requiring clarification were discussed with a senior member of the research team who is also a clinician at the cancer center. Any discrepancies or uncertainties were discussed as a team, and a consensus was reached. This study was approved as an exempt study by the University of Pittsburgh Institutional Review Board prior to initiation.

Women who met the following criteria were included in the study: (a) had been aged 18 years or older; (b) had been given a diagnosis of MBC, including de novo diagnosis (metastatic at diagnosis); (c) had been diagnosed with triple-negative subtype (estrogen receptor–negative/progesterone receptor–negative/HER2-negative); (d) had received cancer treatment at the University of Pittsburgh Medical Center Magee-Womens Hospital; and (e) had died between November 1, 2016, and March 1, 2021. Patients were excluded who (a) were male and (b) whose treatment course was not directed at the clinic where the database is kept. Male patients were excluded because there were very few male patients, and their disease course has unique features distinct from that of women with MBC. Patients who came to the clinic for a consultation or a second opinion only were excluded because there was limited information regarding their treatment course.

Chart Review

Data retrieved from electronic health records included race, date of birth, date of metastatic diagnosis, and date of death. First-line MBC treatment information was extracted, including the medication name, the dosage prescribed, and the dosage received. The last listed address in the electronic health record was used to calculate ADI. To measure stress and anxiety associated with living in areas of high socioeconomic deprivation, self-reported anxiety (Generalized Anxiety Disorder 2-Item) (Kroenke et al., 2007) and depression (Patient Health Questionnaire–2) (Manea et al., 2016) screening scores at the time of first clinic visit following MBC diagnosis were also obtained from the electronic health record. Higher scores indicate a greater number of symptoms. If the screening items are endorsed by the patient, the two-item screening questions for both anxiety and depression open to the full questionnaires: the Generalized Anxiety Disorder–7, which has a possible score range of 0–21, with higher scores indicating greater anxiety; and the Patient Health Questionnaire–9, which has a possible score range of 0–27, with higher scores indicating more severe depression. Both screening tools assess symptoms that occurred during the past two weeks. These scores are routinely collected in clinical care via electronic tablet at every medical oncology clinic visit and then embedded into the electronic health record in time for the patient encounter.

Survival: PMOS and TTFP were calculated in number of days from metastatic diagnosis. PMOS was calculated by subtracting the date of MBC diagnosis from the date of death. TTFP was calculated by subtracting the date of MBC diagnosis from the date of first progression. Higher values of PMOS and TTFP indicate greater survival.

RDI: RDI of the first prescribed treatment for MBC was calculated by taking the percentage of dose prescribed versus dose received for each medication (chemotherapy) individually and then adding together the RDI for each medication, divided by the number of medications. This method has been used in other research (Yamaguchi et al., 2011). Higher values signify that a greater percentage of the prescribed dose was received. This information is easily gathered from the Epic electronic health record under the Synopsis page where chemotherapy doses are documented after administration. The prescribed dose was obtained from the first medical oncology visit for MBC where a treatment option was prescribed and explained to the patient.

ADI: To determine ADI, the patient's full address was entered into the Neighborhood Atlas® interactive website from the University of Wisconsin School of Medicine and Public Health (2021). The ADI ranking for the census block group that contained each address was recorded. ADI is calculated as national percentile rankings from 1 to 100, where higher numbers indicate greater "disadvantage." For the purpose of this analysis, the authors used the median score to dichotomize high versus low ADI.

Data Analysis

Group-specific descriptive statistics, consistent with each variable's level of measurement and observed distribution, were calculated. Between-group differences were examined using independent samples t tests for interval/ratio variables and chi-square tests of independence or Fisher's exact tests for cells with small numbers of participants. RDI and survival variables (TTFP and PMOS) were not normally distributed, so nonparametric testing was performed.

For aim 1, descriptive statistics were calculated for the total sample, by race (Black versus White), and by ADI (low versus high), comparing for differences between the groups. For aim 2, a one-way analysis of variance was used to examine for an interaction effect between race and ADI and the impact on survival. Effect sizes were calculated for each of the variables. Hedges's g was chosen as the measure of effect sizes because of the small, unequal sample sizes. Interpretation of Hedges's g was guided by the general rule of thumb put forth by Cohen (1988): 0.2–0.49 = small effect, 0.5–0.79 = medium effect, and 0.8 or greater = large effect.

Results

Aims

Demographic characteristics, treatment, and survival are shown by race in Table 1 and by ADI in Table 2. Women with MBC included in this study were aged an average of 56.3 years, and most were White (n = 45). In the study sample, Black women were more likely than White women to live in more deprived areas (p = 0.002). Comparison by race showed higher anxiety and depressive symptomatology among Black women than among White women, without statistical significance. There were small effect sizes for both anxiety (Hedges's g = 0.48) and depression (Hedges's g = 0.25). There was minimal difference in RDI for first-line MBC treatment between Black women (RDI = 0.88, or 88%) and White women (RDI = 0.84, or 84%). Black women experienced shorter TTFP (5.5 months versus 8.2 months) and PMOS (10.3 months versus 18.4 months), although neither difference reached statistical significance. There were small effect sizes for TTFP (Hedges's g = 0.25) and PMOS (Hedges's g = 0.41).

Interaction Effect

To examine the interaction between race and area deprivation, ADI was dichotomized by the median ADI level of the total sample. There was only one Black woman in the "less disadvantaged" ADI group; thus, the authors were unable to make comparisons by race in the less disadvantaged group. Descriptive

TABLE 1. Descriptive Statistics by Race (N = 54)

	White (N = 45)		Black (N = 9)			
Variable	$\bar{X}$	SD	$\bar{X}$	SD	Statistic	Hedges's g
ADI	55.6	19.5	74.9	19.3	t = 3.664, p = 0.002	0.99
Age (years)	56.3	12.9	55.3	13	t = –0.198, p = 0.844	0.08
GAD	6.1	5.8[a]	9.3	9.5[b]	t = 1.047, p = 0.305	0.48
PHQ-9	4.2	5.1[c]	5.7	7[b]	t = 0.554, p = 0.252	0.25
PMOS (months)	18.4	21.2	10.3	5.4	MWU = 165.5, p = 0.441	0.41
RDI	0.84	0.2	0.88	0.15	t = 0.643, p = 0.523	0.21
TTFP (months)	8.2	11.7	5.5	3.1	MWU = 194, p = 0.924	0.25

[a] N = 22
[b] N = 6
[c] N = 21
ADI—area deprivation index; GAD—Generalized Anxiety Disorder; MBC—metastatic breast cancer; MWU—Mann–Whitney U test; PHQ-9—Patient Health Questionnaire–9; PMOS—postmetastasis overall survival; RDI—relative dose intensity of first-line MBC treatment; TTFP—time to first progression
Note. Scores for the GAD can range from 0 to 21, with higher scores indicating more severe anxiety. The GAD-2 comprises the first 2 items of the GAD-7. If a patient answers the GAD-2 positively, assessment continues with the remaining GAD-7 questions. Scores for the PHQ-9 can range from 0 to 27, with higher scores indicating greater depression.
Note. RDI is the ratio of the delivered dose to the recommended dose. RDI was calculated by taking the percentage of the dose administered versus dose prescribed for each chemotherapy medication individually, adding together the RDI for each medication, and dividing by the number of medications. PMOS and TTFP were calculated in time from metastatic diagnosis. PMOS was calculated by subtracting the date of MBC diagnosis from the date of death. TTFP was calculated by subtracting the date of MBC diagnosis from the date of first progression. Higher values of PMOS and TTFP indicate greater survival.

TABLE 2. Descriptive Statistics by ADI (N = 53)

	ADI 1–58 (N = 27)		ADI 59–100 (N = 26)			
Characteristic	**$\bar{X}$**	**SD**	**$\bar{X}$**	**SD**	**Statistic**	**Hedges's g**
Age (years)	58.9	11.9	55.3	13.8	t = 0.441, p = 0.661	0.07
GAD	6.8	7[a]	6.3	6.9[b]	t = 0.411, p = 0.684	0.07
PHQ-9	4.2	5.9[a]	4.9	5.3[c]	t = –0.36, p = 0.722	0.13
PMOS (months)	14.2	15	20.1	23.4	MWU = 332.5, p = 0.742	0.3
RDI	0.81	0.21	0.88	0.17	MWU = 286.5, p = 0.155	0.37
TTFP (months)	7.5	12.5	8	8.9	MWU = 324.5, p = 0.637	0.03
Race		**n**		**n**	**Statistic**	**Hedges's g**
Black		1		8	p = 0.011[d]	0.28

[a] N = 13
[b] N = 15
[c] N = 14
[d] Fisher's exact test
ADI—area deprivation index; GAD—Generalized Anxiety Disorder; MBC—metastatic breast cancer; MWU—Mann–Whitney U test; PHQ-9—Patient Health Questionnaire–9; PMOS—postmetastasis overall survival; RDI—relative dose intensity of first-line MBC treatment; TTFP—time to first progression
Note. Scores for the GAD can range from 0 to 21, with higher scores indicating more severe anxiety. The GAD-2 comprises the first 2 items of the GAD-7. If a patient answers the GAD-2 positively, assessment continues with the remaining GAD-7 questions. Scores for the PHQ-9 can range from 0 to 27, with higher scores indicating greater depression.
Note. RDI is the ratio of the delivered dose to the recommended dose. RDI was calculated by taking the percentage of the dose administered versus dose prescribed for each chemotherapy medication individually, adding together the RDI for each medication, and dividing by the number of medications. PMOS and TTFP were calculated in time from metastatic diagnosis. PMOS was calculated by subtracting the date of MBC diagnosis from the date of death. TTFP was calculated by subtracting the date of MBC diagnosis from the date of first progression. Higher values of PMOS and TTFP indicate greater survival.
Note. An ADI of 1–58 indicates a less disadvantaged neighborhood. An ADI of 59–100 indicates a more disadvantaged neighborhood.

statistics by race and ADI are shown in Table 3. In the "more disadvantaged" ADI group, Black women tended to have higher levels of anxiety (9.3 versus 4.3), to live in more deprived areas (ADI 80.3 versus 74.3), and to experience poorer survival (TTFP 5.4 months versus 9.1 months; PMOS 9.9 months versus 24.6 months) than White women, although none of these variables reached statistical significance. The authors found a small effect size for TTFP (Hedges's g = 0.42) and medium effect sizes for anxiety (Hedges's g = 0.72), ADI (Hedges's g = 0.57), and PMOS (Hedges's g = 0.64).

Discussion

This study describes area deprivation, anxiety, depression, first-line MBC RDI, and survival in Black and White women with triple-negative MBC and investigates whether an interaction effect exists between race and ADI. These results suggest that although this study's analysis did not reach statistical significance, in the study sample of women with triple-negative MBC, Black women tended to live in areas of higher deprivation, reported higher levels of anxiety and depression, and experienced poorer survival (TTFP and PMOS) compared with White women.

Many past studies have found racial survival disparities among women with breast cancer, often assumed to be explained by later-stage presentation and more aggressive subtype (Hardy & Du, 2021). Even after equalizing stage and subtype, the current study found differences in survival as measured by TTFP and PMOS between Black and White women, which warrants further investigation. However, this survival disparity was particularly acute when seen through the lens of neighborhoods deprivation.

A possible explanatory pathway, similar to the SEMOARS model (McCall et al., 2020), is that the lifetime experience of living in areas of higher deprivation, coupled with racial discrimination, may result in higher levels of anxiety and depressive symptoms ultimately leading to high allostatic load and worse overall triple-negative MBC survival.

Racial Differences

The interesting finding that the effects of neighborhood deprivation on cancer outcomes were not as profound among White patients has been reinforced in the literature. In a 2022 analysis of area deprivation and all-cause mortality, Ribeiro et al. found that among individuals who lived in more deprived neighborhoods, survival was worse among those who had lower education levels (used as a surrogate for income) than among those with higher educational attainment. This reinforces the authors' findings that individuals with higher income may have access to mitigation strategies dampening the effect of neighborhood deprivation on health outcomes.

Racism

It is clear from these findings that race and racism must be considered as a distinct entity when evaluating neighborhoods with high deprivation. The interaction of race and the experience of racism is not often considered because of the retrospective nature of many data-based analyses and the historic practice of controlling for race rather than fully considering the implication of structural and interpersonal racism encountered by Black patients in the U.S. cancer care system directly and indirectly (Ioannidis et al., 2021). Directly affecting Black patients, as demonstrated through these data, is the effect of disadvantaged neighborhoods. Eldridge and Berrigan (2022) demonstrated that when racism was measured through structural racism measures such as poor educational attainment, criminal justice system outcomes, and community engagement (e.g., political participation), there were greater odds of developing triple-negative breast cancer overall, with notable racial disparities for Black women. Cancer outcomes were not examined.

TABLE 3. Descriptive Statistics by ADI and Race (N = 52)

	ADI 1–58		ADI 59–100							
	White (N = 26)		White (N = 18)		Black (N = 8)		Total (N = 26)			
Variable	$\bar{X}$	SD	$\bar{X}$	SD	$\bar{X}$	SD	$\bar{X}$	SD	Statistic	Hedges's g
ADI	42	12	74.3	10.1	80.3	11.4	76.2	10.7	t = 1.324, p = 0.198	0.57
Age (years)	56.8	12.2	55.8	14.4	54.1	13.3	55.3	13.8	t = –0.285, p = 0.778	0.12
GAD	7.38	6.6[a]	4.3	4.3[b]	9.3	9.5[c]	6.4	7.1	t = 1.224, p = 0.265	0.72
PHQ-9	4.2	5.9[a]	4.4	4.1[b]	5.7	7[c]	4.9	5.3	t = 0.436, p = 0.671	0.24
PMOS (months)	14.6	15.8	24.6	26.9	9.9	5.6	20.1	23.4	MWU = 51, p = 0.243	0.64
RDI	0.84	0.18	0.88	0.18	0.9	0.16	0.88	0.17	MWU = 67, p = 0.757	0.11
TTFP (months)	7.9	13.2	9.1	10.3	5.4	3.3	8	8.9	MWU = 60, p = 0.505	0.42

[a] N = 13
[b] N = 8
[c] N = 6
ADI—area deprivation index; GAD-2—Generalized Anxiety Disorder; MBC—metastatic breast cancer; MWU—Mann–Whitney U test; PHQ-9—Patient Health Questionnaire–9; PMOS—postmetastasis overall survival; RDI—relative dose intensity of first-line MBC treatment; TTFP—time to first progression
Note. Scores for the GAD can range from 0 to 21, with higher scores indicating more severe anxiety. The GAD-2 comprises the first 2 items of the GAD-7. If a patient answers the GAD-2 positively, assessment continues with the remaining GAD-7 questions. Scores for the PHQ-9 can range from 0 to 27, with higher scores indicating greater depression.
Note. RDI is the ratio of the delivered dose to the recommended dose. RDI was calculated by taking the percentage of the dose administered versus dose prescribed for each chemotherapy medication individually, adding together the RDI for each medication, and dividing by the number of medications. PMOS and TTFP were calculated in time from metastatic diagnosis. PMOS was calculated by subtracting the date of MBC diagnosis from the date of death. TTFP was calculated by subtracting the date of MBC diagnosis from the date of first progression. Higher values of PMOS and TTFP indicate greater survival.

Structurally, the redlining practices that were present in the United States since the 1930s through activities of the Home Owners' Loan Corporation and Federal Housing Administration are foundational to the existence of deeply racially segregated, economically deprived neighborhoods that have been found to contribute to poor health outcomes (Goel et al., 2022; Swope et al., 2022). On an interpersonal level, there is evidence that quotidian microaggressions and encounters of perceived racism and discrimination contribute to lifetime stress burden and subsequent poor health outcomes among Black Americans (Miller & Peck, 2020). Within health care, interpersonal racism is often measured through provider communication, which is thought to be of poorer quality and less participatory among Black patients than among White patients (Williams & Cooper, 2019). Challenges toward mitigation of racism and associated poor health outcomes include specific, discrete measurements and linkage to specific outcomes (Neblett, 2019). Unfortunately, the authors were unable to directly compare anxiety, depression, and survival outcomes in Black versus White women living in less disadvantaged areas because of the small sample size. The authors were also unable to more fully explore the concept of allostatic load as influenced by disadvantaged neighborhoods and its effect on MBC outcomes. A more robust sample will help to better elucidate these very preliminary findings.

Limitations

There are several limitations to acknowledge. First, this study was a retrospective chart review; thus, the authors were limited by the data available in electronic health records. Second, the small sample sizes, which were also unequal, did not provide adequate power for hypothesis testing. Although there were clinically significant findings, the lack of statistical significance was likely a result of the small sample size. Third, the study's sample did not include an adequate number of Black women living in less disadvantaged areas, which prevented the authors from comparing the effect of neighborhood deprivation, specifically among Black women with triple-negative MBC. Fourth, the authors recognize that the experience of living with MBC, particularly for Black women, is likely greatly affected by the high segregation present in the authors' region and even found within the study sample. A similar study conducted in an area with more diverse neighborhoods may yield different findings. Fifth, women in this study received numerous and varied chemotherapies as part of first-line MBC treatment. The authors took a cumulative approach to calculating RDI; a much larger sample may allow for investigation of RDI of specific medications rather than collectively, which may result in different findings.

KNOWLEDGE TRANSLATION

- Clinically important differences in time to first progression and overall survival among Black women and White women with metastatic breast cancer (MBC), all of whom had a diagnosis of triple-negative breast cancer, indicate that broader, structural factors must be examined.
- Higher rates of anxiety and depression among Black versus White women are reported during MBC treatment.
- Neighborhood deprivation and its associated effects on health outcomes are important considerations in the assessment of patients as they embark on the chronic, likely life-ending illness of MBC.

Conclusion

Although statistically significant differences in survival between Black and White women with triple-negative MBC were not found, a three-month difference in TTFP and an eight-month difference in PMOS are clinically meaningful. The lack of statistical significance was likely because of the study's small sample size. When examining the interaction between race and ADI, the authors also did not find statistically significant results; however, the effect sizes point to the need for future research in this area.

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No financial relationships to disclose.

Rosenzweig and Nugent contributed to the conceptualization and design, provided the analysis, and contributed to the manuscript preparation. Rosenzweig and McGuire completed the data collection. Rosenzweig provided statistical support.

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