

Neighborhood Socioeconomic Status in Relation to Serum Biomarkers in the Black Women's Health Study

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ABSTRACT Lower neighborhood socioeconomic status (SES) is associated with higher cardiovascular disease (CVD) risk. Black women have a higher CVD risk and are more likely to live in poor neighborhoods than white women. We examined the association of neighborhood SES with several CVD biomarkers using data from the Black Women's Health Study (BWHS), a follow-up study of US black women reporting high levels of education and income. Blood specimens of 418 BWHS participants were assayed for C-reactive protein (CRP), hemoglobin A1C (hgA1C), and high-density lipoprotein (HDL) cholesterol. US Census block group data were linked to the women's addresses to reflect neighborhood SES. Multivariable-adjusted mixed linear regression models that adjusted for person-level SES and for cardiovascular risk factors were used to assess CRP, hgA1C, and HDL levels in relation to quintiles of neighborhood SES. Women living in the poorest neighborhoods had the least favorable biomarker levels. As neighborhood SES increased, CRP decreased (P for trend=0.01), hgA1C decreased (P for trend=0.07), and HDL increased (P for trend=0.19). These associations were present within strata of individual educational level. The present findings suggest that neighborhood environments may affect physiological processes within residents independently of individual SES.

KEYWORDS Neighborhood socioeconomic status, Serum biomarkers, African-Americans, Women

INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of death in the USA, representing the underlying cause for nearly 40 % of all deaths.^{1,2} Morbidity and mortality from CVD are higher among black Americans than among white, Hispanic, and Asian Americans.^{2,3}

Neighborhood socioeconomic status (SES) has been found to be inversely associated with CVD risk.^{4,5} In addition, compared to residents of wealthier neighborhoods, residents of disadvantaged neighborhoods are more likely to be

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overweight or obese,⁶⁻⁸ to smoke,^{5,9} and to have higher blood pressure,^{5,8,10} lipid levels,^{4,8} and glucose levels.^{8,11} Inflammation plays a critical role in all stages of the CVD disease process.^{12,13} Studies examining the association between neighborhood SES and physiologic indicators of inflammation, including C-reactive protein, interleukin-6 (IL-6),¹⁴ and serum albumin,¹⁵ have found higher levels of^{14,15} proinflammatory markers in residents of disadvantaged communities than in wealthier communities.^{14,15}

Black women at all levels of education are more likely to live in poor neighborhoods than are white women¹⁶⁻¹⁹; thus, it is important to determine whether low neighborhood SES is associated with cardiovascular risk factors independent of individual-level SES. Previous studies of neighborhood SES and biomarkers that included black women were limited to low SES communities^{5,20} and the elderly²¹ or had too few subjects to allow for specific analyses of black women across SES.¹⁴ A study of African-American adults living in Jackson, MS, found that neighborhood disadvantage was associated with higher cumulative biological risk.²⁰ One study which analyzed black women across SES found conflicting results.⁸

In the present analyses, we examined the association of neighborhood SES with biomarkers of inflammation, metabolic disease, and CVD risk using data from the Black Women's Health Study (BWHS), a cohort study of US black women including large numbers of women at all levels of neighborhood and individual SES. Our analyses took into account individual-level SES as well as important cardiovascular risk factors. We have previously reported inverse associations between neighborhood SES and incidence of hypertension,¹⁰ diabetes,²² and obesity⁶ in the BWHS.

METHODS

The Black Women's Health Study

The Black Women's Health Study (BWHS) is a prospective cohort study established in 1995, when approximately 59,000 African-American women aged 21 through 69 years from across the USA filled out health questionnaires. The baseline questionnaire elicited data on demographic and lifestyle factors, reproductive history, dietary intake, and medical conditions. The cohort has been followed biennially through mailed questionnaires. Follow-up of the baseline cohort has been successful for 88 % of potential person-years through the last completed follow-up, 2013. The study was approved by the institutional review board of Boston University.

Blood Specimen Collection and Assays

The present analyses are based on blood specimens collected from BWHS participants in three geographic areas in a study to assess the feasibility of collecting blood specimens within the large geographically dispersed population of the BWHS. From July 2006 through July 2007, 1500 participants aged 40 years and older without a history of cancer were randomly selected from BWHS participants in New York, NY, Chicago, IL, and Atlanta, GA, and invited to provide blood specimens. Each potential participant was sent a study packet containing an introductory letter and brochure, consent forms, instructions for locating a blood collection site near her home, and a pre-printed laboratory requisition form. Blood specimens were collected and tested by Quest Diagnostics (Madison, NJ www.QuestDiagnostics.com).

com), an accredited national clinical laboratory, according to the standards set by the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88).^{23,24}

Blood specimens were collected from 532 women. The participating women were similar to non-participants with regard to important characteristics that have been associated with risk of CVD, including age, body mass index, education, income, alcohol consumption, vigorous exercise, menopausal hormone use, and prevalence of diabetes, hypertension, and high cholesterol. The prevalence of current smoking was higher among non-participants (18 %) than participants (12 %). We excluded women whose residential addresses could not be geocoded (e.g., post office boxes and non-residential addresses; $N=46$) and who reported current use of cholesterol-lowering medications ($N=68$), for a total of 418 women in the analytic cohort.

From among the following panel of biomarkers (C-reactive protein, hemoglobin A1c, high-density lipoprotein, total cholesterol, low-density lipoprotein, triglycerides, apolipoprotein A1, apolipoprotein B, and lipoprotein A), we focused on three biomarkers strongly associated with inflammation,²⁵ metabolic disease,²⁶ and cardiovascular risk.^{25,27-34} Thus, the analyses presented are limited to C-reactive protein (CRP), hemoglobin A1C (hgA1C), and high-density lipoprotein (HDL) cholesterol.

Neighborhood Socioeconomic Status

All BWHS participant residential addresses have been geocoded for each questionnaire cycle since 1995. For the present analyses, we linked 2005 addresses to US Census data at the block group level. Based on factor analysis with Varimax rotation, six variables were selected to represent neighborhood SES from among 29 block group census variables measuring dimensions of education, income, and wealth: median household income; median housing value; percent households receiving interest, dividends, or net rental income; percent adults aged ≥ 25 that have completed college; percent employed persons aged ≥ 16 in white collar occupations; and percent of families with children not headed by a single female.³⁵ The SES factor explained 67 % of the variability of the six variables that contributed to it. Regression coefficients from the factor analysis were used to weight the variables for a combined neighborhood score, with higher scores representing higher neighborhood SES. A categorical variable based on quintiles of the distribution of the neighborhood score was created.

Covariates

Individual SES was measured as total years of education (reported in 1995 and 2003). Body mass index in 2005 (weight in kg/height m^2) was calculated from adult height (reported in 1995) and current weight (2005). Age, smoking status, marital status, alcohol consumption, insurance status, menopausal status, and female hormone use as reported in 2005 (or on the most recently returned questionnaire if 2005 data were missing), and family income (reported in 2003) were considered in the analyses. Vigorous physical activity, moderate physical activity, walking for exercise, and sitting/television viewing were reported in 2001. High cholesterol, hypertension, and diabetes were reported by participants at baseline in 1995, and new occurrences were reported on follow-up questionnaires through 2005.

Statistical Analysis

CRP was log-transformed due to its skewed distribution. Mixed linear regression models that adjusted for within-block group correlation (PROC GENMOD, SAS,

version 9.3; SAS Institute Inc., Cary, NC) were used to assess mean serum biomarker levels in relation to quintiles of neighborhood SES. Regression analyses controlled for age, body mass index (<25, 25–29, ≥ 30 kg/m²), education (≤ 12 , 13–15, ≥ 16 years), household income ($\leq \$25,000$, $\$25,001$ – $\$50,000$, $> \$50,000$, missing), household size (1, 2, 3, 4, ≥ 5 people), number of alcoholic beverages consumed per week (<1, 1–6, ≥ 7 , missing), number of cigarettes smoked per day (none, 1–14, ≥ 15 , missing), insurance status (yes, no), hours of vigorous physical activity per week (none, <5, ≥ 5 , missing), hours of moderate physical activity per week (none, <5, ≥ 5 , missing), hours of walking for exercise per week (none, <5, ≥ 5 , missing), hours of sitting/television viewing per week (none, <5, ≥ 5 , missing), menopausal status (postmenopausal, pre-menopausal, missing), current use of female hormones (yes, no), hypertension (yes, no), diabetes (yes, no), Western dietary pattern³⁶ (e.g., red meat and fried foods; quintiles), and prudent dietary pattern³⁶ (e.g., fruits and vegetables). Tests of linear trend were performed by entering the ordinal form of the neighborhood SES variable into the model.³⁷ We repeated the analyses within strata of education (<16 years, ≥ 16 years) and tested for interaction using the Wald chi-square test. Analyses were also confined to women who were born in the USA ($N=398$), and to those who did not move between 1995 and 2005 ($N=250$).

The “traditional” P value for statistical significance is $P < 0.05$. In the present analyses, we assessed three biomarkers. To account for multiple testing, a “statistically significant” result would be $P < 0.05/3$, or $P < 0.017$.

RESULTS

Characteristics of participants according to quintile of neighborhood SES score are shown in Table 1. Years of education, household income, hours of vigorous physical

TABLE 1 Participant characteristics according to quintile of neighborhood SES score

	Quintile of neighborhood SES score				
	1 (low)	2	3	4	5 (high)
Number of participants	84	111	94	76	59
Age (years) (median)	55	52	53	49	53
Body mass index (kg/m ²) (median)	31.3	28.7	28.4	29.2	28.2
16+ years of education (%)	31	51	53	58	70
Family income $\geq \$50,000$ (%)	32	52	50	50	63
5+ hours vigorous activity per week (%)	2	9	6	8	9
5+ hours moderate activity per week (%)	29	28	31	29	26
5+ hours walking for exercise per week (%)	13	19	11	14	17
5+ hours sitting/watching TV per week (%)	25	18	18	18	11
Health insurance (%)	88	95	89	86	94
Current smokers (%)	19	11	10	8	7
Current alcohol drinkers (%)	37	58	58	50	68
History of hypertension (%)	45	50	55	42	48
History of hyperlipidemia (%)	30	26	29	25	31
History of diabetes (%)	16	11	11	11	15
Postmenopausal (%)	66	63	69	53	68
Current female hormone use (%)	12	13	11	13	24
Prudent dietary pattern, quintile 5 (%)	14	23	20	16	27
Western dietary pattern, quintile 5 (%)	15	14	14	20	13

activity, alcohol consumption, and female hormone use were positively associated with neighborhood SES score, while body mass index and smoking were inversely associated with score.

Table 2 presents the age- and multivariable-adjusted mean values of CRP, hgA1C, and HDL according to quintile of neighborhood SES. CRP mean values were back-transformed from their log-transformed values. Overall, women living in the most deprived neighborhoods (lowest quintile of SES score) had the least favorable biomarker levels, while women in the most affluent neighborhoods (highest quintile of SES score) generally had the most favorable levels. The age-adjusted mean of CRP was 1.24 mg/dL greater in the lowest quintile of neighborhood SES than in the highest quintile. After adjustment for individual SES and CVD risk factors, the difference was 1.03 mg/dL, with $P=0.013$ for trend across quintiles. In age-adjusted analyses, mean of % hgA1C was 0.36 greater in the lowest quintile of neighborhood SES than in the highest quintile, and the multivariable-adjusted mean was 0.34 greater, with $P=0.29$ for trend across quintiles. HDL was 8.8 mg/dL higher in the top quintile of neighborhood SES than in the lowest quintile in age-adjusted analyses, and 5.6 mg/dL higher in multivariable analyses, with $P=0.188$ for trend across quintiles. In additional analyses confined to women who were born in the USA, or confined to women who had not moved between 1995 and 2005, results were similar to those presented.

We repeated the analyses of each biomarker within strata of individual level of education (<16 and ≥ 16 years; Table 3). Women with ≥ 16 years of education had more favorable values for CRP than those with <16 years of education, but within both strata of education values of CRP decreased as level of neighborhood SES score increased. HDL values were more favorable among women with ≥ 16 years of education than those with <16 years; values increased with increasing neighborhood SES within each strata of education. Values of hgA1C also decreased as neighborhood SES increased within both strata of education, although hgA1C was not itself associated with education. Of note, among women with ≥ 16 years of education, the P trend for increasing levels of CRP and HDL, and decreasing level of hgA1C with increasing quintile of neighborhood SES were 0.08, 0.07, and 0.07, respectively. Results were similar when analyses were repeated according to levels of household income.

DISCUSSION

In this geographically diverse sample of US black women, low neighborhood SES was associated with less favorable levels of CRP, hgA1C, and HDL. The associations were present within levels of individual SES as measured by level of education.

CRP is a non-specific, acute phase marker of inflammation that has been shown in numerous epidemiological studies to predict incident cardiovascular events, including myocardial infarction, stroke, and death.^{25,38} Values of <1 , 1 to 3, and >3 mg/L represent low, moderate, and high risk for future cardiovascular events.³⁸ In the present study, women in the lowest quintile of neighborhood SES approached the high-risk cutoff, and those in the lowest quintile and who had <16 years of education exceeded the high-risk cutoff. Hemoglobin A1C is considered the best measure of a timed-averaged blood glucose over the prior 3 months.³⁹ It is fundamental to the screening and management of diabetes, and it is a risk factor for CVD.⁴⁰ Values of 6.5 % and higher are considered diagnostic for the condition.⁴¹ In the present study, the mean hgA1C value of women residing in the lowest SES

TABLE 2 Age and multi-variable adjusted mean values of C-reactive protein, hemoglobin A1C, and high-density lipoprotein according to quintile of neighborhood SES score ($n = 418$)

	Quintiles of neighborhood SES					Mean difference between Q1 and Q5	P for ordinal trend
	1 (Lowest)	2	3	4	5 (highest)		
Immune							
C-reactive protein (mg/L) ^a							
Model 1 ^b	2.72 (2.18–3.41)	2.19 (1.75–2.74)	2.25 (1.77–2.87)	1.85 (1.41–2.43)	1.48 (1.03–2.13)	1.24	0.004
Model 2 ^c	2.60 (2.07–3.28)	2.07 (1.73–2.47)	2.43 (2.02–2.93)	1.82 (1.41–2.35)	1.57 (1.11–2.22)	1.03	0.013
Metabolic							
Hemoglobin A1C (% of total hemoglobin)							
Model 1 ^b	6.14 (5.97–6.32)	5.99 (5.85–6.14)	5.91 (5.80–6.03)	6.02 (5.84–6.20)	5.78 (5.60–5.96)	0.36	0.022
Model 2 ^c	6.07 (5.94–6.21)	5.98 (5.87–6.09)	5.96 (5.86–6.07)	6.04 (5.88–6.20)	5.78 (5.61–5.94)	0.29	0.074
Cardiovascular							
High-density lipoprotein (mg/dL)							
Model 1 ^b	57.9 (54.8–61.3)	61.2 (58.5–64.1)	62.7 (59.5–66.0)	60.8 (57.7–64.1)	66.7 (62.1–71.7)	8.8	0.009
Model 2 ^c	59.8 (56.8–62.9)	61.7 (59.1–64.4)	61.9 (59.0–64.9)	60.3 (57.5–63.2)	65.4 (60.7–70.6)	5.6	0.188

^aValues are back-transformed means from log-transformed CRP values

^bModel 1: adjusted for age

^cModel 2: adjusted for age, menopausal status, alcohol consumption, vigorous physical activity, moderate physical activity, walking for exercise, sitting/television viewing, insurance status, cigarette smoking, history of diabetes, female hormone use, household income, number of people in the household, history of hypertension, years of education, body mass index, western dietary pattern, and prudent dietary pattern

TABLE 3 Multi-variable adjusted mean values of C-reactive protein, hemoglobin A1C, and high-density lipoprotein according to level of education within quintiles of neighborhood SES score

Quintiles of neighborhood SES	1 (lowest)	2	3	4	5 (highest)	Mean difference between Q1 and Q5	P for ordinal trend
Immune							
C-reactive Protein (mg/L) ^a							
<16 years of education	2.91 (2.26–3.74)	2.11 (1.64–2.72)	2.41 (1.76–3.30)	1.85 (1.26–2.71)	1.75 (0.96–3.18)	1.16	0.06
≥16 years of education	2.21 (1.47–3.33)	2.07 (1.64–2.62)	2.45 (1.95–3.07)	1.77 (1.30–2.41)	1.43 (0.92–2.21)	0.78	0.08
P for interaction							0.74
Metabolic							
Hemoglobin A1C (% of total hemoglobin)							
<16 years of education	6.08 (5.91–6.27)	6.06 (5.92–6.20)	5.96 (5.79–6.14)	6.06 (5.79–6.33)	5.88 (5.48–6.31)	0.20	0.47
≥16 years of education	6.15 (5.90–6.40)	5.83 (5.70–5.96)	5.99 (5.86–6.13)	6.05 (5.89–6.22)	5.68 (5.53–5.83)	0.47	0.07
P for interaction							0.37
Cardiovascular							
High-density lipoprotein (mg/dL)							
<16 years of education	58.6 (54.8–62.6)	59.4 (55.8–63.2)	60.1 (55.7–64.9)	57.9 (54.4–61.7)	63.7 (55.5–73.2)	5.1	0.60
≥16 years of education	61.0 (56.4–66.0)	63.5 (60.4–66.8)	62.3 (59.1–65.7)	62.6 (58.9–66.5)	69.2 (63.4–75.5)	8.2	0.07
P for interaction							0.95

<16 years of education, n = 201; ≥16 years of education, n = 217. All values adjusted for age, menopausal status, alcohol consumption, vigorous physical activity, moderate physical activity, walking for exercise, sitting/television viewing, insurance status, cigarette smoking, history of diabetes, female hormone use, household income, number of people in the household, history of hypertension, body mass index, western dietary pattern (red meat/fried foods), and prudent dietary pattern (fruits and vegetables)

^aValues are back-transformed means from log-transformed CRP values

neighborhoods, regardless of educational level, exceeded 6.0 %. Importantly, the mean level of hgA1C was highest among women with ≥ 16 years of education who also lived in the lowest quintile of neighborhood SES, suggesting that high individual resources do not protect African-American women from the harmful effects of residing in a low-resource environment. HDL cholesterol is considered cardioprotective, with low values, < 50 mg/dL in women, representing increased CVD risk.⁴²⁻⁴⁴ In the present study, women in the lowest SES neighborhoods had the lowest HDL values.

Neighborhood SES has been shown to play an important role in health. Several studies have found that persons living in poorer residential neighborhoods have an increased prevalence of cardiovascular risk factors⁵ and higher incidence of hypertension,¹⁰ diabetes,²² obesity,⁶ and CVD.^{4,45} Diez-Roux and colleagues observed that residence in lower SES neighborhoods was associated with increased odds of smoking, elevated systolic blood pressure, and serum cholesterol levels after adjustment for individual-level variables in the Atherosclerosis Risk in Communities (ARIC) study.⁵ A later study by Diez-Roux et al. reported a significant direct association between quartiles of neighborhood SES and HDL values among 860 black women in the CARDIA study, but an inverse association between neighborhood SES and a combined measure of the insulin resistance syndrome was present only among those in the high-income and high-education groups; in the low-income and low-education groups, insulin resistance increased with increasing neighborhood SES.⁸ In a cross-sectional analysis of 1081 black and white adults in the Pittsburgh Adult Health and Behavior (AHAB) project, Petersen et al. found that community-level SES was inversely associated with circulating CRP concentrations but that this association was greatly diminished with multivariable control for behavioral factors including smoking, alcohol consumption, and body mass index.¹⁴ In a study of diabetic patients from the University of California Davis Health System where the mean hgA1C of patients was 7.26 % (range, 4.0 to 18/4 %), Geraghty and colleagues found an inverse association between neighborhood SES and serum hgA1C levels.¹¹ More recently, a cross-sectional analysis of data from the Jackson Heart Study found that cumulative biological risk, measured by biomarkers including CRP, hgA1C, and HDL, was directly associated with increased neighborhood disadvantage.²⁰ Moreover, while there was some degree of SES heterogeneity in the Jackson Heart Study, the overall household poverty rate of Jackson, MS, was 17.6 % compared to 11.3 % for the rest of the USA, and 73 % of the sample was classified as residing in the "most disadvantaged" neighborhoods.²⁰ The current analysis extends these findings in that the BWHS is a sample of black women with generally high levels of education and income. Overall, 80 % of participants have completed education beyond high school, and 55 % report a household income of \$50,000 or higher.

Neighborhood SES shapes the social, service, and physical environments of residents,^{16,19,46,47} thereby exposing them to behaviors (e.g., physical activity and diet)⁴⁸⁻⁵² and essential resources (e.g., education, employment, and community services)⁵³⁻⁵⁵ that may be beneficial or detrimental to health.⁵⁴ Levels of air pollution also tend to be higher in poor compared to wealthier neighborhoods,⁵⁶ and poor neighborhoods lack safe and accessible places to walk and exercise, as well as sources of healthy foods.⁵⁷⁻⁶⁰ A higher prevalence of poor health behaviors in disadvantaged neighborhoods has been hypothesized to account for variation in CVD risk factors by neighborhood SES. However, in the present study and others,^{4-6,10} a deleterious effect of low neighborhood SES persisted after control

for various personal factors (e.g., physical activity and smoking), but we were unable to control for many factors associated with neighborhood, e.g., sources of healthy foods and air pollution.

The crime, noise, and lack of municipal services that characterize disadvantaged neighborhoods may increase chronic stress levels.⁶¹⁻⁶³ Stress has been hypothesized to produce chronic dysfunction of the body's regulatory systems affecting the autonomic, metabolic, and immune systems, primarily through the hypothalamic-pituitary-adrenal (HPA) axis.^{64,65} The resulting physiological disturbances may accelerate cell aging and death leading to several adverse health outcomes, including CVD.⁶⁶ In a cross-sectional study of 6814 participants in the Multi-Ethnic Study of Atherosclerosis (MESA), higher levels of psychosocial stress, measured as cynical distrust and chronic stress, were associated with higher levels of CRP, and IL-6.⁶⁷ Kulenovic examined plasma lipid levels in relation to posttraumatic stress disorder (PTSD) in a study of male war veterans in Bosnia⁶⁸ and observed significantly lower levels of HDL among those veterans suffering from PTSD compared to those who were not. Other studies in civilian populations^{67,69} have found direct associations between levels of psychosocial stress and triglycerides, A1C, and inverse associations with HDL. Higher levels of education might be expected to be associated with lower levels of stress in that those with more education may possess the resources needed to successfully cope with stressful neighborhood conditions. However, studies suggest that the health benefits of educational attainment are lower for African-Americans compared to Whites, particularly at higher levels of education.⁷⁰ Studies have also shown that at the same level of personal education and income, African-Americans possess only one tenth of the wealth of white Americans and are more likely than whites to live in poorly resourced neighborhoods.^{16,55} Our data from previous analyses in the BWHS showed a significant inverse association between neighborhood SES (measured as median housing value) and hypertension in the BWHS, and the association was present among women with high levels of education (≥ 16 years)¹⁰ In the present study, the association of biomarkers and neighborhood SES was apparent in women at low and high levels of education, although the biomarker profile was in general more favorable in the more highly educated women.

A strength of our study is the high accuracy of biomarker values. Biomarker levels are affected by method of collection, processing, and storage.⁷¹ All blood specimens were obtained and assayed in fully accredited clinical laboratories which followed established, standardized procedures. We were able to control for a large number of important potentially confounding factors. We chose to characterize neighborhood SES as a composite score of six variables identified through factor analysis. Other studies have taken this approach,⁴ and the consistency of our findings of higher rates of diabetes incidence and obesity with neighborhood SES in BWHS is evidence of the validity of this approach.^{6,22,72} The blood samples were obtained from a study intended to assess the feasibility of collecting samples within the BWHS, a large geographically dispersed population. Participants and non-participants were generally similar in terms of important variables, and both groups were similar to the overall BWHS sample. Currently, blood sample collection is proceeding in the entire BWHS cohort, and in the future, it will be possible to assess associations in much larger samples and to assess changes in biomarker levels over time.

In conclusion, the present findings add further evidence that neighborhood SES can translate into measurable, physiological processes independent of individual

characteristics. Understanding the role that residential neighborhoods play in health risk can assist primary care physicians and other caregivers as they implement disease management programs for their patients. It can also inform public health interventionists and health policy advocates as they work to improve the health of communities.

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COMPLIANCE WITH ETHICAL STANDARDS

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