Adverse Housing and Neighborhood Conditions and Inflammatory Markers among Middle-Aged African Americans

Mario Schootman, Elena M. Andresen, Fredric D. Wolinsky,
Theodore K. Malmstrom, John E. Morley, and Douglas K. Miller

ABSTRACT *Adverse housing and neighborhood conditions are independently associated with an increased risk of various diseases and conditions. One possible explanation relates to systemic inflammation, which is associated with these adverse health outcomes. The authors investigated the association between housing and neighborhood conditions with inflammatory markers using data about 352 persons aged 49–65 years from the African American Health study. Participants were identified by a multistage random selection process in 2000 to 2001 (response rate, 76%). Blood was analyzed for soluble cytokine receptors (interleukin-6, tumor necrosis factor α), C-reactive protein, and adiponectin. Neighborhood and housing characteristics consisted of five observed block face conditions (external appearance of the block on which the subject lived), four perceived neighborhood conditions, four observed housing conditions (home assessment by the interviewers rating the interior and exterior of the subject's building), and census-tract level poverty rate from the 2000 census. Differences in some inflammatory markers were found by age, gender, chronic conditions, and body mass index (all Bonferroni-adjusted $p < 0.0034$). There was no association between any of the housing/neighborhood conditions and the pro-inflammatory markers and potential associations between some housing/neighborhood conditions and adiponectin ($p < 0.05$, Bonferroni-adjusted $p > 0.0034$). Inflammation does not appear to be a mediator of the association between poor housing/neighborhood conditions and adverse health outcomes in middle-aged African Americans.*

KEYWORDS *Neighborhood, African American, Disparity, Geography, Inflammation*

Schootman is with the Division of Health Behavior Research, Departments of Medicine and Pediatrics, School of Medicine, Washington University, Saint Louis, MO, USA; Andresen is with the Department of Epidemiology and Biostatistics, College of Public Health and Health Professions, University of Florida, Gainesville, FL, USA; Wolinsky is with the Department of Health Management and Policy, College of Public Health, University of Iowa, Iowa City, IA, USA; Malmstrom is with the Department of Neurology & Psychiatry, School of Medicine, Saint Louis University, St. Louis, MO, USA; Morley is with the Division of Geriatric Medicine, School of Medicine, Saint Louis University, St. Louis, MO, USA; Morley is with the GRECC, VA Medical Center, St. Louis, MO, USA; Miller is with the Indiana University Center for Aging Research and Regenstrief Institute, Inc., School of Medicine, Indiana University, Indianapolis, IN, USA.

Correspondence: Mario Schootman, PhD, Division of Health Behavior Research, Departments of Medicine and Pediatrics, School of Medicine, Washington University, Saint Louis, MO, USA. (E-mail: mschootm@dom.wustl.edu)

Electronic supplementary material The online version of this article (doi:10.1007/s11524-009-9426-8) contains supplementary material, which is available to authorized users.

INTRODUCTION

Adverse neighborhood and housing attributes have been associated with an increased risk of various diseases and conditions, including cardiovascular disease, diabetes mellitus, disability, neurobehavioral deficits, and cancer.¹⁻⁷ Only recently has research focused on the mechanisms by which adverse neighborhood and housing conditions affect health and disease outcomes as potential means for targeting interventions in a context-sensitive manner.⁸ There are several hypothesized, interrelated, and mediating pathways that could provide such opportunities for intervention, including contextual attributes of place (e.g., availability of grocery stores selling fruits and vegetables), health behavior (e.g., physical activity, alcohol consumption), diseases and conditions (e.g., body mass index (BMI)), and psychosocial factors (e.g., anxiety, stress, and depression).⁹

One possible mediating pathway relates to systemic inflammation. Pro-inflammatory markers (e.g., interleukin (IL) 6, tumor necrosis factor (TNF) α , C-reactive protein (CRP)) and anti-inflammatory adipokine (adiponectin) have been linked to increased risk of multiple diseases and conditions, such as cardiovascular disease, diabetes mellitus, disability, and possibly cancer.¹⁰⁻¹⁷ However, few studies have examined the variation of these markers across neighborhood and housing conditions.¹⁸⁻²⁰ In general, these studies have found modest associations, but only area-based measures of socioeconomic status have been used as indicators of neighborhood conditions. Further research is warranted that examines the association of multiple spatial levels with inflammatory markers.

Few studies examining the inflammation-disease/condition association have been conducted among urban African Americans, who appear to have elevated levels of disease and disability relative to other racial and ethnic groups. To our knowledge, only one study has examined the association between adverse neighborhood conditions and inflammatory markers among African Americans,¹⁹ who also appear to have elevated levels of inflammatory markers.^{19,20} Inflammation may play a role in the relationship between adverse housing/neighborhood conditions and increased risk of diabetes and lower-body functional limitations we have observed in the St. Louis African American Health study.^{3,6} Specifically, our adjusted analysis showed that African Americans who lived in neighborhoods with 4 to 5 versus 0 to 1 conditions rated as fair or poor were three times more likely to develop lower-body functional limitations.³ Also, African Americans who lived in houses rated as fair or poor were more likely to develop diabetes than those living in houses rated as good or excellent.⁶ Various individual characteristics were unable to explain these associations, but inflammation was not examined.

In order to explore the possible mediating pathway (inflammation) by which adverse neighborhood and housing conditions are linked with the risk of adverse health outcomes, we examined the cross-sectional association of observed, perceived, and census-based neighborhood and housing conditions with soluble receptors for three pro-inflammatory markers (IL-6, TNF α 1, and CRP) and an anti-inflammatory adipokine (adiponectin) among African Americans. There are three requirements that all need to be fulfilled for mediation to be present: (1) the mediator (inflammation) needs to be predicted by adverse neighborhood/housing conditions, (2) the mediator predicts the adverse health outcome (diabetes, lower-body functional limitations), and (3) the mediator is on the causal pathway between adverse neighborhood/housing conditions and diabetes/lower-body functional limitations.²¹ To examine the first of the three requirements for mediation,

inflammatory markers (the purported mediators) need to be associated with adverse housing/neighborhood conditions (i.e., the exposure of interest),²¹ which is the focus of this study.

METHODS

Study Sample

The sampling design of the African American Health (AAH) cohort has been described elsewhere.²² Briefly, AAH is a population-based cohort study of 998 noninstitutionalized African Americans recruited in 2000 to 2001 using multistage probability sampling. All participants lived in one of two geographic sampling strata: either a poor, inner-city area (St. Louis, MO, USA) or more heterogeneous suburbs just northwest of the City of St. Louis. Interviewers (two thirds of whom were African American) with extensive study-specific training screened households for eligibility criteria, which involved self-reported Black or African American race, birth date from 1936 through 1950, and Mini-Mental State Examination scores ≥ 16 . This age group was selected to examine the progression of subclinical disability to more overt disability. Participants were paid volunteers. Sampling proportions were set to recruit approximately equal numbers of participants from both areas (sampling strata).

All participants received in-home, baseline evaluations between September 2000 and July 2001. Baseline response was 76% (998 out of 1,320). The eligible study sample for the current analysis included 368 AAH participants who donated blood at baseline. All participants were given the opportunity to donate blood, but only 37% of those who participated in the baseline evaluations did. The current cross-sectional analysis was limited to 352 AAH participants for whom complete data were available on all laboratory measures. All procedures were approved by the Institutional Review Boards of the involved institutions.

Inflammatory Markers

Blood was drawn for laboratory analyses shortly after the baseline assessment or at the time of further clinical examinations required for special substudies. Serum was stored at -700°F until the cytokine analyses were performed in 2006. We used plasma concentrations of soluble receptors of IL-6 (expressed in nanograms per milliliter) and TNF α (type 1, expressed in nanograms per milliliter), which reflect the history of inflammatory immune activation rather than actual values of the inflammatory markers, which are more variable.¹⁴ These receptors were selected based on their association with skeletal muscle mass and strength, which are predictors of lower-body functional limitations, disability, and diabetes.^{14,16,17}

Soluble, extracellular, ligand-binding portions of cytokine receptors occur naturally in body fluids and are believed to regulate the biologic activities of cytokines. Thus, soluble receptors may be better markers of chronic cytokine activity.²³ Receptors of IL-6 are stimulated by circulating IL-6²⁴ while TNF α receptors neutralize the effects of TNF α .²⁵ Higher values of these receptors indicate greater inflammation. Soluble IL-6 receptor (IL-6R; expressed in milligrams per liter) was measured with an ELISA kit from ICN-Biomedicals (Costa Mesa, CA, USA). The intra- and interassay coefficients of variation (CV) were 5.0% and 5.9%, respectively. Soluble TNFR1 and sTNFR2 were measured using ELISA kits (BioSource, Camarillo, CA, USA). Intra- and interassay CVs were 4.1% and 7.3%

for sTNFR1 and 5.1% and 8.6% for sTNFR2. CRP was measured with a commercially available High Sensitivity Enzyme Immunoassay (hsCRP 7ELISA) kit from MP Biomedicals (Orangeburg, NY, USA). The intra- and interassay CVs were 4.5% and 4.1%, respectively. Adiponectin was determined using a commercially available radioimmunoassay kit (Linco Research, St. Charles, MO, USA), with intra- and interassay CVs of 5.3% and 8.1%, respectively, and expressed in micrograms per milliliter. Lower values of adiponectin indicate more inflammation.

Adverse Neighborhood and Housing Conditions

Neighborhood and housing characteristics consisted of observed, global impressions of block face conditions (external appearance of the block on which the subject lived), perceived neighborhood conditions reported by AAH participants, observed housing conditions (home assessment by the interviewers rating the interior and exterior of the subject's building), and census-tract level poverty rate from the 2000 census. An observed global impression of the external appearance of the block face (neighborhood) in front of the homes where the participants resided was done by the survey team using a previously published assessment tool²⁶ during household enumeration, which occurred an average of 7 months before the participants were recruited. Using a four-point scale (excellent, good, fair, poor), observers rated each of five characteristics: condition of houses, amount of noise (from traffic, industry, etc.), air quality, condition of the streets, and condition of the yards and sidewalks in front of homes where participants lived. Reliability was acceptable, with weighted interrater Kappa statistics ranging from 0.58 (air quality) to 0.84 (condition of yards and sidewalks).²⁷

We also obtained a perceived measure of neighborhood conditions from respondents at baseline: neighborhood as a place to live (excellent, very good, good, fair, poor), general feelings about the neighborhood (delighted, pleased, mostly satisfied, mixed, mostly dissatisfied, unhappy, terrible), attachment to the neighborhood (very strongly, strongly, undecided, not strongly, not at all), and neighborhood safety from crime (extremely, quite, slightly, not at all).²⁸ Participant responses were dichotomized for each condition (see [Online table](#) and Tables 2, 3, and 4).

Assessment of housing conditions was measured by the interviewer's subjective ratings at the baseline interview of the cleanliness inside the building, physical condition of the interior, condition of furnishings, condition of the exterior of the building, and a global rating (all rated as excellent, good, fair, or poor). The test-retest reliability was at least 0.68 for each condition.⁶ In the present analysis, each block face condition and each housing condition were dichotomized as either fair or poor versus good or excellent.

Using geocoded baseline street addresses, we used the percentage of the population living below the US federal poverty line from the 2000 census for the census-tract level in which each participant lived (average participants per tract=8.4). Street addresses for all subjects were successfully matched to census tracts using three methods: (1) ArcView 3.2 with records preprocessed by ZP4, (2) Centrus GeoCoder for ArcGIS, and (3) a commercial address matching service. Conflicts resulting from the three methods were compared against the 2000 redistricting TIGER file to recover the most accurate source. If none was accurate, the Internet-based EZ-Locate system was used as an alternate source. The poverty rate measure is robust in its association with various diseases and levels of geography; it has potential policy implications and is comparable over time.^{29,30} We not only used the poverty rate as a continuous variable but also grouped

it into three levels similar to previous research³¹—less than 10% (low-poverty rate), 10–19%, 20%, or greater (high-poverty rate)—to allow for nonlinear effects.

Covariates

Covariates included in the analysis were patterned after other research.^{19,20} Covariates involved sampling stratum (inner city, suburb), age, gender, household income (<\$20,000, \$20,000 to <\$50,000, \$50,000, or more, unknown income), and a count of the number of self-reported physician-diagnosed severe chronic conditions ever experienced (asthma, diabetes, chronic airway obstruction, heart failure, heart attack, angina, stroke, chronic kidney disease, arthritis, and cancer other than a minor skin cancer). Also reported were height and weight to calculate BMI (<25, 25–29.9, 30+, unknown), smoking status (current, former, never), and risk of alcohol abuse (score of at least 2 on the CAGE questionnaire).³²

Statistical Analysis

Since values for the inflammatory markers were not normally distributed, these variables were log-transformed. Chi-square tests were used to compare baseline characteristics of the AAH participants who donated blood (study sample) and those who did not or who had missing data on one or more cytokines. We used *t* tests and linear regression to examine the association of each of the adverse neighborhood and housing conditions with each of the inflammatory markers. First, we constructed unadjusted models. Second, we adjusted for age, gender, income, stratum (city or suburban), the number of severe chronic conditions, BMI, smoking status, and risk of alcohol abuse since these covariates were associated with inflammatory markers.¹⁸ When examining census-tract poverty rate, we used a two-level model with the random components assessed at the individual and census-tract level. Least square mean levels of the inflammatory markers were calculated for each level of the neighborhood and housing conditions by exponentiation of parameter estimates. Because of the large number of comparisons, we used the Bonferroni-adjusted alpha level of 0.0034 as statistically significant as well. All analyses were performed in SAS (version 9.1).

RESULTS

Overall, current study participants ($n=352$) were similar to those AAH participants not in the current study ($n=646$), except that the former were more likely to be older (p (uncorrected for multiple testing) <0.01) and to have less education ($p<0.05$) and less likely to be a current smoker ($p<0.01$) and to be male ($p<0.05$) than the latter group (Online table). No significant differences were found between groups for any of the neighborhood or housing conditions. The only significant p value after Bonferroni multiple test correction was for smoking status.

Table 1 displays the unadjusted values of the inflammatory markers and those stratified by the covariates. Because of the high correlation between sTNFR1 and sTNFR2 (Pearson correlation=0.79), we only focused on sTNFR1 values in the current study. Participants who were male, aged 49–55 years, with lower incomes, those with more chronic conditions, and those with higher BMI typically showed more inflammation on some but not all of the markers than their respective counterparts.

Table 2 shows that there were no statistically significant differences in unadjusted (model A) values of any of the inflammatory markers between categories

TABLE 1 Unadjusted least square means for levels of inflammatory markers by covariate value for African American Health participants in the current study ($n=352$)

Covariate	Number	sIL-6R	sTNFR1	CRP	Adiponectin
Total sample	352	56.2	2.74	4.0	6.9
Stratum					
Inner city	156	56.2	2.9	4.0	7.1
Suburban	196	55.6	2.6	4.1	6.6
Gender					
Male	116	74.1 ^{***}	2.5 ^{***}	2.6 ^{***}	5.4 ^{***}
Female	236	49.0	2.9	5.0	7.7
Age group					
49–55	147	55.0	2.5 ^{***}	4.3	6.5
56–65	205	56.9	3.0	3.8	7.2
Income					
<\$20,000	138	58.9	3.1 ^{***}	4.3	7.2
\$20,000 to <\$50,000	149	52.5	2.6	4.2	6.9
\$50,000 or more	57	60.3	2.3	3.4	5.8
Unknown	8	49.0	3.0	3.0	7.6
Number of chronic conditions					
0	52	56.2	2.1 ^{***}	3.2	6.8
1 to 2	175	55.0	2.5	3.8	6.8
3+	125	56.2	3.4	4.8	6.9
Body mass index (kg/m ²)					
<25.0	62	54.6	2.6	1.7 ^{***}	8.4*
25.0–29.9	114	58.8	2.5	3.4	6.4
30.0+	169	53.7	3.0	6.2	6.7
Unknown	7	66.1	2.6	4.3	8.7
Smoking status					
Smoker	88	56.2*	2.9	3.9	6.2
Former smoker	133	58.9	2.8	4.3	6.8
Never smoked	131	52.5	2.6	3.9	7.4
Risk of alcohol abuse (CAGE ≥ 2)					
Yes	63	61.7	2.9	3.2	6.5
No	282	55.0	2.7	4.3	6.9
Unknown	7	53.7	4.0	2.3	9.7

sIL-6R soluble IL6 receptor, sTNFR1 soluble tumor necrosis factor alpha receptor 1, CRP C-reactive protein

* $p<0.05$; ** $p<0.01$; *** $p<0.0034$ (Bonferroni adjusted) between covariate groups

of the five block face conditions before or after using the Bonferroni-adjusted correction. Adding the covariates (model B) to these models showed that persons who lived on block faces where housing conditions and sidewalk quality were rated as good or excellent had higher values of adiponectin before Bonferroni adjustment but not after this adjustment. Persons who lived on block faces or yards and sidewalks rated as good or excellent had higher adiponectin values ($p<0.05$, but Bonferroni-adjusted $p>0.0034$). There were no statistically significant differences after using the Bonferroni-adjusted correction in values of the inflammatory markers between categories of the five housing conditions (Table 3) or between categories of each of the four perceived neighborhood conditions (Table 4) with either model A or model B adjustments. However, persons who lived in buildings rated as good or excellent had higher adiponectin values ($p<0.05$, but Bonferroni-adjusted $p>0.0034$). Also, there were no associations between census-tract

TABLE 2 Unadjusted and adjusted least square means for levels of inflammatory markers by observed block face condition for African American Health participants in the current study (*n*=352)

Observed block face condition	sIL-6R		sTNFR1		CRP		Adiponectin	
	Model A	Model B	Model A	Model B	Model A	Model B	Model A	Model B
Housing conditions								
Fair–poor	55.1	53.7	2.9	2.7	4.4	4.2	6.6	6.3*
Good–excellent	56.7	57.5	2.7	2.8	4.0	3.9	7.1	7.4
Noise level from traffic, industry, etc.								
Fair–poor	56.4	55.8	2.8	2.7	3.9	3.9	7.0	7.1
Good–excellent	55.9	56.0	2.7	2.8	4.0	4.1	6.8	6.8
Air quality								
Fair–poor	56.3	55.0	2.9	2.8	4.2	4.0	6.7	6.6
Good–excellent	56.0	56.2	2.7	2.8	4.0	4.0	6.9	6.9
Street and road quality								
Fair–poor	54.1	53.7	2.9	2.8	4.2	4.4	6.7	6.6
Good–excellent	56.9	56.2	2.7	2.8	4.0	3.9	7.0	6.9
Yard and sidewalk quality								
Fair–poor	54.7	53.7	2.7	2.7	4.1	4.2	6.7	6.2*
Good–excellent	56.9	57.5	2.9	2.8	4.0	3.9	7.1	7.6

sIL-6R soluble IL6 receptor, sTNFR1 soluble tumor necrosis factor alpha receptor 1, CRP C-reactive protein, Model A unadjusted, Model B adjusted for age, gender stratum, income, alcohol use, smoking, chronic conditions, and body mass index

p*<0.05; *p*<0.01; ****p*<0.0034 (Bonferroni adjusted)

TABLE 3 Unadjusted and adjusted least square means for levels of inflammatory markers by observed housing condition for African American Health participants in the current study (*n*=352)

Observed housing condition	sIL-6R		sTNFR1		CRP		Adiponectin	
	Model A	Model B	Model A	Model B	Model A	Model B	Model A	Model B
Cleanliness inside building								
Fair–poor	54.2	53.7	2.7	2.7	4.0	4.0	6.4	6.3
Good–excellent	56.9	56.2	2.7	2.8	4.0	4.0	7.1	7.1
Physical condition inside building								
Fair–poor	55.3	53.7	2.8	2.7	4.1	4.2	6.2*	6.2*
Good–excellent	56.4	56.2	2.7	2.8	4.0	4.0	7.2	7.2
Furnishings inside building								
Fair–poor	57.3	56.2	2.8	2.7	3.8	3.8	6.6	6.6
Good–excellent	58.5	56.2	2.7	2.8	4.2	4.2	7.0	7.1
Condition on outside of building								
Fair–poor	57.5	56.2	2.9	2.8	4.1	4.1	6.6	6.6
Good–excellent	55.4	56.2	2.7	2.7	4.0	4.0	7.0	7.1
Overall condition of dwelling								
Fair–poor	57.9	56.2	2.8	2.8	4.1	3.9	6.2*	6.3
Good–excellent	55.3	56.2	2.7	2.8	3.8	4.1	7.2	7.1

sIL-6R soluble IL6 receptor, sTNFR1 soluble tumor necrosis factor alpha receptor 1, CRP C-reactive protein, Model A unadjusted, Model B adjusted for age, gender, stratum, income, alcohol use, smoking, chronic conditions, and body mass index

p*<0.05; *p*<0.01; ****p*<0.0034 (Bonferroni adjusted)

TABLE 4 Unadjusted and adjusted least square means for levels of inflammatory markers by perceived neighborhood condition for participants African American Health participants in the current study (*n*=352)

Perceived block face condition	sIL-6R		sTNFR1		CRP		Adiponectin	
	Model A	Model B	Model A	Model B	Model A	Model B	Model A	Model B
Rating of neighborhood								
Fair–poor	56.5	55.0	3.0*	2.9	3.7	3.8	6.8	6.6
Good–excellent	55.9	56.2	2.6	2.7	4.2	4.2	6.9	7.1
General feeling about neighborhood								
Mixed or terrible	53.5	53.7	2.8	2.7	4.1	4.0	6.7	6.5
Mostly satisfied–delighted	57.2	57.5	2.7	2.8	4.0	4.1	6.9	7.1
Attachment to neighborhood								
Undecided or not at all	56.8	57.5	2.8	2.8	4.3	4.3	6.8	6.8
Strongly–very strongly	55.5	55.0	2.7	2.7	3.8	3.9	7.0	7.1
Neighborhood safety								
Slightly safe–not at all	57.2	57.5	2.9	2.8	4.2	4.2	6.9	6.8
Quite safe–extremely safe	55.1	55.0	2.7	2.8	3.9	3.9	6.8	7.1

sIL-6R soluble IL6 receptor, sTNFR1 soluble tumor necrosis factor alpha receptor 1, CRP C-reactive protein, Model A unadjusted, Model B adjusted for age, gender stratum, income, alcohol use, smoking, chronic conditions, and body mass index

p*<0.05; *p*<0.01; ****p*<0.0034 (Bonferroni adjusted)

poverty rate and any of the inflammatory markers in an age–sex–stratum–income adjusted model (all *p* values>0.05) or when also adding risk of alcohol abuse, smoking, chronic conditions, and BMI to this model (all *p* values>0.05). This observation held true when using poverty rate as either a continuous or categorical variable (data not shown).

DISCUSSION

Attributes of subject location were not associated with pro- and anti-inflammatory markers in our study of urban-dwelling African Americans after Bonferroni adjustment. However, higher adjusted values were found for adiponectin for persons who lived on block faces where housing conditions and yard and sidewalk quality were rated as good or excellent prior but not after Bonferroni adjustment. Also, persons who lived in buildings where the physical condition was rated as good or excellent had higher adiponectin value prior but not after Bonferroni adjustment. To our knowledge, there is only one published study available for comparison. Pollitt and colleagues¹⁹ failed to show an association between census-tract socioeconomic position and pro-inflammatory markers among African Americans in adjusted analysis. Our data confirm these findings, based on our use of census-tract poverty rate. Our study goes beyond their findings by showing that the results are the same when examining observed block face, observed housing, and self-reported neighborhood conditions after Bonferroni adjustment. Because one of the three requirements that need to be fulfilled for mediation is that a mediator is associated with the independent variable of interest,²¹ inflammation is unlikely to be a mediator for the association of adverse housing and neighborhood conditions with the risk of diabetes and lower-body functional limitations we previously observed in the African American Health study population based on the lack of a cross-sectional association in the current study.^{3,6} We used soluble receptors of IL-6 and TNFα

because these are more long lived in the circulation and represent evidence of activation of the pro-inflammatory system.

The association between adverse neighborhood conditions and inflammatory markers may differ by race and sociocultural constructs. Studies have shown an association among Whites,¹⁹ a population in Glasgow, Scotland,¹⁸ and among a population-based sample comprised of 23% African Americans,²⁰ but not among African Americans *per se*.¹⁹ Therefore, the mediating pathway of inflammation by which adverse neighborhood and housing conditions affect health and disease may vary by race and sociocultural constructs.

Although the identified associations between adverse block face/housing conditions and adiponectin were neither highly significant nor consistently found across all conditions, the potential for a mediating role by adiponectin is intriguing. Adiponectin is an insulin-sensitizing, anti-inflammatory, and antiproliferative adipokine that decreases with increased adiposity and has shown inverse associations with incident diabetes mellitus, coronary artery disease progression, and severity of peripheral arterial disease.^{33–35} Notably, African Americans have lower adiponectin and higher arterial stiffness (an indicator of adverse effects on arteries) than Whites, and adiponectin has been shown to be independently associated with arterial stiffness in Blacks but not in Whites.³⁶ Additionally, peripheral arterial disease has been shown to be twice as prevalent in Blacks as in Whites³⁷ and to independently predict decline in lower-body functioning.³⁸ Hence, adiponectin may have played a potential role in the effect of adverse block face/housing conditions on declines in lower-body functioning and risk of diabetes that we showed in this population^{3,6} through its effects on peripheral arteries. Because of the tentative nature of our findings, future studies should explore this in more detail.

As with any negative study, lack of statistical power may have been an issue. Although there were only 352 participants available for analysis, lack of power is unlikely to have been an issue in our study since generally the differences in values of the inflammatory markers between categories of the neighborhood and housing conditions were very small and the expected statistical association between these markers and some of the covariates were demonstrable (Table 1).

It also can be hypothesized that our null findings are the result of our use of a limited number of inflammatory markers. However, Pollitt and colleagues observed no association of census-tract socioeconomic position with fibrinogen and white blood cell counts in addition to CRP, suggesting that our use of sIL-6R, sTNF α , and adiponectin unlikely influenced our results. Second, we used soluble receptors of the inflammatory markers rather than their actual serum values. In contrast to cytokines, soluble receptors tend to have longer half-lives and as such may be better markers of chronic cytokine activity. This suggests that neither acute inflammation, based on Pollitt's use of serum cytokines,¹⁹ nor chronic inflammation, based on our use of soluble receptors, plays a role in risk of diabetes and lower-body functional limitations among African Americans.

A third possible reason for our null findings is that the effect of adverse neighborhood and housing conditions on inflammatory markers may have been buffered by anti-inflammatory mechanisms. Some persons who lived under these adverse circumstances may have developed coping mechanisms or a social network that buffered the hypothesized association.^{26,39} Another hypothesis is that anti-inflammatory medication use may have been higher among those living under adverse neighborhood and housing conditions. This is unlikely to be an explanation for our null results because use of nonsteroidal anti-inflammatory drugs (NSAID)

does not vary dramatically among large geographic areas.^{40,41} Unfortunately, less is known about NSAID use across smaller geographic areas.

A fourth possible reason for our findings might be that our study population lived in two relatively small geographic areas, which may have limited the variability in housing and neighborhood conditions. An argument against this is that prior analyses of these data showed that these housing and neighborhood conditions did increase the risk of developing lower-body functional limitations and diabetes.^{3,6}

A fifth potential reason for our observed lack of an association is our use of general methods of housing and neighborhood conditions. Adverse health effects and inflammatory markers could be associated with more specific housing conditions, such as fungi, mold, and moisture, but they were not measured.⁴² Future studies could examine this using more detailed housing and neighborhood assessments.^{43,44}

The strengths of our study include the use of a single race (which helps reduce the effects of the strong interrelationship between race and socioeconomic status) and the use of multiple levels of spatial aggregation and its associated conditions. However, the results of our study may not be generalizable because we included only a single racial group with a restricted age range from one metropolitan area. Nonetheless, we found that adverse conditions at the census-tract, block face, dwelling unit, and self-reported neighborhood satisfaction levels were not associated with the inflammatory markers among urban African Americans, suggesting that inflammation is likely not a mediator of the relationship between adverse housing/neighborhood conditions and risk of disease and disability in the African American Health study.

Funding. This work was supported by the National Institutes of Health (AG-10436 to D.K.M). Dr. Wolinsky is supported, in part, as a Research Scientist at the Department of Veterans Affairs Medical Centers of Iowa City, IA, USA.

REFERENCES

1. Pickett K, Pearl M. Multilevel analyses of neighborhood socioeconomic context and health outcomes: a critical review. *J Epidemiol Community Health*. 2001;55:111-122.
2. Kawachi I, Berkman L. Introduction. In: Kawachi I, Berkman L, eds. *Neighborhoods and Health*. New York: Oxford University Press; 2003:1-19.
3. Schootman M, Andresen E, Wolinsky F, Malmstrom T, Miller J, Miller D. Neighborhood conditions and risk of incident lower-body functional limitations among middle-aged African Americans. *Am J Epidemiol*. 2006;163:450-458.
4. Stjarne MK, Fritzell J, De Leon AP, Hallqvist J. Neighborhood socioeconomic context, individual income and myocardial infarction. *Epidemiology*. 2006;17(1):14-23.
5. Eschbach K, Mahnken J, Goodwin J. Neighborhood composition and incidence of cancer among Hispanics in the United States. *Cancer*. 2005;103(5):1036-1044.
6. Schootman M, Andresen EM, Wolinsky FD, et al. The effect of adverse housing and neighborhood conditions on the development of diabetes mellitus among middle-aged African Americans. *Am J Epidemiol*. 2007;166:379-387.
7. World Health Organization Regional Office for Europe. *Report on the WHO technical meeting on quantifying disease from inadequate housing. Bonn, Germany, November 28-30, 2005*. Copenhagen, Denmark 2005.
8. Cummins S, Curtis S, Diez-Roux AV, Macintyre S. Understanding and representing 'place' in health research: a relational approach. *Soc Sci Med*. 2007;65(9):1825-1838.

9. Daniel M, Moore S, Kestens Y. Framing the biosocial pathways underlying associations between place and cardiometabolic disease. *Health Place*. 2008;14(2):117-132.
10. Ridker P. Inflammatory biomarkers and risks of myocardial infarction, stroke, diabetes, and total mortality: implications for longevity. *Nutr Rev*. 2007;65(s3):S253-S259.
11. Pradhan AD, Manson JE, Rifai N, Buring JE, Ridker PM. C-reactive protein, interleukin 6, and risk of developing type 2 diabetes mellitus. *JAMA*. 2001;286(3):327-334.
12. Heikkilä K, Ebrahim S, Lawlor DA. Systematic review of the association between circulating interleukin-6 (IL-6) and cancer. *Eur J Cancer*. 2008;44(7):937-945.
13. Seruga B, Zhang H, Bernstein LJ, Tannock IF. Cytokines and their relationship to the symptoms and outcome of cancer. *Nat Rev Cancer*. 2008;8(11):887-899.
14. Haren M, Malmstrom T, Miller D, et al. Higher C-reactive protein and soluble tumor necrosis factor receptor levels are associated with poor physical function and disability: a cross-sectional analysis of a cohort of late middle-aged African Americans. *J Gerontol Med Sci*. 2010; in press.
15. Brinkley TE, Leng X, Miller ME, et al. Chronic inflammation is associated with low physical function in older adults across multiple comorbidities. *J Gerontol A Biol Sci Med Sci*. 2009;64A(4):455-461.
16. Toth MJ, Ades PA, Tischler MD, Tracy RP, LeWinter MM. Immune activation is associated with reduced skeletal muscle mass and physical function in chronic heart failure. *Int J Cardiol*. 2006;109(2):179-187.
17. Duncan BB, Schmidt MI, Pankow JS, et al. Adiponectin and the development of type 2 diabetes. *Diabetes*. 2004;53(9):2473-2478.
18. Welsh P, Woodward M, Rumley A, Lowe G. Associations of plasma pro-inflammatory cytokines, fibrinogen, viscosity and C-reactive protein with cardiovascular risk factors and social deprivation: the fourth Glasgow MONICA study. *Br J Haematol*. 2008;141(6):852-861.
19. Pollitt RA, Kaufman JS, Rose KM, Diez-Roux AV, Zeng D, Heiss G. Cumulative life course and adult socioeconomic status and markers of inflammation in adulthood. *J Epidemiol Community Health*. 2008;62(6):484-491.
20. Petersen KL, Marsland AL, Flory J, Votruba-Drzal E, Muldoon MF, Manuck SB. Community socioeconomic status is associated with circulating interleukin-6 and C-reactive protein. *Psychosom Med*. 2008;70(6):646-652.
21. MacKinnon DP. *Introduction to Statistical Mediation Analysis*. New York: Lawrence Erlbaum Associates; 2008.
22. Miller DK, Malmstrom TK, Joshi S, Andresen EM, Morley JE, Wolinsky FD. Clinically relevant levels of depressive symptoms in community-dwelling middle-aged African Americans. *J Am Geriatr Soc*. 2004;52(5):741-748.
23. Morley JE, Baumgartner RN. Cytokine-related aging process. *J Gerontol A Biol Sci Med Sci*. 2004;59(9):M924-M929.
24. Novick D, Shulman LM, Chen L, Revel M. Enhancement of interleukin 6 cytostatic effect on human breast carcinoma cells by soluble IL-6 receptor from urine and reversion by monoclonal antibody. *Cytokine*. 1992;4(1):6-11.
25. Mohler KM, Torrance DS, Smith CA, et al. Soluble tumor necrosis factor (TNF) receptors are effective therapeutic agents in lethal endotoxemia and function simultaneously as both TNF carriers and TNF antagonists. *J Immunol*. 1993;151(3):1548-1561.
26. Krause N. Neighborhood deterioration, religious coping, and changes in health during late life. *Gerontologist*. 1998;38(6):653-664.
27. Andresen E, Malmstrom T, Miller D, Wolinsky F. Reliability and validity of observer ratings of neighborhoods. *J Aging Health*. 2006;18:28-36.
28. Chandola T. The fear of crime and area differences in health. *Health Place*. 2001;7:105-116.
29. Singh G, Miller B, Hankey B, Edwards B. *Area Socioeconomic Variations in U.S. Cancer Incidence, Mortality, Stage, Treatment, and Survival, 1975-1999*. Bethesda: National Cancer Institute; 2003.

30. Krieger N, Chen J, Waterman P, Soobader M, Subramanian S, Carson R. Geocoding and monitoring of socioeconomic inequalities in mortality and cancer incidence: does the choice of area-based measure and geographic level matter? *Am J Epidemiol*. 2002;156:471-482.
31. Schootman M, Andresen EM, Wolinsky FD, Malmstrom TK, Miller JP, Miller DK. Neighbourhood environment and the incidence of depressive symptoms among middle-aged African Americans. *J Epidemiol Community Health*. 2007;61(6):527-532.
32. Mayfield D, McLeod G, Hall P. The CAGE questionnaire: validation of a new alcoholism screening instrument. *Am J Psychiatry*. 1974;131:1121-1123.
33. Li S, Shin HJ, Ding EL, van Dam RM. Adiponectin levels and risk of type 2 diabetes: a systematic review and meta-analysis. *JAMA*. 2009;302(2):179-188.
34. Liang K-W, Sheu WH-H, Lee W-L, et al. Decreased circulating protective adiponectin level is associated with angiographic coronary disease progression in patients with angina pectoris. *Int J Cardiol*. 2008;129(1):76-80.
35. Golledge J, Leicht A, Crowther RG, Clancy P, Spinks WL, Quigley F. Association of obesity and metabolic syndrome with the severity and outcome of intermittent claudication. *J Vasc Surg*. 2007;45(1):40-46.
36. Nguyen QM, Srinivasan SR, Xu J-H, Chen W, Berenson GS. Racial (black-white) divergence in the association between adiponectin and arterial stiffness in asymptomatic young adults: the Bogalusa Heart Study. *Am J Hypertens*. 2008;21(5):553-557.
37. Selvin E, Erlinger TP. Prevalence of and risk factors for peripheral arterial disease in the United States: results from the National Health and Nutrition Examination Survey, 1999-2000. *Circulation*. 2004;110(6):738-743.
38. McDermott M, Tian L, Ferrucci L, et al. Associations between lower extremity ischemia, upper and lower extremity strength, and functional impairment with peripheral arterial disease. *J Am Geriatr Soc*. 2008;56(4):724-729.
39. Ford ES, Loucks EB, Berkman LF. Social integration and concentrations of C-reactive protein among US adults. *Ann Epidemiol*. 2006;16(2):78-84.
40. Glasser SP, Cushman M, Prineas R, et al. Does differential prophylactic aspirin use contribute to racial and geographic disparities in stroke and coronary heart disease (CHD)? *Prev Med*. 2008;47(2):161-166.
41. Shahar E, Folsom AR, Romm FJ, et al. Patterns of aspirin use in middle-aged adults: the Atherosclerosis Risk in Communities (ARIC) Study. *Am Heart J*. 1996;131(5):915-922.
42. Hardin B, Kelman B, Saxon A. Adverse human health effects associated with molds in the indoor environment. *J Occup Environ Med*. 2003;45(5):470-478.
43. Centers for Disease Control and Prevention and U.S. Department of Housing and Urban Development. *Healthy Housing Inspection Manual*. Atlanta: US Department of Health and Human Services; 2008.
44. U.S. Department of Housing and Urban Development and U.S. Census Bureau. *Current housing reports, series H170/04-59, American Housing Survey for the St. Louis Metropolitan Area*; 2004.