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Sharlene D. Newman

sdnewman@ua.edu

The University of Alabama

D. Nichole Pompey

The University of Alabama

Linda Knol

The University of Alabama

Wanda Burton

The University of Alabama

Paige Johnson

The University of Alabama

Letisha Scott

The University of Alabama

Amie Brunson

The University of Alabama

Matthew Hudnall

The University of Alabama

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Heterogeneity in the Association Between Anemia and Blood Pressure in a Rural Population

Sharlene D. Newman¹, D. Nichole Pompey¹, Linda Knol², Wanda Burton³, Paige Johnson³,
Letisha Scott³, Amie Brunson⁴, Matthew Hudnall⁵

1. Alabama Life Research Institute, The University of Alabama, Tuscaloosa, AL

2. Department of Human Nutrition, Hospitality and Sport Management The University of
Alabama, Tuscaloosa, AL

3. Capstone College of Nursing, The University of Alabama, Tuscaloosa, AL

4. School of Social Work, The University of Alabama, Tuscaloosa, AL

5. Culverhouse Business School, The University of Alabama, Tuscaloosa, AL

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Corresponding Author

Sharlene D. Newman, Ph.D.

Executive Director, Alabama Life Research Institute

Professor, Psychology Department

Adjunct Professor, Electrical and Computer Engineering

The University of Alabama

1402B NE Medical Building, Box 870328

Tuscaloosa, AL 35487

sdnewman@ua.edu

Abstract

Objective: The relationship between anemia and blood pressure remains incompletely understood, with previous studies reporting inconsistent findings. We examined whether the association between anemia and blood pressure differed across demographic groups in a rural population.

Methods: Clinical data from the Alabama State Health Information Exchange were analyzed for 1,212 adults (579 African American, 633 White). Multivariable linear models were used to examine the independent and interactive effects of anemia, race, gender, and age on systolic and diastolic blood pressure. Significant interactions were further evaluated using sex-stratified models and least squares mean comparisons.

Results: Significant race $\times$ anemia and race $\times$ gender $\times$ anemia interactions were observed for both systolic and diastolic blood pressure. Sex-stratified analyses showed that these interactions were driven primarily by men, whereas no significant race $\times$ anemia interactions were observed among women. Among men, African American participants with anemia had higher systolic and diastolic blood pressure than African American men without anemia, whereas the association between anemia and blood pressure was attenuated or reversed among White men. These findings demonstrate that the association between anemia and blood pressure is not uniform across the study population but differs across demographic groups.

Conclusions: We found evidence that the relationship between anemia and blood pressure is heterogeneous. Demographic variables identified this heterogeneity, but the mechanisms underlying these differences were not measured and likely involve differing biological, clinical, environmental, and psychosocial exposures rather than race itself. These findings highlight the importance of considering effect modification when evaluating the relationship between anemia

50 and hypertension and suggest that future studies should directly measure the biological and
51 social factors underlying this heterogeneity to better understand hypertension risk.

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53 Key words: blood pressure, anemia, race, gender

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Introduction

Hypertension remains one of the leading modifiable risk factors for cardiovascular disease and premature mortality worldwide [1, 2]. Although improvements in screening and treatment are capable of reducing the burden of uncontrolled hypertension [3], substantial disparities persist across racial, gender, and geographic populations [4, 5]. African American adults experience an earlier onset of hypertension, higher prevalence, poorer blood pressure control, and greater risks of cardiovascular disease than White adults in the United States [6, 7]. Similarly, rural populations experience a disproportionate burden of hypertension [8, 9], reflecting differences in healthcare access, socioeconomic conditions, environmental exposures, and other social determinants of health. These persistent disparities suggest that blood pressure regulation is influenced not only by traditional cardiovascular risk factors but also by the broader biological, environmental, and structural contexts in which individuals live.

Anemia is another common condition that disproportionately affects many of the same populations that experience elevated risk for hypertension. National data indicate that anemia is more prevalent among women than men and among African American adults compared with White adults, with the highest prevalence observed among African American women [10]. Despite the overlap in populations affected by hypertension and anemia, the relationship between these conditions remains incompletely understood. Anemia reduces oxygen-carrying capacity and initiates compensatory cardiovascular responses that may alter vascular resistance, cardiac output, and autonomic regulation [11]. Hemoglobin concentration also influences blood viscosity, providing an additional mechanism through which anemia may affect blood pressure [12,13]. However, previous studies have reported inconsistent findings, with both lower and higher hemoglobin concentrations associated with blood pressure and some studies reporting an inverse relationship between anemia and hypertension [14,15]. These

inconsistencies suggest that the relationship between anemia and blood pressure may vary according to the biological and social contexts in which individuals live.

Recent evidence supports a bidirectional relationship in which anemia and hypertension may each contribute to the development or progression of the other [16]. One example is the interrelationship among anemia, chronic kidney disease, and cardiovascular disease. The triad of anemia, renal insufficiency, and heart failure, termed the cardio-renal anemia syndrome (CRS), represents a vicious cycle in which each condition exacerbates the others, accelerating cardiovascular events and increasing mortality, although the underlying mechanisms are complex and multifactorial [17,18,19]. Factors that may underlie the relationship between blood pressure and anemia are likely those that have been found to affect blood pressure including underlying biological, clinical, environmental, and psychosocial factors; factors that differ across both race and gender. Race and gender may therefore be viewed as markers of these broader exposures rather than as causal determinants themselves [20,21,22]. However, relatively few studies have examined whether the association between anemia and blood pressure varies across demographic groups, particularly in rural populations where both hypertension and anemia are highly prevalent.

West Alabama, including parts of the Alabama Black Belt, a region named after its rich soil [23], provides an important setting in which to investigate these relationships. The region experiences a disproportionate burden of cardiovascular disease, hypertension [24,25], and socioeconomic disadvantage [26] and includes a large rural population with persistent inequities in health outcomes [27]. Using clinical data from the Alabama State Health Information Exchange (HIE), we examined the independent and interactive associations of anemia, race, gender, and age with systolic and diastolic blood pressure. We hypothesized that the association between anemia and blood pressure would differ across demographic groups defined by race and gender, reflecting differences in the underlying biological, clinical, environmental, and

psychosocial factors represented by these characteristics. Identifying such heterogeneity may provide insight into the mechanisms contributing to hypertension risk and help explain the inconsistent findings reported in previous studies.

Methods

Study Design and Data Source. This study is part of a larger project designed to better understand and address factors that may underlie the high rate of hypertension in West Alabama. A retrospective analysis of blood pressure data from Alabama's HIE from West Alabama counties from February 4, 2026 to March 19, 2026 was conducted. The authors obtained minimally identifiable protected health information. All data were transferred to a secure server and stored in a HIPAA-compliant environment, with access restricted to research team members approved by the Institutional Review Board (IRB). The sample included single clinic visits of 3,462 adult participants with available demographic and clinical information, including race, gender, age, blood pressure, and anemia lab measures (e.g., hematocrit, hemoglobin or red blood cell count) values. All analyses were conducted using SAS 9.4, with significance defined at alpha level 0.05.

Ethics Statement. The study was approved by the University of Alabama IRB (# 23-08-6857). A waiver of written informed consent was obtained from the IRB.

Statistical Analyses. Continuous variables were not normally distributed; however, given the large sample size (N=1,212) and balanced group structure, general linear models (GLMs) was retained because of its robustness to moderate departures from normality. Separate GLMs were estimated for systolic and diastolic blood pressure. Independent variables included race, gender, age, anemia, and selected interaction terms. Both models included race × gender, race × anemia, gender × anemia, age × anemia, and the three-way interaction of race × gender × anemia; the systolic blood pressure model additionally included an age × gender interaction.

Participant Description. The analytic sample included 1,212 participants, of whom 579 (47.8%) were African American, 633 (52.2%) White, 332 (27.4%) men, and 880 (72.6%) women. Anemia was defined using hemoglobin, hematocrit, and red blood cell count values (See Table S1). Overall, anemia was more prevalent among African American participants than White participants and among women than men. The prevalence of anemia was highest among African American women (105/444, 23.6%), followed by African American men (23/135, 17.0%), White women (46/436, 10.6%), and White men (20/197, 10.2%). Table 1 presents a description of the participants.

Table 1: Participant Description							
Data Statistic	Overall N = 1212	Women N = 880	Men N = 332	White N = 633	African American N = 579	Not Anemic N = 1018	Anemic N = 194
Age (years)	48.61	46.85	53.29	48.51	48.73	49.15	45.79
Mean (SD)	(17.4)	(17.44)	(16.5)	(16.6)	(18.3)	(17.0)	(19.0)
Median	48	45	56.5	49	47	49	41
Min, Max	18, 99	18, 99	18, 79	18, 87	18, 99	18, 99	18, 88
Systolic	123.55	122.89	125.34	121.55	125.71	123.39	124.38
Mean (SD)	(17.2)	(17.15)	(17.1)	(16.8)	(17.4)	(16.9)	(18.6)
Median	121.5	120	124	120	124	122	121
Min, Max	81, 194	81, 190	85, 194	81, 194	91, 190	81, 194	85, 194
Diastolic	78.47	79.04	76.91	76.71	80.37	78.51	78.28
Mean (SD)	(10.2)	(10.7)	(8.70)	(9.2)	(11.0)	(9.9)	(11.9)
Median	78	78	78	77	79	78	77
Min, Max	48, 121	48, 121	54, 104	48, 108	59, 121	48, 121	49, 108

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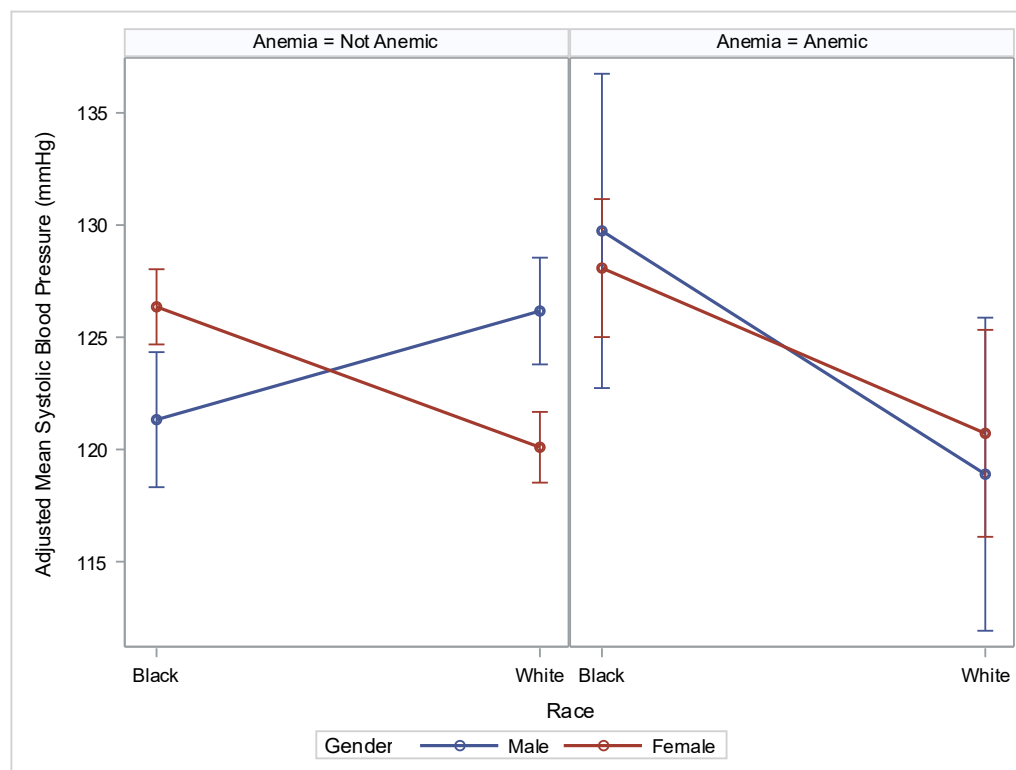


Figure 1: The figure depicts the 3-way interaction between race, gender and anemia status. As shown, the association between race and anemia status is similar for women (red line) showing that systolic BP is lower in White women compared to Black women. However, for men the association between race and systolic BP varies with anemia status (blue line).

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Results

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Systolic Blood Pressure. A GLM identified significant main effects of age ($F = 53.36$, $p <$

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0.0001), race ($F = 10.23$, $p = 0.0014$), and gender ($F = 5.33$, $p = 0.0212$) on systolic blood

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pressure (see Table S2.1 for complete results). Significant interactions were observed for age $\times$

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gender ($F = 7.36$, $p = 0.0068$), race $\times$ anemia ($F = 7.50$, $p = 0.0063$), and the three-way

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interaction of race $\times$ gender $\times$ anemia ($F = 5.65$, $p = 0.0176$; see Figure 1), indicating that the

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association between anemia and systolic blood pressure differed by both race and gender.

Adjusted least-squares means are presented in Table S2.3. Among African American men, anemia was associated with an 8.4 mmHg higher adjusted systolic blood pressure compared with non-anemic African American men, representing the largest difference observed. In contrast, anemia was associated with a 7.2 mmHg lower adjusted systolic blood pressure among White men. Differences associated with anemia were minimal among women (+1.7 mmHg for African American women and +0.6 mmHg for White women). Pairwise comparisons

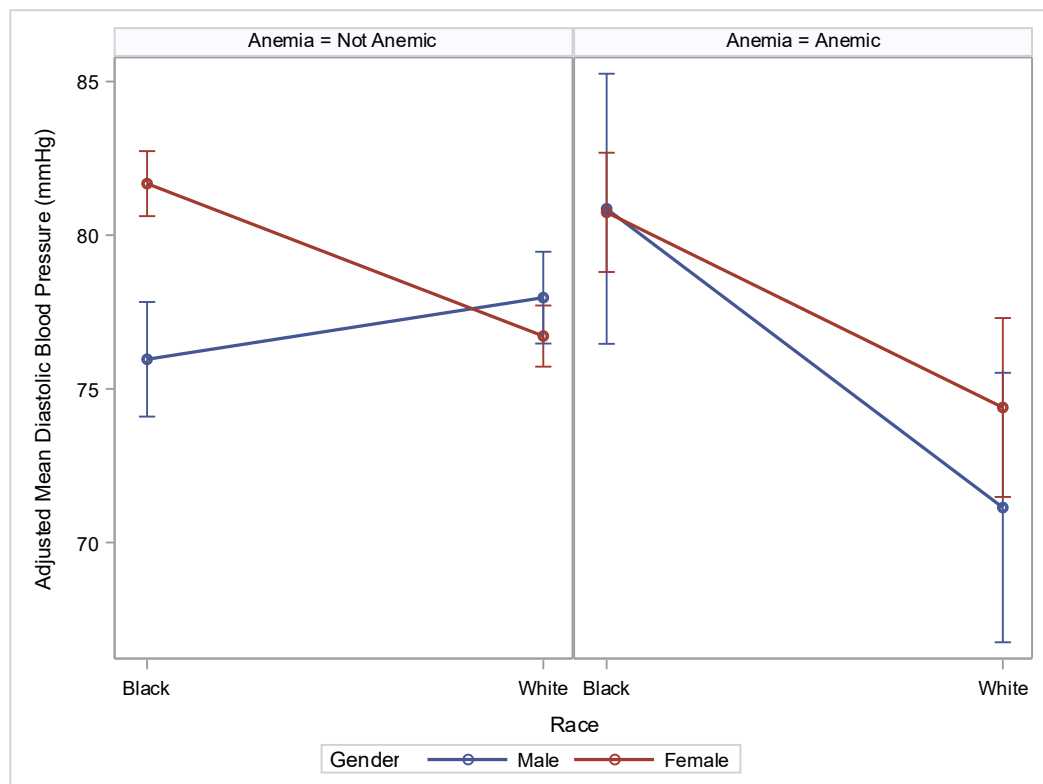


Figure 2. The figure depicts the 3-way interaction between race, gender and anemia status. As shown, the association between race and anemia status is similar for women (red line) showing that diastolic BP is lower in White women compared to Black women. However, for men the association between race and diastolic BP varies with anemia status (blue line).

showed that African American women, regardless of anemia status, had significantly higher adjusted systolic blood pressure than non-anemic White women, and anemic African American women had higher adjusted mean systolic blood pressure than non-anemic African American men ($p = 0.0430$). Complete pairwise comparisons are provided in Supplementary Table S2.3.

Diastolic Blood Pressure. A multivariable linear model evaluated the effects of race, gender, age, anemia status, and their interactions on diastolic blood pressure. Race was a significant predictor of diastolic blood pressure ($F = 24.15$, $p < 0.0001$), while gender showed a marginal association ($F = 3.61$, $p = 0.0578$). Significant interactions were observed between race and anemia status ($F = 11.48$, $p = 0.0007$) and among race, gender, and anemia status ($F = 7.14$, $p = 0.0077$; see Figure 2), indicating that the association between anemia and diastolic blood pressure differed by race and gender. See Table S3.1 for complete results.

Adjusted least squares mean comparisons demonstrated that African American men with anemia had a 4.9 mmHg higher adjusted mean diastolic blood pressure compared with African American men without anemia, representing the largest anemia-associated increase (Table S3.3). In contrast, anemia was associated with lower adjusted mean diastolic blood pressure among White men and White women. Pairwise comparisons showed that African American anemic men had significantly higher adjusted mean diastolic blood pressure than White anemic men ($p = 0.0422$). African American women had significantly higher adjusted mean diastolic blood pressure than African American men and White women regardless of anemia status (p -values ≤ 0.0120). Overall, these findings indicate that the relationship between anemia and diastolic blood pressure varies according to the combined effects of race and gender.

Models by Gender. Because the significant three-way interaction indicated potential gender-specific effects, separate models were estimated for men and women. The observed three-way interaction was primarily driven by differences among men. Among women, there was no evidence of a race $\times$ anemia interaction for systolic blood pressure ($F_s < 1$). In contrast, men demonstrated significant race $\times$ anemia interactions for both systolic ($F(1,321) = 8.08$, $p = 0.0048$) and diastolic blood pressure ($F(1,321) = 18.19$, $p < 0.0001$). Detailed results from the gender-stratified models are provided in the Supplementary Materials.

Discussion

This study examined the relationship between anemia and blood pressure in a rural population while considering potential effect modification by race and gender. The principal finding was that the association between anemia and blood pressure was not uniform across the study population but differed across demographic groups defined by race and gender. Significant race $\times$ anemia and race $\times$ gender $\times$ anemia interactions were observed for both systolic and diastolic blood pressure, indicating heterogeneity in the association between anemia and blood pressure across these groups. Although the prevalence of anemia in our sample differed somewhat from national estimates, with lower rates among African American men and women and higher rates among White men and women [28] compared to the national averages, these differences do not explain the observed interactions. Rather, the findings suggest that the relationship between anemia and blood pressure varies across populations. While race identified this heterogeneity, it should be interpreted as a marker of underlying biological, clinical, environmental, and psychosocial factors rather than as a biological determinant itself. Gender-stratified analyses demonstrated that these interactions were driven primarily by men, whereas no race $\times$ anemia interaction was observed among women.

Among men, African American participants with anemia had higher systolic and diastolic blood pressure than African American men without anemia, whereas the relationship between anemia and blood pressure was attenuated or reversed among White men. Although some individual subgroup comparisons were not statistically significant, the overall interaction pattern indicates that the factors represented by race and gender influence the relationship between anemia and blood pressure. These findings emphasize that averaging effects across heterogeneous populations may obscure clinically meaningful differences and that identifying the underlying mechanisms responsible for these differences is more informative than simply describing demographic variation.

The mechanisms underlying these findings are likely multifactorial. Anemia results in compensatory physiological responses, including increased cardiac output, reduced blood viscosity, and activation of neurohormonal pathways [29], all of which may influence vascular resistance and blood pressure. These responses are further modified by underlying cardiovascular disease, chronic inflammation, and iron status, supporting the concept of a bidirectional relationship between anemia and hypertension. However, these physiological mechanisms occur within broader social and environmental contexts that also influence cardiovascular risk. Chronic psychosocial stress, including stress associated with structural racism, socioeconomic disadvantage, and adverse neighborhood conditions, has been linked to vascular dysfunction and elevated blood pressure [30,31]. Likewise, unequal access to healthcare, differences in health behaviors, environmental exposures, and chronic disease burden may influence both anemia and hypertension. Thus, the observed interactions likely reflect the cumulative influence of these biological, clinical, environmental, and psychosocial factors rather than race itself. Future work should determine which biological and social mechanisms account for this heterogeneity.

Although African American women had higher blood pressure and a greater prevalence of anemia than White women, anemia was not differentially associated with blood pressure across racial groups among women. Gender differences in vascular physiology, hormonal regulation, iron metabolism, and cardiovascular adaptation to anemia may contribute to these differing associations [32,33,34]. Psychosocial factors may also play a role. In our previous study of African American adults residing in the Alabama Black Belt, men reported increasing stress, anxiety, and depression with age, whereas women did not [35]. Although these findings cannot explain the present results directly, they suggest that cumulative psychosocial stress may contribute to the stronger association between anemia and blood pressure observed among

men. Additional research is needed to identify the biological and social mechanisms underlying these gender-specific differences.

Strengths and Limitations. This study has several strengths. It included a community-based sample from rural West Alabama, a region with a disproportionately high burden of hypertension and cardiovascular disease and substantial racial diversity. The analytic approach evaluated interactions among anemia, race, and gender rather than assuming that the association between anemia and blood pressure was homogeneous across the population. These interaction effects identified heterogeneity that may have been overlooked using conventional models limited to main effects alone.

Several limitations should be acknowledged. The cross-sectional design precludes causal inference, and the temporal relationship between anemia and blood pressure cannot be established. In addition, the data represent a single clinical snapshot, and information regarding the etiology of anemia, iron status, kidney function, inflammatory biomarkers, treatment status, medication use (including iron supplementation), healthcare access, and other social determinants of health was unavailable. Consequently, we were unable to directly evaluate the biological, clinical, and psychosocial factors that may underlie the observed differences across demographic groups. Because chronic kidney disease is closely linked to both anemia and hypertension, future studies should incorporate measures of renal function and other potential mechanistic factors. Finally, although significant interaction effects were identified, some subgroup sample sizes were relatively small, and these findings should be considered hypothesis-generating pending confirmation in larger prospective studies.

Conclusions. The present study reports evidence that the relationship between anemia and blood pressure is heterogeneous, with demographic variables identifying this heterogeneity. Although race was useful for identifying this heterogeneity, the study was not designed to determine the mechanisms underlying these differences. Rather than suggesting that race itself

is causal, these findings indicate the need for future studies that directly measure the factors represented by race, including chronic psychosocial stress, socioeconomic conditions, inflammation, iron deficiency, kidney function, healthcare access, and other social determinants of health, thereby taking a precision medicine approach to understanding these relationships. Identifying these mechanisms will inform more effective approaches to hypertension prevention and management.

Declarations

Clinical trial not applicable

Ethics approval and consent to participate: The study was approved by the University of Alabama Institutional Review Board. A waiver of consent was obtained.

Consent for publication: Not applicable

Availability of data and materials: The datasets generated and/or analyzed during the current study are not publicly available. The datasets generated and/or analyzed during the current study contain clinical health information obtained through the Alabama State Health Information Exchange under an IRB-approved protocol and are subject to privacy and data-use restrictions. However, the data are available from the corresponding author on reasonable request.

Competing interests: There are no competing interests.

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276 **Authors' contributions:** DNP cleaned and analyzed the data. SDN interpreted the results and
 277 wrote the draft. All authors read and edited the manuscript.

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282 **Data Availability Statement:** Data will be made available upon request.

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