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Race, African ancestry, and *Helicobacter pylori* infection in a low-income United States population

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Abstract

Background—Gastric cancer incidence in African Americans is twice that of whites, and differing prevalence of *Helicobacter pylori* strain-specific isolates may help explain the disparity.

Methods—Serum levels of antibodies to each of 15 *Helicobacter pylori* proteins were assessed using multiplex serology for a sample of 689 African American and white participants from the Southern Community Cohort Study. African and European admixture was estimated using a panel of 276 ancestry genetic markers, with “low”, “medium”, and “high” categories of African ancestry defined as <85%, 85-95%, and ≥95%.

Results—The majority (79%) of our study population were sero-positive for *Helicobacter pylori*. African American race was associated with a 2- to 6-fold increased odds for sero-positivity to 8 *Helicobacter pylori* proteins, including the cancer-associated virulence constituents CagA (odds ratio, 6.4; 95% confidence interval, 4.5-9.1), and VacA (odds ratio, 2.3; 95% confidence interval, 1.5-3.5). Compared to whites, African Americans of low, medium, and high African ancestry had 1.6-, 4.1-, and 5.2-fold increased odds of sero-positivity to *Helicobacter pylori*, primarily related to CagA sero-positive strains, for which increasing African ancestry led to 2.5-, 9.6-, and 13.1-fold increased odds. Among African Americans alone, compared to those of low African ancestry, African Americans of medium and high African ancestry had 2.5- and 3.4-fold increased odds of sero-positivity to *Helicobacter pylori*, and 3.5-and 4.9-fold increased odds of CagA sero-positive *Helicobacter pylori* strains.

Conclusions—Host genetic variation and/or lifestyle factors associated with African ancestry contribute to the likelihood of infection with *Helicobacter pylori*, particularly its virulent strains, in this low-income U.S. southern population.

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Impact—Our findings that low-income African Americans of high African ancestry have a particularly high prevalence of antibodies against *Helicobacter pylori* provides a framework for further research into better detection and prevention of gastric cancer in this population.

Keywords

Helicobacter pylori; racial disparities; African ancestry; gastric cancer

Introduction

Although distal gastric cancer rates have been declining over the past century, gastric cancer remains second only to lung cancer as the most common cause of death from cancer worldwide (1). In the United States, gastric cancer incidence shows a large racial disparity, with an incidence in African Americans almost twice that in whites, and mortality differentials even greater (2). African Americans are also more likely to be infected with *Helicobacter pylori (H. pylori)*, a gram-negative spiral bacterium that colonizes the stomach of approximately half of the world's population. *H. pylori* is generally acquired in childhood, and is currently the strongest known risk factor for gastric cancer (3). Overall *H. pylori* prevalence in the US is estimated to be approximately 30%, but African Americans as a high-risk group are thought to have a prevalence around 50-60% (4-6).

H. pylori was officially classified as a human carcinogen in 1994 (7). However, only a fraction of persons infected with *H. pylori* ever develop neoplasia, and cancer risk is dependent upon strain-specific factors as well as host characteristics (8). These observations, in conjunction with evidence that carriage of certain *H. pylori* strains is *inversely* related to risk of esophageal adenocarcinoma, a usually fatal malignancy currently increasing in incidence (9-12), as well as possibly asthma, allergies, and gastroesophageal reflux disease (13-17) underscore the importance of understanding the heterogeneous nature of the bacterium.

Because of the large variation in *H. pylori* isolates and associated variability in risk profile, characterization of this diversity is crucial to identify high-risk populations for cost-effective disease prevention and potential new risk markers to further classify *H. pylori* into high- and low-risk groups. The most well-studied marker to date is the *H. pylori* protein cytotoxin-associated antigen (CagA), present in approximately 60% of US *H. pylori* strains (18). CagA is a component of a type IV bacterial secretion system termed the *cag* island, and *cagA*-positive strains of *H. pylori* inject CagA into host cells, altering host cell physiology and the adaptive immune response in a manner that permits *H. pylori* persistence (19,20). Emerging immunoproteomics studies have identified additional *H. pylori* antigens (21), and new epidemiologic research on 15 distinct human *H. pylori* antibodies has revealed important implications for gastric cancer risk (22,23). Specifically, Gao et al. have reported that the simultaneous presence of the *H. pylori* vacuolating toxin (VacA), *Helicobacter* cysteine-rich protein C (HcpC), and the chaperonin GroEL, in addition to CagA, increased the risk of chronic atrophic gastritis (a precursor lesion to gastric cancer) 18-fold (23), and that GroEL may be a new independent risk marker for gastric cancer (22).

The current investigation seeks to characterize overall *H. pylori* prevalence and sero-positivity for 15 *H. pylori* proteins in the primarily low-income population as captured in the Southern Community Cohort Study (SCCS), a study designed to investigate cancer disparities among African Americans and whites. In addition, given the excess burden of gastric cancer among African Americans, an important aim was to evaluate, for the first time, the association between level of African ancestry and *H. pylori* biomarkers of gastric cancer risk.

Materials and Methods

Study Population

Between 2002 and 2009, the SCCS, a prospective cohort study, recruited approximately 86,000 men and women aged 40-79 from 12 southeastern states at community health centers (CHCs, ~86%) and by mail (~14%) (24). All participants completed a baseline survey, which for those enrolled at a CHC involved a comprehensive computer-assisted in-person interview. A validated food frequency questionnaire was used to collect information on regular diet (25,26). Participants self-reported their race using a printed card with instructions to choose all applicable racial/ethnic categories. At the time of the baseline interview at the CHCs, venous blood samples (20 mL) were collected, refrigerated, and shipped overnight to Vanderbilt University to be centrifuged the next day and stored at -80°C. Among participants who enrolled in the SCCS from March 2002 to October 2004 and donated a blood sample at baseline (N=12,162), 792 were randomly selected using a 2×2×3×3 factorial design, with 22 individuals selected within each of the 36 strata defined by self-reported race (African American/white), sex, smoking status (current/former/never), and body mass index (18-24.9/25-29.9/30-45 kg/m^2). This design provided a balanced distribution across these factors in consideration of other blood biomarkers being measured in addition to *H. pylori*. Fifty μl of serum samples were aliquoted for *H. pylori* assays.

Helicobacter pylori Multiplex Serology

H. pylori multiplex serology, a new antibody detection technology based on fluorescent polystyrene beads (Luminex) and recombinant glutathione *S*-transferase (GST) fusion protein capture (27,28) was performed as recently described (29). Fifteen *H. pylori* proteins (UreA, Catalase, GroEL, NapA, CagA, CagM, Cagδ, HP0231, VacA, HpaA, Cad, HyuA, Omp, HcpC, HPO0305) were used as antigens. All sera were analyzed once within a single assay day. For all 15 antigens, antigen-specific cut-point values previously determined in a validation study (29) were applied using a bridging panel of 78 previously characterized sera containing 38 *H. pylori* negative sera and 40 *H. pylori* positive sera. *H. pylori* sero-positivity was defined as sero-positivity to >3 proteins, which has shown good agreement (kappa=0.70) with commercial serological assay classification (29). To test the reliability of the assay within our population, two individuals were randomly selected to have 5 replicate samples sent to the lab; the determination of sero-positivity for all of the *H. pylori* proteins detected was strongly consistent (only 1 (0.3%) replicate of 30 was not identical with the others).

Genetic Analysis and Ancestry Estimation

Genomic DNA was extracted from buffy coat using QIAamp DNA kits (Qiagen, Valencia, CA) according to manufacturer's instructions, and genotyping was carried out using the Illumina GoldenGate genotyping platform (Illumina Inc., San Diego, CA). Laboratory personnel were blinded to the status of the samples. Blinded quality control samples (N=29) and another 171 pairs of duplicate samples were included and the consistency rate was 99.9%. As described previously (30), a set of 276 single nucleotide polymorphisms were selected to estimate African and European ancestry levels, using a Bayesian clustering approach implemented using STRUCTURE software (version 2.2.3) (31). STRUCTURE identifies groups of individuals with similar allele frequency profiles and estimates the shared ancestry of individuals based solely on their genotypes under an assumption of Hardy-Weinberg equilibrium and linkage equilibrium in ancestral populations. It identifies a specified number (*K*) of ancestry population clusters (*K*=2 in this study) and assigns individual admixture estimates for each, with the estimates summing to 1 across these clusters. An admixture estimate (from 0.00 to 1.00) for both African ancestry and European ancestry was thus generated for each participant.

Statistical Analysis

The present study includes 686 (86.6%) of the 792 originally sampled participants, as the available serum was depleted from other assays performed on this group for 77 (9.7%), samples for 3 (0.4%) individuals were unusable because of serum handling issues, 3 individuals (0.4%) were missing information on antibiotic use, and the ancestry estimates for 23 (2.9%) were highly discordant with self-reported race, implying potential data entry errors.

Participants were classified by race based on their self-identification as African American only or white only. Ancestry estimates were modeled both as continuous variables for trend and as the categorical variables “white” (all whites), and “low”, “medium”, and “high” African ancestry based on previously utilized cut-points of <85%, 85% to 94.99%, and ≥95% African ancestry level (30). The outcomes of sero-positivity for *H. pylori* as well as for the 15 individual *H. pylori* proteins were modeled as dichotomous variables (yes/no).

Unconditional logistic regression was used to calculate odds ratios (ORs) and 95% confidence intervals (CIs) for the prevalence of *H. pylori* infection and for the presence of antibodies to specific *H. pylori* proteins by race and ancestry level. Statistical adjustment was made for age at enrollment, sex, smoking status, and body mass index, and also education (<high school education/high school or GED/>high school education) and antibiotic prescriptions in the past year (0/1 or more), chosen because they were associated with both race and *H. pylori* sero-positivity in the data. Crude and adjusted polytomous logistic regression models were also created to explore the association between race and ancestry level and the three outcomes of sero-negativity, sero-positivity to *H. pylori* but not to CagA (*H. pylori*+, CagA−), and sero-positivity to both *H. pylori* and CagA (*H. pylori*+, CagA+). For these analyses, the 5 (0.7% of the population) individuals (2 African American and 3 white) who were found to be sero-negative to *H. pylori* but sero-positive to CagA were excluded. The associations of African ancestry levels and sero-positivity to each of the 15 individual *H. pylori* proteins were also explored using multivariable logistic regression. All statistical analyses were performed using SAS 9.2 (SAS Institute, Cary, NC).

Results

Because of the stratified study design, the percentage of individuals in each category of sex, cigarette smoking status, and body mass index are comparable between the self-identified African Americans and whites in this study (Table 1). Other demographic and lifestyle characteristics were also similar in most respects, although African Americans were more likely to have a lower level of education, be in the highest category of fruit and vegetable intake, be hypertensive, and less likely to have asthma, emphysema, duodenal or gastric ulcer, arthritis, or to have been given a prescription for antibiotics in the past year. The median estimated percentage of African ancestry among self-identified African Americans was 97.0% (range 50.5-99.9%); among self-identified whites the median percentage African ancestry was 0.4% (range 0.1-17.1%).

In this sample of low-income African Americans and whites, 89% of African Americans (88% of men and 90% of women) and 69% of whites (69% of both men and women) were sero-positive for *H. pylori*. African Americans, compared to whites, had a 2- to 6-fold increased odds of sero-positivity to 8 of the 15 *H. pylori* proteins examined, including CagA (OR, 6.4; 95% CI, 4.5-9.1), and VacA (OR, 2.3; 1.5-3.5), the two previously established markers for gastric cancer risk, as well as GroEL, HcpC, Omp, Cad, HP 0305, and HpaA (Table 2). None of the 15 *H. pylori* proteins was recognized as significantly more common among whites.

Overall, compared to whites, African Americans had more than three times the odds (adjusted OR, 3.5; 95% CI, 2.3-5.4) of being *H. pylori*-positive (Table 3). Odds ratios significantly increased with increasing percentage of African ancestry, with ORs of 1.6 (95% CI, 0.8-3.0), 4.1 (95% CI, 2.0-8.6), and 5.2 (95% CI, 2.8-9.5) for low, medium, and high African ancestry, respectively. Examining the association among African Americans alone, compared to African Americans of low African ancestry, African Americans of medium African ancestry had an over two-fold increased risk (OR, 2.5; 95% CI, 1.0-6.6) and African Americans of high African ancestry had an over three-fold increased risk (OR, 3.4; 95% CI, 1.4-8.0). When separating outcomes using joint *H. pylori* and CagA status, the increased risk among African Americans was primarily related to CagA sero-positivity, for which African Americans were at 8.1-fold (95% CI, 5.0-13.1) increased odds, and African Americans of low, medium, and high African ancestry had ORs of 2.5 (95% CI, 1.2-5.3), 9.6 (95% CI, 4.3-21.5), and 13.1 (95% CI, 6.8-25.3), respectively. Again, when examining these associations among African Americans only, African Americans of medium and high African ancestry were of significantly greater risk of CagA-positive *H. pylori* strains than African Americans of low African ancestry (OR. 3.5; 95% CI, 1.3-10.0 and OR, 4.9; 95% CI,2.0-12.4, respectively).

Discussion

Among the generally low-income individuals in the southeastern US included in the present study, 79% were sero-positive for *H. pylori*. Self-reported African American race and increasing percentage of genetic estimation of African ancestry were strongly associated with prevalence of *H. pylori* infection, particularly with CagA sero-positivity. The racial difference is noteworthy because socioeconomic differences by race were minimized by study design (both blacks and whites tended to be of low income and education level) and by statistical adjustment for residual differences. Furthermore, the strong gradient in risk of infection, especially for CagA+ strains, with percent African ancestry is a new finding with potentially major implications regarding susceptibility to this common infection.

Another new finding arising from this research concerns information on the distribution of African ancestry in an African American population spanning rural as well as urban areas of 12 southern states. We found that the levels of African ancestry among African Americans in our population (median, 97%; mean, 92%) tended to be higher than those seen generally in previous studies among African Americans (32-35), but comparable to estimates among Gullah-speakers in South Carolina (36). Although beyond the scope of this report, we observed notable geographic variation in percent African ancestry suggesting that clustering of black populations with very high percent African ancestry many exist in multiple areas of the South.

The estimates of *H. pylori* prevalence in this study (89% for African Americans and 69% for whites) are much higher than the previously reported prevalence of 30% for the US overall, and 50-60% for African Americans (5). Worldwide, *H. pylori* prevalence has generally been reported to be higher in developing than developed countries, with estimates of 25% in Australia (37); 28-65% in Europe (lower in Western European than Eastern European countries) (38,39); 64-72% in the Middle East, China and Japan (5,39-41); and around 80-90% in many countries in South America and Africa (5,42). Of note, in the present study only 2 (0.6%) of the African Americans and 9 (2.7%) of the whites were born outside of the US.

In line with our findings, the few studies that have specifically examined US racial differences in *H. pylori* prevalence have consistently found higher rates among African Americans, but none have shown the exceptionally high rates of infection, especially for

CagA+ strains, reported herein. In the Third National Health and Nutrition Examination Survey (NHANES) reflective of the entire adult US population in 1988-91, 54% of African Americans vs. 28% of non-Hispanic whites were *H. pylori* positive (6); among those with less than 12 years education and considered at "high risk", the subset closest to our sample, 60% of African Americans and 41% of non-Hispanic whites were sero-positive. In NHANES 1999-2000, the prevalence remained nearly the same among blacks (53%) but declined to 22% among whites (4). Other surveys have shown that the racial disparity tends to begin early in life; for example African American children aged 5-9 years have been observed to have an *H. pylori* infection prevalence of about 30%, compared to 12% for the overall child infection rate in the United States (43). While an inverse association between socioeconomic status and *H. pylori* infection has been one of the most consistent findings (44), even among African American and white children attending the same schools, a longitudinal study in Louisiana observed that over the 12-year follow-up period, African American children had a 4-fold greater acquisition rate than whites, and only 4% of African American children proceeded to lose the infection, compared to 50% of the white children (45).

In terms of strain-specific *H. pylori* infection, the NHANES data revealed that approximately 60% of adults that were *H. pylori* positive were also CagA+ (46). In a small series of *H. pylori*-positive dyspepsia patients undergoing upper endoscopy in Nashville, Tennessee, 61% of non-Hispanic whites versus 90% of African Americans were sero-positive for CagA (47). Higher prevalences of CagA sero-positivity among blacks have also been reported in other series (48,49). In the current study, among *H. pylori*-positive individuals, 36% of whites and 75% of African Americans were CagA+. While this difference is substantial, the trend in CagA sero-positivity was even more striking when analyzed within the context of African ancestry level.

To the best of our knowledge, the current study is the first to examine the association between African ancestry level (characterized using ancestry informative genetic markers) and *H. pylori* infection. The environmental factor most consistently associated with *H. pylori* infection is low socioeconomic status (40,50), but we could eliminate all but very minor influences of education, income and other demographic factors in the observed black/white differences because of the fairly homogenous population studied, and because we were able to adjust in detail for education level. Educational level was the only socioeconomic status variable adjusted for, as it was the only one significantly associated with both race/African ancestry and *H. pylori* status. Additional adjustment for household income and household size was examined as well, but these factors had little impact on the main results. Furthermore, when examining the associations between race and African ancestry and *H. pylori* prevalence among only those without a high school education (n=210), the strong association between increasing African ancestry and increasing likelihood of *H. pylori* prevalence seen in the larger study was replicated in this sub-group defined by low educational status (data not shown). However, we cannot rule out the possibility that unmeasured lifestyle factors associated with African ancestry may influence *H. pylori* infection. While we did not have information on history of treatment for *H. pylori*, we did adjust for antibiotic use in the previous year, a factor that while different by race (African American versus white), was not associated with level of African ancestry among African Americans. Our results raise the possibility of an increased genetic susceptibility to *H. pylori* infection that may operate in conjunction with greater opportunities for environmental exposure in low-income populations to yield higher *H. pylori* infection rates.

The associations we observed could reflect the genetics of *H. pylori* itself. A study comparing a polymorphic *H. pylori* DNA sequence found a 180-bp insertion in 100% of West African isolates, 45% of South African isolates, 23% of Spanish isolates and 10% of

North American isolates, and 56% of isolates from African Americans compared to 17% of isolates from Caucasian Americans ($p<0.05$), suggesting that *H. pylori* strains colonizing African Americans today retain residual characteristics of those in Africa (51). Unfortunately, we had no endoscopy specimens from which we could isolate the bacteria, and are not aware of other investigations which have classified *H. pylori* origins among African Americans.

A German study of the association of the 15 *H. pylori* proteins measured here with gastric outcomes found that all 15 were positively associated with chronic atrophic gastritis (23), a precursor to intestinal-type gastric cancer, and 7 were significantly associated with gastric cancer (22). However, the few other population-based epidemiologic studies examining an assortment of *H. pylori* antigens, using different methods for detection, have not found the same associations (52,53). In our study, antibodies to 12 of the 15 *H. pylori* proteins were more common among African Americans than whites, including 6 of the 7 proteins identified as risk factors for gastric cancer. Furthermore, all of these associations were heightened when examining prevalence by increasing African ancestry levels (see Supplemental Table). Additionally, the proteins GroEL, Cad, HP 0305, and HpaA were significantly associated with African American race and African ancestry level independent of the known gastric cancer virulence factor CagA (data not shown).

Our findings that low-income African Americans and whites have developing country levels of *H. pylori* infection, and that African Americans, especially those of higher percentage of African ancestry, have a particularly high prevalence of antibodies against the *H. pylori* virulence factor CagA, now provides a framework for further research into better detection and prevention of gastric cancer in this population. Additional research may help delineate those at highest risk for increased surveillance and candidacy for *H. pylori* eradication. Examination of bacterial samples may help clarify the ancestral origins of the *H. pylori* strains and their links to cancer risks. *H. pylori* strain-specific research in high-risk populations such as the one in the present study also may help to inform as well as contribute to ongoing efforts at vaccine development. Ultimately, studies such as the current investigation may help identify determinants, and means of amelioration, of the long-standing higher rates of gastric cancer among African Americans.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Demographic and lifestyle characteristics, by race, of a sample of participants in the Southern Community Cohort Study, recruited from 12 southeastern states between 2002 and 2004

	All N = 686	African-American N = 346	White N = 340
Age (y), mean (SD)	52.4 (9.3)	51.5 (9.0)	53.3 (9.6)
Sex, n (%)*			
Female	362 (52.8)	182 (52.6)	180 (52.9)
Male	324 (47.2)	164 (47.4)	160 (47.1)
Cigarette smoking*			
Never	229 (33.4)	115 (33.2)	114 (33.5)
Former	229 (33.4)	118 (34.1)	111 (32.7)
Current	228 (33.2)	113 (32.7)	115 (33.8)
Body mass index (kg/m^2)*			
18.0-24.9	221 (32.2)	111 (32.1)	110 (32.4)
25.0-29.9	236 (34.4)	118 (34.1)	118 (34.7)
30.0-45.0	229 (33.4)	117 (33.8)	112 (32.9)
Education, n (%)†			
Less than high school	210 (30.6)	120 (34.7)	90 (26.5)
High school or GED	280 (40.8)	141 (40.8)	139 (40.9)
More than high school	196 (28.6)	85 (24.6)	111 (32.7)
Household income ($), n (%)			
<15,000	413 (60.7)	208 (60.6)	205 (60.7)
≥15,000 to <25,000	146 (21.4)	84 (24.5)	62 (18.3)
≥25,000	122 (17.9)	51 (14.9)	71 (21.0)
Household size, n (%)			
1-2	423 (61.7)	203 (58.7)	220 (64.7)
3-4	189 (27.6)	100 (28.9)	89 (26.2)
5+	74 (10.8)	43 (12.4)	31 (9.1)
Fruit and vegetable intake (times/d), n (%)†			
0-1	133 (19.4)	53 (15.3)	80 (23.5)
2-4	435 (63.4)	213 (61.6)	222 (65.3)
5+	118 (17.2)	80 (23.1)	38 (11.2)
Have health insurance			
Yes	393 (57.3)	203 (58.7)	190 (55.9)
No	293 (42.7)	143 (41.3)	150 (44.1)
1° family history of stomach cancer			
Yes	25 (3.6)	14 (4.0)	11 (3.2)
No / do not know / refused	661 (96.4)	332 (96.0)	329 (96.8)
Medical conditions, n (%)			
Diabetes	117 (17.1)	65 (18.8)	52 (15.3)

	All N = 686	African-American N = 346	White N = 340
Hypertension†	365 (53.2)	208 (60.1)	157 (46.2)
Coronary heart disease	43 (6.3)	16 (4.6)	27 (7.9)
Stroke	41 (6.0)	13 (3.8)	28 (8.2)
Asthma†	109 (15.9)	43 (12.4)	66 (19.4)
Emphysema†	89 (13.0)	29 (8.4)	60 (17.7)
Ulcer†	95 (13.9)	34 (9.8)	61 (17.9)
Arthritis†	231 (33.7)	95 (27.5)	136 (40.0)
Antibiotic prescription in the past year, n (%)†			
Yes	335 (48.8)	148 (42.8)	187 (55.0)
No	351 (51.2)	198 (57.2)	153 (45.0)

*matching factor

†significant difference ($p<0.05$) between African Americans and whites

Table 2

Sero-prevalence for antibodies to *H. pylori* proteins in relation to race among a sample of participants in the Southern Community Cohort Study, recruited from 12 southeastern states between 2002 and 2004

	Sero-positive n (%)	Sero-negative n (%)	Crude OR (95% CI)	Adjusted OR* (95% CI)
CagA				
White	88 (25.9)	252 (74.1)	1.00 (Reference)	1.00 (Reference)
African American	234 (67.6)	112 (32.4)	5.98 (4.30–8.33)	6.41 (4.53–9.09)
GroEL				
White	195 (57.4)	145 (42.7)	1.00 (Reference)	1.00 (Reference)
African American	273 (78.9)	73 (21.1)	2.78 (1.99–3.89)	2.84 (2.00–4.05)
HcpC				
White	143 (42.1)	197 (57.9)	1.00 (Reference)	1.00 (Reference)
African American	230 (66.5)	116 (33.5)	2.73 (2.00–3.72)	2.57 (1.86–3.54)
Omp				
White	175 (51.5)	165 (48.5)	1.00 (Reference)	1.00 (Reference)
African American	253 (73.1)	93 (26.9)	2.57 (1.87–3.53)	2.46 (1.77–3.43)
Cad				
White	49 (14.4)	291 (85.6)	1.00 (Reference)	1.00 (Reference)
African American	101 (29.2)	245 (70.8)	2.45 (1.67–3.58)	2.39 (1.62–3.54)
VacA				
White	259 (76.2)	81 (23.8)	1.00 (Reference)	1.00 (Reference)
African American	303 (88.7)	39 (11.3)	2.46 (1.62–3.73)	2.27 (1.48–3.49)
HP 0305				
White	91 (26.8)	249 (73.2)	1.00 (Reference)	1.00 (Reference)
African American	153 (44.2)	193 (55.8)	2.17 (1.57–2.99)	2.02 (1.45–2.81)
HpaA				
White	78 (22.9)	262 (77.1)	1.00 (Reference)	1.00 (Reference)
African American	133 (38.4)	213 (61.6)	2.10 (1.50–2.93)	2.00 (1.42–2.82)
Cagδ				
White	25 (7.4)	315 (92.7)	1.00 (Reference)	1.00 (Reference)
African American	32 (9.3)	314 (90.8)	1.28 (0.74–2.22)	1.34 (0.77–2.35)
Catalase				
White	215 (63.2)	125 (36.8)	1.00 (Reference)	1.00 (Reference)
African American	231 (66.8)	115 (33.2)	1.17 (0.85–1.60)	1.11 (0.80–1.54)
CagM				
White	106 (31.2)	234 (68.8)	1.00 (Reference)	1.00 (Reference)
African American	116 (33.5)	230 (66.5)	1.11 (0.81–1.53)	1.10 (0.79–1.52)
UreA				
White	213 (62.7)	127 (37.4)	1.00 (Reference)	1.00 (Reference)
African American	225 (65.0)	121 (35.0)	1.11 (0.81–1.51)	1.08 (0.79–1.49)
NapA				

	Sero-positive n (%)	Sero-negative n (%)	Crude OR (95% CI)	Adjusted OR* (95% CI)
White	127 (37.4)	213 (62.7)	1.00 (Reference)	1.00 (Reference)
African American	131 (37.9)	215 (62.1)	1.02 (0.75–1.39)	0.97 (0.70–1.33)
HP 0231				
White	98 (28.8)	242 (71.2)	1.00 (Reference)	1.00 (Reference)
African American	100 (28.9)	246 (71.1)	1.00 (0.72–1.40)	0.95 (0.68–1.34)
HyuA				
White	102 (30.0)	238 (70.0)	1.00 (Reference)	1.00 (Reference)
African American	90 (26.0)	256 (74.0)	0.82 (0.59–1.15)	0.82 (0.58–1.16)

*odds ratios from an unconditional logistic regression model adjusted for age, sex, smoking status, body mass index, education, and antibiotics prescriptions.

Table 3

Sero-prevalence for antibodies to *H. pylori* in relation to race and African ancestry level among a sample of participants in the Southern Community Cohort Study, recruited from 12 southeastern states between 2002 and 2004

	Sero-positive* n (%)	Sero-negative n (%)	Crude OR (95% CI)	Adjusted OR† (95% CI)
H. pylori+				
Model 1‡				
Reference: White/European	234 (68.8)	106 (31.2)	1.00 (Reference)	1.00 (Reference)
African American	308 (89.0)	38 (11.0)	3.67 (2.44–5.52)	3.53 (2.31–5.38)
Model 2‡				
Reference: White/European	234 (68.8)	106 (31.2)	1.00 (Reference)	1.00 (Reference)
African – Low (<85%)	42 (73.7)	15 (26.3)	1.27 (0.67, 2.39)	1.55 (0.81, 2.99)
African – Medium (85-94.9%)	88 (90.7)	9 (9.3)	4.43 (2.15, 9.13)	4.11 (1.97, 8.56)
African – High (≥95%)	178 (92.2)	14 (7.8)	5.76 (3.19, 10.40)	5.18 (2.83, 9.49)
Model 3‡				
Reference: African – Low	42 (73.7)	15 (26.3)	1.00 (Reference)	1.00 (Reference)
African – Medium (85-94.9%)	88 (90.7)	9 (9.3)	3.49 (1.41, 8.63)	2.51 (0.96, 6.59)
African – High (≥95%)	178 (92.2)	14 (7.8)	4.54 (2.04, 10.13)	3.37 (1.42, 8.00)
H. pylori+ by CagA status				
H. pylori+, CagA-				
Model 1‡				
Reference: White/European	149 (59.1)	103 (40.9)	1.00 (Reference)	1.00 (Reference)
African American	76 (67.9)	36 (32.1)	1.46 (0.91–2.33)	1.41 (0.87–2.28)
Model 2‡				
Reference: White/European	149 (59.1)	103 (40.9)	1.00 (Reference)	1.00 (Reference)
African – Low (<85%)	18 (54.6)	15 (45.5)	0.83 (0.40-1.72)	0.98 (0.46-2.08)
African – Medium (85-94.9%)	23 (74.2)	8 (25.8)	1.99 (0.86-4.62)	1.87 (0.80-4.37)
African – High (≥95%)	35 (72.9)	13 (27.1)	1.86 (0.94-3.69)	1.68 (0.84-3.38)
Model 3‡	18 (54.6)	15 (45.5)		
Reference: African – Low	23 (74.2)	8 (25.8)	1.00 (Reference)	1.00 (Reference)
African – Medium (85-94.9%)	35 (72.9)	13 (27.1)	2.40 (0.83, 6.89)	1.94 (0.63, 5.93)
African – High (≥95%)	23 (74.2)	8 (25.8)	2.24 (0.88, 5.72)	1.88 (0.68, 5.16)
H. pylori+, CagA+				
Model 1‡				
Reference: White/European	85 (45.2)	103 (54.8)	1.00 (Reference)	1.00 (Reference)
African American	232 (86.6)	36 (13.4)	7.81 (4.96–12.29)	8.12 (5.04–13.08)
Model 2‡				
Reference: White/European	85 (45.2)	103 (54.8)	1.00 (Reference)	1.00 (Reference)
African – Low (<85%)	24 (61.5)	15 (38.5)	1.94 (0.96-3.93)	2.54 (1.22-5.33)
African – Medium (85-94.9%)	65 (89.0)	8 (11.0)	9.85 (4.47-21.66)	9.60 (4.29-21.45)

	Sero-positive* n (%)	Sero-negative n (%)	Crude OR (95% CI)	Adjusted OR† (95% CI)
African – High (≥95%)	143 (91.7)	13 (8.3)	13.33 (7.05-25.19)	13.10 (6.78-25.32)
Model 3‡				
Reference: African – Low	24 (61.5)	15 (38.5)	1.00 (Reference)	1.00 (Reference)
African – Medium (85-94.9%)	65 (89.0)	8 (11.0)	5.08 (1.91, 13.50)	3.54 (1.26, 9.97)
African – High (≥95%)	143 (91.7)	13 (8.3)	6.87 (2.91, 16.24)	4.93 (1.96, 12.40)

*sero-positivity to *H. pylori* defined as sero-positivity to at least 4 *H. pylori* proteins.

†adjusted for age, sex, smoking status, body mass index, education, and antibiotic prescriptions.

‡model 1 presents the odds ratios for *H. pylori* sero-positivity for those self-identifying as African American-only, compared to those self-identifying as white-only; model 2 presents the odds ratios for sero-positivity for African Americans of low, medium, and high African ancestry, compared to whites; model 3 presents the odds ratios for sero-positivity among African Americans *only*, comparing risk for African Americans of medium and high African ancestry to that of African Americans of low African ancestry.