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Racial differences in *Helicobacter pylori* CagA sero-prevalence in a consortium of adult cohorts in the United States

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Abstract

Background: Prevalence of *Helicobacter pylori* infection, the main risk factor for gastric cancer, has been decreasing in the US; however, there remains a substantial racial disparity. Moreover, the time-trends for prevalence of CagA-positive *H. pylori* infection, the most virulent form, are unknown in the US population. We sought to assess prevalence of CagA-positive *Helicobacter pylori* infection over time by race, in the US.

Methods: We utilized multiplex serology to quantify antibody responses to *H. pylori* antigens in 4,476 participants across 5 cohorts that sampled adults from 1985 to 2009. Using log-binomial regression models, we calculated prevalence ratios (PRs) and 95% confidence intervals (CIs) for the association between *H. pylori*-CagA sero-prevalence and birth year by race.

Results: African Americans were 3-times more likely to be *H. pylori*-CagA sero-positive than whites. After adjustment, *H. pylori*-CagA sero-prevalence was lower with increasing birth year among whites (P_{trend}=0.001), but remained stable for African Americans. When stratified by sex and education separately, the decline in *H. pylori*-CagA sero-positivity among whites remained only for females (P_{trend}<0.001) and was independent of educational attainment. Among African Americans, there was no difference by sex; further, sero-prevalence increased with increasing birth year among those with a high-school education or less (P=0.006).

Conclusions: Among individuals in the US born from the 1920s to 1960s, *H. pylori*-CagA sero-prevalence has declined among whites, but not among African Americans.

Impact: Our findings suggest a widening racial disparity in the prevalence of the most virulent form of *Helicobacter pylori*, the main cause of gastric cancer.

Keywords

Cytotoxin associated gene A; CagA; Antibodies; *Helicobacter pylori*; Prevalence; Racial differences

INTRODUCTION

Infection with the gastric bacterium, *Helicobacter pylori,* is the single greatest risk factor for the development of non-cardia gastric cancer (1). Although nearly half the world's population carries this bacterium, its prevalence varies strongly by geographical region and ethnicity, coinciding mainly with gastric cancer incidence in the respective populations (2–7). In the United States (US), there are pronounced ethnic and racial disparities in both *H. pylori* prevalence and gastric cancer incidence whereby non-white populations are at an approximately two-fold increased risk for both (3, 6, 8–10). However, only a minority of *H. pylori* infected individuals will eventually develop gastric cancer. One determinant for this is the heterogeneity of *H. pylori*, as not all *H. pylori* strains have the same level of virulence and consequently carcinogenic properties. One strain-specific *H. pylori* virulence factor that augments cancer risk is the cytotoxin-associated gene (*cag*) pathogenicity island (11). The *cag* pathogenicity island encodes for a type 4 secretion system which translocates the oncoprotein CagA into host cells (11). The CagA protein is highly immunogenic and serum antibody responses to CagA persist throughout the life-time of an infection, and can even persist after *H. pylori* is eradicated (12, 13). Meta-analyses and observational studies from

around the world have consistently demonstrated that infection with CagA-positive *H. pylori* strains is associated with increased risk of non-atrophic gastritis and non-cardia gastric cancers (12, 14–20). As such, serum antibody responses to CagA have been used as markers for cancer risk in diverse population groups, including African Americans and Asian Americans in the US (3, 4, 9, 21).

Although gastric cancer incidence has been on the decline for decades across the globe, there remains a need to monitor *H. pylori* infection to help further reduce the burden of this cancer (22–24). In the US alone, it is estimated that there will be 27,600 new gastric cancer cases and 11,010 deaths from gastric cancer in 2020 (25). However, there exist scant data examining racial differences in prevalence and trends over time for infection with *H. pylori* and, more importantly CagA-positive *H. pylori,* especially taking into consideration the large disparity in gastric cancer incidence by race previously found in the US. Therefore, we sought to examine trends by race in *H. pylori*-CagA sero-prevalence over time in a subset of participants from 5 highly diverse prospective cohorts in the US, specifically: the Southern Community Cohort Study (SCCS) (26); NYU Women's Health Study (NYUWHS) (27); Women's Health Initiative (WHI) (28) ; the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial (PLCO) (29); and the Multiethnic Cohort (MEC) (30).

MATERIALS AND METHODS

Study participants

This study was conducted within a larger prospective consortium assembled to examine the associations between *H. pylori* blood biomarkers and colorectal cancer risk as described previously (31). Briefly, the consortium comprises prospectively ascertained colorectal cancer (CRC) cases and 1:1 controls matched on age, sex, self-reported race, and date of blood collection, nested within ten different US cohort studies. Because the present study is primarily focused on disparities between African Americans and whites (including both non-Latino and Latino whites) in *H. pylori* prevalence, we included only those cohorts, across the larger consortium of 10 cohorts, with at least 50 African American participants (NYUWHS, PLCO, SCCS, and WHI, and MEC). We did not include participants from the other five cohorts in the consortium as each cohort had specific inclusion criteria and target populations that require within-cohort comparisons for race-specific analyses. For the purposes of this prevalence study, we also supplemented the five cohorts with 177 CRC cases and 351 controls who were from the SCCS but had been included in a previous nested case-control study of the *H. pylori* and CRC association (32). In total, our analyses included 4,550 participants, 2,188 prospectively ascertained colorectal cancer cases and 2,362 controls. Covariates collected from participating cohorts included case-control status, age, sex, body mass index (BMI, missing n=62), smoking status (missing n=37), and education (missing n=74) as a measure of socioeconomic status. We then removed all participants missing education – who did not differ from the included subjects by age, sex, BMI, or smoking status – as we consider adjustment for socioeconomic status a necessity in these analyses, resulting in a final population of 4,476 individuals.

Institutional Review Board approval was obtained from all participating institutions.

H. pylori multiplex serology

We applied multiplex serology in sera from consortium participants to detect antibodies against 13 recombinantly expressed *H. pylori* antigens from strains 26695 and G27 as described previously (31, 33). Cutoff values for sero-positivity to each *H. pylori* antigen were calculated as defined previously (31, 33). Being sero-positive to 4 or more individual *H. pylori* antigens defined overall *H. pylori* sero-positivity. Those who were, in addition, sero-positive to *H. pylori*-CagA defined the CagA sero-positive group.

Statistical analysis

H. pylori-CagA sero-prevalence in our population was not rare (>10%) and, thus, odds ratios are not an appropriate approximation of relative risk. We therefore estimated prevalence ratios (PR) and 95% confidence intervals (CI) for the association of race with *H. pylori* and *H. pylori*-CagA sero-prevalence using log-binomial regression models (34). The association was assessed with three models: 1) a crude, unadjusted model; 2) a multivariable-adjusted model including age (continuous), sex, case-control status, and education (≤ high school [HS] or General Education Diploma [GED]; technical school or some college; ≥college degree), to remove the potential mediation of the association by socio-economic status; and 3) model 2 with further adjustment for BMI (<30 kg/m^2, ≥30kg/m^2) and smoking status (ever, never) as these additional two factors were associated both with race and *H. pylori*-CagA sero-positivity in our study (Table 1 and 2).

Year of birth was categorized into 5 groups (<1925, 1925-1935, 1936-1945, 1946-1953, and ≥1954) based on the distribution among the participants of the cohorts with the exception of WHI (which was not able to provide the variable year of birth) (Supplementary figure S1). We plotted the proportion of *H. pylori*-CagA sero-positive individuals by year of birth category. To determine the PR, 95% CI and two-sided *P*-values for trends, year-of-birth categories were treated as a linear continuous variable with the lowest year of birth category considered as reference for each cohort. Log-binomial regression models were adjusted for sex, case-control status, and education. No further adjustment was made for BMI and smoking status in this analysis as the PR and 95% CI were not changed by more than 10%. Separate models were constructed by race with further stratification by sex and education (≤HS, and >HS). We were unable to adjust for age in the year of birth analyses because age and year of birth were highly correlated, r/rho = 0.81, $P < 0.001$.

As a sensitivity analysis, because disease status might alter *H. pylori*-CagA sero-status, all models were repeated among controls only, and no qualitative differences were found (see Supplemental Tables S3–S6), so only the results among cases and controls combined are presented here.

In order to expand the scope of our prevalence study beyond differences between whites and African Americans, we secondarily analyzed 995 additional CRC cases and controls from the MEC, in which there were 570 Japanese Americans, 329 Latinos, and 96 Native Hawaiians, in addition to the 226 non-Latino white and 280 African American MEC participants included in the larger study. Analyses in the MEC to calculate PRs and 95% CIs were conducted as described above.

RESULTS

Study characteristics by race and *H. pylori* and *H. pylori*-CagA sero-status

In our study population, compared to whites, African Americans were younger and, thus, over-represented in the younger birth cohorts. Moreover, they were more likely to be male, of lower educational achievement, ever smokers, and obese (BMI ≥30 kg/m^2) (Table 1). *H. pylori,* as well as *H. pylori*-CagA, sero-positive individuals also were more likely to be younger, born in a later year, male, of lower educational achievement, and ever smokers and to have higher BMI than their respective sero-negative groups (Table 2).

H. pylori and *H. pylori*-CagA sero-prevalence by race and birth cohort

Differences in sero-prevalence of *H. pylori* were found by race, specifically *H. pylori* sero-prevalence was 33% among whites and 71% among African Americans. Of those *H. pylori* sero-positive, 59% of whites and 87% of African Americans were also CagA sero-positive, leading to an overall *H. pylori*-CagA sero-prevalence of 19% among whites and 62% among African Americans (Table 3). This racial difference in the sero-prevalence of *H. pylori* and *H. pylori*-CagA was consistent for each of the cohorts. In crude analyses, African Americans were twice as likely to be *H. pylori* sero-positive compared to whites (PR: 2.17; 95% CI: 2.05, 2.31) and three times as likely to be *H. pylori*-CagA sero-positive (PR: 3.19; 95% CI: 3.94, 3.47). After adjusting for age, sex, case-control status, and education, being African American remained associated with an almost two-fold increase in odds of *H. pylori* sero-prevalence (PR: 1.96; 95% CI: 1.83, 2.09) and an almost three-fold increase in odds of *H. pylori*-CagA sero-prevalence (PR: 2.83; 95% CI: 2.59, 3.10). This association did not change when additionally adjusting for BMI and smoking (*H. pylori*: PR: 1.96; 95% CI: 1.84, 2.10; *H. pylori*-CagA: PR: 2.87; 95% CI: 2.62, 3.14).

When examining trends over time, among all cohorts except for WHI, which did not provide year of birth, both *H. pylori* and *H. pylori*-CagA sero-prevalence were lower across later years of birth among whites (for a one increment increase in year of birth category: *H. pylori*: PR: 0.83; 95% CI: 0.77, 0.91; *H. pylori*-CagA: PR: 0.83; 95% CI: 0.75, 0.93; both $P_{trend} < 0.001$). However, among African Americans, sero-prevalence of both were stable across birth years (*H. pylori*: PR: 1.01; 95% CI: 0.97, 1.05, $P_{trend} = 0.625$; *H. pylori*-CagA: PR: 1.04; 95% CI: 1.00, 1.09, $P_{trend} = 0.078$) (Table 4 and Figure 1A). As seen in Table 4, the decline in sero-prevalence across birth years among whites was primarily driven by white study participants from NYUWHS and PLCO, whereas whites in SCCS and MEC did not show such a decline.

Stratifying by sex (Figure 1B) revealed that it was only white females who had lower prevalence across later years of birth (*H. pylori*: PR: 0.81; 95% CI: 0.73, 0.89, $P_{trend} < 0.001$; *H. pylori*-CagA: PR: 0.79; 95% CI: 0.68, 0.90, $P_{trend} < 0.001$). Stratifying on level of education (≤HS compared to >HS) showed that there was a lower *H. pylori* and *H. pylori*-CagA sero-prevalence across later years of birth among whites, regardless of educational level attained. In contrast, the association between *H. pylori* sero-positivity with birth year remained stable for African Americans independent of their educational level attained and sero-prevalence of *H. pylori*-CagA was higher in later birth years for African Americans

with a high school education or less (PR: 1.08; 95% CI: 1.02, 1.14, P_{trend} = 0.006; *P* for interaction by education among African Americans = 0.04) (Figure 1C).

Secondary analysis of *H. pylori* and *H. pylori*-CagA sero-prevalence among the five racial/ethnic groups in the Multiethnic Cohort

In our Multiethnic Cohort study population, compared to non-Latino whites, Native Hawaiians were younger, and Native Hawaiians were likewise more likely to be born in later cohorts, while African Americans and Latinos were more likely to be born in earlier cohorts (Supplemental Table S1). African Americans were also more likely to be obese (BMI ≥30 kg/m^2) than non-Latino whites, while Japanese Americans were less likely to be obese than non-Latino whites (Supplemental Table S1). Unlike in the multi-cohort study reported above, *H. pylori,* as well as *H. pylori*-CagA, sero-positive individuals were more likely to be older and born in an earlier year than their respective sero-negative groups, but were similarly more likely to have lower educational achievement (Supplemental Table S2).

Similar to our multi-cohort study reported above, ethnic/racial minorities in the MEC were more likely to be *H. pylori* and *H. pylori*-CagA sero-positive than non-Latino whites (Table 5). Specifically, compared to non-Hispanic whites, and adjusting for age, sex, case-controls status, and education, African Americans, Latinos, and Native Hawaiians were two- to three-fold more likely to be *H. pylori*-CagA sero-positive (PR: 3.05; 95% CI: 2.29, 4.06; PR: 2.55; 95% CI: 1.91, 3.41; and PR: 2.11; 95% CI: 1.47, 3.02, respectively), and Japanese Americans were 1.7-fold more likely to be *H. pylori*-CagA sero-positive (PR: 1.71; 95% CI: 1.28, 2.30) (Table 5). Additionally, the trends in sero-prevalence remained stable by year of birth for all races except for Japanese Americans, for whom there was a lower prevalence of *H. pylori*-CagA sero-positivity across later years of birth (PR: 0.72; 95% CI: 0.63, 0.83, P_{trend} < 0.001) (Table 4).

DISCUSSION

Although the overall prevalence of *H. pylori* has been declining in the US for several decades (3, 35), this study provides evidence that it persists as a common infection, especially among ethnic/racial minorities. Current estimates of *H. pylori* prevalence in the US have been based on National Health and Nutrition Examination Surveys (NHANES) collected in 1988–1994 and 1999–2000. The overall age-standardized sero-prevalence of *H. pylori* has decreased from 34.0% to 30.7% among adults between the surveys; however, this decrease was driven entirely by non-Latino whites (3). Concordantly, small cohort studies of *H. pylori* prevalence in non-white populations have suggested a stable, or even increasing prevalence (4, 9, 36, 37). Data on sero-positivity to the strongly gastric cancer-associated *H. pylori* virulence factor CagA in US populations, however, are rare, and trends over time have not been reported previously.

This racially diverse study of 4,476 participants demonstrates that the racial disparities in the prevalence of sero-positivity to *H. pylori* – and, more importantly, to *H. pylori*-CagA – infection remain high and, particularly for African Americans, are not changing over time. Our secondary analyses of the MEC show that these same trends also apply to Latinos and Native Hawaiians. These data also confirm our previous, smaller study within the SCCS,

where African American individuals were shown to be approximately twice as likely to be sero-positive to *H. pylori* and *H. pylori*-CagA than whites (4). The observations regarding prevalence of *H. pylori* sero-positivity across birth cohorts are concordant with previous reports from NHANES data, in which no declines over time were observed among African Americans or Latinos (3, 35). We here add important information to the literature, namely that prevalence of sero-positivity to *H. pylori*-CagA is not declining among African Americans, Latinos, or Native Hawaiians in the US.

This study has several strengths and weaknesses. It is composed of a large (4,476 participants in the primary analyses, 995 additional in the MEC), highly diverse population of US adults that encompasses groups not commonly included in large national surveys, notably low-income African Americans in the southeastern US as well as Native Hawaiians and Japanese Americans. We were also able to assess *H. pylori* sero-positivity through a comprehensive panel of 13 *H. pylori* antigens, including the cancer-associated CagA toxin, an assay that has been previously used to assess *H. pylori* in other large national and international cohorts (13, 38–41). Future work, beyond the scope of the current analyses, could delve more deeply into the differences by race in terms of the magnitude of fluorescence intensity of individual antigens.

Socio-economic status is strongly associated with both race and *H. pylori* sero-prevalence, and a limitation of the current study is that we adjusted for this potentially important variable with educational attainment alone. Although this may not necessarily be sufficient to capture variation in socio-economic status, we have previously conducted studies in the SCCS of *H. pylori* sero-prevalence in which we examined race, African ancestry, and both individual and neighborhood-level socioeconomic status (SES) factors including employment, education, and home value (from census block groups) (9). All of these SES factors were associated with *H. pylori* sero-prevalence, even separately among race/ancestry groups. However, once adjusted for, none of these SES factors explained the strong association between race and the prevalence of sero-positivity to the most virulent CagA-positive *H. pylori* strains. We did not have this level of SES data in the current study but our data, combined with previous studies, suggest that SES alone does not account for the observed racial disparities in *H. pylori* and *H. pylori*-CagA sero-prevalence. We hypothesize that other factors such as host genetics, other bacterial factors, and environmental factors, may also contribute to differences in *H. pylori* prevalence by race.

Another limitation of our study is that the inclusion criteria for the study and the larger consortium was incident CRC diagnosis and controls matched on age, sex, and race. Thus, these individuals do not represent the entire underlying cohort populations, limiting the generalizability of our findings. However, secondary analyses among only the control individuals found no qualitative differences from cases and controls together (fully adjusted PRs for *H. pylori* and *H. pylori*-CagA sero-positivity for African Americans, compared to whites, among controls only: PR: 1.91; 95% CI: 1.74, 2.10 and PR: 2.81; 95% CI: 2.47, 3.20, respectively). Additionally, our consortium includes a large proportion of less-educated individuals and, by implication, low SES individuals, thereby potentially overestimating the *H. pylori* and *H. pylori*-CagA sero-prevalence compared to the general US population. We were also unable to assess more recent birth cohorts for *H. pylori* and *H. pylori*-CagA sero-

prevalence, due to the time periods and age ranges from which the cohorts recruited participants. Another limitation of our study is that *H. pylori* serology cannot distinguish between current and past infection. However, infection typically occurs in childhood and lasts for a lifetime unless the individual is treated with eradication therapy (42–44). Therefore, in this instance, *H. pylori* serology is a close approximation to a measure of current infection.

H. pylori is the greatest risk factor for the development of gastric cancer and is the leading causative agent of infection-associated cancers in highly developed countries. Although the overall prevalence of this bacterium is decreasing in the US (3), our data reaffirm that *H. pylori* and *H. pylori*-CagA sero-prevalence remains high in ethnic/racial minorities and, moreover, in these populations it is not lower among individuals born in later years (3, 35, 36). Simultaneously, trends in gastric cancer incidence mirror those of *H. pylori* prevalence whereby substantial racial disparities are observed (6, 45–47). *H. pylori* erradication strategies have been estimated to be cost-effective in reducing the burden of gastric diseases including gastric cancer, even in low-incidence countries such as the US (48). However, nationwide *H. pylori* screening and eradication to reduce gastric cancer incidence requires a comprehensive understanding of prevalence and associated risk factors to allow for targeted treatment and prevention strategies.

In conclusion, our study highlights the large differences in the prevalence of *H. pylori* and *H. pylori*-CagA sero-positivity by race, and suggests that other factors beyond education are responsible for this disparity. Thus, continued surveillance of *H. pylori* prevalence by race is needed to inform how this treatable infection can be selectively eradicated to benefit high cancer-risk populations and ultimately reduce the widening racial disparity in both infection and gastric cancer incidence in the US.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

−	sero-negative
+	sero-positive
BMI	body mass index

CagA	cytotoxin-associated gene A
CI	confidence interval
GED	General Education Diploma
HS	high school
H. pylori	*Helicobacter pylori*
MEC	Multiethnic Cohort Study
n	number
NYUWHS	New York University Women's Health Study
PLCO	Prostate, Lung, Colorectal, and Ovarian Cancer Screening Study
PR	prevalence ratio
Ref	reference
SCCS	Southern Community Cohort Study
SES	socioeconomic status
US	United States
WHI	Women's Health Initiative

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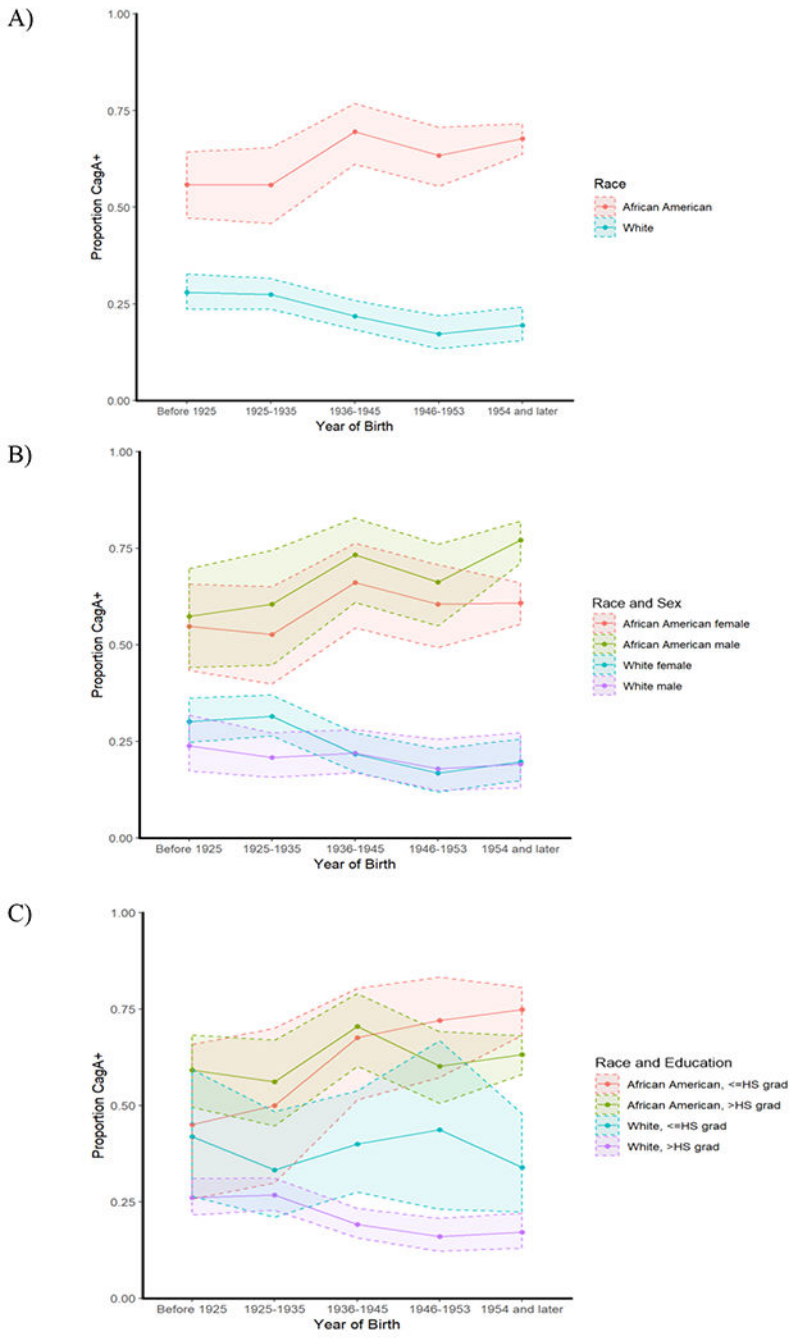

Figure 1.

H. pylori-CagA sero-positivity in CRC cases and controls in all cohorts excluding the WHI by year of birth category and stratified by A) Race (whites n=1,908, African American n=1,023); B) Race and sex (female/white n=1,135, female/African American n=571, male/white n=773, male/African American n=452) C) Race and education (≤HS/white n=703, ≤HS/African American n=583, >HS/white n=1,205, >HS/African American n=440)

Table 1.

Study Characteristics by Race, in a Subset of the *H. pylori*-Colorectal Cancer Consortium (NYUWHS, PLCO, SCCS, WHI, and MEC), 1985–2009

	Whites[a] (n = 3,292)		African Americans (n = 1,184)	
	n	%	n	%
Age, years[b]				
<60	784	24	555	47
60-69	1656	50	406	34
≥70	852	26	223	19
Year of birth[b, c]				
Before 1925	278	15	94	9
1925 – 1935	1020	53	247	24
1936 – 1945	468	25	270	26
1946 – 1953	97	5	218	21
1954 or later	45	2	194	19
Missing	1,384		161	
Cohort[b]				
NYUWHS	412	13	280	24
PLCO	1098	33	55	5
SCCS	172	5	98	8
WHI	1384	42	590	50
MEC	226	7	161	14
Sex[b]				
Female	2,519	77	732	62
Male	773	23	452	38
Education[b]				
≤HS	998	30	629	53
Technical school or some college	1,080	33	339	29
≥College	1,214	37	216	18
BMI, [kg/m^2][b]				
<30	2,385	73	670	58
≥30	867	27	492	42
Missing	40		22	
Smoking[b]				
Never	1,515	47	443	38
Ever	1,743	53	738	62
Missing	34		3	

Abbreviations: HS, high school:, BMI, body mass index.

[a]Includes non-Latino and Latino whites.

[b] $P < 0.05$ in Chi-Square test, two-sided.

[c] WHI did not provide data on year of birth.

Table 2.

Study Characteristics by *H. pylori* and *H. pylori*-CagA Sero-status, in a Subset of the *H. pylori*-Colorectal Cancer Consortium (NYUWHS, PLCO, SCCS, WHI, and MEC), 1985–2009

	***H. pylori* − (n = 2,550)**		***H. pylori* + (n = 1,926)**		***H. pylori*− and/or CagA− (n = 3,106)**		***H. pylori*+ and CagA+ (n = 1,370)**	
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Age, years[a]								
<60	698	27	641	33	838	27	501	37
60-69	1235	48	827	43	1490	48	572	42
≥70	617	24	458	24	778	25	297	22
Year of birth[a, b]								
Before 1925	171	12	201	14	232	13	140	13
1925 – 1935	696	48	571	39	871	48	396	36
1936 – 1945	397	27	341	23	474	26	264	24
1946 – 1953	121	8	194	13	163	9	152	14
1954 or later	70	5	169	11	88	5	151	14
Missing	1,095		450		1,287		267	
Cohort[a]								
NYUWHS	240	9	227	12	314	10	153	11
PLCO	760	30	436	23	910	29	286	21
SCCS	223	9	539	28	319	10	443	32
WHI	1095	43	450	23	1278	41	267	19
MEC	232	9	274	14	285	9	221	16
Sex[a]								
Female	1,955	77	1,296	67	2,364	76	887	65
Male	595	23	630	33	742	24	483	35
Race[a]								
White[c]	2,211	87	1,081	56	2,654	85	638	47
African American	339	13	845	44	452	15	732	53
Education[a]								
≤HS	714	28	913	47	945	30	682	50
Technical school or some college	845	33	574	30	1,021	33	398	29
≥College	991	39	439	23	1,140	37	290	21
BMI, [kg/m^2][a]								
<30	1,791	71	1,264	66	2,157	70	898	66
≥30	721	29	638	34	905	30	454	34
Missing	38		24		44		18	
Smoking[a]								
Never	1,157	46	801	42	1,407	46	551	41
Ever	1,371	54	1,110	58	1,672	54	809	59

	H. pylori − (n = 2,550)		*H. pylori* + (n = 1,926)		*H. pylori*− and/or CagA− (n = 3,106)		*H. pylori*+ and CagA+ (n = 1,370)	
	n	%	n	%	n	%	n	%
Missing	22		15		27		10	

Abbreviations: −, sero-negative; +, sero-positive; HS, high school; BMI, body mass index.

[a] $P < 0.05$ in Chi-Square test, two-sided, compared to respective sero-negative group.

[b] WHI did not provide data on year of birth.

[c] Includes non-Latino and Latino whites.

Table 3.

H. pylori and *H. pylori*-CagA Sero-Prevalence by Race and Cohort, in a Subset of the *H. pylori*-Colorectal Cancer Consortium (NYUWHS, PLCO, SCCS, WHI, and MEC), 1985–2009

Cohort	*H. pylori* +										*H. pylori* + CagA +									
	Whites[a]		African Americans								Whites[a]		African Americans							
	n	%	n	%	PR[b]	95%CI	PR[c]	95%CI	PR[d]	95%CI	n	%	n	%	PR[b]	95%CI	PR[c]	95%CI	PR[d]	95%CI
Total	1,081	33	845	71	**2.17**	**2.05, 2.31**	**1.96**	**1.83, 2.09**	**1.96**	**1.84, 2.10**	638	19	732	62	**3.19**	**2.94, 3.47**	**2.83**	**2.59, 3.10**	**2.87**	**2.62, 3.14**
NYUWHS	193	47	34	62	**1.32**	**1.05, 1.66**	**1.41**	**1.12, 1.77**	**1.34**	**1.04, 1.73**	125	30	28	51	**1.68**	**1.25, 2.26**	**1.68**	**1.25, 2.26**	**1.70**	**1.25, 2.32**
PLCO	373	34	63	64	**1.89**	**1.60, 2.24**	**1.80**	**1.52, 2.13**	**1.85**	**1.55, 2.20**	233	21	53	54	**2.55**	**2.06, 3.16**	**2.39**	**1.93, 2.97**	**2.46**	**1.97, 3.07**
SCCS	85	49	454	77	**1.56**	**1.33, 1.82**	**1.52**	**1.30, 1.78**	**1.51**	**1.29, 1.77**	41	24	402	68	**2.86**	**2.18, 3.75**	**2.75**	**2.09, 3.62**	**2.76**	**2.10, 3.63**
WHI	361	26	89	55	**2.12**	**1.80, 2.50**	**2.10**	**1.78, 2.47**	**2.03**	**1.71, 2.41**	196	14	71	44	**3.11**	**2.51, 3.87**	**3.17**	**2.53, 3.96**	**3.16**	**2.51, 3.98**
MEC	69	31	205	73	**2.40**	**1.95, 2.96**	**2.27**	**1.83, 2.81**	**2.28**	**1.84, 2.82**	43	19	178	64	**3.34**	**2.52, 4.44**	**3.23**	**2.43, 4.31**	**3.23**	**2.43, 4.30**

Abbreviations: +, sero-positive; CagA, Cytotoxin-associated gene A; CI, confidence interval; MEC, Multiethnic cohort study; n, number; NYUWHS, New York University Women's Health Study; PLCO, Prostate, Lung, Colorectal, and Ovarian Cancer Screening Study; PR, prevalence ratio; SCCS, Southern Community Cohort Study; WHI, Women's Health Initiative.

[a] Includes non-Latino and Latino whites.

[b] Log-binomial regression models without further adjustment.

[c] Log-binomial regression models with adjustment for age (continuous), sex, education (≤HS, technical school or some college, ≥college), and case-control status.

[d] Log-binomial regression models with adjustment for age (continuous), sex, education (≤HS, technical school or some college, ≥college), case-control status, BMI (non-obese/obese), and smoking status (ever/never).

Table 4.

Association of *H. pylori* and *H. pylori*-CagA Sero-Prevalence with Year of Birth, Overall and by Cohort, in a Subset of the *H. pylori*-Colorectal Cancer Consortium (NYUWHS, PLCO, SCCS, and MEC), 1985–2009

		***H. pylori* +**			***H. pylori* + CagA +**		
Cohort	**n**	**PR**[a]	**95% CI**[a]	P_{trend}[a]	**PR**[a]	**95% CI**[a]	P_{trend}[a]
All							
Whites[b]	1,908	**0.83**	**0.77, 0.91**	**<0.001**	**0.83**	**0.75, 0.93**	**0.001**
African American	1,023	1.01	0.97, 1.05	0.625	1.04	1.00, 1.09	0.078
NYUWHS							
Whites[b]	412	**0.79**	**0.69, 0.90**	**<0.001**	**0.76**	**0.62, 0.92**	**0.006**
African American	55	0.99	0.74, 1.31	0.920	0.92	0.66, 1.29	0.630
PLCO							
Whites[b]	1,098	**0.85**	**0.74, 0.98**	**0.020**	0.85	0.71, 1.03	0.094
African American	98	1.03	0.81, 1.30	0.815	1.13	0.82, 1.55	0.449
SCCS							
Whites[b]	172	0.92	0.80, 1.06	0.258	1.07	0.83, 1.39	0.589
African American	590	1.02	0.97, 1.06	0.447	1.03	0.98, 1.09	0.231
MEC							
Whites[c]	226	0.82	0.65, 1.05	0.120	0.92	0.67, 1.28	0.635
African American	280	0.94	0.86, 1.02	0.120	0.98	0.89, 1.07	0.609
Japanese American	570	**0.78**	**0.70, 0.87**	**<0.001**	**0.72**	**0.63, 0.83**	**<0.001**
Latino	329	0.98	0.91, 1.07	0.667	0.96	0.85, 1.09	0.538
Native Hawaiian	96	1.04	0.77, 1.40	0.810	1.06	0.77, 1.45	0.739

Abbreviations: +, sero-positive; CagA, Cytotoxin-associated gene A; CI, confidence interval; MEC, Multiethnic cohort study; n, number; NYUWHS, New York University Women's Health Study; PLCO, Prostate, Lung, Colorectal, and Ovarian Cancer Screening Study; PR, prevalence ratio; SCCS, Southern Community Cohort Study.

[a] PR and 95% CI estimated for one increment increase in year of birth category (<1925, 1925-1935, 1936-1945, 1946-1953, and ≥1954) estimated by Log-binomial regression adjusted for sex, education (≤HS, technical school or some college, ≥college), and case control status; for each cohort the lowest year of birth category was considered as reference.

[b] Includes both non-Latino and Latino whites.

[c] Non-Latino whites only.

Table 5.

Secondary Analysis, *H. pylori* and *H. pylori*-CagA Sero-Prevalence by Race in the Multiethnic Cohort (MEC), 1995–2006

	***H. pylori*−**		***H. pylori*+**							***H. pylori*−/ CagA−**		***H. pylori* +CagA+**							
Race	**n**	**%**	**n**	**%**	**PR[a]**	**95% CI[a]**	**PR[b]**	**95% CI[b]**	**PR[c]**	**95% CI[c]**	**n**	**%**	**n**	**%**	**PR[a]**	**95% CI[a]**	**PR[b]**	**95% CI[b]**	**PR[c]**	**95% CI[c]**
White[d]	157	69	69	31	1.00	Ref	1.00	Ref	1.00	Ref	183	81	43	19	1.00	Ref	1.00	Ref	1.00	Ref
African American	75	27	205	73	**2.40**	**1.95, 2.96**	**2.21**	**1.79, 2.73**	**2.21**	**1.79, 2.73**	102	36	178	64	**3.34**	**2.52, 4.44**	**3.05**	**2.29, 4.06**	**3.07**	**2.31, 4.08**
Japanese American	334	59	236	41	**1.36**	**1.09, 1.69**	**1.32**	**1.06, 1.65**	**1.34**	**1.07, 1.66**	381	67	189	33	**1.74**	**1.30, 2.34**	**1.71**	**1.28, 2.30**	**1.71**	**1.27, 2.29**
Latino	78	24	251	76	**2.50**	**2.03, 3.07**	**2.24**	**1.82, 2.76**	**2.25**	**1.82, 2.77**	153	47	176	53	**2.81**	**2.11, 3.75**	**2.55**	**1.91, 3.41**	**2.57**	**1.92, 3.43**
Native Hawaiian	52	54	44	46	**1.50**	**1.12, 2.01**	**1.44**	**1.07, 1.93**	**1.44**	**1.07, 1.93**	56	58	40	42	**2.19**	**1.53, 3.13**	**2.11**	**1.47, 3.02**	**2.12**	**1.48, 3.04**

Abbreviations: −, sero-negative; +, sero-positive; CagA, Cytotoxin-associated gene A; CI, Confidence interval; PR, Prevalence ratio; Ref, Reference.

[a]Log-binomial regression models without further adjustment.

[b]Log-binomial regression models with adjustment for age (continuous), sex, education (≤HS, technical school or some college, ≥college), and case-control status.

[c]Log-binomial regression models with adjustment for age (continuous), sex, education (≤HS, technical school or some college, ≥college), case-control status, BMI (non-obese/obese), and smoking status (ever/never).

[d]Non-Latino whites only.