

ORIGINAL RESEARCH—CLINICAL

Time Trends and Demographic Disparities in *Helicobacter pylori* Burden in a Large, Community-Based Population in the United StatesDan Li,^{1,2,*} Sophie A. Merchant,^{1,*} Jessica M. Badalov,¹ and Douglas A. Corley^{1,3}

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BACKGROUND AND AIMS: There are minimal recent population-based data on the epidemiology of *Helicobacter pylori* (*H. pylori*) in the United States. **METHODS:** This retrospective cohort study evaluated *H. pylori* positivity rates in adult members of a large, community-based US population in 2000–2019. Time trends, demographic disparities, and birth cohort effects on *H. pylori* test positivity rates were analyzed. **RESULTS:** Among 751,322 individuals tested for *H. pylori*, the overall nonserological and serological test positivity rates were 18.2% (95% confidence interval [CI], 18.1%–18.4%) and 36.8% (95% CI, 36.6%–36.9%), respectively. Nonserological positivity rate (95% CI) was significantly higher among Asian (23.2% [22.8%–23.6%]), Black (25.1% [24.4%–25.8%]), and Hispanic (28.1% [27.7%–28.5%]) individuals than non-Hispanic White individuals (10.0% [9.8%–10.2%]), and was significantly higher among individuals with a non-English language preference (32.9% [32.3%–33.5%]) than those with English language preference (15.8% [15.6%–15.9%]). Patterns were similar for serological positivity, although with substantially higher rates. Serological positivity rates decreased over 2 decades but nonserological positivity rates initially decreased and then stabilized over the past decade. There was a significant decrease in both nonserological and serological positivity rates from older to younger birth cohorts. Older age, non-White race or Hispanic ethnicity, male sex, and non-English language preference were associated with high odds of *H. pylori* positivity. **CONCLUSION:** The burden of *H. pylori* decreased over 2 decades, although the rates of active infection plateaued over the past decade in a diverse, community-based US population, likely attributable to birth cohort effects and demographic changes. Asian, Black, and Hispanic individuals had 2–3-fold higher rates of active *H. pylori* infection than non-Hispanic White individuals. These findings should inform targeted screening and eradication of *H. pylori* in high-risk US populations.

United States, non-White racial and ethnic groups had substantially higher prevalence of *H. pylori* compared with non-Hispanic White population.^{3–5} Chronic *H. pylori* infection is a main cause of peptic ulcer disease and nonvariceal upper gastrointestinal hemorrhage as well as the most important risk factor for noncardia gastric adenocarcinoma.^{3,6–10} Accordingly, multiple US and international guidelines recommend screening and eradication for *H. pylori* among individuals who are at increased risk of developing important *H. pylori*-related adverse health outcomes.^{11–15}

Contemporary population-based or community-based data on *H. pylori* prevalence in the United States are very limited. Most of the population-based epidemiological studies on *H. pylori* infection in the United States were conducted more than 15 years ago.^{16–21} A recent nationwide study based on the veteran population showed significant racial and ethnic disparities on *H. pylori* test positivity rates.²² However, it remains unclear whether the *H. pylori* burden in community-based US populations has changed over time, with any substantial racial and ethnic disparities, or is different by birth cohorts. With increasing racial and ethnic diversity in the US populations, reassessing the burden of *H. pylori* in the general population becomes important and relevant, as the findings may inform strategies to improve *H. pylori* screening and eradication among high-risk populations.^{12,13,23,24}

To address these knowledge gaps, we investigated the positivity rates of *H. pylori* using nonserological and serological testing methods in a large, diverse, community-based US population over 2 decades, stratified by race and

Keywords: *Helicobacter pylori*; Prevalence; Race and ethnicity; Disparity

*Authors share co-first authorship.

Abbreviations used in this paper: CI, confidence interval; *H. pylori*, *Helicobacter pylori*; KPNC, Kaiser Permanente Northern California; OR, odds ratio.

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Introduction

Helicobacter pylori (*H. pylori*) infection is one of the most common bacterial infections in humans, affecting at least half of the world population.^{1,2} In the

ethnicity, birth cohorts, and other patient-level variables. We also assessed the predictors of *H. pylori* positivity among tested individuals.

Methods

Setting

This study was conducted within Kaiser Permanente Northern California (KPNC), a large integrated health system which provides comprehensive medical care to approximately 4.5 million members in suburban, urban, and semi-rural regions throughout Northern California. The KPNC member population is socially, racially, and ethnically diverse and closely approximates the census demographics of the population in Northern California.²⁵ This study was approved by the KPNC Institutional Review Board, with informed consent waived.

Study Population

We identified all KPNC health plan members who were aged 18 years and more and received their first *H. pylori* test in 2000–2019; members with a history of total gastrectomy were excluded (Figure A1). Participants were censored at the earliest occurrence of (1) a positive *H. pylori* test; (2) health plan membership termination; (3) death; or (4) end of the study period on December 31, 2019. We decided to end the data collection on December 31, 2019 to avoid any confounding effect of COVID-19 pandemic on *H. pylori* testing in our study population.

Data Sources

Sociodemographic data (age, sex, race and ethnicity, language preference, education level) and clinical data (body mass index [BMI], smoking status, family history of gastric cancer, comorbidities) were obtained from electronic health records. Regarding race and ethnicity by subregional groups, 39.3% of Asians had subregional racial and ethnic information in their membership file, while the rest were registered as “Asians”. Only 2.2% Hispanic individuals, 0.26% non-Hispanic White individuals, and <0.1% Black individuals had subregional racial and ethnic information. Death data were sourced from health plan administrative databases, Social Security Administration vital status files, and state death certificate files. Education level was ascertained through census-level sociodemographic records and recorded as percent with a college education for the census block where the patient was residing at the time of data collection. To evaluate the birth cohort effects, study participants were divided based on their birth year into 5-year birth cohorts (1915–1919, 1920–1924, ... 1995–2000).

Ascertainment of *H. pylori* testing. *H. pylori* infection was tested by either serological methods for the presence of *H. pylori* antibody or nonserological methods, including stool antigen, urea breath test, rapid urease test on the biopsy specimens of the stomach, or histology of the biopsy specimens of the stomach (Table A1).^{12,13} To accurately ascertain the *H. pylori* infection status on pathology, we established and validated a natural language processing tool using SAS Pearl Regular Expression. Validation of this natural language processing query tool compared with manual medical record review as the gold standard showed a sensitivity of

97.4%, specificity of 99.2%, positive predictive value of 95.0%, and negative predictive value of 99.6% for the presence of *H. pylori* based on the pathology reports.¹⁰

Outcomes

H. pylori test positivity rate was defined as the proportion of patients who tested positive for *H. pylori* per total number of patients who received a test. Test-specific positivity rate reflected the rate of positivity among those who received non-serological tests or those who received serological tests. Only the first positive test was included for the calculation of positivity rate of that test category (nonserological or serological test). For individuals who underwent more than 1 test using the same test category, a positive result overrode the prior negative results in the same testing category for the calculation of positivity rate in that test category. Patients who received both serological and nonserological tests are counted in both testing method strata.

Statistical Analyses

Mean and standard deviation were used to describe the demographic and clinical patient characteristics. Student's *t*-test for means and Pearson's chi-square tests for proportions were used to compare patterns in testing methods across patient characteristics. Missing values were imputed using the Multivariate Imputation by Chained Equations method, generating 10 datasets. Multivariate logistic regression models adjusted for age, sex, race and ethnicity, language preference, education level, smoking status, BMI, family history of gastric cancer, and Charlson comorbidity index were applied to each dataset, and estimates were averaged across the datasets to identify potential predictors of *H. pylori* test positivity. Significance was defined as a 2-sided *P* value of <.05 for all statistical comparisons. All analyses were performed using SAS version 9.4.

Results

Among the 751,322 adult KPNC members who received at least 1 *H. pylori* test between January 1, 2000 and December 31, 2019, 207,181 (27.6%) received their initial test using nonserological methods and 544,141 (72.4%) received their initial test using serological methods (Figure A1 and Table 1). At their initial test, individuals were more likely to be non-Hispanic White (44.7%), female (59.7%), and have English language preference (84.9%), with an average age of 49.5 years.

H. pylori Positivity Rates Among Tested Individuals

Among individuals who received nonserological tests for *H. pylori*, the overall positivity rate was 18.2% (95% confidence interval [CI], 18.1%–18.4%); among individuals who received serological tests, the overall positivity rate was 36.8% (95% CI, 36.6%–36.9%) (Table 2). Positivity rates by each of the nonserological testing methods are included in Table A2.

Positivity rate by race and ethnicity. The non-serological positivity rate was highest in those who were

Table 1. Patient Characteristics at the Initial *Helicobacter pylori* Testing at KPNC in 2000–2019

Characteristic	Total	Nonserological		Serological		P value
	N (%)	N	%	N	%	
Overall	751,322	207,181	27.6	544,141	72.4	
Race and ethnicity						<.001
American or Alaskan Native	4010 (0.5)	1096	27.3	2914	72.7	
Asian	140,996 (18.8)	41,569	29.5	99,427	70.5	
Black	47,695 (6.3)	13,635	28.6	34,060	71.4	
Hispanic	162,059 (21.6)	44,527	27.5	117,532	72.5	
Non-Hispanic White	336,004 (44.7)	94,323	28.1	241,681	71.9	
Other or unknown ^a	64,568 (8.6)	13,127	20.3	51,441	79.7	
Mean age, y (SD)	49.5 (16.2)	54.6 (16.4)		47.5 (15.7)		<.001
Sex						<.001
Female	448,638 (59.7)	119,296	26.6	329,342	73.4	
Male	302,640 (40.3)	87,870	29.0	214,770	71.0	
Other or unknown	44 (0.0)	15	34.1	29	65.9	
Language preference						<.001
English	638,155 (84.9)	176,833	27.7	461,322	72.3	
Non-English	102,915 (13.7)	28,067	27.3	74,848	72.7	
Unknown	10,252 (1.4)	2281	22.2	7971	77.8	
Percent college educated in patient residing area						<.001
<40%	207,675 (27.6)	88,059	42.4	119,616	57.6	
40%–59.9%	85,801 (11.4)	36,382	42.4	49,419	57.6	
60%–79.9%	47,610 (6.3)	20,447	42.9	27,163	57.1	
≥80%	7371 (1.0)	3160	42.9	4211	57.1	
Unknown	402,865 (53.6)	59,133	14.7	343,732	85.3	
Body mass index, kg/m ²						<.001
<18.5	10,230 (1.4)	4158	40.6	6072	59.4	
18.5–24.9	178,232 (23.7)	61,767	34.7	116,465	65.3	
25–29.9	182,111 (24.2)	62,723	34.4	119,388	65.6	
≥30	170,497 (22.7)	58,014	34.0	112,483	66.0	
Unknown	210,252 (28.0)	20,519	9.8	189,733	90.2	
Smoking status						<.001
Ever smoker	262,209 (34.9)	82,630	31.5	179,579	68.5	
Never smoker	328,707 (43.8)	110,921	33.7	217,786	66.3	
Unknown	160,406 (21.3)	13,630	8.5	146,776	91.5	
Family history of gastric cancer						<.001
Yes	10,355 (1.4)	5805	56.1	4550	43.9	
No	740,967 (98.6)	201,376	27.2	539,591	72.8	
Charlson comorbidity index						<.001
0	495,797 (66.0)	107,662	21.7	388,135	78.3	
1	140,181 (18.7)	44,147	31.5	96,034	68.5	
2	51,058 (6.8)	21,383	41.9	29,675	58.1	
≥3	64,286 (8.6)	33,989	52.9	30,297	47.1	

KPNC, Kaiser Permanente Northern California; SD, standard deviation.

^aIncludes American and Alaskan Native and multiracial groups.

Hispanic (28.1%; 95% CI, 27.7%–28.5%), followed by those who were Black (25.1%; 95% CI, 24.4%–25.8%), Asian (23.2%; 95% CI, 22.8%–23.6%), and non-Hispanic White (10.0%, 95% CI, 9.8%–10.2%) (Table 2). Similar patterns were seen using serological methods but with substantially higher rates. The positivity rate ratios comparing people who were Asian, Black, and Hispanic vs non-Hispanic White using nonserological methods were 2.32 (95% CI, 2.26–2.37), 2.51 (95% CI, 2.43–2.59), and 2.81 (95% CI, 2.74–2.87), respectively (Figure 1). When stratified by variable patient characteristics among each racial and ethnic group (Table 3), the nonserological *H. pylori* positivity rates

as well as serological positivity rates were significantly higher among Asian, Black, and Hispanic individuals compared to non-Hispanic White individuals across almost all patient characteristics. When stratified by subregional race and ethnicity, Southeast Asian individuals (34.5%, 95% CI, 29.4%–40.3%) or Korean individuals (33.6%, 95% CI 27.5%–41.0%) had the highest nonserological positivity rates as well as serological positivity rates among Asians (Table A3). The *H. pylori* positivity rates by subregional racial and ethnic groups for Black, Hispanic, and non-Hispanic White individuals are not shown due to insufficient information.

Table 2. *Helicobacter pylori* Positivity Rates Among KPNC Members Tested by Nonserological and Serological Methods in 2000–2019

Characteristic	Tested by nonserological methods			Tested by serological methods		
	Total	Test positivity		Total	Test positivity	
	N	N	% [95% CI]	N	N	% [95% CI]
Overall	292,958	53,347	18.2 [18.1, 18.4]	556,849	204,807	36.8 [36.6, 36.9]
Race and ethnicity						
Asian	59,174	13,707	23.2 [22.8, 23.6]	101,759	43,197	42.5 [42.1, 42.9]
Black	18,746	4704	25.1 [24.4, 25.8]	34,928	17,127	49.0 [48.3, 49.8]
Hispanic	63,475	17,819	28.1 [27.7, 28.5]	119,940	67,590	56.4 [55.9, 56.8]
Non-Hispanic White	132,810	13,285	10.0 [9.8, 10.2]	247,965	55,394	22.3 [22.2, 22.5]
Other or unknown ^a	18,753	3832	20.4 [19.8, 21.1]	52,257	21,499	41.1 [40.6, 41.7]
Age, y						
18–29	20,711	3268	15.8 [15.2, 16.3]	78,449	20,943	26.7 [26.3, 27.1]
30–39	45,026	8226	18.3 [17.9, 18.7]	126,320	42,166	33.4 [33.1, 33.7]
40–49	56,919	10,610	18.6 [18.3, 19.0]	131,955	47,367	35.9 [35.6, 36.2]
50–59	66,579	11,613	17.4 [17.1, 17.8]	114,113	40,756	35.7 [35.4, 36.1]
60–69	61,209	9711	15.9 [15.6, 16.2]	77,241	27,900	36.1 [35.7, 36.5]
70–79	39,761	6716	16.9 [16.5, 17.3]	40,696	16,938	41.6 [41.0, 42.3]
80–89	15,798	2896	18.3 [17.7, 19.0]	16,952	7703	45.4 [44.4, 46.5]
≥90	1725	307	17.8 [15.9, 19.9]	2215	1034	46.7 [43.9, 49.6]
Sex						
Female	175,142	29,766	17.0 [16.8, 17.2]	337,239	117,718	34.9 [34.7, 35.1]
Male	117,799	23,577	20.0 [19.8, 20.3]	219,581	87,080	39.7 [39.4, 39.9]
Other or unknown	17	4	23.5 [8.8, 62.7]	29	9	31.0 [16.1, 59.6]
Language preference						
English	250,042	39,382	15.8 [15.6, 15.9]	472,441	149,731	31.7 [31.5, 31.9]
Non-English	40,273	13,250	32.9 [32.3, 33.5]	76,309	51,729	67.8 [67.2, 68.4]
Unknown	2643	715	27.1 [25.1, 29.1]	8099	3347	41.3 [39.9, 42.8]
Percent college educated in patient residing area						
<40%	131,712	23,827	18.1 [17.9, 18.3]	140,479	43,220	30.8 [30.5, 31.1]
40%–59.9%	56,236	7955	14.1 [13.8, 14.5]	58,919	14,637	24.8 [24.4, 25.2]
60%–79.9%	31,017	4346	14.0 [13.6, 14.4]	31,720	7664	24.2 [23.6, 24.7]
≥80%	4688	588	12.5 [11.6, 13.6]	4873	1080	22.2 [20.9, 23.5]
Unknown	84,478	16,631	19.7 [19.4, 20.0]	348,149	138,206	39.7 [39.5, 39.9]
Smoking status						
Ever smoker	118,978	19,508	16.4 [16.2, 16.6]	192,926	66,650	34.5 [34.3, 34.8]
Never smoker	159,291	28,995	18.2 [18.0, 18.4]	235,949	80,082	33.9 [33.7, 34.2]
Unknown	18,310	4844	26.5 [25.7, 27.2]	147,541	58,075	39.4 [39.0, 39.7]
Body mass index, kg/m ²						
<18.5	6518	942	14.5 [13.6, 15.4]	7083	2122	30.0 [28.7, 31.3]
18.5–24.9	93,354	15,000	16.1 [15.8, 16.3]	129,523	40,378	31.2 [30.9, 31.5]
25–29.9	94,183	16,170	17.2 [16.9, 17.4]	134,575	46,024	34.2 [33.9, 34.5]
≥30	84,369	14,013	16.6 [16.3, 16.9]	125,359	41,253	32.9 [32.6, 33.2]
Unknown	27,021	7222	26.7 [26.1, 27.4]	190,941	75,030	39.3 [39.0, 39.6]
Family history of gastric cancer						
Yes	9446	1485	15.7 [14.9, 16.5]	5672	1973	34.8 [33.3, 36.4]
No	284,553	51,862	18.2 [18.1, 18.4]	551,889	202,834	36.8 [36.6, 36.9]
Charlson comorbidity index						
0	158,560	29,043	18.3 [18.1, 18.5]	397,540	142,012	35.7 [35.5, 35.9]
1	67,993	11,786	17.3 [17.0, 17.6]	108,060	37,098	34.3 [34.0, 34.7]
2	33,066	5280	16.0 [15.5, 16.4]	35,532	12,245	34.5 [33.9, 35.1]
≥3	48,382	7238	15.0 [14.6, 15.3]	37,204	13,452	36.2 [35.6, 36.8]

CI, confidence interval; KPNC, Kaiser Permanente Northern California.

^aIncludes American and Alaskan Native and multiracial groups.

Positivity rates by age. The nonserological positivity rates of *H. pylori* were slightly higher in 30–59 years age groups and in people aged 70 years or more. The serological positivity rates increased significantly by age (Table 2 and Figure 1).

Positivity rates by sex. The positivity rate of *H. pylori* was higher in men than in women using both nonserological and serological methods (Table 2). When further stratified by race and ethnicity, positivity rates by nonserological methods were highest in Hispanic men

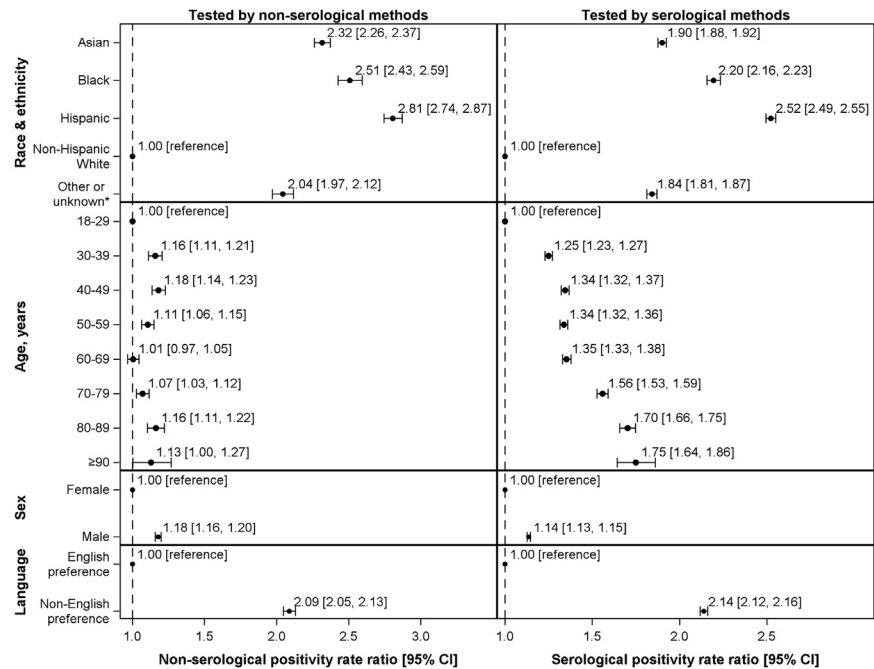


Figure 1. *Helicobacter pylori* positivity rates ratios across demographic characteristics among KPNC members who received serological and nonserological testing in 2000–2019. * Includes American and Alaskan Native and multiracial groups. CI, confidence interval; KPNC, Kaiser Permanente Northern California.

(30.8%, 95% CI, 30.2%–31.6%) and lowest in non-Hispanic White women (9.4%, 95% CI, 9.2%–9.6%) (Table 3).

Positivity rates by language preference. The positivity rates of *H. pylori* among people with non-English language preference were significantly higher than those with English language preference (Table 2 and Figure 1). When stratified by race and ethnicity, among individuals with English language preference, both serological and nonserological positivity rates were higher among people who were Asian, Black, or Hispanic than those who were non-Hispanic White (Table 3). By contrast, among individuals with non-English language preference, the positivity rate for non-Hispanic White individuals was similar to the rate for Black and Hispanic individuals but higher than the rate for Asian individuals by both nonserological and serological methods (Table 3).

Trends in *H. pylori* Positivity Rates Over Two Decades

H. pylori positivity rates by both serological and non-serological testing methods declined from 2000 to 2010 (Figure 2A). Starting 2010, trends in positivity rates diverged, with serological positivity continuing to decline ($P < .001$), while nonserological positivity stabilized to slightly increased ($P < .001$). When comparing 2000 and 2019, there was an absolute decrease in both serological and nonserological positivity rates across race and ethnicity, age, sex, and language preference (Figure 3A, Table A4). However, when comparing 2010 and 2019, a reverse, increasing trend in nonserological positivity rates was noted in people who were Asian (rate increase: 2.6%; 95% CI, 0.8%–4.4%) or Hispanic (rate increase: 2.3; 95% CI, 0.4%–4.2%), with borderline changes noted in those who were Black and

other or unknown, although decreasing trends were noted in those who were non-Hispanic White (Figure 3B, Table A4). Increases in nonserological positivity rates were also seen in younger persons (aged <60 years), men, and those with a non-English language preference.

Trends of *H. pylori* Test Positivity Rates by Birth Cohort

Both serological and nonserological *H. pylori* positivity rates were highest in the older birth cohorts and lower in the younger cohorts (Figure 2B). Serological positivity rates decreased for consecutive cohorts born circa 1915 through 1950, after which the positivity rates plateaued for consecutive cohorts until 1970s and then decreased again through cohort 2000 (Figure 2B). For nonserological positivity rates, a similar decrease was observed for consecutive cohorts from 1915 to 1950, with a slight increase from 1950 to 1980 and a decrease again through cohort 2000. Overall similar trends were observed by birth cohorts when stratified by race and ethnicity, sex, and language preference, although the decrease in both serological and nonserological positivity was more pronounced for older birth cohorts (1915–1950) in non-Hispanic White individuals and those with English language preference, compared with other groups (Figure A2).

Predictors of *H. pylori* Test Positivity

Factors associated with increased odds of *H. pylori* nonserological test positivity included older age (adjusted odds ratio [aOR], 1.06; 95% CI, 1.05–1.07), male sex (aOR, 1.29; 95% CI, 1.27–1.32), being Asian (aOR, 2.48; 95% CI, 2.41–2.55), Black (aOR, 3.12; 95% CI, 3.00–3.24), Hispanic (aOR, 2.97; 95% CI, 2.89–3.06), having a non-English

Table 3. *Helicobacter pylori* Test Positivity Rates Across Racial and Ethnic Groups Among KPNC Members Tested by Nonserological and Serological Methods in 2000–2019

Characteristic	Asian	Black	Hispanic	Non-Hispanic White	Other or unknown ^a
	% [95% CI]	% [95% CI]	% [95% CI]	% [95% CI]	% [95% CI]
Tested by nonserological methods					
Overall	23.2 [22.8, 23.6]	25.1 [24.4, 25.8]	28.1 [27.7, 28.5]	10.0 [9.8, 10.2]	20.4 [19.8, 21.1]
Age, y					
18–29	20.0 [18.7, 21.3]	19.4 [16.9, 22.2]	21.5 [20.4, 22.7]	7.1 [6.5, 7.7]	18.7 [16.7, 20.9]
30–39	21.4 [20.6, 22.3]	20.7 [19.0, 22.5]	26.8 [25.9, 27.7]	8.1 [7.7, 8.6]	19.7 [18.2, 21.3]
40–49	21.6 [20.8, 22.4]	22.5 [21.1, 24.1]	28.5 [27.7, 29.4]	8.3 [7.9, 8.7]	19.6 [18.2, 21.1]
50–59	22.6 [21.8, 23.4]	24.5 [23.1, 26.0]	27.7 [26.9, 28.6]	8.7 [8.4, 9.1]	19.4 [18.1, 20.8]
60–69	22.7 [21.9, 23.6]	25.1 [23.6, 26.7]	26.2 [25.2, 27.3]	9.0 [8.6, 9.3]	18.1 [16.8, 19.5]
70–79	23.1 [21.9, 24.3]	27.1 [25.1, 29.2]	26.5 [25.2, 27.9]	11.6 [11.2, 12.0]	19.9 [18.2, 21.7]
80–89	22.4 [20.4, 24.6]	29.4 [26.0, 33.2]	26.2 [24.1, 28.5]	14.6 [13.9, 15.4]	21.5 [18.8, 24.7]
≥90	22.0 [16.4, 29.4]	30.0 [20.1, 44.8]	27.4 [20.3, 36.9]	14.5 [12.4, 16.8]	23.1 [15.6, 34.3]
Sex					
Female	21.1 [20.6, 21.6]	22.5 [21.6, 23.4]	26.4 [25.9, 26.9]	9.4 [9.2, 9.6]	19.2 [18.4, 20.0]
Male	25.9 [25.3, 26.5]	29.5 [28.3, 30.8]	30.8 [30.2, 31.6]	10.9 [10.6, 11.2]	22.2 [21.2, 23.3]
Language preference					
English	21.5 [21.1, 21.9]	24.8 [24.1, 25.6]	23.9 [23.4, 24.4]	9.5 [9.3, 9.7]	18.7 [18.1, 19.4]
Non-English	28.3 [27.4, 29.2]	37.1 [28.3, 48.5]	35.7 [34.9, 36.4]	33.3 [30.6, 36.2]	33.5 [31.2, 36.1]
Unknown	33.9 [27.8, 41.3]	41.4 [33.4, 51.4]	30.7 [24.5, 38.4]	24.7 [22.4, 27.1]	18.3 [13.1, 25.6]
Percent college educated in patient residing area					
<40%	22.9 [22.2, 23.5]	23.0 [22.1, 24.0]	27.2 [26.7, 27.7]	8.1 [7.9, 8.3]	19.1 [18.1, 20.1]
40%–59.9%	20.0 [19.3, 20.7]	21.4 [19.6, 23.2]	23.0 [22.0, 24.0]	7.3 [7.0, 7.6]	17.2 [15.9, 18.7]
60%–79.9%	19.9 [19.0, 20.8]	22.2 [19.5, 25.3]	21.6 [19.9, 23.3]	7.9 [7.5, 8.4]	17.3 [15.6, 19.2]
≥80%	18.7 [16.7, 21.0]	26.7 [18.3, 39.0]	13.9 [10.1, 19.0]	7.7 [6.7, 8.9]	14.7 [10.9, 19.6]
Unknown	24.2 [23.4, 25.0]	27.7 [26.3, 29.1]	29.2 [28.4, 30.1]	13.3 [13.0, 13.7]	21.6 [20.5, 22.7]
Smoking status					
Ever smoker	24.2 [23.4, 25.0]	24.6 [23.6, 25.6]	27.1 [26.4, 27.8]	9.7 [9.4, 9.9]	18.2 [17.2, 19.1]
Never smoker	21.6 [21.2, 22.1]	23.9 [22.9, 25.0]	27.4 [26.9, 27.9]	8.8 [8.5, 9.0]	20.4 [19.5, 21.3]
Unknown	31.9 [30.1, 33.8]	35.7 [32.1, 39.5]	37.1 [35.1, 39.3]	19.0 [18.2, 20.0]	27.0 [24.7, 29.5]
Body mass index, kg/m ²					
<18.5	19.4 [17.7, 21.3]	23.4 [18.4, 29.8]	16.1 [13.1, 19.8]	8.7 [7.7, 9.8]	19.1 [15.3, 23.8]
18.5–24.9	21.4 [20.9, 21.9]	24.0 [22.5, 25.6]	23.8 [23.0, 24.6]	8.5 [8.2, 8.7]	18.7 [17.6, 19.9]
25–29.9	21.5 [20.8, 22.2]	23.6 [22.3, 24.9]	27.4 [26.8, 28.1]	8.7 [8.4, 9.0]	18.7 [17.7, 19.9]
≥30	21.9 [20.8, 23.1]	22.2 [21.2, 23.3]	26.5 [25.9, 27.2]	8.2 [7.9, 8.5]	17.5 [16.3, 18.7]
Unknown	33.8 [32.1, 35.5]	35.9 [33.2, 38.9]	37.9 [36.2, 39.8]	19.5 [18.8, 20.3]	27.3 [25.3, 29.4]
Family history of gastric cancer					
Yes	17.8 [16.2, 19.5]	17.8 [15.0, 21.1]	22.7 [20.8, 24.7]	8.3 [7.4, 9.3]	19.6 [16.3, 23.6]
No	23.3 [22.9, 23.7]	25.3 [24.6, 26.1]	28.2 [27.7, 28.6]	10.0 [9.8, 10.2]	20.4 [19.8, 21.1]
Charlson comorbidity index					
0	21.7 [21.3, 22.2]	24.7 [23.6, 25.8]	28.5 [27.9, 29.0]	9.3 [9.0, 9.5]	20.8 [19.9, 21.6]
1	23.9 [23.1, 24.8]	24.4 [23.0, 25.8]	26.0 [25.2, 26.8]	9.5 [9.2, 9.9]	18.5 [17.2, 19.8]
2	22.8 [21.6, 24.1]	23.5 [21.7, 25.6]	23.4 [22.2, 24.7]	9.8 [9.4, 10.3]	18.0 [16.2, 19.9]
≥3	20.6 [19.6, 21.7]	22.5 [21.2, 24.0]	22.8 [21.7, 23.9]	9.6 [9.3, 10.0]	17.0 [15.6, 18.5]
Tested by serological methods					
Overall	42.5 [42.1, 42.9]	49.0 [48.3, 49.8]	56.4 [55.9, 56.8]	22.3 [22.2, 22.5]	41.1 [40.6, 41.7]
Age, y					
18–29	29.3 [28.4, 30.2]	30.7 [29.1, 32.4]	40.9 [40.1, 41.8]	11.5 [11.1, 11.9]	31.1 [30.1, 32.2]
30–39	35.8 [35.1, 36.5]	39.5 [38.1, 40.9]	52.1 [51.3, 52.9]	14.8 [14.5, 15.2]	37.8 [36.8, 38.8]
40–49	40.9 [40.1, 41.7]	46.5 [45.1, 47.9]	57.3 [56.4, 58.1]	17.9 [17.5, 18.3]	41.8 [40.6, 42.9]
50–59	44.9 [44.1, 45.9]	51.4 [49.8, 53.0]	59.6 [58.5, 60.6]	20.4 [20.0, 20.7]	44.0 [42.7, 45.5]
60–69	47.2 [46.0, 48.4]	55.7 [53.6, 58.0]	60.8 [59.4, 62.3]	24.2 [23.8, 24.7]	43.2 [41.5, 45.0]
70–79	48.6 [46.7, 50.5]	63.4 [60.1, 66.9]	64.1 [61.9, 66.3]	33.2 [32.5, 33.9]	48.4 [45.8, 51.2]
80–89	48.1 [44.9, 51.5]	63.9 [58.6, 69.8]	63.4 [59.8, 67.2]	40.7 [39.6, 41.9]	49.1 [45.1, 53.6]
≥90	42.1 [33.7, 52.6]	63.6 [50.1, 80.6]	64.1 [53.7, 76.4]	43.5 [40.4, 46.9]	53.2 [41.8, 67.7]
Sex					
Female	39.9 [39.4, 40.4]	45.8 [45.0, 46.7]	53.7 [53.2, 54.2]	21.4 [21.1, 21.6]	39.0 [38.3, 39.7]
Male	46.4 [45.7, 47.1]	55.1 [53.8, 56.5]	60.5 [59.8, 61.2]	23.9 [23.6, 24.2]	43.8 [42.9, 44.6]
Language preference					
English	38.7 [38.3, 39.2]	48.6 [47.9, 49.4]	46.9 [46.4, 47.4]	21.4 [21.3, 21.6]	35.8 [35.3, 36.4]
Non-English	56.6 [55.6, 57.6]	75.6 [66.4, 86.0]	72.7 [71.9, 73.5]	71.6 [68.6, 74.7]	68.6 [66.9, 70.4]
Unknown	42.4 [38.1, 47.2]	61.5 [54.8, 69.0]	56.8 [51.6, 62.6]	37.0 [35.4, 38.7]	40.9 [37.4, 44.8]

Table 3. Continued

Characteristic	Asian	Black	Hispanic	Non-Hispanic White	Other or unknown ^a
	% [95% CI]	% [95% CI]	% [95% CI]	% [95% CI]	% [95% CI]
Percent college educated in patient residing area					
<40%	34.9 [34.2, 35.7]	39.7 [38.5, 40.9]	47.0 [46.4, 47.7]	16.0 [15.7, 16.3]	32.8 [31.5, 34.1]
40%–59.9%	33.4 [32.4, 34.3]	37.4 [35.1, 39.9]	40.5 [39.2, 41.8]	14.6 [14.2, 15.1]	28.5 [26.8, 30.3]
60%–79.9%	33.3 [32.2, 34.5]	36.8 [33.2, 40.8]	38.1 [35.9, 40.3]	14.6 [14.1, 15.3]	27.6 [25.4, 30.0]
≥80%	31.9 [29.3, 34.7]	31.9 [22.1, 45.9]	34.9 [28.8, 42.1]	13.7 [12.3, 15.2]	21.6 [16.8, 27.7]
Unknown	45.9 [45.4, 46.5]	52.1 [51.1, 53.0]	60.6 [60.1, 61.2]	25.1 [24.8, 25.3]	43.0 [42.3, 43.6]
Smoking status					
Ever smoker	42.6 [41.7, 43.4]	50.9 [49.7, 52.0]	54.1 [53.4, 54.9]	23.6 [23.3, 23.9]	38.1 [37.1, 39.0]
Never smoker	38.6 [38.0, 39.1]	43.1 [41.9, 44.2]	51.8 [51.2, 52.4]	18.1 [17.8, 18.4]	38.5 [37.5, 39.4]
Unknown	44.8 [44.0, 45.7]	49.0 [47.6, 50.6]	60.5 [59.6, 61.3]	23.0 [22.7, 23.4]	43.0 [42.2, 44.0]
Body mass index, kg/m ²					
<18.5	36.9 [34.6, 39.2]	56.0 [48.0, 65.3]	38.2 [33.5, 43.7]	18.6 [17.1, 20.2]	34.3 [29.8, 39.5]
18.5–24.9	39.1 [38.5, 39.7]	45.8 [43.9, 47.7]	45.9 [45.0, 46.9]	18.8 [18.4, 19.1]	35.9 [34.7, 37.1]
25–29.9	38.4 [37.7, 39.2]	46.5 [45.0, 48.1]	54.0 [53.2, 54.8]	19.8 [19.5, 20.2]	38.9 [37.7, 40.1]
≥30	35.8 [34.6, 37.0]	42.9 [41.8, 44.1]	51.0 [50.2, 51.7]	19.4 [19.1, 19.8]	35.4 [34.1, 36.7]
Unknown	45.7 [44.9, 46.5]	50.8 [49.5, 52.1]	60.8 [60.0, 61.5]	24.4 [24.1, 24.7]	42.6 [41.8, 43.4]
Family history of gastric cancer					
Yes	37.7 [34.7, 40.9]	40.4 [33.9, 48.2]	48.3 [44.9, 52.1]	22.0 [20.0, 24.1]	35.4 [29.9, 41.9]
No	42.5 [42.1, 42.9]	49.0 [48.3, 49.8]	56.4 [55.9, 56.8]	22.3 [22.1, 22.5]	41.1 [40.6, 41.7]
Charlson comorbidity index					
0	41.1 [40.7, 41.6]	46.6 [45.7, 47.5]	55.9 [55.4, 56.4]	19.9 [19.7, 20.2]	40.4 [39.7, 41.0]
1	40.9 [40.0, 41.9]	46.6 [45.1, 48.2]	52.1 [51.2, 53.0]	21.4 [21.0, 21.8]	38.7 [37.4, 40.0]
2	41.2 [39.5, 43.0]	48.4 [45.8, 51.1]	52.4 [50.6, 54.3]	24.8 [24.1, 25.5]	39.9 [37.4, 42.5]
≥3	41.3 [39.6, 43.1]	52.9 [50.4, 55.5]	51.0 [49.1, 53.0]	28.5 [27.8, 29.2]	39.9 [37.5, 42.5]

CI, confidence interval; KPNC, Kaiser Permanente Northern California.

^aIncludes American and Alaskan Native and multiracial groups.

language preference (aOR, 1.65; 95% CI, 1.61–1.70), living in an area with < 40% college attainment (aOR, 1.12; 95% CI, 1.03–1.23), and having a BMI of ≥25 (Table 3). Having a family history of gastric cancer was associated with lower odds of *H. pylori* nonserological test positivity (aOR 0.79, 95% CI, 0.74–0.83) but did not affect the odds of serological positivity. The odds of *H. pylori* test positivity were also lower with increasing Charlson comorbidity index and over time (Table 4).

Discussion

In this retrospective cohort study, we provided updated information on *H. pylori* burden in a large, diverse, community-based US population. Overall, there was a marked decrease in the serological positivity of *H. pylori* over 20 years across all age and racial and ethnic groups, but nonserological positivity initially decreased and then stabilized to slightly increased over the last 10 years. We also noted persistent and substantial racial and ethnic disparities in active *H. pylori* burden, with Asian, Black, and Hispanic individuals having 2-fold to 3-fold higher nonserological positivity rates than non-Hispanic White individuals. In addition, people with a non-English language preference had significantly higher positivity rates across all racial and ethnic groups, including non-Hispanic White individuals. Furthermore, both serological and nonserological positivity rates decreased substantially from older to

younger birth cohorts. These findings demonstrated an overall decreasing *H. pylori* burden over the past 2 decades but with persistent demographic disparities, particularly by race and ethnicity and by language preference, in a community-based US population.

We noted an overall 2-fold higher positivity rate using serological methods than nonserological methods. It is possible that a substantial proportion of individuals who tested negative by nonserological methods received treatment with successful eradication before cohort entry in our study. It is also possible that many individuals were exposed to antibiotics for different indications that inadvertently eradicated *H. pylori*, leading to negative nonserological test results, while their *H. pylori* serology remained positive. Another possibility is that some serological results were false positive, particularly in populations with low prevalence rates, although this seems less likely to be the main contributor overall given that the doubling rates using serological methods were also seen in populations with much higher *H. pylori* prevalence such as Asian, Black, and Hispanic individuals. The overall nonserological positivity rate in our study participants was 18.2% (95% CI, 18.1%–18.4%) which was lower than the prevalence rates reported previously,^{4,13,20,26} but similar to a recently reported pool prevalence rate of 17.6 (95% CI, 16.0%–98.4%).² Given the substantially lower nonserological positivity rates which are indicative of active infection compared with the serological positivity rates which are unable to differentiate between a

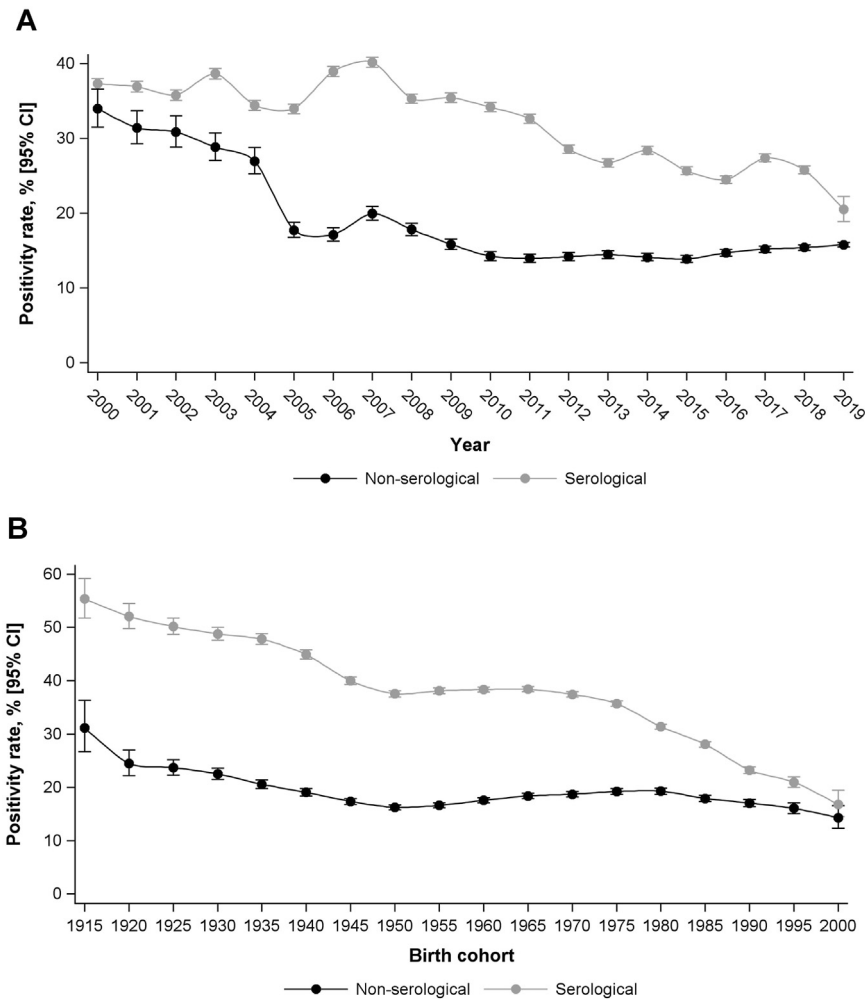


Figure 2. Trends in *Helicobacter pylori* positivity rates (A) over time and (B) by birth cohort among KPNC members who received serological and non-serological testing in 2000–2019. CI, confidence interval; KPNC, Kaiser Permanente Northern California.

prior vs current infection, our findings provide further evidence supporting the use of nonserological methods to identify active *H. pylori* infection in clinical practice.^{12,13}

We noted substantial racial and ethnic disparities in *H. pylori* positivity, with people who were Asian, Black, and Hispanic having approximately 2–3-fold higher positivity rates than people who were non-Hispanic White. In a systematic review of 25 studies (most of which used data collected prior to 2005), the prevalence ratio of *H. pylori* for Black vs non-Hispanic White individuals ranged from 1.3 to 5.4 and the ratio for Hispanic to non-Hispanic White individuals ranged from 1.8 to 4.4.²⁷ Similarly, in a recent nationwide study based on the veteran population, *H. pylori* test positivity rates among people who were non-Hispanic Black, Hispanic, and non-Hispanic White were 40.2% (95% CI, 40.0%–40.5%), 36.7% (95% CI, 36.4%–37.1%), and 20.1% (20.0%–20.2%), respectively.²² Overall, our findings extend the current literature suggesting significant racial and ethnic disparities in *H. pylori* burden across different populations in the United States, with persistently higher *H. pylori* burden in Asian, Black, and Hispanic populations who may benefit from targeted screening and eradication of *H. pylori*.

Our findings showed that people with non-English language preference had an approximately 2-fold higher positivity rate of *H. pylori* than primary English speakers using both nonserological and serological methods, consistent with several prior studies.^{5,26,28,29} Importantly, non-Hispanic White individuals who preferred to speak non-English languages had comparable positivity rates to Black and Hispanic individuals and higher positivity rates than Asian individuals, suggesting language preference may be considered a useful tool to identify subpopulations at high risk of *H. pylori* infection across all racial and ethnic groups, including non-Hispanic White individuals.

The temporal decrease in *H. pylori* positivity rates over 2 decades using both nonserological and serological methods through 2019 extends a prior analysis showing a decrease in pooled prevalence in the United States from 42.2% (95% CI, 22.9%–61.5%) in 1970–1999 to 26.6% (95% CI, 19.0%–34.1%) in 2000–2016,²⁶ and are consistent with a recent Veterans Health System study which showed *H. pylori* test positivity decreased from 35.9% in 1999–2006 to 18.4% in 2013–2018.²² A main factor contributing to the declining *H. pylori* burden could be the birth cohort effect.³⁰ Individuals who were born in more recent years have a lower

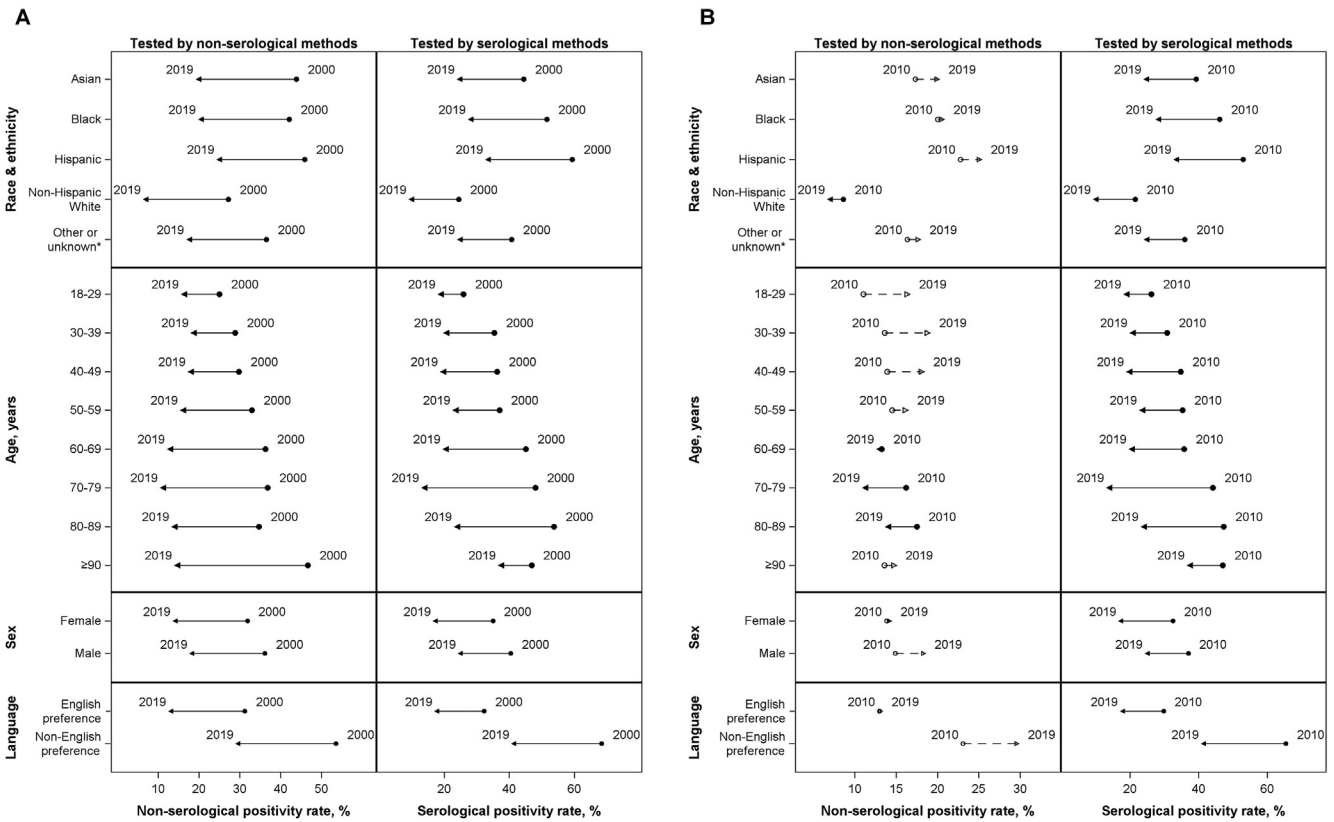


Figure 3. Changes in *Helicobacter pylori* positivity rates from (A) 2000 to 2019 and (B) 2010–2019 across demographic characteristics among KPNC members who received serological and nonserological testing. * Includes American and Alaskan Native and multiracial groups. KPNC, Kaiser Permanente Northern California.

risk of *H. pylori* exposure, particularly during childhood, and higher likelihood of antibiotic use for a variety of reasons leading to eradication of *H. pylori*.^{4,31} The plateauing of the decrease in nonserological positivity rate after 2010 with a mild increase primarily seen in people who were aged less than 60 years, Asian or Hispanic individuals, or those with a non-English language preference may be explained by recent changes in racial and ethnic distribution, and in particular, recent trends in immigration to California. Data from the Department of Homeland Security noted the number of new immigrants, international students, and temporary workers in California increased from 847,565 in 2010 to 1,230,708 in 2019.³² In addition, new immigrants to the United States during this period were younger and most likely to be from Asia and the Pacific Islands (39.7%), Mexico and Central and South America (31.7%), or Africa and the Caribbean Islands (19.0%), where the prevalence rates of *H. pylori* are substantially higher than in the general US population.²⁶

To our knowledge, this study represents the largest contemporary observational study on *H. pylori* epidemiology in a demographically diverse, community-based population in the United States over the past 2 decades. Strengths of this study include a population approximating the region’s large, underlying population in regards to demographic and sociodemographic characteristics, increasing

the generalizability of the study findings; a long observation period over 2 decades; comprehensive assessment of all available testing methods for *H. pylori* to decrease potential misclassifications; assessment of multiple patient-level demographic and clinical variables as well as birth cohorts to allow evaluation of independent risk factors; and accuracy in data ascertainment from well-maintained electronic databases.

Our study has several limitations. First, we were only able to measure *H. pylori* burden in the tested individuals, which is a shared limitation in the majority of prior studies on *H. pylori* prevalence in the United States.^{1,22,26,33,34} Although we did not have the detailed information regarding the clinical indications for the *H. pylori* testing, in the current US practice the testing is generally performed for symptomatic individuals or for individuals who are considered at high risk for *H. pylori* infection. Because routine screening for *H. pylori* in asymptomatic individuals is not the current standard of care, it would not be possible to precisely measure the prevalence among the general population. Nonetheless, the present study with an exceedingly large dataset provided important information on the contemporary *H. pylori* burden in a community-based US population. It is reasonable to assume that the time trends and demographic disparities in positivity rates of the tested individuals in our study approximate those in the

Table 4. Predictors of *Helicobacter pylori* Test Positivity

Variable	Tested by nonserological methods		Tested by serological methods	
	OR [95% CI] ^a	P value	OR [95% CI] ^a	P value
Race and ethnicity				
Asian	2.48 [2.41, 2.55]	<.001	2.52 [2.48, 2.57]	<.001
Black	3.12 [3.00, 3.24]	<.001	3.85 [3.76, 3.94]	<.001
Hispanic	2.97 [2.89, 3.06]	<.001	4.03 [3.96, 4.10]	<.001
Non-Hispanic White	1.00 [reference]	-	1.00 [reference]	-
Other or unknown ^b	2.14 [2.06, 2.23]	<.001	2.36 [2.31, 2.41]	<.001
Age, y ^c	1.06 [1.05, 1.07]	<.001	1.25 [1.24, 1.25]	<.001
Sex				
Female	1.00 [reference]	-	1.00 [reference]	-
Male	1.29 [1.27, 1.32]	<.001	1.29 [1.28, 1.31]	<.001
Language preference				
English	1.00 [reference]	-	1.00 [reference]	-
Non-English	1.65 [1.61, 1.70]	<.001	2.67 [2.62, 2.72]	<.001
Percent college educated in patient residing area				
<40%	1.12 [1.03, 1.23]	.011	1.06 [0.99, 1.13]	.076
40%–59.9%	1.03 [0.94, 1.12]	.531	1.03 [0.96, 1.09]	.424
60%–79.9%	1.05 [0.96, 1.15]	.309	1.02 [0.96, 1.09]	.513
≥80%	1.00 [reference]	-	1.00 [reference]	-
Smoking status				
Ever smoker	1.00 [0.98, 1.02]	.883	1.00 [0.98, 1.01]	.791
Never smoker	1.00 [reference]	-	1.00 [reference]	-
Body mass index, kg/m²				
<18.5	1.00 [0.93, 1.07]	.913	1.01 [0.96, 1.06]	.732
18.5–24.9	1.00 [reference]	-	1.00 [reference]	-
25–29.9	1.03 [1.01, 1.06]	.005	1.03 [1.01, 1.05]	.007
≥30	1.04 [1.01, 1.07]	.005	1.02 [1.00, 1.04]	.037
Family history of gastric cancer	0.79 [0.74, 0.83]	<.001	1.03 [0.97, 1.09]	.372
Charlson comorbidity index				
0	1.00 [reference]	-	1.00 [reference]	-
1	0.94 [0.92, 0.97]	<.001	0.94 [0.93, 0.95]	<.001
2	0.87 [0.84, 0.90]	<.001	0.93 [0.91, 0.95]	<.001
≥3	0.75 [0.73, 0.78]	<.001	0.89 [0.86, 0.91]	<.001
Year ^c	0.96 [0.96, 0.96]	<.001	0.96 [0.96, 0.96]	<.001

CI, confidence interval; OR, odds ratio.

^aMultivariable logistic regression analysis, adjusted for year, age, sex, race, ethnicity, language preference, education level, smoking status, body mass index, family history of gastric cancer, and Charlson comorbidity index. Missing values were imputed using multiple imputations with chained equations and estimates were averaged over 40 imputed datasets.

^bIncludes American and Alaskan Native and multiracial groups.

^cEstimate corresponds to 1 unit increase.

overall population. These findings should still have relatively high generalizability to other population-based US settings and can inform strategies to improve targeted screening and eradication of *H. pylori* in high-risk groups. Second, we were unable to ascertain data on *H. pylori* testing or treatment conducted prior to the participants' KPNC membership commencement. Therefore, some negative test results, particularly by nonserological methods, could reflect eradication from prior treatment. Third, proton pump inhibitors (PPIs) use may decrease the sensitivity of nonserological *H. pylori* testing. In our study participants with a history of PPI use, it was not possible to precisely ascertain the information with regard to the time and duration of their PPI use, and in particular, whether PPI was taken within 2 weeks before *H. pylori* nonserological testing. In addition, a substantial proportion of study participants

took over-the-counter PPIs which are unable to be ascertained. Therefore, the PPI effect on the nonserological testing positivity rates could not be accurately evaluated. That said, it is the common practice in our setting that providers recommend stopping PPIs for 2 weeks before taking nonserological *H. pylori* tests. Fourth, individual-level income or education data were not available; thus, we used census-level data of percent attainment of a college education as a proxy method for socioeconomic status.

In conclusion, we provided a comprehensive analysis of *H. pylori* burden in a large, diverse, community-based US population over 2 decades. *H. pylori* serological positivity rates markedly declined over the past 2 decades, while nonserological positivity rates initially decreased and then stabilized to slightly increased over the recent 10 years. There remained persistent and significant demographic

disparities in active *H. pylori* burden, with 2–3 higher folds in nonserological positivity rates among Asian, Black, and Hispanic individuals compared with non-Hispanic White individuals, and among those with non-English language preference. These findings should inform strategies to allocate resources to improve screening and eradication of *H. pylori* in US populations, particularly among groups with a high risk of infection, to reduce *H. pylori*-associated adverse health outcomes.

Supplementary Materials

Material associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.gastha.2024.04.008>.

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Dan Li: Study concept and design, acquisition of data, analysis and interpretation of data, drafting of the manuscript, article guarantor, and manuscript editing. Sophie A. Merchant: Acquisition of data, analysis and interpretation of data, drafting of the manuscript, and manuscript editing. Douglas A. Corley: Analysis and interpretation of data and manuscript editing. Jessica M. Badalov: Analysis and interpretation of data and manuscript editing. All authors have approved the final draft submitted.

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Data, analytic methods, and study materials are available upon request, although certain computer programs and analytic codes or macros used in this study are specific to Kaiser Permanente Northern California.

Reporting Guidelines:

STROBE.