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SYSTEMATIC REVIEW AND META-ANALYSES

Racial Differences in *Helicobacter pylori* Prevalence in the US: A Systematic Review

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BACKGROUND AND AIMS: *Helicobacter pylori* remains an important risk factor for noncardia gastric cancer and a spectrum of disease from *H. pylori* infection to gastric cancer. As a step toward improved clinical strategies for gastric cancer prevention, we assessed racial differences in prevalence of *H. pylori* from studies across the United States. This systematic review provides a comprehensive evaluation of the literature regarding racial differences in *H. pylori* in the United States. **METHODS:** MEDLINE, Embase, and Web of Science database searches were performed through May 26, 2021. Ultimately, 25 studies that reported *H. pylori* infection prevalence by race were included. **RESULTS:** All studies included in the review documented higher *H. pylori* prevalence in Blacks and Hispanics than in whites. The ratio of *H. pylori* prevalence for Blacks compared to non-Hispanic whites ranged from 1.3 to 5.4, and the ratio for Hispanics compared to non-Hispanic whites ranged from 1.8 to 4.4. Of the 5 studies that examined *H. pylori* CagA prevalence by race, 4 found higher prevalence among Blacks and Hispanics compared to whites, with CagA prevalence ranging from 19% to 77% in whites, 62% to 90% in Blacks, and 64% to 74% in Hispanics. **CONCLUSION:** In this review, across 25 studies, varying in underlying population, time period, and geographic location, Blacks and Hispanics appeared to have a higher prevalence of *H. pylori* infection than whites. This increased prevalence of *H. pylori* among populations also at a higher risk of gastric cancer is relevant in the clinical setting for decision-making related to *H. pylori* testing and gastric cancer prevention.

Keywords: *H. pylori*; Race/Racial; Systematic Review

Introduction

Recent studies suggest a worldwide prevalence of *Helicobacter pylori* infection as high as 4.4 billion, representing over half the world's population.[1] Notably, *H. pylori* is estimated to be responsible for 89% of noncardia gastric adenocarcinomas (GCs),[2] a highly fatal cancer with a 5-year relative survival of only 32%.[3] In the US population as a whole, the overall incidence of both *H. pylori* and gastric cancer have declined over time.[4] However, disparities related to GC persist: Blacks remain at an increased risk of gastric cancer compared to non-Hispanic whites[5] and when compared to all cancers, GC is the cancer associated with the greatest disparity in cancer mortality between Black and white Americans.[5] Addressing disparities in GC risk factors such as *H. pylori* infection may offer important opportunities to prevent gastric cancer in high-risk groups.

In addition to GC, *H. pylori* infection has been associated with a variety of clinical conditions encountered by gastroenterologists, including chronic gastritis, peptic ulcer disease, and mucosa-associated lymphoid tissue lymphoma.[6] In 2017, the American College of Gastroenterology expanded indications for *H. pylori* testing and recommended treating all *H. pylori* infections regardless of symptomatic or pathologic burden, followed by eradication testing.[7] However, despite these wider testing and treatment guidelines, *H. pylori* infection remains undertreated, and retesting for eradication to confirm successful treatment is inconsistently performed.[8]

Recently, the Houston Consensus Conference recommended *H. pylori* testing in patients who have migrated from *H. pylori*–endemic countries. Although the Houston Consensus has suggested that Blacks and Hispanics be considered for *H. pylori* testing due to suspected higher prevalence rates of infection in these groups,[9] there have been no definitive recommendations, and we currently lack clear guidelines about the clinical utility of *H. pylori* testing in the United States among high-risk populations.

Furthermore, work elucidating the carcinogenic mechanism of *H. pylori* has identified 2 proteins, CagA and VacA, as

Abbreviations used in this paper: **CI, confidence interval; GC, gastric adenocarcinoma; GI, gastrointestinal; OR, odds ratio; PR, prevalence ratio; RR, risk ratio; VA, Veterans Affairs.**

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high-risk virulence factors.[10] Currently, there are no clinical guidelines for utilizing *H. pylori* virulence factor testing as a method for risk stratification in infected individuals.

Once a diagnosis of *H. pylori* has been established, current guidelines for *H. pylori* treatment suggest incorporating individual prior exposure as well as regional prevalence of antibiotic-resistant infection when determining the optimal antibiotic regimen.[7] Unfortunately, data on *H. pylori* antibiotic resistance in the United States remain scarce, making implementation of treatment guidelines difficult. Interestingly, recent studies have suggested incorporating patient demographics into the treatment algorithm in refractory cases.[11]

Overall, the goal of our systematic review was to assess and interpret the current literature of racial differences between Blacks and non-Hispanic whites in *H. pylori* prevalence in the United States, given the lack of consistent prior reporting in those groups. This represents a first step to improving health and addressing disparities related to *H. pylori* infection toward the prevention of gastric cancer.

Methods

Information Sources and Search Strategy

Our search strategy for this systematic review was devised and conducted with an experienced medical librarian (SC). In order to ensure a comprehensive approach, we searched MEDLINE (via PubMed), Embase (via Elsevier), and Web of Science Core Collection (via Clarivate) from the date of database inception forward with the understanding that *H. pylori* was first reported in the literature in 1984.[12] The original searches were conducted on April 16, 2020; a search update was conducted on May 26, 2021, in order to identify newly published studies.

The comprehensive search strategy included a combination of keywords and database-specific subject headings for the following concepts: *Helicobacter pylori* or stomach (or gastric) cancer or gastritis and Blacks (or African Americans) or disparities. No restrictions were placed by date or language. Editorials, letters, conference abstracts, and comments were excluded. The full, reproducible search strategies for all included databases are located in Appendix 1.

All citations identified were then imported into Covidence (Melbourne, Australia), a systematic review screening software (https://www.covidence.org/). Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and checklist were consulted, as detailed in Appendix 6.

Eligibility Criteria and Selection Process

We established eligibility criteria for the abstract screen by defining initial inclusion and exclusion criteria in Covidence; inclusion and exclusion criteria were determined *a priori* and are listed as Appendix 2. Initially, our search strategy cast a broad net with articles with a primary outcome of *H. pylori*, intestinal metaplasia, or gastric cancer included in the abstract review phase. We excluded manuscripts where race was not a primary comparison or where the focus was on esophageal or proximal gastric cancer. Three reviewers K.G., H.T., and H.B. independently screened references by title and abstract in the Covidence systematic review screening software. Conflicts from the abstract review process were resolved by a fourth, independent arbitrator, ME.

Next, we evaluated full-text versions of the 230 abstracts selected for full manuscript review. During the full-text review, the included articles were screened by 2 independent reviewers (K.G. and H.T.), and conflicts were discussed as a team. At this stage, manuscripts with data collection prior to 1990 were excluded due to the fact that *H. pylori* was only discovered in 1984.[12] We then narrowed the scope of papers selected for this systematic review to those focused on *H. pylori*; papers with focus on intestinal metaplasia or gastric cancer were separated into a separate data set for future review.

As detailed in Figure 1, 4142 references were initially imported into Covidence. After duplicates and irrelevant studies were excluded, 230 references underwent full-text review, resulting in 30 manuscripts focused on *H. pylori* and race in the United States included in this systematic review (Appendix 4). Twenty-five studies reported prevalence of *H. pylori* infection by race. In addition, 2 studies that reported CagA+ and/or VacA+ *H. pylori* prevalence by race and 3 studies that reported antibiotic resistance patterns by race were also included. Furthermore, as part of the full manuscript review, some primary authors were contacted by the study team in order to determine dates of data collection. The majority of study authors responded to requests for the data collection period; studies whose data collection period we were unable to confirm were denoted in tables with the year of publication rather than the data collection period.

Data Collection Process

For manuscripts that used the same database (such as Surveillance, Epidemiology, and End Results (SEER) data or National Health and Nutrition Examination Survery (NHANES) data), the most comprehensive and representative papers were prioritized for data abstraction, although all related references were reviewed. Selected manuscripts were reviewed, and population information including race, ethnicity, region, age, and reported prevalence of *H. pylori* were extracted.

Data Items

The data abstracted for this review included the study location and population, and specifically the data source (eg, SEER, NHANES, and so on), as appropriate. For both serologic and histologic studies, the primary outcome abstracted was reported prevalence of *H. pylori* in the population by race/ethnicity. When applicable, statistics such as odds ratios (OR) and confidence intervals (CIs) were also included in order to assess precision of measurements reported by individual studies. In relevant manuscripts, exposure to *H. pylori* virulence factors CagA and VacA was determined by antigen-specific seropositivity. Exposure to these virulence factors as well as data related to *H. pylori* antibody resistance were abstracted as secondary outcomes.

Study Bias

We utilized the Newcastle-Ottawa quality assessment scale, adapted for cross-sectional analyses,[13] to assess the quality of papers included in Tables 1 and 2. Of the 25 studies assessed,

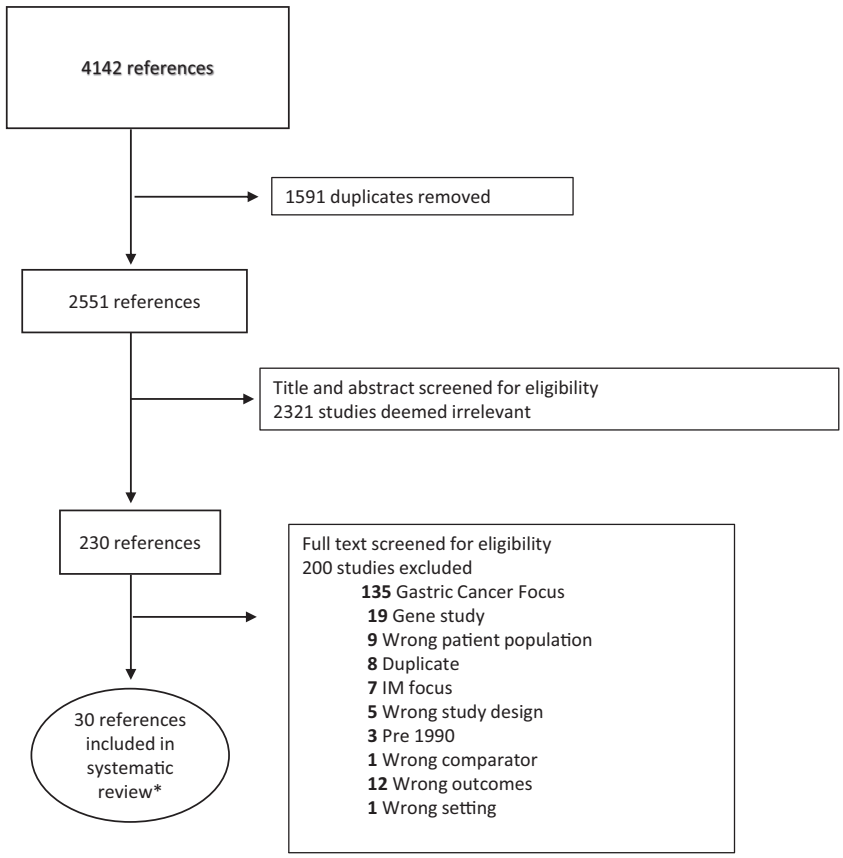

Figure 1. Flow diagram of studies included in the systematic review. Twenty-five studies reported prevalence of *Helicobacter pylori* infection by race, the primary outcome of this review. Five additional studies were included which pertained to secondary outcomes such as oncoprotein prevalence rates and antibiotic resistance rate by race. *5 of the studies pertained to oncoprotein prevalence (CagA and/or VacA + *H. pylori*) rates by race and/or antibiotic susceptibility by race and were evaluated separately although included in the schematic.

14 studies were of good quality,[14–27] 2 were fair,[28,29] and 9 were of poor quality.[30–38] The poor-quality studies tended to lack rigor in representativeness of cases, cohort selection, and comparability of cases and controls (Appendix 5).

Assessment of Limitations

Study design and analytic approach to the data varied greatly in the manuscripts reviewed. Specifically, the studies selected for this review included diverse study populations, with marked heterogeneity between studies. Of the studies included in this review, in addition to the national databases (eg, SEER, NHANES, Women's Health Initiative, Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial), some studies were state-specific, and Texas and California were particularly well-represented. While we were able to evaluate data from across the United States, generalizability to specific regions may be limited as a result of regional sampling.

Our primary outcome of interest was the relative prevalence of *H. pylori* in the United States by race/ethnicity. While white, Black, and Hispanic rates of *H. pylori* prevalence were represented, data in Asian Americans, American Indians, and Alaskan Natives were sparse and, as such, were not included in this review. For most studies, data were not available for migrant status.

Synthesis Methods

Included studies varied widely in respect to sample population characteristics (population-based vs clinic-based, and of those, some were specific to a very particular population, such as those undergoing bariatric surgery), inclusion and exclusion criteria, and *H. pylori* testing mechanism. Given this pronounced heterogeneity of the included studies, no attempt was made to pool data. Data from individual studies were compiled in Tables 1–3. We compared serologic studies and histologic studies separately. We also compared the prevalence of *H. pylori* virulence factors, CagA and VacA, and *H. pylori* antibiotic resistance, by race/ethnicity. Statistics from individual studies were reported when applicable. Data were compiled by the year of data collection in order to evaluate patterns of *H. pylori* prevalence by race over time.

Results

Serologic Evidence H. pylori Exposure

Differences in serologic evidence of exposure to *H. pylori* by race are shown in Table 1, which includes studies with data collection from 1990 to 2014. Twenty-two studies were included in Table 1, and study population sizes ranged from 150 to 7465 participants. Studies were organized by the year of sample collection. Study populations were diverse and included regional hospital studies as well as large national databases. Regionally specific studies were focused primarily in the West and Southern regions of the United States. In contrast to the large national databases, some special populations, such as Roux-en-Y gastric bypass patients and US army recruits, were also represented. The majority of studies included only adults. The age ranges

Table 1. Prevalence of *Helicobacter pylori* by Race From Serologic Studies of Adults or Children in the United States, 1990–2014

Author, publication year	Region	Study population/site	Date of data collection (mean y)	Study size	Age range	*Helicobacter pylori* seroprevalence		
						White	Black	Hispanic
Correa, 1990[31]	New Orleans, LA	2 Children's hospitals	1990[b]	225	0–18	32%	49%	–
Correa, 1990[31]	New Orleans, LA	LSU Dental School	1990[b]	274	18–84	43%	70%	–
Everhart, 2000[16]	National	NHANS III	1990	7465	>20	26%	53%	62%[a]
Graham, 1991[18]	Houston, TX	General population	1990	490	15–80	34%	70%[c]	–
Hyans, 1995[19]	National	US Marine and Navy recruits	1990	1000	17–50	18%	46%	45%
Kruszon-Moran, 2005[20]	National	NHANES III	1990	7465	≥20	26%	53%	62%[a]
Malaty, 1992[36]	Houston, TX	General population	1990	267	≥20	26%	66%	65%
McQuillan, 2004[22]	National	NHANES III	1990	7465	≥20	28%	54%	63%[a]
Smoak, 1994[29]	Fort Jackson, SC	US Army Recruits	1990	938	17–26	14%	44%	38%
Staat, 1996[25]	National	NHANES III	1990	2851	6–19	17%	40%	42%[a]
Zajacova, 2009[27]	National	NHANES III	1990	7465	≥20	28%	54%	62%[a]
Malaty, 1994[28]	Houston, TX	General population	1993	150	19–49	–	65%	47%
Parsonnet, 1997[23]	Northern California	Kaiser Permanente	1993	152	20–39	50%	79%	64%
Replogle, 1995[24]	Northern California	Kaiser Permanente	1993	567	20–39	10%	32%	44%
Cryer, 1996[32]	Dallas, TX	VA Medical Center	1994	180	18–66	25%	67%	–
Anand, 1996[30]	Houston, TX	Texas Medical Center	1996	190	≥20	38%	58%	70%
Malaty, 2002[35]	Bogalusa, LA	Bogalusa Heart Study	1996	224	19–23	8%	43%	–
Varga, 2020[26]	National	NYUWHS, PLCO, SCCS, WHI, MEC	1997	4476	36–87	33%[d]	71%	–
Grad, 2012[17]	National	NHANES	2000	4032	≥20	21%	52%	64%
Erim, 2008[33]	Weston, FL	Roux-en-Y gastric bypass patients	2004	240	44[c]	50%	80%	72%
Epplein, 2011[15]	Southeast	SCCS	2006	686	40–79	69%	89%	–
Butt, 2020[14]	Southeast	SCSS	2006	686	40–79	69%	89%	–
Long Parma, 2017[21]	Bexar County, TX	SABOR	2014	284	49–79	9%	–	30%

[a]Mexican American.
[b]Date of study publication.
[c]Mean.
[d]Includes non-Latino and Latino whites.

Table 2. Prevalence of *Helicobacter pylori* by Race From Histologic Studies of Adults in the United States, 1994–2000

Author, publication year	Region	Study population/site	HP testing method	Date of data collection (mean y)	Study size	Age range	*H. pylori* prevalence		
							White	Black	Hispanic
Ruiz, 1994[37]	New Orleans, LA	Patients undergoing EGD at Charity hospital	Modified Steiner technique	1994[a]	248 Black: 200 white: 48	18–82	54%	75[b]	–
Fontham, 1995[34]	New Orleans, LA	Patients undergoing EGD at a charity hospital	Modified Steiner technique	1995[a]	321 Black: 245 white: 63	19–72	52%	80%	–
Straus, 2002[38]	New York City, NY	Patients undergoing EGD at 2 inner-city hospitals and 1 suburban hospital	Rapid urease test/histology and PCR	2000	202 Black: 110 white: 71 Hispanic: 20	–	11%	43%	20%

[a]Date of study publication.
[b]Mean.

included in the teen/adult studies ranged from 15 to 87. The studies using NHANES (1999–2000) data included participants older than 19 years, with no upper age cutoff, and NHANES III also included data from children ages 6 to 19 years. There was 1 additional study that included children, with ages ranging from 0 to 18 years.[31] In addition, definitions of ethnicity varied between studies and in studies using the NHANES III database, the Hispanic population included only Mexican Americans. The country of origin was not reported in these studies.

In all the serologic studies, the prevalence of *H. pylori* antibodies was higher in Blacks and Hispanics than in whites. The reported prevalence of *H. pylori* antibodies in whites ranged from 8% to 69%, compared to 32% to 89% in Blacks and 30% to 72% in Hispanics. In children of ages 0–19 years, *H. pylori* seroprevalence was lower than in adults and ranged from 17% to 32% in whites, 40% to 49% in Blacks, and was 42% in Hispanics. After removing the poor-quality studies, the reported prevalence of *H. pylori* antibodies in whites ranged from 9% to 69%, compared to 32% to 89% in Blacks and 30% to 64% in Hispanics.

Endoscopic Evidence of H. pylori *Infection*

Evidence of active *H. pylori* infection as determined at the time of endoscopy is shown in Table 2. Only 3 studies reported active *H. pylori* infection rates using histologic assessment, representing 2 cities: New York City, NY, and New Orleans, LA.[34,37,38] Of note, all 3 histologic studies were deemed to be of poor quality using the Newcastle-Ottowa assessment tool. Both of the New Orleans studies recruited patients from the same hospital, although at different times. All 3 studies were convenience samples and recruited participants presenting for upper endoscopy. Study years ranged from 1994 to 2000, and the participant age ranged from 18 to 82 years. The sample size for the histologic studies was all relatively small, ranging from 202 to 321 participants. Rates of active *H. pylori* infection in whites ranged from 11% to 54%, compared to 43% to 80% in Blacks. In the 1 study that reported rates of active *H. pylori* in Hispanics, 20% were found to have evidence of *H. pylori* during endoscopy, compared to 11% of whites in that population.[38] The method for active *H. pylori* testing varied by the study. The NYC study used a combination of rapid urease testing, histologic staining, and polymerase chain reaction testing to identify positive cases.[38] Both of the New Orleans studies used the modified Steiner technique (a nonselective silver stain to report positive cases of *H. pylori* infection).[39]

Synthesis of H. pylori *Prevalence by Race*

Based on the reported *H. pylori* prevalence, we calculated ratios of *H. pylori* prevalence in Blacks vs whites and Hispanics vs whites, organized by the study region and method of testing (see Figure 2). All the studies represented in Figure 2 are described in detail in either Table 1 or

Table 3. *Helicobacter pylori* CagA and VacA Prevalence by Race Among *H. pylori*–Positive Adults in the United States, 1990–2006

Author, year	Region	Study population	Mean year of data collection	Study size	Age range	CagA prevalence			VacA prevalence		
						White	Black	Hispanic	White	Black	Hispanic
PCR studies (from *H. pylori* isolates grown from biopsy)											
Yamaoka, 2000[40]	Houston, TX	Volunteers	1990	125	–	77%	71%	74%	33%[b]	69%[b]	65%[b]
Parsonnet, 1997[23]	Northern California	Healthy volunteers	1993	152	20–39	50%	79%	64%	–	–	–
Tham, 2001[41]	Nashville, TN	VA patients undergoing EGD for dyspepsia	1997	82	25–87	61%	90%	–	31%[b]	90%[b]	–
Serology studies											
Varga, 2020[26]	National	Participants from 5 cohorts	1997	1926	36–87	59%[a]	87%	–	–	–	–
Butt, 2020[14]	South-eastern US	SCCS cohort participants	2006	542	40–79	36%	75%	–	88%[c]	94%[c]	–

[a]Includes non-Latino and Latino whites.
[b]VacA-m1, genotype.
[c]Presence of VacA antibodies.

Table 2. Figure 2 demonstrates that across this diverse set of studies in the United States, *H. pylori* prevalence was consistently higher in Blacks and Hispanics than in whites. The Black/white *H. pylori* prevalence ratio (PR) ranged from 1.3 to 5.4, and the Hispanic/white *H. pylori* PR ranged from 1.8 to 4.4. The studies with the highest PRs tended to be regional studies with smaller sample sizes. Despite different testing methods, with serology capturing evidence of either prior or current infection and with endoscopy-based studies assessing active infection, we found similar ratios between racial groups. The Black/white and Hispanic/white ratios in serologic studies ranged from 1.3 to 5.4 and 1.8 to 4.4, respectively, and in histologic studies ranged from 1.4 to 3.9 comparing prevalence in Blacks to whites and was 1.8 in the single histologic study that compared Hispanics to whites.

Eleven studies reported ORs, risk ratios (RRs), or PRs for *H. pylori* infection, as shown in Figure 3, grouped by race. These are organized by the date of data collection as given in Table 1. Ten studies reported either an OR or RR, and 1 study reported a PR. Adjusted ORs/RRs/PRs are denoted with an asterisk, and a list of the adjustments made in each study can be found in Appendix 3. Four of the studies used NHANES data. All the reported ORs/RRs/PRs were significant, with CIs as represented in Figure 3. Blacks had 2.6–4.4 times the odds of having an *H. pylori* infection when compared to whites. Hispanics had 1.8–3.9 times the odds of having an *H. pylori* infection when compared to whites.

H. pylori *Virulence Factors*

We also reviewed the data related to *H. pylori* virulence factors CagA and VacA by race (Table 3). As there is no clinically accepted test for *H. pylori* virulence factors, testing methods in these research studies varied. Three studies isolated *H. pylori* from endoscopic biopsies and then used polymerase chain reaction–based testing for virulence factors, while 2 studies used serologic specimens to probe for antibodies to specific *H. pylori* virulence factors.[14,23,26,40,41] Overall, among *H. pylori*–positive adults, the CagA prevalence ranged from 36% to 77% among whites, 71%–90% among Blacks, and 64%–74% among Hispanics. For VacA, 2 studies amplified the m allelic region of *vacA* for genomic characterization and found a higher prevalence of the virulent VacA-m1 genotype among Blacks and Hispanics than among whites.[40,41] Additionally, a third study used multiplex serology to measure the antibody response to the VacA protein and found VacA antibody prevalence to be 88% in whites and 94% in Blacks.[14]

H. pylori *Antibiotic Resistance*

Three studies investigated *H. pylori* antibiotic resistance by race and yielded conflicting results. Given the small size of antibiotic resistance studies, no table was created, and instead, the studies are described here. Talarico et al[42] at the University of Washington in Seattle, WA, included 102 *H. pylori*–positive participants with gastric biopsy samples

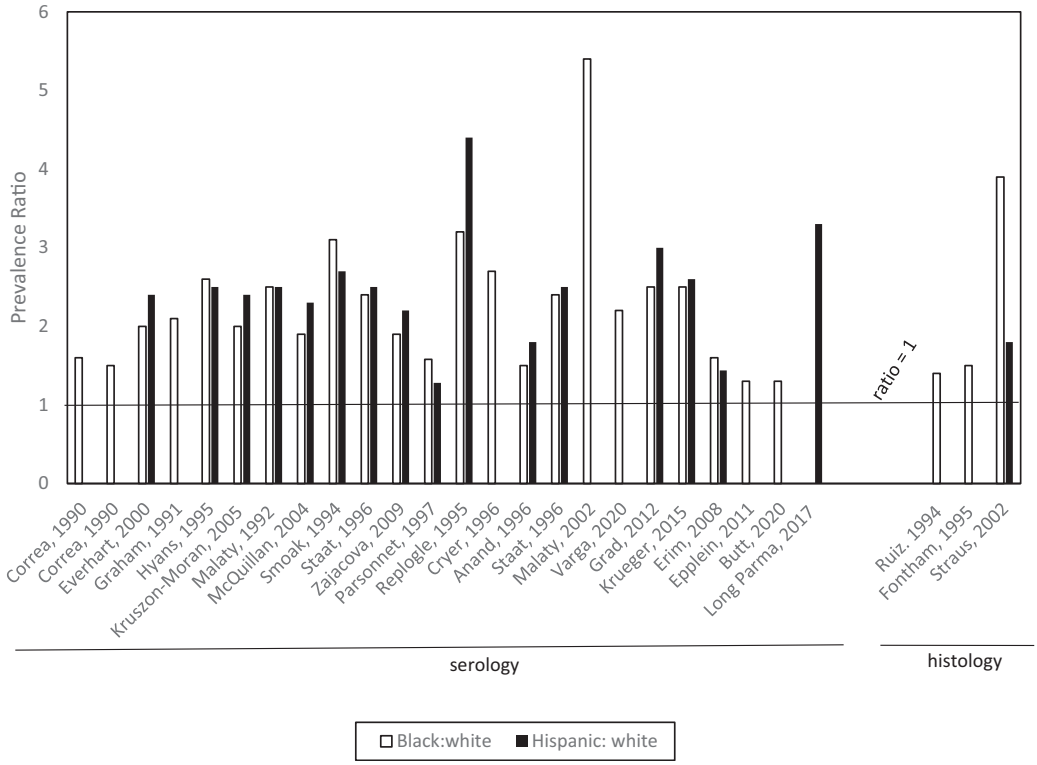

Figure 2. Graph of *Helicobacter pylori* prevalence ratios by race, ordered by the year of study collection, grouped by method of study collection. For Blacks compared to non-Hispanic whites (unshaded), the ratios ranged from 3 to 5.4, and for Hispanics compared to non-Hispanic whites (shaded), the ratios ranged from 1.8 to 4.4.

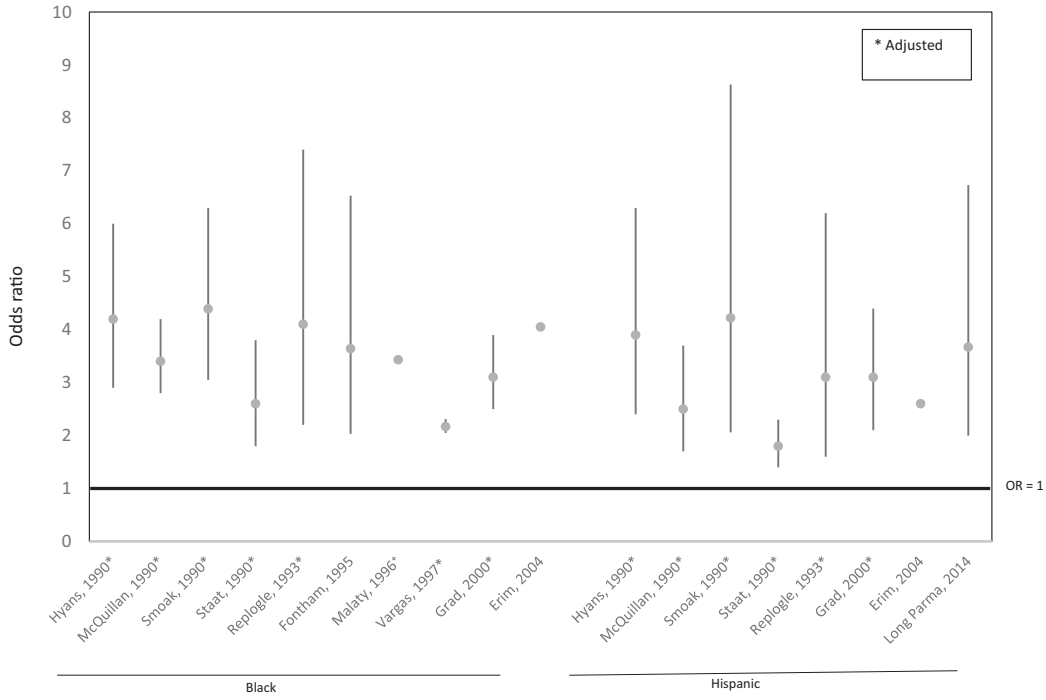

Figure 3. Graph of the odds ratios/risk ratios/prevalence ratios of *H. pylori* infection for Blacks and Hispanics compared to whites as reported by 11 studies; ordered by year of study collection and separated by race. ORs ranged from 2.6 to 4 for Blacks compared to whites and 1.8 to 3.9 for Hispanics when compared to whites. OR = 1 is depicted by solid horizontal line. Confidence intervals are shown.* denotes adjusted ratio. OR, odds ratio.

available from 2014 to 2018, assessing for the presence of clarithromycin-resistant alleles. Clarithromycin-resistant alleles were similarly prevalent in whites and Blacks, 32% and 33%, respectively, compared to 47% in Hispanics and 67% in Asians. A multicenter study of 11 hospital sites across the United States (*Helicobacter pylori* Antimicrobial Resistance Monitoring Project) by Duck et al[43] documented antibiotic resistance in patients undergoing upper endoscopies between 1998 and 2002. A total of 317 participants ranging in age from 3 to 94 years were included, and antimicrobial susceptibility testing for amoxicillin, tetracycline, clarithromycin, and metronidazole was performed on *H. pylori* isolates. In multivariate analyses controlling for *H. pylori* treatment in the last 5 years as well as geographic location, when compared to whites, Blacks had a reported hazard ratio of 2.1 (95% CI: 1.1–3.8) for antibiotic resistance to at least 1 antibiotic. Park et al[44] reported rates of clarithromycin resistance, via sequencing *H. pylori* 23S sRNA, at 4 academic medical centers from around the country using biopsy samples from 124 participants. Interestingly, the study found no statistically significant difference in clarithromycin-resistant *H. pylori* prevalence in Blacks, Hispanics, or whites.

Discussion

This systematic review sought to provide the most current understanding of racial differences in prevalence of *H. pylori* in the United States. All the studies included in this review documented increased prevalence of *H. pylori* in Blacks and Hispanics when compared to whites. This finding of racial disparities in *H. pylori* prevalence was consistent across a wide variety of sample populations from different regions of the United States, strengthening the conclusion reached through this review. Our review focused on disparities in Blacks, as demonstrated by the search strategy emphasis on Blacks, although broader terms such as "minority" were included. As such, this review was not designed to comment broadly on racial disparities in prevalence of *H. pylori* infection in other minority groups, although previous work has noted a large *H. pylori* infection burden in both Asian and American Indian/Alaska Native populations,[45,46] and further research is also urgently needed in these populations that bear some of the highest rates of gastric cancer incidence in the United States.[47–49] This study addresses a knowledge gap and compiles existing data on *H. pylori* in Blacks compared to whites, highlighting the variation in the prevalence of *H. pylori* between racial and ethnic groups, which may allow clinicians to better delineate high-risk populations.

This review included study periods over a wide time span, from 1990 to 2014. A limitation of this review is the paucity of more recent studies. The majority of studies included in this review was conducted more than a decade ago, highlighting the need for more recent, higher-quality studies that investigate not only the differences in *H. pylori* prevalence by race but also delve into the mechanisms underlying these differences.

Based on available data, it is known that overall *H. pylori* prevalence has been decreasing in industrialized countries, specifically in the United States, likely secondary to improved sanitation and urbanization.[16,26] However, a recent systematic review reported that this decline is not reflected in non-white populations,[26,50] Interestingly, our systematic review suggested little decline in *H. pylori* prevalence over time, even in whites. This could be explained by the unique sample populations used in some of the studies included, which was not representative of the US general population. For example, some studies recruited patients being seen for a specific medical reason – such as an upper endoscopy, and/or preparatory to bariatric surgery – patients who would be expected to have a higher underlying prevalence of *H. pylori*. Additionally, *H. pylori* prevalence has consistently been found to be higher among lower socioeconomic status (SES) populations than among higher SES populations, even within the same geographic region, and multiple studies drew patients, both white and non-white, from low SES areas.[16,51]

Studies have consistently found that infection with CagA-postive *H. pylori* increases the risk of gastric cancer.[10,52] In both animal and human ex vivo models, infection with a *cagA* + *H. pylori* strain induced inflammatory and carcinogenic changes in tissue.[53,54] Currently, work is being done to investigate polymorphisms in the *cagA* locus, suggesting different CagA strains may confer differing risk profiles.[55] A recent study found racial disparities in *H. pylori*-CagA seroprevalence with a decline over time in CagA seroprevalence in whites but not in Blacks.[26] Similarly, all *H. pylori* strains are thought to carry the VacA protein, and infection with specific *vacA* allele types, namely s1, s1i, and sm1, is thought to elevate risk of progression to intestinal metaplasia and gastric cancer.[52,56] In this review, studies comparing virulence factors by race described a higher prevalence of both CagA and VacA-s1m1–positive *H. pylori* prevalence in Blacks and Hispanics than in whites, suggesting that variable exposure to *H. pylori* virulence factors may contribute to racial differences in gastric cancer incidence and mortality.

Changes in the landscape of our understanding of *H. pylori* infection have resulted in expanded indications for *H. pylori* testing, with treatment and eradication testing recommended when *H. pylori* is identified.[7] Indeed, *H. pylori* eradication significantly reduces the risk of developing gastric cancer.[57–59] Appropriately, this strategy is used regardless of race. However, current guidelines fall short of a universal test-treat and retest strategy, with a recent paper reporting retesting rates as low as 23.9% in a large, national study using Veteran Health Administration data.[60] Understanding the differential prevalence of *H. pylori* infection by race can assist providers by informing relative pretest probabilities and raising awareness of false negatives in high-risk populations. Indeed, several factors can reduce sensitivity of tests for active *H. pylori* infection, most

notably recent use of proton-pump inhibitors. In the studies we reviewed, the proton-pump inhibitor status was rarely reported in endoscopy-based tests, and this may result in an underestimate of the actual rates of *H. pylori* infection.

Recent questions have emerged regarding selection of antimicrobial treatment for *H. pylori* infection, illustrating the need for improved understanding of *H. pylori* antibiotic resistance patterns.[61] While prior antibiotic use is associated with higher rates of resistance, these data can be difficult to collect.[11] Additionally, although antibiotic resistance is the most likely cause of treatment-resistant *H. pylori* infection, factors such as patient adherence, duration of treatment, and inadequate acid suppression are also associated with treatment failure.[11] Only 1 study concluded that Black race was a significant risk factor for antibiotic-resistant *H. pylori* infection.[43] However, more information is needed in order to interpret these results as it is possible that factors such as treatment cost, adverse medication effects, or even inappropriate treatment prescription may contribute to treatment failure.

There are several other important limitations to this review. Given the over-representation of serologic studies, this review is unable to quantify the rate of active *H. pylori* infection by race, although the studies that reported tests for active infection echoed the racial disparities seen in serologic studies. There was significant variation in the population sampling schemes among the included studies, and there is concern among those using convenience sampling, especially in histologic studies. Additionally, studies did not consistently include data on country of origin, which is particularly important for identifying participants who migrated from countries with endemic rates of *H. pylori*, including parts of Africa, South America, and Asia.[1]

This review did not focus on characterizing racial differences in treatment of *H. pylori*, although this is an important area for future research. A major limitation of the studies reviewed was that they did not include data on prior *H. pylori* infection, treatment, or eradication history. In addressing disparities related to gastric cancer, it will be important to determine whether lack of *H. pylori* treatment and eradication could explain some of the disparities related to gastric cancer.

While this review clearly demonstrates the stark racial differences in *H. pylori* prevalence in the United States, the cause of such differences is not immediately apparent and is likely multifactorial. For example, as noted previously, current understanding of risk factors related to *H. pylori* infection consistently associate low SES with increased prevalence, and we were not able to adjust for SES in this review. However, previous work from our group has found that even after adjusting for both individual- and neighborhood-level indicators of SES, racial differences persist, [15,62] suggesting that factors beyond SES remain that influence differences in prevalence rates by race.

We speculate that differences in early childhood acquisition of the *H. pylori* bacteria, as well as differences in living and sanitation conditions and water sources, may impact prevalence rates.[63] Furthermore, differing treatment patterns and eradication testing rates may factor into the prevalence rates reported. Lack of eradication testing may also be important in understanding racial differences in *H. pylori* prevalence, as it may be that Blacks and Hispanics are less likely to be tested for eradication and therefore more likely to have chronic *H. pylori* infections. When determining factors associated with increased eradication testing, a recent study conducted at Duke University Hospital reported patients with gastrointestinal (GI) follow-up had significantly higher rates of eradication testing than their counterparts .[8] Similarly, in a multicenter Veterans Affairs (VA) study, eradication testing was ordered most consistently by GI Advanced Practice Providers when compared to GI physicians, non-GI physicians, and non-GI Advanced Practice Providers.[60] Interestingly, the VA study found no significant difference in rates of eradication testing by race.[60] However, the Veteran's Health Administration represents a unique healthcare structure, and disparities may be more pronounced in non–VA-associated hospitals. Thus, further studies are needed to access disparities related to eradication testing and treatment.

Racial disparities related to *H. pylori* have been thought to contribute to racial differences in both GC incidence and mortality.[64,65] Interestingly, a large cohort study restricted to patients with *H. pylori* found *H. pylori*–infected Blacks to be at an increased risk for the development of GC compared to *H. pylori*–infected whites and that smoking history also increased the risk.[65] While this recent large VA Health System Study [65] did not provide overall prevalence data for *H. pylori* by race, this can be estimated using available estimates of race within the VA Health System reporting for 2019: 12% Black, 8% Hispanic, and 74% non-Hispanic white patients.[66] In contrast to the overall VA population, of the 371,813 Veterans identified with prior *H. pylori*, 23.8% were Black and 57.8% were white.

When examining risk factors associated with progression to gastric cancer, work is emerging that host-microbe mismatch may infer increased risk for progression to cancer.[67] It may be that the racial differences in adenocarcinoma incidence and mortality are related to more virulent and carcinogenic strains of *H. pylori* in populations that have not coevolved with the microbe. There has also recently been attention given to the rising incidence of noncardia gastric cancer among young non-Hispanic white women, of unknown cause, although autoimmune gastritis has been hypothesized.[68] However, our own very recent analysis in the Finnish Maternity Cohort suggests that while serologic evidence of autoimmune gastritis was associated with an increase in gastric cancer incidence among young (<50 years) white women (OR, 3.09; 95% CI, 1.58–6.02), *H. pylori* remains a particularly strong risk factor in this population (OR, 7.00; 95% CI, 4.93–9.94).[69]

In summary, across all populations, time periods, and geographic locations, this review found a higher prevalence of *H. pylori* among Blacks and Hispanics than in whites. The

available literature suggests that clinicians should be mindful of variable *H. pylori* prevalence by race. Our hope is that this review will inspire new high-quality studies of rigorous design that evaluate association of race with *H. pylori* and associated outcomes in the United States. Studies with clear and representative selection of cases and controls, careful ascertainment of exposure to *H. pylori*, adequate follow-up, and transparent reporting methods are needed in order to help us understand racial differences associated with *H. pylori* so that healthcare providers can address related health disparities. Ultimately, our goal is to personalize gastric cancer prevention and improve outcomes in all patients through improved clinical management and enhanced patient care.

Supplementary Materials

Material associated with this article can be found in the online version at https://doi.org/10.1016/j.gastha.2022.06.001.

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Data Transparency Statement:
Study material available to other researchers by email, contact HannahSofia Brown (htb6@duke.edu).