# Helicobacter pylori infection in the United States beyond NHANES: a scoping review of seroprevalence estimates by racial and ethnic groups



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## **Summary**

Gastric cancer in the United States is characterised by marked racial and ethnic disparities. Widespread declines in Helicobacter pylori prevalence have contributed to declining gastric cancer incidence. However, H pylori prevalence shows the same persistent racial and ethnic disparities seen in gastric cancer. The most recent population estimates of H pylori prevalence in the United States are from the late 1990s and early 2000s and only include three specific racial and ethnic groups. We conducted a scoping review to supplement existing population estimates and assess H pylori seroprevalence trends over by age and birth cohort with available data. We found the extant data suggest considerable variation in H pylori prevalence between racial and ethnic groups in the United States and evidence that age and birth cohort trends may differ between groups. We also found that the extant data were limited in generalizability and insufficient to describe trends in many cases.

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# Introduction

Gastric cancer (GC) is the fourth leading cause of cancer death worldwide1 and, while it is relatively rare in the United States (US),2 it has some of the starkest disparities among any cancer in the nation. As recently as 2020, GC was ranked as the cancer with the largest Hispanic-White and the second largest Black-White disparities in mortality.3,4 GC incidence has declined steadily over the past decades, nevertheless marked racial-ethnic disparities persist.5 Furthermore, mortality for GC in the US has not shown the same decline, staying largely steady over the past few decades, and continuing to show the disparities seen in GC incidence.6 In recent years, there has also been concern about the increasing incidence of GC in young people, including Non-Hispanic White (NHW) women, Hispanic men and Hispanic women.7-10

H pylori is estimated to be responsible for almost 90% of non-cardia GC cases, and about 6.2% of all cancers worldwide. 11,12 Like GC, H pylori prevalence can vary widely between race/ethnicity groups within a single country, and persistent racial-ethnic disparities in H pylori prevalence in the US have been documented for several decades. 13-17 Declines in *H pylori* prevalence have been the main contributor to the simultaneous declines in GC incidence since the 1970s,11,18 however no substantive inquiry has been made into how race/ethnicity group differences in H pylori prevalence over time have affected GC disparities in the US. Currently, population screening for H pylori is not recommended in the US. 19,20 Evidence for targeted screening in groups at high risk for H pylori associated GC (e.g., race/ethnicity groups in the US with evidence of high H pylori prevalence, recent immigrants from countries with high H pylori prevalence, etc.) is mixed and the implementation of existing recommendations in clinical practice is

Understanding changing patterns of *H pylori* prevalence through the lifespan and over time is a critical component of any proposed screening strategy. The age-

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effect pattern of increased *H pylori* seroprevalence by age has been recognised since the 1980s and is seen across many different cultural and economic contexts.<sup>23</sup> Then in the 1990s, evidence emerged that the age effect observed in prior cross-sectional research may have been primarily the result of a cohort effect, in which the age differences are driven not by the age itself but by the year of birth.<sup>24,25</sup> Subsequent research supports the presence of a combination of age effect, with the vast majority of *H pylori* acquisition occurring in childhood,<sup>26</sup> and cohort effect, with younger generations having lower prevalence than older generations at the same ages.<sup>24,25,27,28</sup>

The most recent national estimates of *H pylori* seroprevalence in the US are data from the National Health and Nutrition Examination Survey (NHANES). Unfortunately, these estimates are over 20 years old and contain only three specific racial and ethnic groups; Non-Hispanic Black (NHB), Non-Hispanic White (NHW), and Mexican-American, with all others in the "Other" group. <sup>29,30</sup> The data available suggests persistent racial and ethnic disparities remain <sup>15,16</sup>; however, no studies have investigated how age and cohort effects on *H pylori* prevalence may differ between racial and ethnic groups in the US.

The purpose of this scoping review is to supplement existing *H pylori* seroprevalence estimates from NHANES, to broaden our understanding of race/ethnicity-specific trends in *H pylori* seroprevalence in the US over time and across the lifespan.

# Methods

### Overview

We conducted a scoping review of articles in PubMed and Embase that included race or ethnicity-specific *H pylori* seroprevalence estimates for the US. Studies which used data from NHANES collected in 1991 (NHANES III) or 2000 (NHANES 1999–2000) were excluded from the search because we had access to the primary data.

We used the five mutually exclusive race/ethnicity groups from the Surveillance, Epidemiology, and End Results (SEER) program: Hispanic, all races (Hispanic); Non-Hispanic American Indian/Alaska Native (AI/AN); Non-Hispanic Asian/Pacific Islander (API); Non-Hispanic Black (NHB) and Non-Hispanic White (NHW) for our analysis.<sup>31</sup> These groups were chosen to align with available cancer statistics and population estimates.<sup>31</sup> If more specific racial or ethnic groupings were given in the source articles (e.g., Japanese-American, Mexican-American) they were recoded into the appropriate SEER grouping.

Our review was conducted according to the guidelines laid out in the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping reviews (PRISMA-ScR) checklist<sup>32</sup> (see Supplement A for checklist).

## Data sources and charting

Our search was conducted using PubMed and Embase with an initial search on December 8th 2021 and an updated search on September 28th 2022 using search terms developed with guidance from a research librarian at the Boston Children's Hospital Library (Supplement B for full search enquiry). There were no publication date restrictions imposed on the search. The references of the publications identified in the initial search, as well as any review articles were reviewed to identify additional sources. Additional supplemental searching of publications by key authors and their references was focused on API and AI/AN populations as they were underrepresented in initial search results. Nevertheless, all articles identified through supplemental searching which met inclusion criteria were included for analysis.

Publications were eligible for inclusion if they included data estimating H pylori seroprevalence for specific racial and/or ethnic groups in the US, from data sources other than NHANES and included age data or data that could be used to estimate age. Publications did not need to focus on *H pylori* to be eligible for inclusion nor were they required to have a random or populationbased sample method. Studies were ineligible for inclusion if they combined serology testing with another testing modality (e.g., prevalence of H pylori based on a positive serology test *or* a positive breath test). Studies in which all participants were symptomatic for H pylori at the time of testing and studies in which all participants were seropositive for H pylori were also ineligible, with the exception that if the same group of people were tested for overall H pylori seropositivity and CagA seropositivity with results reported in two different publications, these articles were combined for analyses. In cases where publications reported both eligible and ineligible estimates (e.g., the main results reported H pylori prevalence estimates based on any testing modality, but the supplement reported H pylori prevalence estimates stratified by testing modality), the publication was included, and eligible estimates were extracted.

Publications were screened, extracted by one researcher (MM) using a Google Forms extraction sheet and standardised for analysis (see Supplement C for extraction sheet). Extracted publications were reviewed in a group (MM, FA, JR, ZW, JY) and any disagreements on inclusion or exclusion were resolved by consensus. Where date of data collection was not given in the source (N = 8), the earliest date available in the source (typically the date of paper receipt) was used as a proxy. We extracted the mean or median age from publications directly. If the mean or median age was not reported, we calculated the mean age as a weighted average based on the age group distribution given in the publication. For the birth cohort, we estimated the birth decade based on the year of data collection and the age of the study population. We assigned each study to a US

census region based on the area in which the data was collected (i.e. West [Alaska, Arizona, California, Hawaii, Washington], South [Alabama, Arkansas, Florida, Georgia, Kentucky, Louisiana, Mississippi, North Carolina, South Carolina, Tennessee, Texas, Virginia, West Virginia], Northeast [New York], Midwest [not represented in data]) or designated it as covering multiple census regions.

## Data charting

We extracted seroprevalence data from publications directly and calculated 95% uncertainty intervals (95% UI) using Beta distributions. In addition to the published data extracted from the literature search, we also included weighted seroprevalence data from NHANES III and NHANES 1999–2000 and their 95% CI as these are considered the gold standard for population-level *H pylori* prevalence data available in the US. Data cleaning, processing, and visualisation were performed in R v.4.1.2.

#### Results

## Published data

Data were extracted from 41 publications, representing 56,845 individuals and data collected between 1965 and 2014 (Fig. 1). Most studies were conducted in the West (19/41, 46%) or the South (17/41, 41%) census regions. There was no single study based in the Midwest region though multi-regional studies (5/41, 12%) did contain data from the Midwest (Table 1).<sup>17,30,33-64</sup> 12 publications reported percent foreign-born status among participants, which ranged from 0% to 100%. No single publication included all mutually exclusive race/ethnicity groups. However, among publications that included more than one race/ethnicity group (N = 21), extracted data showed evidence of differences in *H pylori* seropositivity between those groups included.

# Age and cohort effects

To elucidate evidence of age and cohort effects, we combined the NHANES *H pylori* seroprevalence estimates with the published data from our literature search. When all data sources were examined together, collection dates represented varied widely between race/ethnicity groups (see Supplement D for more detailed information on sample size variation within race/ethnicity groups).

When looking at the effect of age alone, the data suggested the expected trend of increasing *H pylori* seroprevalence with increasing age in every race/ethnicity group (Fig. 2, Panel A). Looking at the birth cohort alone, the data provided evidence of decreasing seroprevalence in recent cohorts compared to earlier cohorts in each race/ethnicity group (Fig. 2, Panel B). Differences in magnitude of seroprevalence estimates were apparent when each individual group was visually

compared to all of the other groups combined. The AI/AN group had consistently higher *H pylori* seroprevalence compared to the other groups, while the NHW group had consistently lower seroprevalence compared to the other groups. The API group was generally lower or in the middle, while the Hispanic and NHB groups were generally higher or in the middle compared to the other groups.

When we investigated the effects of age and cohort together, differences in the age and cohort *H pylori* seroprevalence trends between race/ethnicity groups were apparent (Fig. 3). Seroprevalence in NHW group was again consistently lower than the other race/ethnicity groups, while the AI/AN group was consistently the highest among the five groups examined. All race/ethnicity groups showed some evidence of decreasing seroprevalence over time since the 1900–1919 or the 1920–1939 birth cohorts. However, limited data in the API and AI/AN groups impacted the ability to assess evidence of any sustained trends over time.

The H pylori seroprevalence trends by age within birth cohorts varied widely between race/ethnicity groups. In the Hispanic group, the most recent birth cohort (i.e. the 1980-1999 cohort) showed an increase in seroprevalence from birth to age 20 with evidence of a continued increase after age 20, while the 1960-1979 cohort showed an increase in seroprevalence between age 20 and age 60 (Fig. 3). The earlier birth cohorts showed little indication of increasing seroprevalence by age (i.e. the 1920-1939 and 1940-1959 cohorts) or lacked sufficient data to evaluate an age trend (i.e. the 1900-1919 cohort). In the NHW group, only one birth cohort showed evidence of increasing H pylori seroprevalence with age (i.e. the 1940-1959 cohort), while the two most recent birth cohorts showed negligible increase (i.e. the 1960-1979 and 1980-1999 cohorts), and the oldest birth cohorts lacked sufficient data to evaluate a trend. The NHB group also showed increasing seroprevalence in childhood and adolescence in the most recent birth cohort (i.e. the 1980-1999 cohort) and an indication of increasing seroprevalence after age 20 in some earlier cohorts (i.e. the 1960-1979 and 1920-1939 cohorts). Conversely, the 1940-1959 cohort shows little evidence of increasing seroprevalence between age 20 and age 60.

The API group showed evidence of increasing *H pylori* seroprevalence after age 20 in the 1940–1959 birth cohort with the other birth cohorts not showing an increase in seroprevalence by age (i.e. the 1920–1939 cohort), showing evidence of a decrease at the oldest ages (i.e. the 1900–1919 cohort) or lacking sufficient data to evaluate and age trend (i.e. the 1960–1979 cohort). The API group could not be assessed for seroprevalence trends prior to age 20 as no data was available. Conversely, the AI/AN group showed a rapid increase in seroprevalence between birth and age 10 in the most recent birth cohort (i.e.

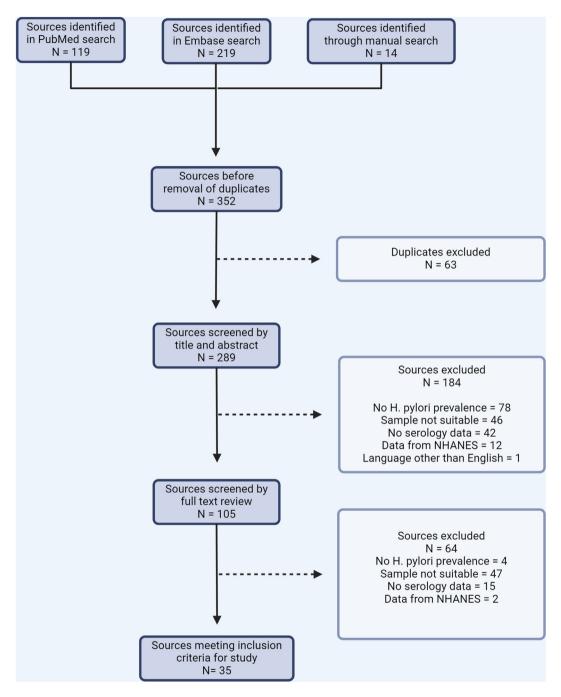


Fig. 1: Study flow diagram. Flow diagram showing exclusion process from search inquiry results to included studies, created with BioRender. Light colored boxes show excluded sources at each step.

the 1980–1999 cohort), with earlier birth cohorts showing little indication of any increasing seroprevalence after adolescence, but lacking data on earlier ages to evaluate the full trend (i.e. the 1940–1959 and 1960–1979 cohorts). Data was limited to published estimates in both the API and the AI/AN groups as they could not be identified among the NHANES data.

## Discussion

Leveraging data from the 41 publications identified in our study, we found that there is a paucity of population-based *H pylori* seroprevalence data available in the US, particularly data that contain information on race/ethnicity group and foreign-born status. The data that do exist are largely from convenience samples or high-risk

Study	N	Census region	Study location	Study population	Race/ Ethnicity groups included	Test	Mean age (Min-Max)	Date of data collection	Percent foreign- born	H pylori seroprevalence					
										Hispanic	White	Black	American Indian/Alaska native	Asian/Pacific Islander	
Dehesa M. et al., 1991 <sup>33</sup>	56	West	Los Angeles, CA	Healthy adults	Hispanic	ELISA	27.1	-	-	79% (67%–88%)	-	-	-	-	
NHANES <sup>65</sup>	17,249	Multiple	United States	Persons living in the United States	NHB, NHW, Hispanic	ELISA		1991, 2000	-	43% (42%-45%)	16% (15%–17%)	43% (42%–45%)	-	-	
Nomura A. et al., 1991 <sup>34</sup>	109	West	Hawaii	Men recruited for heart health study	API	ELISA	59 (48–70)	1965-1968	17%	-	-	-	-	76% (68%–83%)	
Malaty H.M. et al., 1992 <sup>35</sup>	286	South	Houston, TX	Healthy adults	NHB, NHW, Hispanic	ELISA	36 (19-75)	-	33%	67% (57%–76%)	20% (13%–29%)	78% (68%–85%)	-	-	
Malaty H.M., Graham D.Y., 1994 <sup>36</sup>	150	South	Houston, TX	Healthy employed adults	NHB, Hispanic	ELISA	31.2 (19-49)	-	-	47% (37%–57%)	-	65% (52%–76%)	-	-	
Smoak B.L., Kelley P.W., Taylor D.N., 1994 <sup>37</sup>	938	South	Fort Jackson, SC	Army recruits	NHB, Hispanic, NHW	ELISA	20.2 (17–26)	1990	-	38% (25%–53%)	14% (11%–17%)	44% (39%-50%)	-	-	
Replogle M.L. et al., 1995 <sup>38</sup>	567	West	Northern CA	Adults	API, NHB, Hispanic, NHW	ELISA	30.1 (20–39)	1992-1993	-	44% (36%–52%)	10% (6%–15%)	32% (26%–39%)	-	9% (1%-35%)	
Centers for Disease Control, 1999 <sup>39</sup>	86	West	Hooper Bay, AK	Children	AI/AN	ELISA	3.4 (1–5.9)	1999	-	-	-	-	41% (31%-51%)	-	
Namekata T. et al., 2000 <sup>40</sup>	776	West	King County, Seattle, WA	Japanese- American adults recruited through a cardiovascular disease screening program	API	ELISA	52.2 (20–86)	1994	14%	_	-	-	-	25% (22%–28%)	
Opekun A.R. et al., 2000 <sup>41</sup>	797	South	Houston, TX	Children who had blood taken at the hospital	NHB, Hispanic, NHW	ELISA	9.3 (0.5–18)	1995	-	13% (9%–18%)	8% (6%–12%)	17% (12%–22%)	-	-	
Parkinson A.J. et al., 2000 <sup>42</sup>	2080	West	Alaska	Persons living in rural and urban areas	AI/AN	ELISA	27.1	1980-1986	-	-	-	-	80% (78%–81%)	-	
Nomura A. et al., 2002 <sup>43</sup>	261	West	Hawaii	Men recruited for heart health study	API	ELISA	72.5 (50–90)	1967-1975, 1975-1977	16%	-	-	-	-	74% (68%–79%)	
Goodman K.J. et al., 2003 <sup>44</sup>	384	South	El Paso, TX	Low-income pregnant women	Hispanic	ELISA	27.2 (17-47)	1998-2000	-	57% (52%-62%)	-	-	-	-	
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Study I	N	Census region	Study location	Study population	Race/ Ethnicity groups included	Test	Mean age (Min-Max)		Percent foreign- born					
										Hispanic	White	Black	American Indian/Alaska native	Asian/Pacific Islander
(Continued fro	om prev	ious page)												
Perez– Perez G.I. et al., 2003 <sup>66</sup>	131	West	Arizona	Woman and children living on the White Mountain Apache Indian Reservation and San Carlos Apache Reservation	AI/AN	ELISA	16.3 (1.92–34)	1993-1994	-	-	-	-	59% (50%-67%)	-
Lee R.H., Pan V.L., Wing D.A., 2005 <sup>46</sup>	82	West	Los Angeles, CA	Pregnant women	Hispanic	ELISA	41 (18-81)	2002–2004	-	66% (55%-75%)	-	-	-	-
Perez- Perez G.I. et al., 2005 <sup>45</sup>	194	Northeast	New York City, NY	East-Asian-born adults	API	ELISA	51.5 (20-90)	2002	100%	-	-	-	-	56% (49%-63%)
Tsai C.J. et al., 2005 <sup>47</sup>	1537	West	San Francisco, CA	Children	Hispanic, NHW	ELISA & HpSA	3.8	2000–2004	22%	14% (12%–16%)	6% (2%–13%)	-	-	-
Opekun A.R. et al., 2006 <sup>48</sup>	188	South	Houston, TX	Adults	API, NHB, Hispanic	ELISA	46.5 (18-75)	2004	-	52% (41%-63%)	-	53% (31%-73%)	-	44% (33%-57%)
Felkner M. et al., 2007 <sup>49</sup>	147	South	Texas	Pregnant women servings as matched controls for a neural tube defect study	Hispanic	ELISA	25.5 (18-45)	1995-2000	45%	52% (44%–60%)	-	-	-	-
Lutsey P.L. et al., 2009 <sup>50</sup>	6814	Multiple	United States	Diverse adults from across the US recruited for a cardiovascular health study	API, NHB, NHW, Hispanic	ELISA	62.1 (45-84)	2000-2002	-	70% (64%–76%)	25% (22%–30%)	58% (51%–65%)	-	55% (45%-64%)
Bruden D.L. et al., 2011 <sup>51</sup>	280	West	Alaska	Adults undergoing EDG for any reason	AI/AN	ELISA	48 (19-88)	1999-2000	-	-	-	-	67% (61%–72%)	-
Epplein M. et al., 2011 <sup>52</sup>	686	South	Southeastern US	Low-income adults	NHB, NHW	Multiplex Serology	52.4 (48-70)	2002–2009	-	-	69% (64%–74%)	89% (85%–92%)	-	-
Rubicz R. et al., 2013 <sup>53</sup>	801	West	Alaska	Adults	AI/AN	ELISA	45 (18-91)	2000-2004	-	-	-	-	78% (74%–80%)	-
Sealy- Jefferson S. et al., 2013 <sup>54</sup>	1457	West	Sacramento, CA	Elderly adults	Hispanic	ELISA	70.2 (60–101)	1998-2008	52%	66% (63%– 68%)	-	-	-	-
Keck J.W. et al., 2014 <sup>55</sup>	346	West	Alaska	Adults with no known history of gastric cancer	AI/AN	ELISA	41.2	1969-2008	-	-	-	-	82% (78%–86%) (Table 1 continu	= ues on next page

Study	N	Census region	Study location	Study population	Race/	Test	Mean	Date of data collection	Percent foreign- born	H pylori seroprevalence					
					Ethnicity groups included		age (Min-Max)			Hispanic	White	Black	American Indian/Alaska native	Asian/Pacific Islander	
Continued fro	om prev	ious page)													
McLaren G.D. et al., 2015 <sup>56</sup>	1142	Multiple	United States	Matched controls from anemia study	NHB, NHW, Hispanic	ELISA	50.4	2001–2002	-	67% (59%–74%)	23% (20%–26%)	56% (48%–64%)	=	44% (35%–54%)	
Meier H.C.S. et al., 2016 <sup>57</sup>	1562	West	Sacramento, CA	Elderly adults	Hispanic	ELISA	70 (60–101)	1998-1999	-	94% (92%–95%)	-	-	-	-	
Long Parma D. et al., 2017 <sup>58</sup>	284	South	San Antonio, TX	Men with no personal history of prostate cancer	Hispanic, NHW	ELISA	65 (49-79)	2013-2014	-	30% (23%-37%)	8% (4%-13%)	-	-	-	
Miernyk K.M. et al., 2018 <sup>59</sup>	710	West	Alaska	Persons living in rural and urban areas	AI/AN	ELISA	32.7 (2–92)	1996-1997	-	-	-	-	75% (72%–79%)	-	
Butt J. et al., 2019 <sup>60</sup>	3984	Multiple	United States	Diverse adults from across the US serving as matched controls for a colorectal cancer study	API, NHB, Hispanic, NHW	Multiplex Serology	64 <sup>a</sup> (18-89)	-	-	77% (71%–83%)	33% (32%–35%)	65% (60%–69%)	-	39% (34%-45%)	
Namekata T. et al., 2019 <sup>61</sup>	803	West	King County, Seattle, WA	Immigrants	API	ELISA	54.7	2004–2005	96%		-	-	-	36% (32%–39%)	
Simanek A.M. et al., 2019 <sup>62</sup>	771	West	Sacramento, CA	Elderly adults	Hispanic	ELISA	69.4 (60–101)	1998-1999	44%	91% (88%–92%)	-	-	-	-	
Varga M.G. et al., 2020 <sup>63</sup>	4476	Multiple	United States	Adults	NHB, NHW	Multiplex Serology	61.6	1985–2009	-	-	-	71% (69%–74%)	-	-	
Tsang S.H. et al., 2021 <sup>17</sup>	16,144	Multiple	United States	Urban adults	Hispanic	ELISA	41 (18-76)	2008–2011	77%	60% (59%–61%)	-	-	-	-	
Yoon H.S. et al., 2022 <sup>64</sup>	295	South	Southeastern US	Low-income adults serving as matched controls for a lung cancer study	NHB, NHW	Multiplex Serology	57.6 (40-79)	2002–2009	-	-	37% (29%-46%)	61% (53%–68%)	-	-	

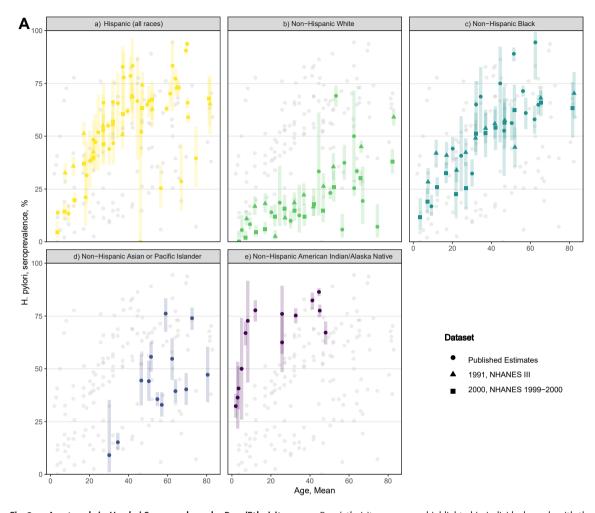


Fig. 2: a. Age trends in H pylori Seroprevalence by Race/Ethnicity group. Race/ethnicity groups are highlighted in individual panels with the Hispanic group shown in yellow, NHW in green, NHB in teal, API in navy blue, and AI/AN in purple. Colored vertical bars indicate the 95% UI for each point. Grey points in the background show all other data points not belonging to the highlighted group. Highlighted data points extracted from published studies are indicated by circles, while those from NHANES are indicated by triangles. The y-axis shows H pylori seroprevalence and the x-axis shows mean age. b. Birth cohort trends in H pylori Seroprevalence by Race/Ethnicity group. Race/ethnicity groups are highlighted in individual panels with the Hispanic group shown in yellow, NHW in green, NHB in teal, API in navy blue, and AI/AN in purple. Colored vertical bars indicate the 95% UI for each point. Grey points in the background show all other data points not belonging to the highlighted group. Highlighted data points extracted from published studies are indicated by circles, while those from NHANES are indicated by triangles. The y-axis shows H pylori seroprevalence and the x-axis shows mean birth year.

populations, which makes it challenging to estimate the true population seroprevalence of *H pylori* in the US. However, the published estimates appear to be in accordance with the estimates available from NHANES for the groups and time periods available, which lends confidence for the generalisability of the non-nationally representative published estimates. Furthermore, most of the available serologic data were collected 20 years ago or longer, which underscores the need for more contemporary estimates of *H pylori* prevalence in the US. One reason for this may be that serological testing has declined over time<sup>67</sup>; consequently, more recent studies may rely on testing methods excluded from the current analysis.

Despite a substantial overall decline since the earliest birth cohorts our findings indicate that *H pylori* sero-prevalence still varies considerably between racial and ethnic groups in the US, consistent with prior findings from NHANES.<sup>15</sup> We found the highest seroprevalence among the AI/AN group, followed by the Hispanic and NHB groups, while the NHW group and API groups had the lowest seroprevalence. Prior studies, both with NHANES data and with other data, have documented the existence of Black-White and Hispanic-White disparities in *H pylori* prevalence, <sup>15,16,68</sup> as well as a pattern of higher *H pylori* prevalence among indigenous populations compared to non-indigenous populations of the same country.<sup>13,14</sup> In contrast, our finding that the API

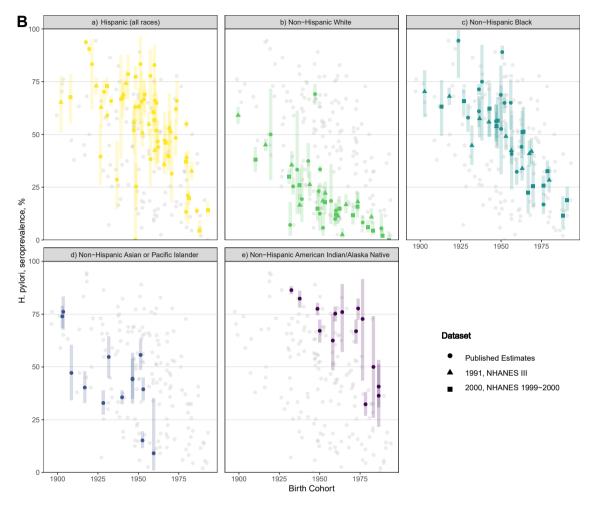


Fig. 2: Continued.

group had lower seroprevalence compared to the other groups was unexpected, as this group is considered "high risk," primarily due to the high prevalence of H pylori in many East Asian countries. 19,45,61 One reason our estimates may differ from expected numbers is that we combined all API subgroups into a single group for our analysis. Prior research suggests that H pylori prevalence varies by ethnicity and national origin within the larger API group, 45,61 which is not reflected in this analysis. The API group is also considered "high risk," while other race/ethnicity groups may not be immediately recognised as such. Consequently, there may also be an element of selection bias underlying the lowerthan-anticipated estimates. For example, persons in the API group may be more likely to be involved in prevalence studies regardless of other risk factors while persons from other race/ethnicity groups may be targeted for prevalence studies only if other risk factors are also present (e.g., recent immigrant, low socioeconomic status, etc.). This highlights the importance of collecting data from diverse populations using an approach that allows direct comparisons across race/ethnicity groups within the same study. We also know that variation exists within the Hispanic and API groups when disaggregated by national origin.<sup>17,45,61,69</sup> Continued and expanded collection of more granular data would allow for a more nuanced understanding of heterogeneous risks within race/ethnicity groups. Furthermore, as race and ethnicity are socially constructed categories, collecting information on other risk factors associated with *H pylori* seroprevalence, such as foreign-born status, geographic location, or household crowding, should be a priority.

When examining seroprevalence trends by age or birth cohort alone, the primary difference between race/ethnicity groups included appeared to be the magnitude of *H pylori* prevalence with the overall pattern appearing relatively similar. However, when examined by age and birth cohort together, differences in the patterns emerged among race/ethnicity groups.

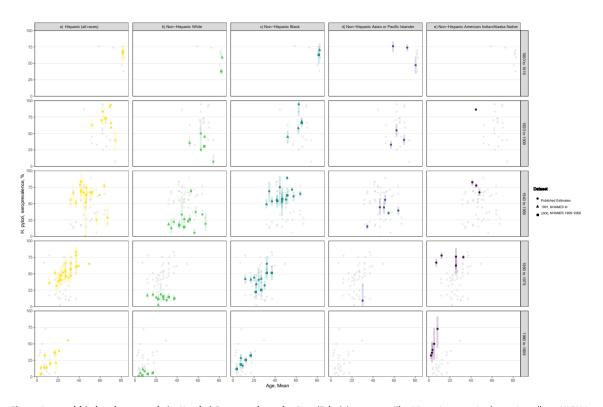


Fig. 3: Age and birth cohort trends in H pylori Seroprevalence by Race/Ethnicity group. The Hispanic group is shown in yellow, NHW in green, NHB in teal, API in navy blue, and AI/AN in purple. Colored vertical bars indicate the 95% UI for each point. Grey points in the background show all other data points not belonging to the highlighted group. Highlighted data points extracted from published studies are indicated by circles, while those from NHANES are indicated by triangles. The y-axis shows H pylori seroprevalence and the x-axis shows mean age. Columns denote race/ethnicity group while rows show birth cohort grouped by mean birth year in 20-year increments.

Most groups show evidence of increasing seroprevalence between birth and age 20 consistent with childhood acquisition of H pylori, with the exception of the API group, for which data before age 20 are not available. Several groups also show evidence of increasing seroprevalence with increasing age following adolescence well into adulthood. This is most strongly apparent in the Hispanic group, and could be present in some birth cohorts in the API and NHB groups. One explanation for the differences in trends is that both the API and the Hispanic groups may contain a higher share of foreign-born persons than the other groups.70 Birth outside of the US is associated with an increased risk of H pylori seroprevalence across all racial and ethnic groups, particularly for those who immigrate as teenagers or adults. 14,40,45,68,71 The AI/AN group, which could be expected to have few to no foreign-born persons, shows essentially no increase in seroprevalence after adolescence and provides some support to this theory. However, we note that the seroprevalence in the AI/AN group during adolescence appears to be twice as high than the next highest group. Prior research suggests that persons in high prevalence populations may acquire infection at an earlier age compared to those in low prevalence populations. $^{72,73}$  Another explanation for differences between groups could be a cohabitation effect. Crowding and household members' H pylori infection status have been linked to H pylori infection and reinfection among AI/AN and Hispanic communities. $^{47,59}$ 

This study has several important limitations. First, the overall paucity of data, particularly between the AI/ AN and the API groups, made it difficult to discern trends by age and birth cohort. Comparisons between race/ethnicity groups and comparisons over time were complicated by the lack of overlapping age and time points to compare. We also relied on estimated birth cohorts and summarised age data to complete our analysis, as more granular data was frequently not reported. Because these estimates may lack precision, we took a conservative approach to interpreting trends in the current study. Second, the nature of the available data was such that the generalizability of some studies included in our analysis may be limited. We incorporated the data from NHANES to address this problem, however, NHANES is only available for three of our five race/ethnicity groups. Additionally, our groups themselves may not be representative. For example, most

studies in the AI/AN group were conducted in Alaska and many tribal nations are not reflected in that data. Nevertheless studies examining active H pylori infection suggest that prevalence is similarly high among the Navajo (Diné) people, a group not represented in our data, and other indigenous groups worldwide. 13,14,74-76 We further made the assumption that persons in the API and AI/AN groups were non-Hispanic in order to maximise the comparability of our data by aligning with the SEER race/ethnicity groups. This is not necessarily reflective of the true data or demographics in the US,77 however it was necessary to make some assumptions, as no information regarding Hispanic ethnicity was reported in most studies which included API or AI/AN groups. Our data is also likely non-representative of the distribution of foreign-born persons in the US population. Most studies in our sample do not report nativity and those studies that have reported nativity tend to be heavily skewed in one direction or the other (e.g., 95% foreign-born, foreign-born excluded from study sample). This limitation underscores the importance of collecting nativity data in future studies of H pylori prevalence as the extant data is of poor quality. We were also unable to assess the effect of sex or gender, factors known to have an effect on H pylori prevalence,38,78 in our study as data was inconsistently reported in the source manuscripts leading to insufficient data for analysis. Lastly, we acknowledge that seroprevalence indicates whether a person has ever been infected with H pylori and does not differentiate between prior and active infection.79

While there is no national screening program in the US, there are already differences in referral for *H pylori* testing between race/ethnicity groups considered highrisk for H pylori.21 The Houston Consensus document on H pylori testing acknowledges that "Latino and African American" patients may be considered at higher risk for H pylori infection and may benefit from being considered for testing, while the American College of Gastroenterology guidelines do not presently address "high-risk" racial or ethnic groups. 19,80 Prior studies have proposed that populations with a high prevalence of H pylori could potentially benefit from a targeted screening program<sup>6-8</sup> however, our results suggest that a greater understanding of how trends in H pylori seroprevalence vary between race/ethnicity groups may be needed to design effective screening and prevention strategies to prevent GC. The population data needed to fully investigate these differences may not be feasible or cost-effective to collect, which suggests alternative approaches such as cohort studies<sup>27,65</sup> or dynamic modelling of population prevalence26 are needed in order to better understand the current state of H pylori seroprevalence in the United States.

In conclusion, we found that the available data suggest trends in *H pylori* seroprevalence vary among race/ethnicity groups in the US. However, extant data are

#### Search strategy and selection criteria

Sources were identified through two rounds of searches in PubMed and Embase using the search terms "United States" and "prevalence or occurrence or incidence" and "Helicobacter pylori or H pylori" and "Race factors or race or African American or Black or Hispanic or Latin or Asian or Native American or Indigenous or White or Caucasian or BIPOC or people of color" and excluding "review or meta-analysis" from results. Search terms were mapped to MESH terms and Emtree as appropriate, and additionally included for title-abstract matching. Truncation and wildcard terms were used to return results matching relevant variations of keywords (e.g., race, racial, racism). Citation and author searching was used to supplement the database searches, with a particular focus on searching for groups underrepresented in the initial search results. All sources identified in supplemental searching which met the inclusion criteria were included in the review.

Sources were eligible for inclusion if they contained race or ethnicity specific *H pylori* seroprevalence data, including information on the age of the study sample, and did not use a study sample selected based on showing symptoms of *H pylori* infection and reported data from a source other than the National Health and Nutrition Examination Survey. Sources in which the study population were persons based in the United States residing outside of the United States for a period of time were also excluded. Sources were identified from database inception to September 28, 2022, with no exclusion based on publication or study date.

insufficient to fully describe the magnitude of variation by age and birth cohort among the subgroups, with very limited population-based data available. As immigration patterns may impact observed *H pylori* seroprevalence, additional research on the role of immigration should be a priority for future research. Our findings suggest that targeted screening programs aimed at gastric cancer prevention should consider variation in *H pylori* seroprevalence both between and within race/ethnicity groups in the US.

### Contributors

MM helped conceptualize the study, designed the study, analyzed the data, drafted the initial manuscript and critically reviewed and revised the manuscript.

CT critically reviewed and revised the manuscript.

ZW helped conceptualize and design the study, helped carry out the analysis and critically reviewed and revised the manuscript.

FAE helped conceptualize and design the study and critically reviewed and revised the manuscript.

MCC critically reviewed and revised the manuscript.

ML critically reviewed and revised the manuscript.

JR helped conceptualize and design the study and critically reviewed and revised the manuscript.

JY secured funding for the study, conceptualized the study, helped design the study, helped carry out the analysis and critically reviewed and revised the manuscript.

# Declaration of interests

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# Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lana.2024.100890.

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