Birth cohort and age-specific trends in global *Helicobacter pylori* seroprevalence: a scoping review

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Summary

Gastric cancer persists around the world as one of the leading causes of cancer-related death, despite declines in recent years. The declining prevalence of *H pylori*, the primary risk factor for gastric cancer, has contributed to this reduction and understanding changes in seroprevalence trends over time may yield further insight into gastric cancer incidence trends. We conducted a scoping review to compile data on *H pylori* seroprevalence in asymptomatic populations to assess global trends by age and birth cohort. We found that published data suggest *H pylori* seroprevalence declined among recent birth cohorts and increased with age, with trends differing between regions and sub-regions subject to data availability. The Americas lacked sufficient data to enable more robust assessment of *H pylori* trends by both age and birth cohort.

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Introduction

Helicobacter pylori (*H pylori*) is a gram-negative bacterium known to infect the human stomach lining and is a class I carcinogen related to the development of gastric cancer.[1] Chronic *H pylori* infection has been associated with gastric cancer as a major risk factor in the development of chronic gastritis, the first pathogenic step in the precancerous cascade.[2,3] As of 2020, gastric cancer remains one of the most common cancers worldwide and was estimated to be the fourth leading cause of cancer death, despite decades-long declines in incidence and mortality.[4] Although a major threat to global public health,[5] prevention strategies for gastric cancer have not been prioritised[6] and leave at-risk populations vulnerable to continued gastric cancer burden.

By using serology testing to detect the immunoglobulin G (IgG) antibody for *H pylori*,[7,8] seroprevalence trends can be assessed through both a birth cohort effect and an age-specific effect. A birth cohort effect refers to differences in the risk of a certain health outcome as a function of year of birth, which tends to correspond with disparity in exposure to specific risk factors over time.[9] In the United States (U.S.), gastric cancer has been shown to decrease in more recent birth cohorts, from the early 1900s[10] through 2000s.[11] A cohort effect has been hypothesised in high-income countries related to *H pylori*, but to our knowledge has not been previously demonstrated on a global scale.[12,13] With factors such as industrialisation and sanitation thought to impact *H pylori* acquisition,[7,14] variation between birth cohorts likely influences *H pylori* trends and thus contributes to secular gastric cancer trends. As for age-specific effects, *H pylori* is thought to be typically acquired during childhood, though prevalence has been shown to increase with age.[15] Determining more robust global trends of *H pylori* infection based on age could help disentangle the relation of infection to gastric cancer trends, expanding work that has been done previously in developed countries.[16] *H pylori* birth cohort and age effects previously examined using the U.S. National Health and Nutrition Examination Survey (NHANES) provide perhaps the most comprehensive birth cohort and age trend data on *H pylori* seroprevalence across the Americas and suggests that U.S. *H pylori* rates have increased with age and decreased over time by birth cohort.[17,18] However, these data provide limited coverage by time period and location and require updating for an

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improved assessment of trends. Recent studies on the global level have primarily focused on *H pylori* risk factor profiles in children and variation in prevalence due to economic or social conditions or time,[14,19–21] but birth cohort or age trends on the global level have remained largely uninvestigated.

To address this gap in our understanding of *H pylori* epidemiology, we performed a scoping review of global studies reporting *H pylori* seroprevalence in asymptomatic individuals of all ages, aiming to assess whether available data from PubMed and Embase provide evidence for *H pylori* seroprevalence trends by birth cohort or age on the global, regional, or sub-regional scale.

Methods

Overview

We conducted a scoping review of publications in PubMed and Embase, including articles that contained regional information and *H pylori* seroprevalence data from non-migrant study participants either designated asymptomatic or with no mention of gastrointestinal symptoms (Supplement 1). Our review was conducted following the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping reviews (PRISMA-ScR) checklist guidelines (Supplement 2).

Data charting

Publications meeting the necessary criteria were screened and data were extracted by one researcher (CT) (Supplement 3). Any publications ambiguous in criteria were reviewed with another researcher (MM). No risk of bias assessment was performed. All relevant characteristics, including *H pylori* seroprevalence, age, and birth cohort data, were extracted from each publication (Supplement 4–6). The data were then organised into regions and sub-regions based on the United Nations (UN) geoscheme, as designated by the UN Statistics Division.[22] To assess age-specific effects, we extracted the mean or median age from each study. If these data were not explicitly reported, we derived proxy values by estimating age using information on distributions of age groups included in the study. For birth cohort assignment, age was subtracted from the year of data collection, then rounded to the nearest 20-year decade increment. If data collection occurred over multiple years, the average year of collection was used, and in the case of no reported data collection year, the earliest date available in the publication was substituted.

From this extracted data, 95% confidence intervals (CIs) were estimated through bootstrapping. Data from NHANES 1999–2000 were included in addition to our literature extracted data. Each seroprevalence value was weighted by sample inverse variance and country population prior to summing the total number of data points and the number of *H pylori* positives individually. These values were then used to calculate the weighted means for the global overall and by region and sub-region as reported in Table 1. Estimates were not age adjusted. UN estimates of country population from the year of data collection[23] were utilised, but in the case of missing data, estimates were pulled from the World Bank for Israel, United Arab Emirates, Sudan, and Poland in 2022, and all San Marino, and Greenland years[24] and from the Organization for Economic Co-operation and Development for 1950s United Kingdom.[25] Data visualisations and descriptive analysis were performed in R v.4.4.1.

Results

Published data

A total of 2069 references were initially identified in PubMed and Embase. 165 were flagged as duplicates and 1451 were deemed irrelevant by selection criteria. Of the 453 papers that underwent a full text review, 148 were excluded for having an unsuitable sample, 53 could not be acquired due to language or restricted access, and 23 lacked serology testing. We yielded a total of 229 papers: 214 of which had one dataset, defined as data collected within one time frame in one country, 11 of which had two datasets, and 4 of which had three datasets, yielding 248 datasets from the literature. When added to the two NHANES datasets as divided by collection date, we collected a total of 250 extractable datasets from 230 references. (Fig. 1).

Our dataset represents 88 countries with samples collected between 1947 and 2023. The majority of the original studies were conducted in Europe and Asia, with 82 and 72 studies respectively (Table 1). Although all regions of the globe were represented, some had few studies such as Africa, with 25, and Oceania, with 12. All extracted data combined for a global weighted *H pylori* seroprevalence of 38.5% (WM; 95% CI: 33.0–46.8), with regional estimates ranging from 16.4% (WM) in Oceania to 62.1% (WM) in Africa and suggesting a high global burden of infection.

Age and birth cohort trends

H pylori seroprevalence increased with age across all UN regions at varying rates when considering age effects in isolation (Fig. 2, Panel a). When assessing birth cohort effect, *H pylori* seroprevalence decreased in more recent cohorts compared to earlier ones (Fig. 2, Panel b). Magnitude of *H pylori* seroprevalence varied across the regions, with Oceania consistently presenting the lowest rates of seroprevalence and Africa and Latin America and the Caribbean the highest. Asia and Europe had the most data and had significant amounts of variation in seroprevalence, whilst North American seroprevalence fell generally in the middle in comparison to the other regions.

The age and birth cohort trends seen in broader UN regions are replicated within the UN sub-regions, with seroprevalence increasing with age and decreasing in more recent birth cohorts (Fig. 3, Panel a and b; Supplement 7). In North America and Latin America and the Caribbean (Americas) particularly, South America shows higher magnitude of seroprevalence compared to the other Americas sub-regions, whilst North America falls toward the lower end of seroprevalence and Central America and the Caribbean presenting middle to high seroprevalence based on limited data.

In looking at age and birth cohort trends in combination, variations in seroprevalence trends between regions and sub-regions became apparent. Overall, there is a visible decrease in *H pylori* seroprevalence across all regions over time since the earliest present birth cohort, with Oceania again maintaining the lowest seroprevalence rates across all birth cohorts while Africa maintained the highest (Fig. 2, Panel c).

In assessing UN sub-regions, there are also differential patterns of decrease in *H pylori* seroprevalence by birth cohort. For example, within South America there is some evidence of a decrease in the 25–50 age group between the 1940–1959 cohort and the 1960–1979 cohort. In contrast, North America had a decrease in *H pylori* between the ages of 0 and 50 from the 1960–1979 cohort to the 1980–1999 cohort and evidence of a decrease around the age 50 from the 1940–1959 cohort to the 1960–1979 cohort (Fig. 3, Panel c). Sub-regions also vary in the amount of available data, limiting insight into either age or birth cohort trends. For example, Central American and Caribbean sub-regions had markedly less data than their counterparts. In Central America, there were decreases in seroprevalence under the age of 25 from the 1960–1979 cohort to the 1980–1999 cohort but little evidence of other changes (Fig. 3, Panel c). The Caribbean had the least amount of data of the Americas sub-regions and trend assessment was limited. See Supplement 7 for further sub-region data and Supplement 8 for data reported by WHO region and sub-region.

UN region	# Datasets[a]	# Data points[b,c]	Average *H pylori* seroprevalence WM % (95% CI)[d]	Average birth cohort[d]	Average age[d,e]
Global	250	376,722	38.5 (33.0–46.8)	1965	39.3
Africa	25	6688	62.1 (41.3–78.2)	1973	27.5
Eastern Africa	7	2104	70.7 (33.0–93.8)	1961	29.1
Middle Africa	1	205	62.4 (55.7–68.9)[f]	1950	53.1
Northern Africa	10	2201	22.2 (13.9–46.0)	1992	16.5
Southern Africa	1	681	65.7 (63.8–67.6)	1980	7.9
Western Africa	6	1497	71.8 (41.0–89.5)	1974	32.1
Asia	72	186,827	37.7 (31.3–47.5)	1966	40.3
Central Asia	2	454	70.6 (47.8–86.9)	1957	44.0
Eastern Asia	26	150,466	37.6 (31.3–47.7)	1966	40.6
South-eastern Asia	12	12,721	28.1 (21.7–38.0)	1964	33.0
Southern Asia	12	13,255	51.8 (44.2–59.8)	1976	25.6
Western Asia	20	9931	46.8 (37.1–56.9)	1978	25.0
Europe	82	105,970	36.2 (26.3–46.2)	1961	32.3
Eastern Europe	11	13,317	50.3 (28.5–69.3)	1969	27.4
Northern Europe	34	38,635	33.0 (25.9–41.6)	1951	32.5
Southern Europe	15	18,413	59.7 (40.6–73.5)	1953	45.2
Western Europe	22	35,605	25.4 (13.3–37.7)	1965	30.2
Latin America and the Caribbean	29	33,868	57.9 (49.5–65.7)	1966	27.1
Caribbean	6	2130	36.9 (21.9–53.8)	1962	31.2
Central America	5	18,572	60.9 (50.1–71.7)	1963	25.6
South America	18	13,166	53.7 (40.9–66.9)	1969	29.1
North America	31	34,119	41.1 (33.1–49.4)	1956	35.1
Oceania	12	9250	16.4 (13.2–20.8)	1966	29.6

UN, United Nations; WM, Weighted mean; CI, Confidence Interval. [a]Multiple papers contained data from two or more countries, hence the number of datasets being greater than the number of papers (Fig. 1). [b]Cohort studies were included in extraction to build out age curves and increase granularity, so there are more data points than participants. [c]A dataset containing the most granular subgroup level data from each paper was created and used for calculations to increase data availability and granularity within age groups and birth cohorts. [d]Average WM, birth cohort, and age values were calculated using inverse-variance and population weighting. 95% CIs for *H pylori* WM were calculate using bootstrapping. [e]In the case of individual studies lacking specific age data, we calculated an average age using the minimum and maximum ages provided. If a paper was more specific about age range and provided N values for specific groupings, we calculated a weighted average age to be as accurate as possible. [f]Middle Africa had only one paper with no subgroup data so uncertainty could not be estimated through bootstrapping. A 95% uncertainty interval was calculated from the Beta distribution instead.

Table 1: **Summary of extracted data on *H pylori* seroprevalence among asymptomatic individuals by UN region and sub-region.**

Discussion

In this scoping review, we extracted data from 229 publications and 1 database, yielding over 375,000 data points collected across 88 countries and spanning over 75 years. Using these data, we compared age and birth cohort trends in asymptomatic populations across regions, contributing to a growing body of evidence that suggests both birth cohort and age must be taken into account to properly assess *H pylori* trends and their effect on gastric cancer. We revealed broad gaps in data availability, yielding particularly limited representative data in locations dubbed low- and middle-income, which limited comparisons across specific age groups or time points. Furthermore, the data that was available often utilised convenience sampling or sampled groups known to be at higher risk of *H pylori* relative to the general population (low-income or rural populations, specific racial groups or indigenous populations, etc.). Nevertheless, we found evidence of decreases in *H pylori* seroprevalence in more recent birth cohorts with most individuals acquiring infections in their early decades of life.

Across all age groups and birth cohorts *H pylori* maintains a notable global presence. Our data estimates the prevalence of infection in the global population across all ages from 1947–2023 to be 38.5% (95% CI: 33.0–46.8) which is consistent with previously published global estimates of *H pylori* infection rates ranging

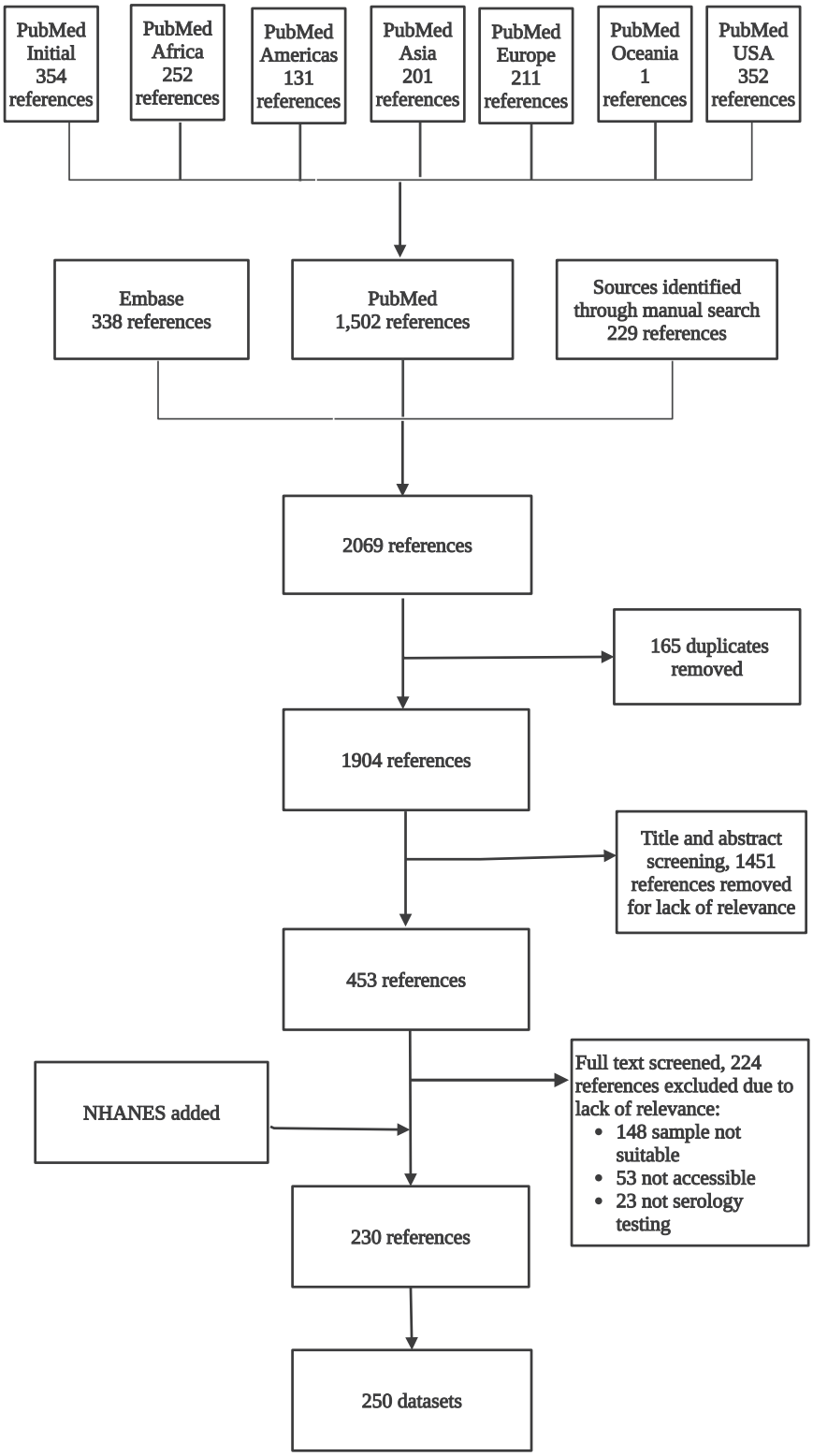

Fig. 1: **Flowchart of study selection process**. Flow diagram showing exclusion process from search, created in Biorender. Sample not suitable refers to a number of reasons for exclusion including: symptomatic individuals included, data post eradication therapy, sample not being stratified in a usable way, and repeating or overlapping data from the same sample set. Not accessible indicates we were unable to acquire the text, typically due to a language barrier. Not serology testing refers to papers that use other styles of testing, such as urea breath tests, stool samples, etc.

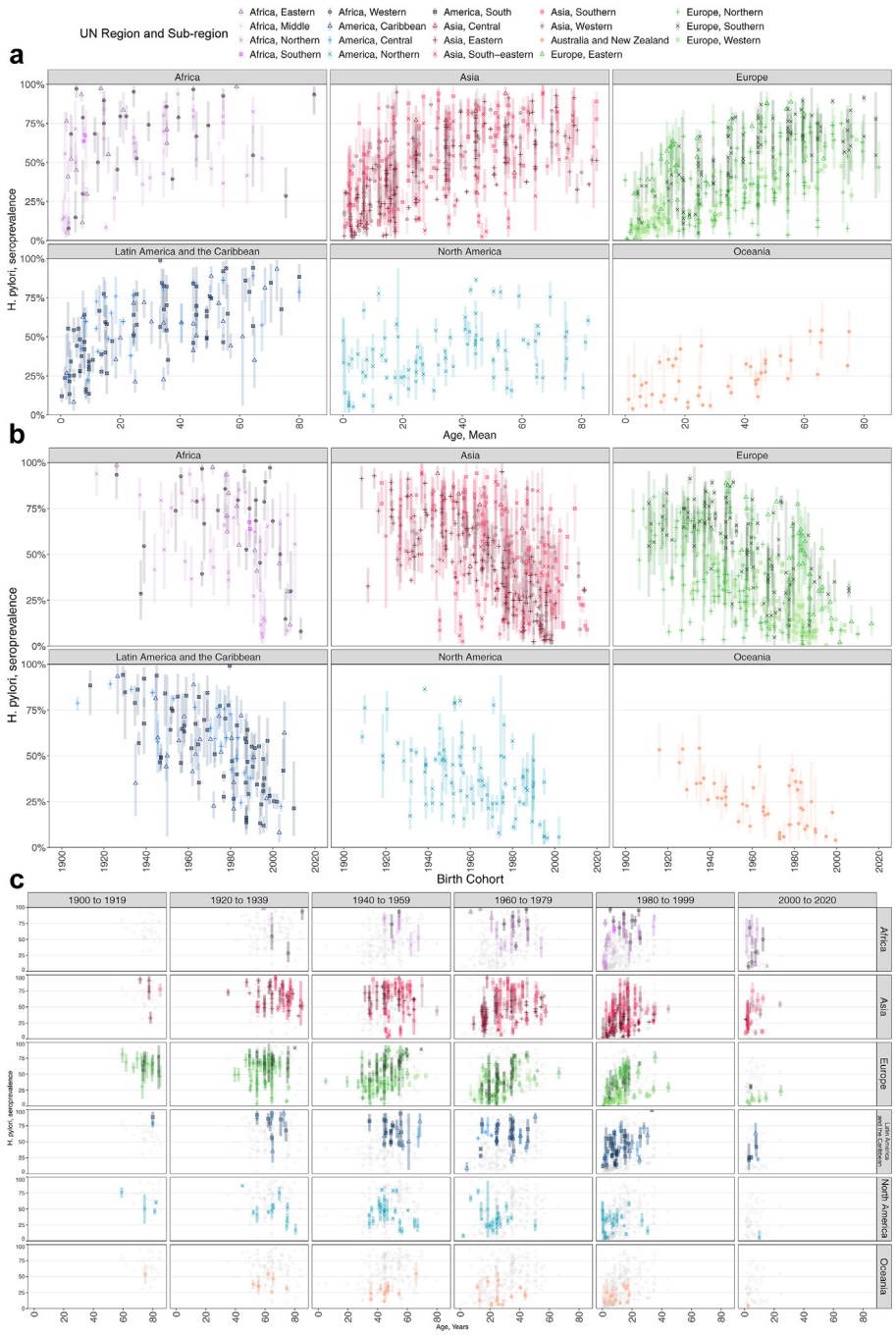

Fig. 2: **Age- and birth cohort-specific trends in *H pylori* seroprevalence among asymptomatic individuals by UN region.** (a) Age-specific trends in *H pylori* seroprevalence across six UN regions. Sub-regions are specified within each region by both color and symbol. Vertical lines represent 95% CIs. (b) Birth cohort-specific trends in *H pylori* seroprevalence across six UN regions. Sub-regions are specified within each region by both color and symbol. Vertical lines represent 95% CIs. (c) Assessment of age and birth cohort trends in combination related to *H pylori* seroprevalence across six UN regions. Grey background points represent all data within a given 20 year birth cohort, while individual sub-regions are specified by both color and symbol. Vertical lines represent 95% CIs.

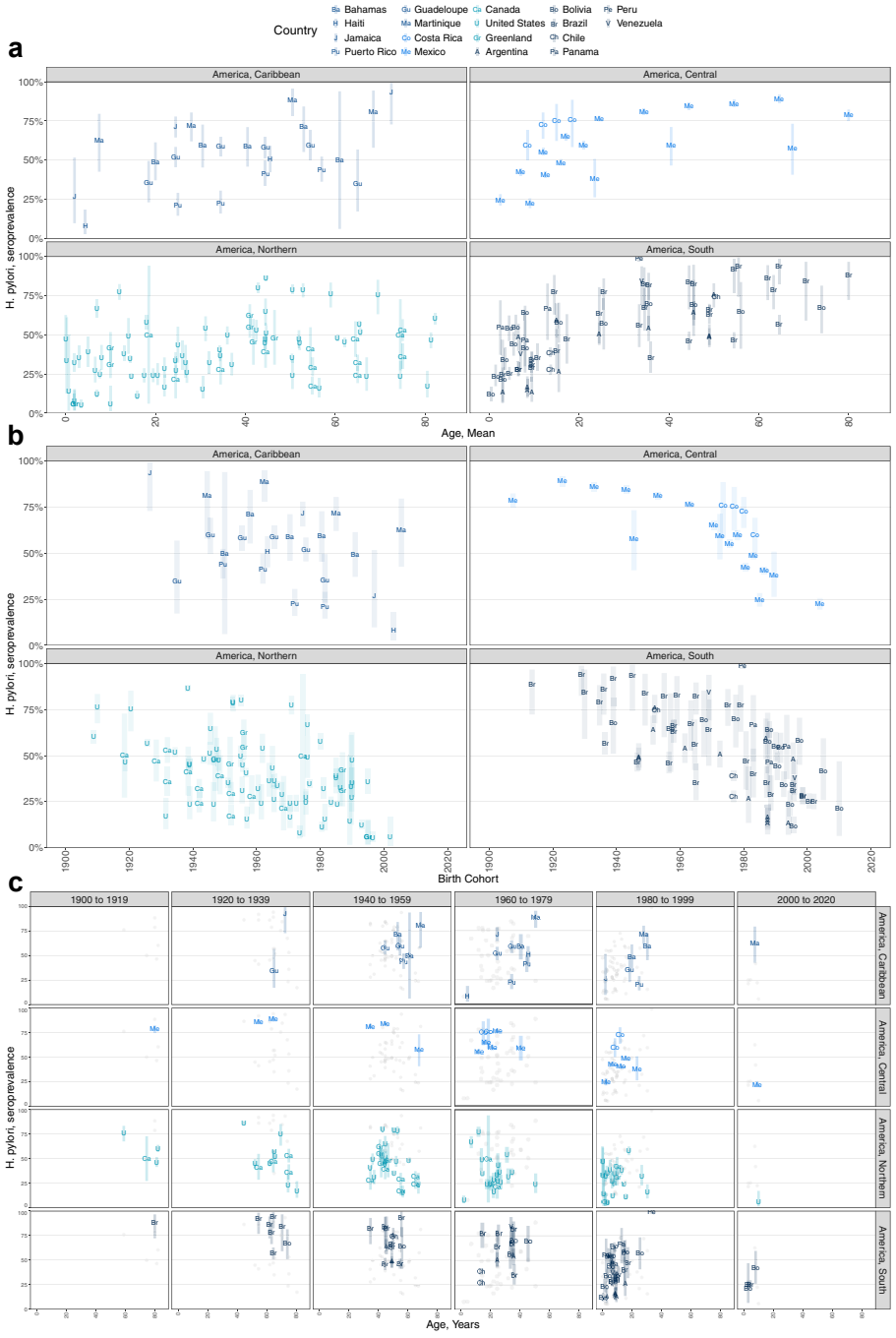

***Fig. 3*: Age- and birth cohort-specific trends in *H pylori* seroprevalence among asymptomatic individuals within UN North America and Latin America and the Caribbean (Americas) sub-regions.** (a) Age-specific trends in *H pylori* seroprevalence within the Americas. Color corresponds to each given sub-region. Individual countries within a sub-region are represented by the first one or two letters of the country name. Vertical lines represent 95% CIs. (b) Birth cohort-specific trends in *H pylori* seroprevalence within the Americas. Color corresponds to each given sub-region. Individual countries within a sub-region are represented by the first one or two letters of the country name. Vertical lines represent 95% CIs. (c) Assessment of age and birth cohort trends in combination related to *H pylori* seroprevalence within the Americas. Grey background points represent all data within a given 20 year birth cohort, while countries are individually labeled by the first letters of their name. Vertical lines represent 95% CIs.

between 27.3% and 51.2%.[14,18–20] The differences in *H pylori* prevalence estimates likely stem from variation in study objectives, with the lowest estimate coming from a review on *H pylori* in children and adolescents[14] and higher estimates from papers focused on socioeconomic factors,[19] different testing methods,[20] or temporal trends.[21] Given the variation in the birth cohorts and age groups included among these studies, direct comparison of our estimates is not possible. Together, the studies underscore the continued public health risk that *H pylori* poses to the global population.

H pylori seroprevalence increased across all UN regions and sub-regions with older age and decreased in more recent birth cohorts. This suggests that older individuals from earlier cohorts were more likely to have acquired an *H pylori* infection in their lifetime. However, upon combined inspection of age and birth cohort trends, more complexity emerges. Despite regional variations in *H pylori* seroprevalence by age when stratified by a 20-year birth cohort, there is evidence of an overall decrease in more recent birth cohorts. Sub-regions with more data present evidence that there is a reduction in *H pylori* seroprevalence in more recent birth cohorts, but in sub-regions with less data it becomes more difficult to elucidate any evidence of trends. This observation suggests that other dimensions may be impacting *H pylori* seroprevalence in addition to age, birth cohort, and location. Global variations in economic and social conditions[19] and *H pylori* eradication[26] are plausible drivers in varied *H pylori* seroprevalence, though more detailed analysis is required to investigate the impact of these variables within an asymptomatic cohort. The role of smoking in *H pylori* acquisition has also been long debated[27–30] and could provide an alternative explanation as to why the magnitude of *H pylori* seroprevalence varies so significantly by UN sub-region. In considering these dimensions, further disaggregation of regions to properly assessing *H pylori* seroprevalence trends should be a priority. Risks within regions are heterogeneous, with socioeconomic and eradication conditions varying not only between UN sub-regions, but between countries and the racial or ethnic groups within them.

Of particular interest is the assessment of trends in the Americas, both North America and Latin America and the Caribbean. Combined, the Americas accounts for almost 20% of all data gathered in this review, behind only Asia and Europe. *H pylori* has been thoroughly reviewed in Asia[31,32] and Europe,[33] leading to eradication guideline campaigns in countries across both regions, albeit with varied integration particularly across Europe.[34,35] However, across the Americas there remains a markedly lower amount of literature in comparison, despite continued high rates of *H pylori* demonstrated in the data collected here. This is important in considering gastric cancer trends. The absolute burden of gastric cancer is estimated to be on the rise in the Americas due to the increasingly large ageing and high-risk populations and the continued lack of *H pylori* eradication interventions across the region will only facilitate this increased burden.[36] Our findings in other regions also reinforce historic trends related to *H pylori* and gastric cancer. In Africa in particular, high rates of *H pylori* persist even in the more recent cohorts of 1980–1999 and 2000–2020 compared to the other UN regions (Fig. 2c), reflecting previous work related to "The African Enigma," wherein African countries tend to have limited gastric cancer rates despite high prevalence of *H pylori* infection.[37]

Our global point estimate is intentionally conservative given our restriction to asymptomatic populations, but even in the absence of symptoms *H pylori* affected more than one in three individuals in this global study. These infections may remain undetected and untreated for years, resulting in a higher lifetime risk for developing gastric cancer. Moreover, *H pylori* is a known contributor to gastritis and other symptomatic gastrointestinal conditions,[2] and symptomatic populations have reported even higher prevalence rates than asymptomatic or general populations. Li et al. (2023) included symptomatic patients in their evaluation of temporal trends from 1980 to 2022 and reported a global seroprevalence estimate of 53.2% (95% CI: 49.8–56.6)[21]; a higher seroprevalence estimate as predicted due to symptomology. In comparison, Zamani et al. (2018) assessed *H pylori* in asymptomatic patients as we did but limited their search to between 2000 and 2017 and found a global seroprevalence of 42.0% (95% CI: 37.7–46.3).[20] We used more data and a wider time period, both of which likely contributed to the differences in estimates. Despite variations in overall *H pylori* seroprevalence, both Li et al. (2023) and Zamani et al. (2018) reported temporal changes, specifically seeing decreases in *H pylori* infection in more recent data.[20,21] This is consistent with the hypothesised decrease in *H pylori* seroprevalence due to better living conditions and reduced exposure to *H pylori* in more recent birth cohorts. Nonetheless, there remain large portions of the global population suffering from *H pylori* infection. Currently no countries in the Americas and few countries across the globe have implemented national eradication strategies in asymptomatic populations, but it is feasible that such prevention efforts may facilitate a bigger impact on accelerating the decline in *H pylori* prevalence globally by targeting these populations that remain at high risk.

Alongside decreases in *H pylori* in more recent birth cohorts, there is also an increase in *H pylori* seroprevalence persisting well past 20 years old, suggesting that acquisition of *H pylori* does not solely occur in childhood. It is often claimed that childhood is the main period during which individuals are infected with *H pylori*,[13] though there is contradicting evidence that prevalence continues to increase by age.[15] Our data

reinforces the idea that prevalence may continue to increase with age, regardless of the birth cohort of an individual. However, more robust data is required to clearly distinguish between true increases due to age and increases due to variations in risk factor exposure by birth cohort. The possible acquisition of *H pylori* in adulthood reinforces the common clinical focus on treating older populations, but eradication of *H pylori* at younger ages is associated with a reduced risk of gastric cancer.[38] Subsequently, *H pylori* surveillance and treatment in children may be useful in reducing the commencement of the precancerous cascade, particularly as early-onset gastric cancer becomes more common in the United States.[39]

There are several notable limitations of this study. The first is that we did not identify enough representative data to estimate trends of interest in certain regions. Most countries were lacking in nationally representative published data comparable to the U.S. NHANES dataset, which presents the most complete single-country *H pylori* birth cohort and age trends: *H pylori* seroprevalence declines at age 20 in the more recent cohorts between 1881 and 2020[18] and increases in all race/ethnicity groups through age 70.[17] Though NHANES primary data was included in our dataset, for many countries we had to rely on much smaller, less representative, and more variable samples. These studies may only be representative of a smaller locality due to variations in risk factors across regions within a single country. This reliance on small studies likely contributed to heterogeneity in our results, and the inconsistencies in age and birth cohort effects may be a function of limited data availability as opposed to true differences between regions or sub-regions. We acknowledge that variation in serology test performance adds to the heterogeneity in our results. In addition to serology testing not differentiating between active and past *H pylori* infection, specific testing methods varied across the included studies, with at least ten different methods reported, introducing variability due to differences in sensitivity and specificity of tests as well as performance within specific age groups. Testing for the IgG antibody through serology in young children has been shown to have lower sensitivity compared to adults,[40] and therefore we may be undercounting infection in childhood.

Additionally, we found limited data in some regions across the globe. For example, African countries in our dataset provided less than 2% of all data points despite representing 12.5% of the global population.[41] Russia and China also accounted for fewer publications than expected based on population size and national research frameworks, but the main issue was the language barrier as many relevant titles were published in Russian or Chinese. Thus, data extracted in this review may not be entirely globally representative and analysis would benefit from the curation of nationally representative datasets and a broader multilingual assessment through the expansion of the team to more than one data extractor and the use of additional databases such as Scopus or Web of Science. Further, as *H pylori* seroprevalence is known to be higher among migrants compared to native populations,[42,43] limited data reporting migrant status may obscure true age trends if adult infections reflect migration rather than new infections. Further investigation is needed to understand the extent to which migration patterns impact *H pylori* seroprevalence trends and how migration may differentially affect *H pylori* seroprevalence trends in different regions or countries.

The information gathered in this review provides the first insights into global age and birth cohort specific trends of *H pylori* seroprevalence and is integral to understanding the role of *H pylori* in gastric cancer burden. In recent years there has been an unexplained increase in early-onset gastric cancer incidence and a slowing in the decades-long decline of overall gastric cancer incidence.[39] Concerns for future trends have been preliminarily assessed by modelling gastric cancer burden through 2040, projecting an increase in cases and deaths[44] and an urgent need for prevention work. Integrating birth cohort and age effect data related to *H pylori* into these models will contribute to more accurate projections and influence gastric cancer screening or prevention programs by indicating the most at-risk populations. Simulation models have been used previously to analyse the impact of *H pylori* on U.S. national gastric cancer incidence in conjunction with other factors, such as smoking[18,45] and utilising our data in this type of model on the global scale will identify further opportunities for harm reduction within the gastric cancer prevention landscape.

In this scoping review we have summarised global *H pylori* seroprevalence data and provided insight into

Search strategy and selection criteria

References for this review were identified through searches of PubMed, using search terms "Prevalence or occurrence or incidence," "*Helicobacter pylori* or H pylori," "Population or population surveillance or global burden of disease or national," and "Africa or Americas or Asia or Europe or Oceania" while excluding "gastritis," and of Embase, using search terms "Eastern or Western Hemisphere," "Prevalence or Serology," "*Helicobacter pylori*," and "asymptomatic." Further searches were conducted targeting countries with limited literature, using country search terms and citation searching. Articles were identified from database inception until June 20, 2024. Exclusion criteria included articles published in a language other than English, Spanish, or French, using non-serological testing methods, or focusing on symptomatic or mobile populations. The final reference list was compiled based on presence of original and extractable *H pylori* seroprevalence data.

birth cohort and age-specific infection trends in individuals born as early as 1900–1919, showing possible reductions in *H pylori* in more recent birth cohorts and increased *H pylori* with age. This data lends itself to future use in modelling changes in gastric cancer and understanding the influence of its greatest risk factor, *H pylori*, on secular trends. Nevertheless, further research in the form of larger, nationally representative datasets with more Americas, Africa, and Oceania coverage should be future research priorities to elucidate robust age and birth cohort trends and ultimately further aid attempts in reducing the global gastric cancer burden.

Contributors

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

MM helped conceptualize the study, designed the study, helped carry out the analysis, and 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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ML reports institutional research funding from AI Medical Service.

MCC declares no competing 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.2024.100877.

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