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Global Prevalence of *Helicobacter pylori* Infection: Systematic Review and Meta-Analysis

James K. Y. Hooi,[1,*] Wan Ying Lai,[1,*] Wee Khoon Ng,[1,2,*] Michael M. Y. Suen,[1,*] Fox E. Underwood,[3] Divine Tanyingoh,[3] Peter Malfertheiner,[4] David Y. Graham,[5] Vincent W. S. Wong,[1] Justin C. Y. Wu,[1] Francis K. L. Chan,[1] Joseph J. Y. Sung,[1] Gilaad G. Kaplan,[3,§] and Siew C. Ng[1,§]

[1]Department of Medicine and Therapeutics, Institute of Digestive Disease, State Key Laboratory of Digestive Diseases, LKS Institute of Health Science, Chinese University of Hong Kong, Hong Kong, China; [2]Department of Gastroenterology and Hepatology, Tan Tock Seng Hospital, Singapore; [3]Departments of Medicine and Community Health Sciences, University of Calgary, Calgary, Alberta, Canada; [4]Department of Gastroenterology, Hepatology and Infectious Diseases, Otto-von-Guericke University of Magdeburg, Magdeburg, Germany; and [5]Gastroenterology, Baylor College of Medicine, Houston, Texas

BACKGROUND & AIMS: The epidemiology of *Helicobacter pylori* infection has changed with improvements in sanitation and methods of eradication. We performed a systematic review and meta-analysis to evaluate changes in the global prevalence of *H pylori* infection. **METHODS:** We performed a systematic search of the MEDLINE and EMBASE databases for studies of the prevalence of *H pylori* infection published from January 1, 1970 through January 1, 2016. We analyzed data based on United Nations geoscheme regions and individual countries. We used a random effects model to calculate pooled prevalence estimates with 95% confidence intervals (CIs), weighted by study size. We extrapolated 2015 prevalence estimates to obtain the estimated number of individuals with *H pylori* infection. **RESULTS:** Among 14,006 reports screened, we identified 263 full-text articles on the prevalence of *H pylori* infection; 184 were included in the final analysis, comprising data from 62 countries. Africa had the highest pooled prevalence of *H pylori* infection (70.1%; 95% CI, 62.6−77.7), whereas Oceania had the lowest prevalence (24.4%; 95% CI, 18.5−30.4). Among individual countries, the prevalence of *H pylori* infection varied from as low as 18.9% in Switzerland (95% CI, 13.1−24.7) to 87.7% in Nigeria (95% CI, 83.1−92.2). Based on regional prevalence estimates, there were approximately 4.4 billion individuals with *H pylori* infection worldwide in 2015. **CONCLUSIONS:** In a systematic review and meta-analysis to assess the prevalence of *H pylori* infection worldwide, we observed large amounts of variation among regions—more than half the world's population is infected. These data can be used in development of customized strategies for the global eradication.

Keywords: Bacteria; Incidence; Europe; Stomach.

Helicobacter pylori (HP) is a gram-negative microaerophilic bacterium that infects the epithelial lining of the stomach. The discovery of HP as a cause of peptic ulcer disease in 1983 resulted in a change of what was once a difficult and debilitating disease into one that could be reliably cured with a course of antibiotics, albeit with escalating concerns due to mounting antibiotic resistance.[1−3] In many countries, the incidence of HP infection has been decreasing in association with improved standards of living.[4,5] Yet the prevalence of this bacterium is still ubiquitous, especially in the Far East.[4] It is the main cause of chronic gastritis and the principal etiological agent for gastric cancer and peptic ulcer disease.[2,6] In most regions, the main mechanism of spread is intrafamilial transmission.[7] The prevalence remains high in most developing countries and is generally related to socioeconomic status and levels of hygiene. Global and regional HP prevalence has not been systematically reported until now.

Recent interest has focused on HP eradication as a strategy of eliminating gastric cancer. However, the epidemiology and clinical manifestations of the infection has been changing, especially in developed countries. For example, gastric cancer and peptic ulcer incidence has continued to fall in Western Europe, the United States, and Japan. Global eradication strategies require up-to-date information regarding HP prevalence and disease burden.

We performed a systematic review of population-based studies reporting HP prevalence of different countries over different time periods, with the premise that these data would provide crucial updates about HP global disease burden and the information to plan appropriate strategies for allocating health care resources. We pooled HP prevalence estimates in different regions and countries, examined the trend in HP prevalence over the past 4 decades, and estimated the number of people infected with HP globally. Understanding the global epidemiologic patterns of HP will aid us in prioritizing and customizing public health efforts to better manage the burden of this disease.

*Authors share co-first authorship; §Authors share co-senior authorship.

Abbreviations used in this paper: CI, confidence interval; HP, *Helicobacter pylori*; UN, United Nations.

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EDITOR'S NOTES

BACKGROUND AND CONTEXT

There are multiple reports on individual countries' *Helicobacter pylori* (HP) prevalence over the past few decades. However, global and regional HP prevalence and their trend with time is not well reported.

NEW FINDINGS

This is the first study to summarize comprehensive global HP prevalence. HP prevalence in different regions of the world is stable or decreasing.

LIMITATIONS

This study contains reports from 62 out of 196 countries, with data lacking in several developing countries. Reports were also conducted at different time periods, with several countries lacking recent data, limiting accuracy for inter-region comparison.

IMPACT

This review estimates that more than half the world's population is infected with HP. Our data can be used to prioritize public health efforts in countries with the highest HP prevalence.

Materials and Methods

Literature Search and Study Selection

This systematic review was performed in accordance to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) 2009 guidelines.[8] A search using keywords from a combination of Medical Subject Headings and free text including terms related to HP and prevalence was performed in MEDLINE and EMBASE via OvidSP. All suitable published papers from January 1, 1970 to January 1, 2016 were identified and subsequently catalogued using EndNote X7. The search strategy is described in the Supplementary Table 1.

Comprehensive inclusion and exclusion criteria were predefined (Table 1) to facilitate objective screening of papers. Only published original observational reports on the prevalence of HP in study populations that were reflective of the general population at national or sub-national levels were included. Systematic reviews, meta-analyses, conference presentations, and letters or correspondences were excluded. Suitable reports identified in hand searches were also included for review. Reports that focused only on specific sub-groups that were not reflective of the general population were excluded (eg, migrants and prisoners). The first phase involved a group of 3 reviewers (J.H., W.Y.L., and M.S.) who independently catalogued all reports using the set criteria. Outcome of this initial categorization was then cross-checked by a different reviewer within this group to ensure its accuracy with a 90% level of agreement. In the second phase, full-text papers were obtained for all identified potential reports for detailed analysis of inclusion suitability. All conflicts of opinion and uncertainties were discussed and resolved by consensus with third-party reviewers (W.K.N., W.T., and S.C.N.). The search was not limited by language. Reports written in neither English nor Chinese had been translated by Google Translate or by colleagues proficient in that language for evaluation of their suitability. Attempts were also made to clarify with the corresponding authors regarding any uncertainties or missing data (eg, study periods not explicitly stated) in selected reports. The reports were then grouped by countries and subsequently into regions based on the United Nations (UN) geoscheme devised by the UN Statistics Division.[9] Figure 1 details the process of report selection.

Data Extraction and Quality Appraisal

Full-text review was performed for all the selected papers and data extracted and sorted by the following variables: name of study, leading author, journal, publication year, study period, type of study, study location (country and sub-national region), HP diagnostic methods used, participant details (number, age, sex ratio), total number of participants, number of HP positive participants, and HP crude prevalence rate. Data on prevalence as a percent of the number of HP-positive participants relative to total number tested were recorded or calculated with 95% confidence intervals (CIs). Papers with missing data, despite attempts to contact the corresponding authors, were excluded. The quality of the remaining papers was rated with the Cochrane Collaboration–endorsed Newcastle-Ottawa Quality Assessment Scale,[10] which was designed to assess aspects of population-based studies of prevalence. The quality assessment of each paper is shown in Supplementary Table 2.

Summarization of Data

HP prevalence for each country was estimated by pooling the data from eligible papers. We used a random effects model to calculate pooled prevalence estimates with 95% CIs. Heterogeneity was assessed using the I^2 measure and the Cochran Q-statistic. The following stratified analyses were conducted to address sources of heterogeneity: (1) geographic region based on classification by UN; (2) time period of evaluating prevalence of HP split into 1970 to 1999 and 2000 to 2016; (3) restricting analysis to adult only (aged 18 years and older); and (4) primary modality of testing HP, including serology, urea breath test, stool antigen, *Campylobacter*-like organism or histopathology, and serology or urea breath test.

The prevalence data were grouped by geographic region based on the UN geoscheme: Northern America, Latin America and the Caribbean, Europe (Northern, Southern, Western, Eastern), Africa, Asia (Central, Eastern, Southern, South-Eastern, Western), and Oceania. Reports that focused on the indigenous population in the United States and Australia were analyzed separately from the respective general population of the country. When prevalence was reported for a multi-year period that extended over more than one time period, the study was included in the time period that captured the most updated data. If multiple studies reported prevalence for the same country and time period, the pooled estimate was taken.[11] Quartiles of prevalence data were used to create choropleth map. Next, we created a web-based interactive map to display comments associated with the prevalence of HP for each country. The static and interactive maps were created using QGIS 2.16.3[12] with the HTML Image Map Plugin[13] for the interactive map. The geographic data were created by the Natural Earth Community.[14]

Population-based studies that reported HP prevalence with two or more time points for the same country were included for temporal trend analyses. For the assessment of potential changes of HP prevalence over time, we stratified prevalence

Table 1. Study Selection Criteria

Criteria
Selection, grading, and clarification of studies
HP diagnosis must be confirmed by one of the following tests: HP serology, HP stool antigen, urea breath test, biopsies for *Campylobacter*-like organism test, rapid urease test, histology, or culture
The study participants must be reflective of the general population in the region
Data from multicenter and multinational studies were extracted separately and sorted by countries and regions
Studies were classified as national (if stated in the report or multicenter study involving multiple regions in the country), sub-national (if only a particular region was evaluated), and city level
Clarifications with the corresponding authors of studies with missing data were made if possible (eg, without specified HP diagnostic method or study period)
Attempts were made to rectify any data errors found in the studies, in consultation with the corresponding authors whenever possible
Exclusion criteria
Publication type
Guidelines
Perspectives, correspondence, letters
Conference abstract or presentation without formal publication
Systematic reviews or meta-analyses
Surveillance registration or national notifiable disease reports of HP
Studies without defined study periods
Study type
Economic analyses
Modeling, time series, or transmission studies; mortality or survival analyses; diagnostic assay or test performance studies; animal studies
Study Population
Study populations that are typically associated with higher prevalence of HP (eg, patients with gastric cancer, peptic ulcers)
High-risk population groups (migrants, refugees, prisoners, individuals [groups] classified as low socioeconomic status, homeless people, adoptees)
Study participants that were restricted to selected age groups (eg, children, elderly)
Testing
HP diagnosis made from methods other than the 4 conventional tests stated above
Studies not reporting the method of HP diagnosis
Self-reported HP infection
Studies not reporting the number of individuals on which the prevalence estimate was based

estimates into two time periods, 1970−1999 and 2000−2016. To obtain the number of people affected with HP, we extrapolated our prevalence estimates to the total 2015 population living in countries and regions as per the UN Population Division. We assumed that countries with missing data in a region had comparable prevalence to our pooled mean prevalence.

R Studio, version 0.99.903, was used for statistical analysis. The R-metafor package was used to generate 95% CIs from logistic regression models then converted to prevalence using the expit transformation. The results of the pooled prevalence estimates were then organized by geographical region.

Role of Funding Source

There was no funding source for this study. The corresponding authors had full access to all data in the study and had final responsibility for the decision to submit for publication.

Results

A total of 14,006 records were identified from both databases, of which 6188 records were duplicates, 7611 records were excluded based on selection criteria, 22 records were removed due to inaccessible full text, and 3 records could not be translated for review (Figure 1). Two records were found in hand searches, and a total of 184 papers were included after full-text review (11 from Africa, 75 from Asia, 66 from Europe, 13 from Latin America and Caribbean, 13 from Northern America, and 6 from Oceania), reporting HP prevalence in 62 countries with 257,768 (48.5%) participants tested HP-positive, out of a total of 531,880 participants. The countries with the highest number of reports were China (n = 21), Korea (n = 12), Japan (n = 11), United States (n = 10), Germany (n = 8), and Iran (n = 8). A summary of the distribution of papers by regions is shown in Supplementary Table 3 and details of individual papers (including age range, sex, and methods to diagnose HP) in Supplementary Tables 4 and 5.

Prevalence of HP in the indigenous population of the United States and Australia was higher than the general population. In Australia, the pooled HP prevalence estimate for the general population was 24.6% (95% CI, 17.2%−32.1%), but was as high as 76.0% (95% CI, 72.3%−79.6%) in the rural Western Australian indigenous community. In the United States, the pooled HP prevalence estimate for the general population was 35.6% (95% CI, 30.0%−41.1%), but it was 74.8% (95% CI, 72.9%−76.7%) in the Alaskan indigenous population. The countries with

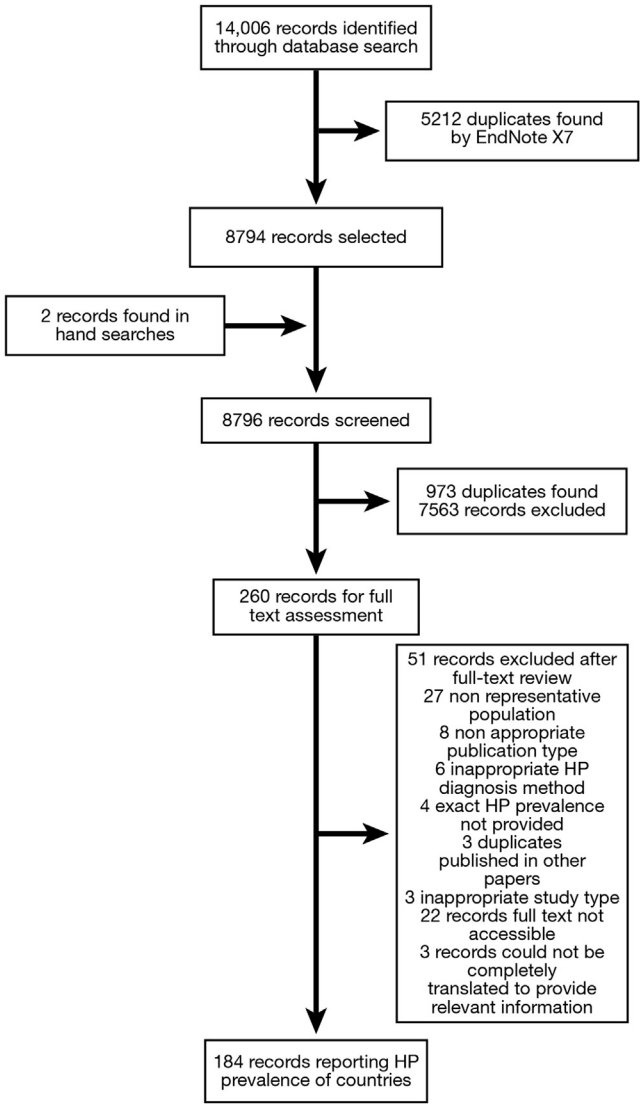

Figure 1. Flowchart of study selection

the highest HP burden were Nigeria (87.7%; 95% CI, 83.1%−92.2%), Portugal (86.4%; 95% CI, 84.9%−87.9%), Estonia (82.5%; 95% CI, 75.1%−90.0)%, Kazakhstan (79.5%; 95% CI, 74.9%−84.2%), and Pakistan (81.0%; 95% CI, 75.6%−86.4%). Countries with the lowest HP prevalence were Switzerland (18.9%; 95% CI, 13.1%−24.7%), Denmark (22.1%; 95% CI, 17.8%−26.5%), New Zealand (24.0%; 95% CI, 21.4%−26.5%), Australia (24.6%; 95% CI, 17.2%−32.1%), and Sweden (26.2%; 95% CI, 18.3%−34.1%).

Regions with the highest reported HP prevalence were Africa (70.1%; 95% CI, 62.6%−77.6%), South America (69.4%; 95% CI, 63.9%−74.9%), and Western Asia (66.6%; 95% CI, 56.1%−77.0%). Regions with the lowest reported HP prevalence were Oceania (24.4%; 95% CI, 18.5%−30.4%), Western Europe (34.3%; 95% CI, 31.3%−37.2%), and Northern America (37.1%; 95% CI, 32.3%−41.9%). HP prevalence and the number of people with HP living in the general population in the 6 UN regions were reported in Tables 2 and 3. Forest plots of pooled HP prevalence stratified by country and UN region are shown in Supplementary Table 6. Significant heterogeneity was observed for pooled analyses in each region (Supplementary Table 6). In order to assess potential sources of heterogeneity, pooled prevalence was stratified by modality of testing for HP (Supplementary Table 7) and adult-only studies (Supplementary Table 8).

Two time periods (1970−1999 and 2000−2016) were used to analyze the HP prevalence trend with time. HP prevalence after 2000 was lower than before in Europe from 48.8% (95% CI, 39.4%−58.2%) to 39.8% (95% CI, 34.2%−45.3%), Northern America 42.7% (95% CI, 32.7%−52.6%) to 26.6% (95% CI, 19.0%−34.1%), and Oceania 26.6% (95% CI, 20.4%−32.8%) to 18.7% (95% CI, 11.6%−25.7%). In contrast, the prevalence of HP positivity was similar in Asia (53.6% before 2000 vs 54.3% after 2000), and Latin America and the Caribbean (62.8% before 2000 vs 60.2% after 2000). Summary of the time trend prevalence for each country and region is shown in Supplementary Table 9. After extrapolation to the 2015 world population, 4.4 billion individuals were estimated to be HP-positive globally (Table 3).

Discussion

HP infection continues to be a major public health issue worldwide. This global systematic review shows that in 2015, approximately 4.4 billion individuals worldwide were estimated to be positive for HP. This is the most comprehensive and up-to-date systematic review of the worldwide prevalence of HP. We confirmed a wide variation in the prevalence of HP between regions and countries. Prevalence is highest in Africa (79.1%), Latin America and the Caribbean (63.4%), and Asia (54.7%). In contrast, HP prevalence is lowest in Northern America (37.1%) and Oceania (24.4%). At the turn of the 21st century, the prevalence of HP has been declining in highly industrialized countries of the Western world, whereas prevalence has plateaued at a high level in developing and newly industrialized countries. The widening differential gap in prevalence has important implications on the future worldwide prevalence of sequelae associated with HP, including peptic ulcer disease and gastric cancer. These differences in HP prevalence likely reflect the level of urbanization, sanitation, access to clean water, and varied socioeconomic status. There are significant differences in the HP prevalence even within the same country. Different racial groups in the United States have different HP prevalence. It was reported that the prevalence in non-Hispanic whites ranges from 18.4% to 26.2% and that in non-whites ranges from 34.5% to 61.6%.[15,16] Prevalence can be as high as 75.0% in the Alaskan Native population.[17]

Our review demonstrated that there is still a significant burden of HP in most of the world. Even in Switzerland, which had the lowest reported HP prevalence (18.9%), there were still approximately 1.6 million infected individuals. Eradication of gastric cancer will require additional efforts and research focused on prevention of HP acquisition and HP eradication. Innovative strategies will

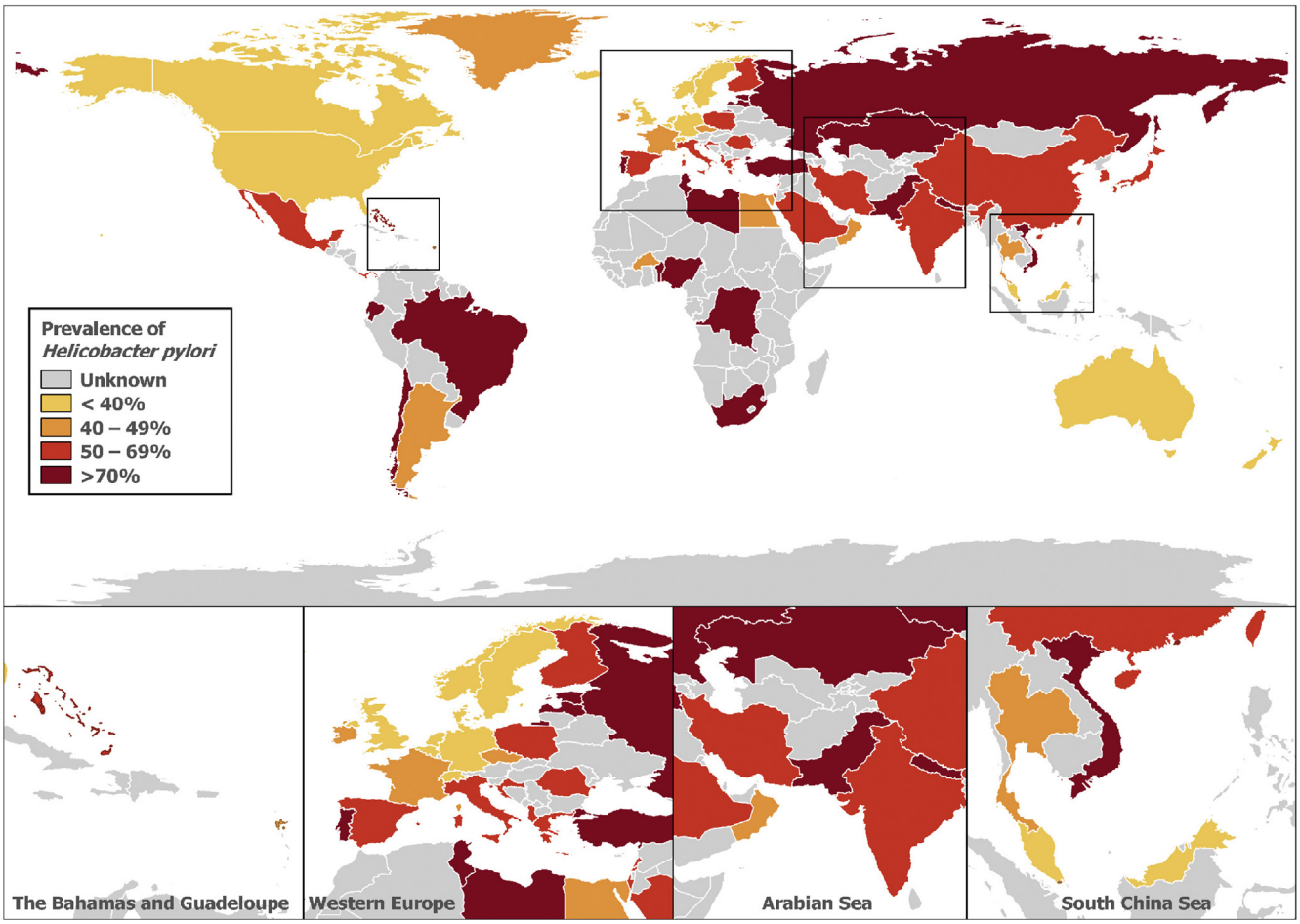

Figure 2. Global prevalence of HP choropleth map. Certain regions are magnified to better display the smaller countries. The online interactive global map showing the HP prevalence can be found at the following URL: https://people.ucalgary.ca/~ggkaplan/HP2016.html.

likely be needed to reduce HP prevalence in areas such as Africa, India, and South America, where access to health care and resources may be limited.

HP has been identified as a Group I carcinogen by the International Agency for Research on Cancer and currently is considered a necessary but insufficient cause of gastric adenocarcinoma.[18–22] Approximately 89% of all gastric cancers can be attributable to HP infection.[23] Gastric cancer remains the third most common cancer worldwide, with more than half coming from China, Japan, and Korea. Prognosis is poor, with only 1 in 5 patients surviving longer than 5 years after diagnosis. HP eradication has been associated with a reduction of gastric cancer incidence and this benefit is present irrespective of risk group.[24–26] There is also evidence that screening and eradication of HP in young adults in China would be cost-effective and could help in preventing 1 gastric cancer in every 4 to 6 cases.[26] The appropriate strategy may differ between countries and is further complicated by increasing antibiotic resistance, which could prove to be a major hindrance to eradication. Increasing prophylactic HP vaccination appears to be an option.[27] The development of HP vaccine has been challenging, but there is yet to be an effective vaccine available in the market. One promising phase 3 trial of an oral vaccine in China has demonstrated vaccine-mediated protection against HP, leading to a reduced risk of HP acquisition among the younger population.[28] The high global prevalence of HP in many parts of the world and the non-diminishing HP prevalence in developed countries should serve as the impetus for researchers to hasten the process to create an effective vaccine. Of interest, HP vaccination has also been demonstrated to be cost-effective in the United States, which has one of the lowest HP prevalences globally.[29]

In Africa, despite the high HP prevalence, the reported incidence of gastric cancer was considerably lower compared with China or Japan and was postulated to be related to the predominant non-atrophic gastritis pattern in Africa; the archetypal hpAfrica2 type strain largely restricted in South Africa, which lacks cag A pathogenicity island; and lastly intestinal parasitic infestation modulating the immune response against HP toward a Th2 type (anti-inflammatory), which may reduce risk of gastric cancer.[30,31] The now defunct phenomenon known as "African enigma" was attributed to the inadequate sampling of the African population obtained through endoscopic data, limited access

Table 2. *Helicobacter pylori* Prevalence and Number of People Living With *H pylori* in the General Population Within Each Country Grouped by United Nations Regions

Variable	No. of reporting studies	No. of participants	Prevalence estimates, % (95% CI)	Population size per country[a]	HP-positive population
UN African region					
Benin	1	446	74.1 (70.0–78.1)	10,880,000	8,056,640
Burkina Faso	1	188	46.8 (39.7–53.9)	18,106,000	8,475,419
Democratic Republic of Congo	1	133	77.4 (70.3–84.6)	77,267,000	59,835,565
Egypt	1	200	40.9 (15.4–66.4)	91,508,000	37,435,923
Libya	1	360	76.4 (72.0–80.8)	6,278,000	4,795,764
Nigeria	2	648	87.7 (83.1–92.2)	182,202,000	159,700,053
South Africa	2	1539	77.6 (59.8–95.5)	54,490,000	42,306,036
Tunisia	2	348	72.8 (53.7–91.9)	11,254,000	8,191,787
UN Latin American and Caribbean region					
Argentina	1	493	49.1 (44.7–53.5)	43,417,000	21,313,405
Bahamas	1	204	57.8 (51.1–64.6)	388,000	224,419
Brazil	6	2937	71.2 (66.0–76.4)	207,848,000	147,946,206
Chile	1	2615	74.6 (72.9–76.2)	17,948,000	13,383,824
Ecuador	1	90	72.2 (63.0–81.5)	16,144,000	11,659,197
Guadeloupe[b]	1	854	49.0 (35.3–62.8)	468,000	229,367
Mexico	2	11,820	52.5 (24.7–80.3)	127,017,000	66,709,328
Panama	1	74	54.1 (42.7–65.4)	3,929,000	2,123,625
UN Northern American region					
Canada	1	316	38.0 (32.6–43.3)	35,940,000	13,646,418
Greenland	2	756	41.4 (37.9–44.9)	56,000	23,178
United States[c]	8	16,235	35.6 (30.0–41.1)	321,774,000	114,455,012
UN Asian region					
Central Asia (n = 1)					
Kazakhstan	1	288	79.5 (74.9–84.2)	17,625,000	14,013,638
Eastern Asia (n = 47)					
China	22	103,128	55.8 (51.8–59.9)	1,376,049,000	768,110,552
Japan	11	48,979	51.7 (44.7–58.7)	126,573,000	65,387,612
Korea	11	121,493	54.0 (50.1–57.8)	25,155,000	13,571,123
Taiwan	3	10,616	53.9 (36.6–71.2)	23,381,000	12,600,021
Southern Asia (n = 13)					
Iran	8	5256	59.0 (51.5–66.5)	79,109,000	46,658,488
India	2	407	63.5 (53.4–73.5)	1,311,051,000	831,861,860
Lebanon	1	308	52.0 (46.4–47.5)	5,851,000	3,039,595
Nepal	1	383	70.1 (65.9–75.1)	28,514,000	19,974,057
Pakistan	1	205	81.0 (75.6–86.4)	188,925,000	152,991,465
South-Eastern Asia (n = 8)					
Malaysia	3	9168	28.6 (19.0–38.2)	30,331,000	8,677,699
Singapore	2	953	40.8 (37.7–43.9)	5,604,000	2,287,553
Thailand	1	179	43.6 (36.3–50.8)	67,959,000	29,616,532
Vietnam	2	1241	70.3 (63.3–77.4)	93,448,000	65,712,634
Western Asia (n = 8)					
Israel	2	688	68.9 (62.7–75.1)	8,064,000	5,555,290
Oman	2	499	49.1 (11.5–86.7)	4,491,000	2,205,081
Saudi Arabia	1	364	65.9 (61.1–70.8)	31,540,000	20,794,322
Turkey	3	6036	77.2 (71.4–83.1)	78,666,000	60,761,618
UN European region					
Eastern Europe (n = 10)					
Czech Republic	3	4644	41.2 (24.8–57.6)	10,543,000	4,342,662
Poland	3	7806	66.6 (56.4–76.7)	38,612,000	25,707,870
Romania	1	960	68.5 (65.6–71.5)	19,511,000	13,372,839
Russian Federation	3	4771	78.5 (67.1–89.9)	143,457,000	112,585,054
Northern Europe (n = 22)					
Denmark	2	37,741	22.1 (17.8–26.5)	5,669,000	1,254,550
Estonia	2	2198	82.5 (75.1–90.0)	1,313,000	1,083,356
Finland	1	896	56.8 (46.5–67.0)	5,503,000	3,124,603
Iceland	2	834	36.0 (32.7–39.2)	329,000	118,341
Ireland	1	1000	43.0 (39.9–46.1)	4,688,000	2,015,840

Table 2. Continued

Variable	No. of reporting studies	No. of participants	Prevalence estimates, % (95% CI)	Population size per country[a]	HP-positive population
Latvia	1	3564	79.2 (77.9–80.5)	1,971,000	1,561,229
Norway	3	4068	30.7 (20.5–40.8)	5,211,000	1,597,172
Sweden	5	7149	26.2 (18.3–34.1)	9,779,000	2,563,076
United Kingdom	5	15,098	35.5 (14.5–56.5)	64,716,000	22,974,180
Southern Europe (n = 22)					
Albania	1	101	53.5 (43.7–63.2)	2,897,000	1,549,026
Croatia	3	6538	52.7 (42.5–62.8)	4,240,000	2,234,056
Greece	3	1571	52.1 (40.2–64.0)	10,955,000	5,708,651
Italy	5	9055	56.2 (46.9–65.4)	59,798,000	33,606,476
Portugal	1	2067	86.4 (84.9–87.9)	10,350,000	8,942,400
San Marino	2	3765	47.5 (40.5–54.5)	32,000	15,200
Spain	7	2721	54.9 (48.6–61.1)	46,122,000	25,307,141
Western Europe (n = 16)					
Belgium	3	27,845	32.7 (22.4–43.0)	11,299,000	3,694,773
France[d]	1	64	46.9 (34.7–59.1)	64,395,000	30,188,376
Germany	8	19,015	35.3 (31.2–39.4)	80,689,000	28,483,217
Netherlands	3	8592	35.5 (30.1–41.0)	16,925,000	6,011,760
Switzerland	1	175	18.9 (13.1–24.7)	8,299,000	1,565,191
UN Oceania region					
Australia[c]	4	4485	24.6 (17.2–32.1)	23,969,000	5,905,962
New Zealand	1	1060	24.0 (21.4–26.5)	4,529,000	1,085,148

[a]Based on UN 2015 Revision of World Population Prospects total population estimates.
[b]Insular region of France located in the Caribbean.
[c]Data related to the indigenous population were excluded from this table.
[d]Guadeloupe data not included in the pooled analysis for France due to different demographics.

to health care, and a relatively short life expectancy in the population. More recent and robust data on the African gastric ulcer and cancer prevalence confirmed that it is not as low as reported previously.[32] Ongoing efforts to monitor HP prevalence and its disease burden in a systematic manner is crucial, as it will minimize any skewed data, which can adversely affect the allocation of health care resources.

As has been reported in the literature, our review observed that HP prevalence is lower in certain ethnic groups, like Malay, despite having the similar environmental exposures as other ethnic groups.[4] Malaysia's population consisted of approximately 67.4% Malays[33] and has a low pooled HP prevalence of 28.6%. Among the varied ethnicities in Malaysia, the prevalence of HP in Malays is 19.6%, which is significantly lower than the Chinese (40.0%) and Indians (50.7%).[34] Besides Malaysia, the Malays in Singapore also had a low HP prevalence of 25.0%.[35] Of interest, the age-standardized rate of gastric cancer is 1.7 per 100,000 in Malay males, 1.1 per 100,000 in Malay females, compared to 5.6 per 100,000 in Chinese males and 4.1 per 100,000 in Chinese females.[36] The reasons for a lower prevalence in Malays and some other ethnic groups need to be further investigated, while genetic factors and environmental factors also must be evaluated. Additionally, indigenous populations in developed countries have much higher HP prevalence. For example, Alaskan Natives in the US had a HP prevalence of 75.0%,[17] while the Martu community in Western Australia had a prevalence of 91.0%.[37] These differences likely reflect the disparity in care, reduced sanitation, and lower socioeconomic status that is observed in indigenous populations.

This study has several strengths. It is one of the most comprehensive and up-to-date reviews on the evolution of the global epidemiology of HP in the 21st century. We included only population-based data, which limited selection bias. Secondly, we pooled data to highlight differences within and between different regions around the world. Recent declines in HP prevalence—particularly in more industrialized nations, such as the United States, China, and Japan—are likely due to rising standards of living, and improved sanitation. However, the cohort effect associated with these changes has become gradually less important for consequent stabilization of the prevalence. What remains unclear is whether the prevalence of HP will continue to drop or remain static. Regardless, surveillance cohorts that track disease burden and preventive strategies are paramount to discovering or confirming suspected environmental factors.

This review has some limitations. This systematic review contains reports from only 62 of 196 countries globally. Reports were also conducted at different time periods, with several countries lacking recent data, limiting accuracy for inter-region comparison. HP prevalence is generally higher in developing countries, yet reports for many developing countries are not available. For some reports, only selected

Table 3. *Helicobacter pylori* Prevalence and Number of People Living With *H pylori* in the General Population in the United Nations Regions

Variable	Prevalence estimates, %, 95% CI)	Population size per region/country[a]	HP-positive population (range)
UN Africa region	79.1 (62.6–95.6)	1,186,178,282	938,267,021 (742,547,604–1,133,986,437)
UN Latin American and Caribbean region	63.4 (59.2–67.6)	634,386,567	402,201,083 (375,556,847–428,845,319)
Caribbean	52.6 (45.2–60.0)	43,199,297	22,731,470 (19,526,082–25,919,578)
Central America	53.0 (32.6–73.5)	172,740,074	91,621,335 (56,313,264–126,963,954)
South America	69.4 (63.9–74.9)	418,447,196	290,318,665 (267,387,758–313,416,949)
UN Northern American region	37.1 (32.3–41.9)	357,838,036	132,614,776 (115,581,685–149,934,137)
UN Asian region	54.7 (51.3–58.1)	4,393,296,014	2,403,132,920 (2,253,760,855–2,552,504,984)
Central Asia	79.5 (74.9–84.2)	67,314,033	53,521,388 (50,418,210–56,678,415)
Eastern Asia	54.1 (50.8–57.5)	1,612,286,941	872,892,150 (819,041,766–927,064,991)
Southern Asia	61.6 (55.9–67.4)	1,822,974,074	1,123,134,327 (1,019,042,507–1,228,684,525)
South–Eastern Asia	43.1 (31.5–54.8)	633,489,946	273,287,563 (199,549,332–347,152,490)
Western Asia	66.6 (56.1–77.0)	257,231,020	171,212,967 (144,306,602–198,067,885)
UN European region	47.0 (41.8–52.1)	738,442,070	347,067,773 (308,668,785–384,728,318)
Eastern Europe	62.8 (48.3–77.2)	292,942,778	183,850,887 (141,491,361–226,151,824)
Northern Europe	41.6 (32.4–50.7)	102,357,768	42,550,124 (33,163,916–51,895,388)
Southern Europe	55.0 (49.1–61.0)	152,347,892	83,852,280 (74,802,814–92,932,214)
Western Europe	34.3 (31.3–37.2)	190,793,632	66,396,184 (59,718,406–70,975,231)
UN Oceania region	24.4 (18.5–30.4)	39,331,130	9,608,595 (7,276,259–11,956,663)
Global	—	—	4,356,096,968 (3,750,167,566–4,961,780,681)

[a]Based on United Nations 2015 Revision of World Population Prospects total population estimates.

areas of countries were sampled instead of the entire country (ie, sub-national level), limiting its accuracy to reflect the country's true prevalence. We assumed that countries with missing data in a region have comparable prevalence to our pooled mean prevalence. Future studies are necessary in areas lacking prevalence to HP to confirm our estimates. Also, our pooled analyses demonstrated significant heterogeneity. We explored some sources of heterogeneity, including age, geographic region, time period, and modality of testing. However, a comprehensive evaluation of heterogeneity was limited by the information available in the primary studies. As well, HP is not a notifiable disease in many countries and its prevalence is mainly derived from willing participants of population-based studies. It is likely these reports may underestimate the true prevalence, especially in areas with poorer access to health care facilities. HP is also usually not routinely included in health screening, reducing the chance of identifying this disease in the general population. Furthermore, the reports used different methods and assays for the diagnosis of HP, with different sensitivities and specificities, which may limit the accuracy of inter-region comparison. Additionally, an underestimation of the lifetime prevalence may occur in older subjects, as infection tends to disappear with the progression of gastric lesions caused by the HP, resulting in a decline in the circulating IgG titers. Despite these limitations, IgG serology was commonly used, as it is a relatively simple, less invasive, and convenient method to screen large populations. In the developing world, defining HP prevalence is considerably more challenging because many countries lack health care systems that compile outcomes into population-based registries.

Thus, prevalence rates reported are likely to be underestimated in studies published early in the observation period and in developing countries. This may explain why HP prevalence seemed to have remained stable in parts of Asia and Latin America, and the Caribbean when compared with the developed areas in Europe, North America, and Oceania, due to better diagnostics, but also a declining HP prevalence. HP prevalence is related to the acquisition rate in children, which is related to sanitation and clean water. Despite rapidly falling pediatric HP prevalence in China, Korea, and Japan, HP prevalence remained relatively stable artefactually due to the mixed populations, which will take decades to demonstrate a significant change in rate. Lastly, most primary studies lacked key covariates to conduct regression models to evaluate for any additional factors significantly associated with HP prevalence.

Despite these limitations, this systematic review provides a comprehensive overview of the prevalence of HP. Variation in prevalence of HP observed in different geographic areas and across time suggests that prevalence is influenced by living conditions, such as hygiene status and industrialization of society. Consequently, these data can be used to support regional initiatives to prevent and eradicate HP, with the goal of reducing the complications of HP.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Gastroenterology* at www.gastrojournal.org, and at http://dx.doi.org/10.1053/j.gastro.2017.04.022.

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Author names in bold designate shared co-first authorship.

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Reprint requests
Address requests for reprints to: Siew C. Ng, MBBS, MRCP, PhD, Department of Medicine and Therapeutics, Chinese University of Hong Kong, Hong Kong. e-mail: siewchienng@cuhk.edu.hk; fax: (852) 2637 3852. Gilaad G. Kaplan, MD, MPH, FRCPC, Teaching Research and Wellness Center, 3280 Hospital Drive NW, 6D17 Calgary, Alberta, T2N 4N1, Canada. e-mail: ggkaplan@ucalgary.ca; fax: 1 403 592 5050.

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Conflicts of interest
The authors disclose no conflicts.