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



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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 metaanalysis 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. 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. 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 I² 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 2.16.3¹² with the HTML Image Map Plugin¹³ 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

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