



Prevalence of *Helicobacter pylori* infection in Latin America and the Caribbean populations: A systematic review and meta-analysis

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ABSTRACT

Objective: To describe the prevalence of *Helicobacter pylori* (*H. pylori*) infection in Latin America and the Caribbean (LAC), through systematic review and meta-analysis by age groups and gender.

Methods: Systematic review and meta-analysis of the population-based observational epidemiological studies carried out in LAC, focused on the prevalence of *H. pylori* and published until March, 2018. The databases utilized in the search were MEDLINE, SCIELO and PUBMED. The prevalence described in the meta-analysis and 95% confidence intervals were estimated by the random effects model, and weighted by the size of the study.

Results: The 22 selected studies were carried out in 14 countries of LAC, and included 24,178 individuals. The studies were conducted between 1987 and 2012, and all were representative of at least one city. The prevalence of *H. pylori* infection was 57.57% (CI95%:50.43;64.72) for all ages; in children and adolescents the prevalence was 48.36% (CI95%:38.03;58.70) and in adults 69.26% (CI95%:64.54;76.99). No differences were observed regarding sex.

Conclusion: Prevalence of *H. pylori* infection in LAC is high for all age groups. These data reinforce the necessity of actions towards the prevention and treatment of *H. pylori* infection for all age groups. Treating *H. pylori* infection in young ages probably will reduce gastric cancer incidence in the future.

1. Introduction

Incidence and mortality rates of gastric cancer are high in Latin America. [1,2] In 2018, the estimated age-standardized incidence rates of Gastric cancer for the Caribbean, Central and South America were, respectively, 8.7, 8.1 and 12.7 per 100,000 men and 5.1, 6.3 and 6.9 per 100,000 women [1], demonstrating sex-related disparities in the rates.

Helicobacter pylori (*H. pylori*) is a bacteria associated with gastric adenocarcinoma and mucosa-associated lymphoid tissue lymphoma. [3,4] Of the new cancer cases associated with infectious agents, 35.4% (770,000) of all cases were attributed to *H. pylori* in 2012.⁵ For non-cardia gastric adenocarcinoma (NCGC), the attributable share to *H. pylori* was 89.0%. [5]

In 2018, a compilation of 183 studies carried out between 2000 and 2017 estimated *H. pylori* infection prevalence as 44.3% (95%CI: 40.9–47.7) for the world population, with differences associated with the socioeconomic level of countries.⁶ Prevalence of *H. pylori* varies around the world. In 2017, a meta-analysis that included 263 studies published within the period 1970–2016, estimated the prevalence of *H. pylori* infection between 18.9% (CI95%:13.1;24.7) in Switzerland up to 87.7% (CI95%:83.1;92.2) in Nigeria. In Latin America and the

Caribbean (LAC), prevalence was 62.8% before the year 2000 and 60.2% after that.⁷

Previous studies have estimated prevalence for this region [6,7], but analyses are required to explore the characteristics of this population regarding prevalence by sex and age group, to better comprehend the high prevalences found for *H. pylori* in LAC.

In the light of the above, the study presented herein is a systematic review followed by meta-analysis of observational studies on the prevalence of *H. pylori* in LAC, analyzing age group and sex within population-based observational studies.

2. Methods

This systematic review was followed by meta-analysis, which included population-based observational studies, conducted in LAC. The proposal was registered in the International Perspective Register of Systematic Reviews (PROSPERO) under number CRD42018091631, available at http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42018091631. The systematic review followed the standards of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). [8]

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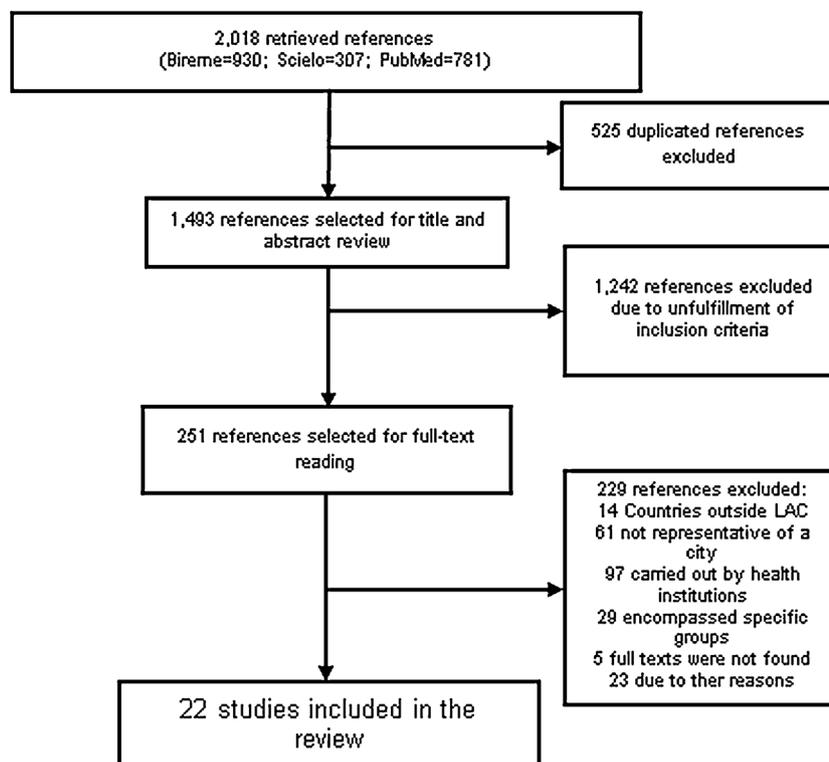


Fig. 1. Search, selection and study inclusion process.

The following databases were utilized for the search: MEDLINE via PubMed, Latin American and Caribbean Center on Health Sciences Information (LILACS) and Scientific Electronic Library Online (SciELO), using the mesh terms described in Supplementary Fig. 1. No restrictions on language, publication date or status were applied. Studies published up to March, 2018 were included (March 1st 2018, updated in November 22th, 2018).

Population-based studies on the prevalence of *Helicobacter pylori* infection were included, along with cross-sectional, and/or cohort and/or case control studies, independent of age, sex or ethnicity, carried out in LAC.

H. pylori infection was established according to one or more of the detection methods: HP serology, HP stool antigen, urea breath test, biopsies for Campylobacter-like organism test, rapid urease test, histology, or culture.

Editorials, case reports, study reviews, ecological studies, bachelor theses and animal studies were excluded. Specific groups of populations were excluded: cancer patients, HIV-positive individuals, and high-risk population groups (migrants, refugees, slum residents). Other exclusion criteria were: studies carried out with non-probabilistic samples; studies that did not represent, at least, one municipality; studies with convenience samples; and samples obtained from health services (health centers, hospitals, blood banks).

Two researchers reviewed the retrieved studies independently; one researcher extracted data and the second confirmed the extraction. A third reviewer resolved any disagreements. A data extraction sheet was developed to collect the following information from the studies: author, year, location (city/region), country, sample, number of cases by gender, age distribution, and the methods utilized for diagnosis and prevalence (and/or frequency) of *Helicobacter pylori* in the available

studies. The Loney criteria was employed to assess the quality of the prevalence studies [9].

The prevalence described in the meta-analysis and the 95% confidence intervals (CI95%) were estimated by the random effects model, weighted by the size of the study. Heterogeneity across studies was analyzed by the fixed effect model of the inverse variance, and the magnitude of inconsistency was estimated by I-square statistics (I^2) [10].

Subgroup analyses were carried out to investigate *H. pylori* prevalence by country, sex, age group (< 18 years old and \geq 18 years old), and period of data collection from the studies (1987–2000 and 2001–2012), when data were available. Meta-regression was also applied to evaluate the effect of the study year, diagnosis methods, and Human Development Index (<https://data.worldbank.org/>) (HDI). This analysis considered the HDI of the country and year of study (or closest year available at the website from world bank). Small study effects were evaluated by visual inspection of the funnel plot and linear regression test of funnel plot asymmetry [11]. All analyses were carried out in R, using the meta package [12].

3. Results

A total of 2018 manuscripts were identified in the period; of these, 525 were duplicated and therefore excluded from the study. After reading the titles and abstracts, 251 papers were selected for full reading; of these, 22 studies [13–34] fulfilled the eligibility criteria and were included (Fig. 1).

The 22 selected studies were carried out in 14 countries of LAC, and included 24,178 individuals. The studies were conducted between 1987 and 2012 (period of data collection), and all were representative of at

Table 1
Characteristics of the included studies.

ID	Author, Year of publication	Year of data collection	Title	Country	Age groups	N event	N Total	Diagnosis method
1	Torres, 1998 [13]	1987	A Community-Based Seroepidemiologic Study of Helicobacter pylori Infection in Mexico	Mexico	0-19 years / 20+ years	7720	11605	HP serology
2	Hopkins, 1993 [14]	1990	Seroprevalence of Helicobacter pylori in Chile: vegetables may serve as one route of transmission	Chile	0 – 34 years	624	1815	HP serology
3	Klein, 1991 [15]	1991	Water source as risk factor for Helicobacter pylori infection in Peruvian children. Gastrointestinal Physiology Working Group	Peru	2 months – 12 years	195	407	Urea breath test
4	Goodman, 1996 [16]	1992	Helicobacter pylori infection in the Colombian Andes: a population-based study of transmission pathways	Colombia	2 – 9 years	472	684	Urea breath test
5	Souto, 1998 [17]	1993	Prevalence of Helicobacter pylori Infection in a Rural Area of the State of Mato Grosso, Brazil	Brazil	10 – 19 years / 20+ years	170	204	HP serology
6	Camargo, 2004 [18]	1999	Age at acquisition of Helicobacter pylori infection: comparison of two areas with contrasting risk of gastric cancer	Colombia	1 – 6 years	394	666	Urea breath test
7	Lindo, 1999 [19]	1999	Seroepidemiology of Helicobacter pylori infection in a Jamaican community	Jamaica	All ages	202	346	HP serology
8	Steinberg, 2004 [20]	1999	Prevalence of infection with waterborne pathogens: a seroepidemiologic study in children 6-36 months old in San Juan Sacatepequez, Guatemala	Guatemala	6 – 36 months	95	522	HP serology
9	Sivapalasingam, 2014 [21]	2000	Recurrence of Helicobacter pylori infection in Bolivian children and adults after a population-based 'screen and treat' strategy	Bolivia	All ages	848	1065	Urea breath test
10	Parente, 2006 [22]	2001	Helicobacter pylori infection in children of low and high socioeconomic status in northeastern Brazil	Brazil	0 – 12 years	115	303	HP serology
11	Aoki, 2004 [23]	2002	Seroprevalences of Helicobacter pylori infection and chronic atrophic gastritis in the united Republic of Tanzania and the Dominican Republic	Dominican Republic	18+ years	742	1215	HP serology
12	Morgan, 2006 [24]	2002	Gastric Cancer and the High Combination Prevalence of Host Cytokine Genotypes and Helicobacter pylori in Honduras	Honduras	18 – 91 years	122	162	HP serology
13	Merino, 2002 [25]	2002	Helicobacter pylori infection in children from Northeast Argentina: seroprevalence and its relation with nutritional status and socio-sanitary conditions	Argentina	4-14 years	126	278	HP serology
14	Ferreccio, 2007 [26]	2003	Gastric cancer is related to early Helicobacter pylori infection in a high-prevalence country	Chile	17+ years	1950	2615	HP serology
15	Holst-Schumacher, 2007 [27]	2003	Prevalence of mild serum vitamin B12 deficiency in rural and urban Costa Rican young adults	Costa Rica	20 – 40 years	85	139	HP serology
16	Cardenas, 2010 [28]	2004	Hyperendemic <i>H. pylori</i> and tapeworm infections in a U.S.-Mexico border population	Mexico	All ages	82	215	HP stool antigen
17	Graham, 2006 [29]	2004	Noninvasive versus histologic detection of gastric atrophy in a Hispanic population in North America	Mexico	17 – 82 years	137	180	HP serology
18	González-Pons, 2018 [30]	2005	Seroprevalence of Helicobacter pylori in Hispanics living in Puerto Rico: A population-based study	Puerto Rico	21 – 64 years	174	528	HP serology
19	Ornelas, 2007 [31]	2005	Protective effect of yoghurt consumption on Helicobacter pylori seropositivity in a Mexican population	Mexico	20+ years	350	464	HP serology
20	Santos, 2005 [32]	2005	Prevalence of Helicobacter pylori infection and associated factors among adults in Southern Brazil: a population-based cross-sectional study	Brazil	20+ years	231	363	Urea breath test
21	O’Ryan, 2015 [33]	2009	Persistent and transient Helicobacter pylori infections in early childhood	Chile	< 57 months	100	302	HP stool antigen
22	Faria, 2012 [34]	2012	Relationship between histology and the test of quantitative breath in gastritis follicular (Helicobacter pylori): Mucuchies-Mérida	Venezuela	18 – 50 years	76	100	Urea breath test

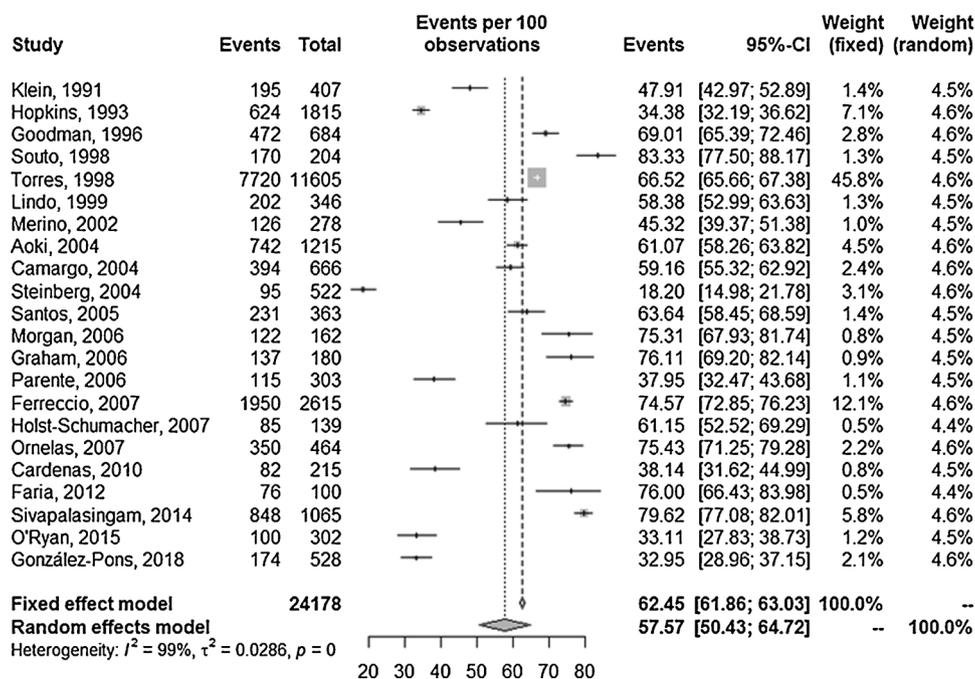


Fig. 2. Prevalence of Helicobacter Pylori in Latin American and Caribbean populations.

least one city. The diagnosis tests for *H. pylori* employed in the studies were HP serology (14 studies) and ureabreath test (6 studies), as shown in Table 1. Except for one study, all presented methodological quality over five points and there were no exclusions due to methodological quality (Supplementary Table 1).

Prevalence of *H. pylori* infection in LAC was 57.57% (CI95%: 50.43; 64.72) for all ages (Fig. 2). Among children and adolescents (≤ 18 years), prevalence was 48.36% (CI95%: 38.03; 58.70) (Fig. 3). Among adults, prevalence was 69.26% (CI95%: 61.54; 76.99) (Fig. 4). There were no statistically significant differences according to sex, across the age groups (Figs. 3 and 4), nor according to the year of study and diagnosis methods (Supplementary Figs. 2 and 3). The estimated prevalence presented elevated heterogeneity in all studies ($I^2 = 99\%$ ($p < 0.01$)), as well as in the subgroup analysis (Figs. 2 and 3, and Supplementary Figs. 2 and 3).

To investigate the possible causes of heterogeneity, studies were evaluated according to the type of diagnosis test, but no significant differences were observed. The results suggested a correlation between HDI and the prevalence of *H. pylori* in LAC (Fig. 5).

The funnel plot on the prevalence of *H. pylori*, the small study effect was discarded after linear regression test of funnel plot asymmetry, for all 22 studies ($p = 0.1827$). The same was observed for the 11 studies carried out in adults ($p = 0.1223$), for the 13 studies carried out between 2001 and 2012 ($p = 0.0987$), and for the 14 studies that utilized serology to diagnose *H. pylori* ($p = 0.2933$) (Supplementary Fig. 4).

4. Discussion

The prevalence of *H. pylori* infection estimated for LAC overall was 57.57%. The estimates obtained herein were lower than those obtained by Hooi et al⁷ (63.4%; CI95%: 59.2; 67.6) and Zamani et al⁶ (59.3%; CI95%: 52.9; 65.6), even with differences regarding inclusion

criteria. The present study also considered the Regional Scielo database (303 studies), and only included population-based studies.

Prevalence of *H. pylori* according to sex did not show differences, suggesting that the habits associated with *H. pylori* infection do not differ across genders in LAC. On the contrary, the findings of Ibrahim [35] show higher prevalence in male adults (OR:1,11) for America as a whole.

Regarding age group, prevalence among adults was higher than in children and adolescents. This increase in prevalence along with age has already been described earlier. [36] Peleteiro et al observed that the prevalence of *H. pylori* in the age group up to 20 years old were high in Latin American countries in comparison with other countries in the world [37], from 30% in Argentina to 70% in Mexico.

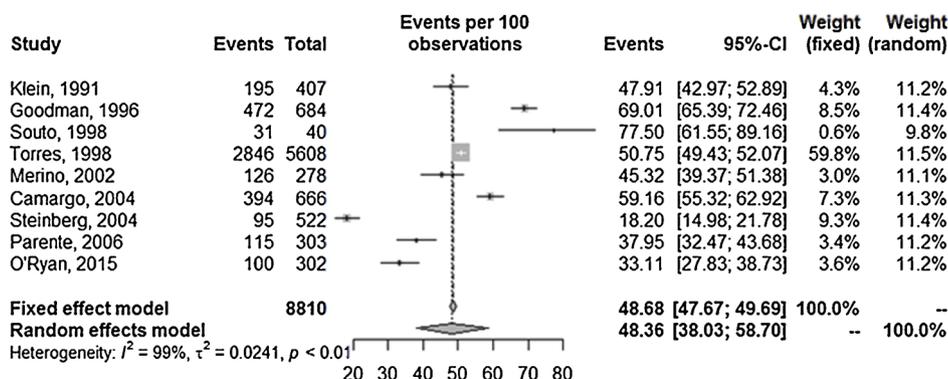
In this meta-analysis, the prevalence of *H. pylori* in LAC was 52% among children and adolescents, which demonstrates a high presence of this infection, especially in younger age groups. The chronic infection can lead to an increase of risk and in the incidence of gastric cancer.

In this study, as well as in Hooi et al and Zamani et al, the prevalence detected in LAC were high, when compared with other regions of the world [6,7]. These differences probably reflect the different levels of urbanization, sanitation, access to clean water and socioeconomic conditions.

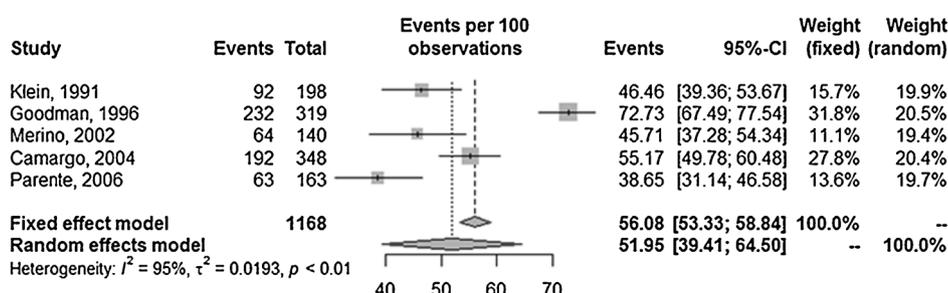
When comparing studies according to the year of data collection (1987–2000 and 2001–2012), no differences were identified in the prevalence of *H. pylori*. Although, Eusebi et al verified a reduction in prevalence in some countries, depending to the studied years. [38] Zamani et al identified differences, according to the study year, for Africa, where prevalence of *H. pylori* infection increased. [6] The socioeconomic and sanitary changes that occurred in LAC do not seem to have influenced the prevalence of *H. pylori* infection in this region.

Difficult access to treatment, frequent recurrences, and discontinuity in treatment lead to this high prevalence for *H. pylori*

A. All



B. Males



C. Females

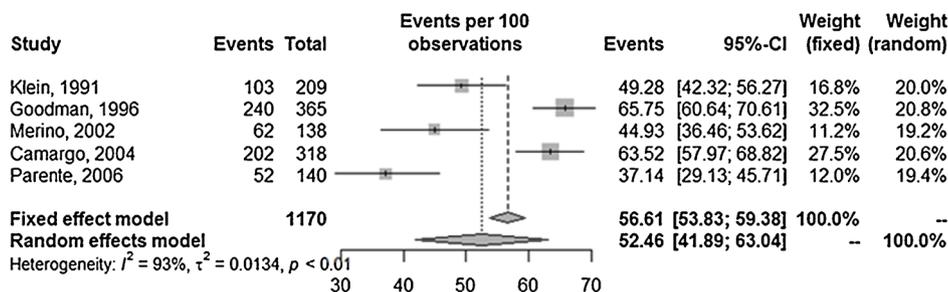


Fig. 3. Prevalence of Helicobacter Pylori in Latin America and the Caribbean: Children and Adolescent population.

infection. [39,40]A meta-analysis conducted by Corral et al estimated a relapse rate of 7.9 (CI95%: 5.3–10.5) per 100 people-year for *H. pylori* infection in Latin America [41].

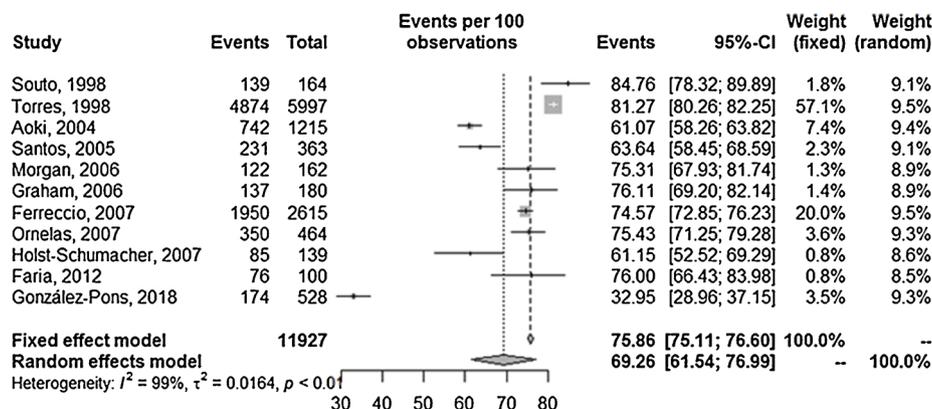
The possible causes for the heterogeneity observed herein were investigated, and the effect of the size of the studies was partially discharged. This effect could not be evaluated in all analyzed subgroups due to few numbers of studies available since for the test to be it is required minimum of ten studies.

It was also investigated whether heterogeneity could be associated

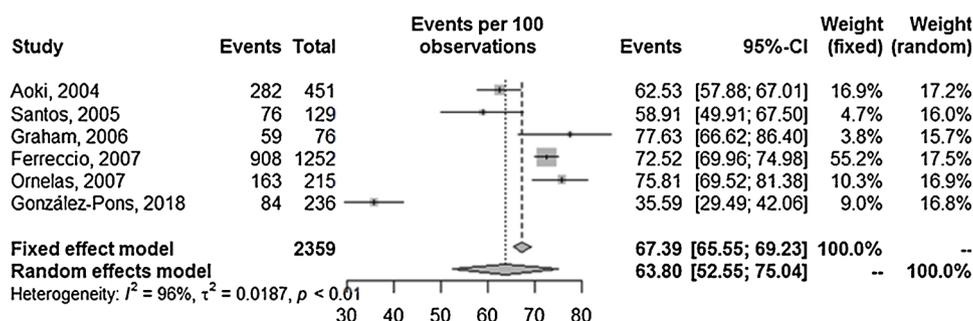
to the diagnosis method in each study, and no changes were observed in the results. For the diagnosis of *H. pylori*, serology is useful in screening tests, as well as the fecal antigen. The urea breath test is the best non-invasive test to diagnosis *H. pylori* infections, with high sensitivity and specificity, and was employed in six out of 22 studies. [42,43]

In this meta-analysis, the correlation between the prevalence of *H. pylori* and the HDI was not significant. However, visual inspection of the graphic revealed a reduction in prevalence with the increase in income per capita, in seven studies. It is known that there is an association

A. All



B. Males



C. Females

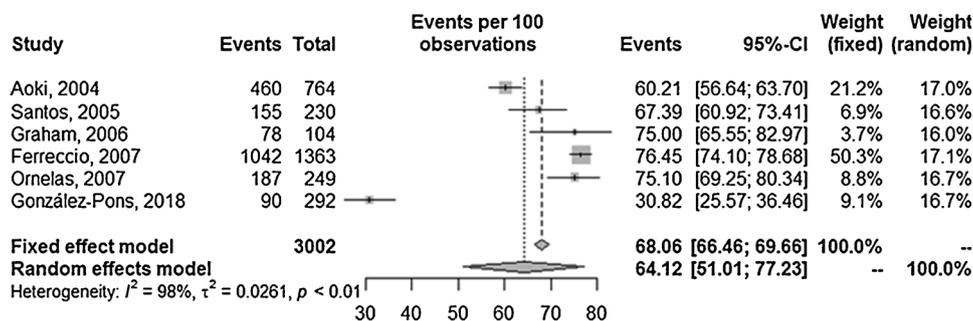


Fig. 4. Prevalence of Helicobacter Pylori in Latin America and the Caribbean: Adult population.

between worse sanitary conditions and low socioeconomic levels with high prevalence of *H. pylori*. [44]

The main limitation of this analysis was testing the indicator for the country and not for the site location where the study was conducted, which could explain the lack of statistical significance found.

Despite these limitations, the present work traces an overview of *H. pylori* infection for LAC. The findings presented here indicate that the prevalence is high, in men and women, for all age groups. The findings presented evidence that the prevalence of *H. pylori* remained high in LAC and that an increase in the HDI did not reduce this prevalence. Effective actions are therefore required to reduce

the prevalence of this agent in LAC.

Authorship contribution statement

MPC and MMO were responsible for the conception and design of the review. MMO and MAF conducted the database search and data collection. MMO was responsible for the data analysis. MPC and MMO were involved in the interpretation of results and drafting the article. All authors reviewed this draft, contributed and approved the final manuscript.

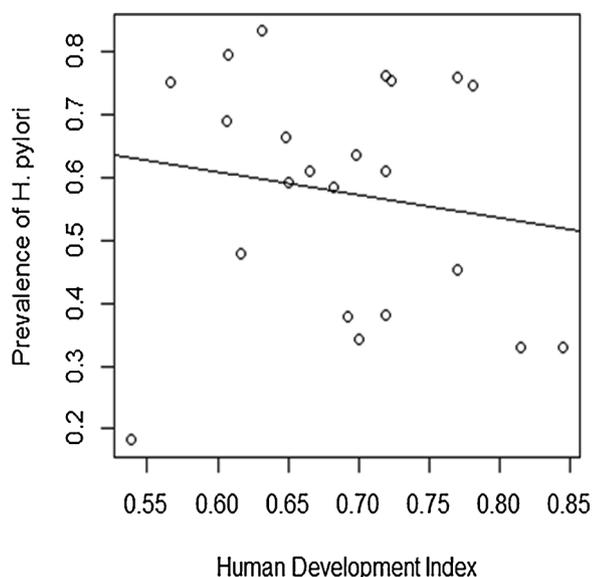


Fig. 5. Correlation between the prevalence of *Helicobacter pylori* and the Human Development Index.

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Conflicts of interest

The authors declare no conflicts of interest.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.canep.2019.04.003>.

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