Helicobacter

Helicobacter ISSN 1523-5378

Epidemiology of *Helicobacter pylori* Infection and Public Health Implications

Khean-Lee Goh,* Wah-Kheong Chan,* Seiji Shiota† and Yoshio Yamaoka†,‡

*Department of Medicine-Gastroenterology and Hepatology, University of Malaya, Kuala Lumpur, Malaysia, †Department of Environmental and Preventive Medicine, Oita University Faculty of Medicine, Yufu, Japan, ‡Department of Medicine-Gastroenterology and Hepatology, Baylor College of Medicine and Michael E. DeBakey Veterans Affairs Medical Center, Houston, TX, USA

Keywords
H. pylori risk factors, transmission, prevalence, incidence.

Reprint requests to: Professor KL Goh, Gastroenterology and Hepatology, Department of Medicine, University of Malaya, 50603 Kuala Lumpur, Malaysia.
E-mail: klgoh56@gmail.com

Abstract

This review summarizes studies on the epidemiology and public health implications of *Helicobacter pylori* published in peer-reviewed journals from April 2010 through March 2011. Prevalence rates vary widely between different geographical regions and ethnic groups. An interesting study from the USA identified the degree of African ancestry as an independent predictor of *H. pylori* infection. Two studies have demonstrated early childhood as the period of transmission of infection and identified an infected sibling as an important risk factor. An oral–oral route of spread has been substantiated with several studies showing the presence of *H. pylori* in the oral cavity. Studies have shown the presence of *H. pylori* in drinking water and the role of poor living conditions and sanitation in *H. pylori* infection, supporting an oral–fecal route of spread. Screening for *H. pylori* as a gastric cancer prescreening strategy has been described in Japan, and the importance of *H. pylori* eradication as a gastric cancer–prevention strategy has now been further emphasized in Japanese guidelines. Two studies have shown a decrease in the burden of dyspepsia and peptic ulcer disease with *H. pylori* eradication.

This article presents a review of the literature concerning the epidemiology and public health implications of *Helicobacter pylori* infection published from April 2010 till March 2011. The authors searched PubMed and Embase using MeSH terms ''Helicobacter infections/epidemiology'' and ''Helicobacter infections/prevention and control'', and repeated the PubMed search independently using MeSH term ''Helicobacter'' alone and using the set operator AND with the terms ''Epidemiology'', ''Prevalence'', ''Incidence'', ''Transmission'', ''Risk Factors'', ''Prevention and Control'' or ''Environment''. The identified literature is summarized below by subtopic: prevalence; incidence; transmission; risk factors; and public health implications.

Prevalence

Serology was the most common method of diagnosis used in these studies, but several studies were endoscopy-based and diagnoses were then made by rapid urease test (RUT), culture, immuno-histochemistry or histology. A few studies utilized the urea breath test (UBT) or the stool antigen test (SAT). In an interesting and important study, Gong et al. [1] compared the accuracy of serological testing to histological diagnosis in a gastric cancer screening field survey in northern China. They found that serological testing using a commercially available kit and utilizing the recommended cut-off level underestimated the prevalence of *H. pylori* by almost 30% and emphasized the need for local validation of serological tests.

We have grouped the studies according to the different geographical regions for ease of reference (Table 1). There were 10 studies from the Asia-Pacific region on adults [2–11] and 4 on children [12–15]. Li et al. [2] reported a well-conducted study which was carried out in Shanghai as part of a systematic investigation of gastrointestinal disease in China. Using a multistage, stratified sampling method, they recorded a *H. pylori* prevalence of 73.3% (2310/3151) by serological testing for all subjects and 71.7% (733/1022) by endoscopy for subjects who agreed for the procedure. In large endoscopy-based studies from Korea [3], Vietnam [4], and Turkey [5], *H. pylori* was detected from 50–70% of the

Table 1 Studies reporting prevalence of *Helicobacter pylori* infection, published between April 2010 and March 2011, tabulated according to different geographical regions

Author	Population studied	Diagnostic test performed	Number of subjects or patients	*H. pylori* prevalence (%)
Asia-Pacific				
Li et al. [2]	Random sample of residents in Shanghai, China (aged 18–80 years old)	Serology	1022	71.7
Nam et al. [3]	Healthy screening population in Korea	Rapid urease test (RUT)	10102	50.8
Nguyen et al. [4]	Patients undergoing gastroscopy in Hanoi and Ho Chi Minh, Vietnam (aged 14–86)	Serology, RUT, culture, histology, immuno-histochemistry	270	65.6
Ozdil et al. [5]	Consecutive dyspeptic patients undergoing gastroscopy in Turkey	Histology	3301	71.3
Tsukanov et al. [6]	Consecutive patients referred for dyspepsia in Eastern Siberia	Serology, RUT, histology	689 ''Europoid'' 1440 ''Mongoloid''	93.6 94.3
Ullah et al. [7]	Fish handlers and non-fish handlers in Bangladesh	Serology	163 fish handlers 72 non-fish handlers	77.3 37.5
Rahim et al. [8]	Aborigines living in northeastern Peninsular Malaysia	Serology	480	19
Pandeya et al. [9]	Australian adults	Serology	1355	15.5
Fraser et al. [10]	Teenage females in high schools in Auckland, New Zealand	Serology	386 Pacific Island 120 Maori 162 Asian 124 European	49.0 26.7 24.7 13.7
Al Faleh et al. [11]	Random sample of students aged 16–18 from 3 regions in Saudi Arabia	Serology	1157	47
Ozen et al. [12]	School children in Istanbul, Turkey	Serology	473	34
Thankachan et al. [13]	Children aged 6–10 in Bangalore, India	Urea breath test (UBT)	543	79
Cherian et al. [14]	African refugee children from resettlement in Australia	Stool antigen test (SAT)	163	84.0
Abdollahi et al. [15]	Children aged 3–18 with reflux symptoms in Iran	RUT, Histology	263	22.4
Africa				
Tanih et al. [16]	Consecutive dyspeptic patients at a hospital in Port Elizabeth, South Africa	Culture, PCR	254	66.1
Joutei et al. [17]	Dyspeptic patients in Morocco	Histology	755	69
Aje et al. [18]	Patients with dyspepsia and controls in Nigeria	Serology, SAT	46 dyspeptics 46 controls	67.4 78.3–91.3
Hestvik et al. [19]	Healthy children aged 0–12 in Kampala, Uganda	SAT	427	44.3
S. America				
Dattoli et al. [20]	Children aged 4–11 in northeastern Brazil	Serology	1104	28.7
Miranda et al. [21]	Children attending a public hospital in Sao Paulo, Brazil	Serology	326	35.6
Janjetic et al. [22]	Children aged 4–16 with upper gastrointestinal symptoms	UBT	395	24.3
Egorov et al. [23]	Children in poor suburbs of Quito, Ecuador.	SAT	124	61
Araf et al. [24]	Adolescents in a public school in Sao Paolo, Brazil (aged 10–16)	UBT	194	40.7
Ortega et al. [25]	Dyspeptic patients in Chile	RUT	5664	78
Fialho et al. [26]	Poor urban community in northeastern Brazil	UBT in children, serology in adults	570 members of 128 households	66.0

Table 1 (*Continued*)

Author	Population studied	Diagnostic test performed	Number of subjects or patients	*H. pylori* prevalence (%)
Europe				
Vendt et al. [27]	Children from ambulatory admission in Estonia	Serology	363	27
Katsanos et al. [28]	Retrospective consecutive Albanian and Greek patients undergoing gastroscopy in western Balkans	Histology	101 Albanian 101 Greek	54 34
N. America				
Epplein et al. [29]	African Americans and whites from the Southern Community Cohort Study	Serology	689	79
Sonnenberg et al. [30]	Central laboratory database of gastric biopsies, USA	Histology	78985	7.5
McJunkin et al. [31]	Patients who underwent endoscopy in Charleston, USA	Histology	251	6.8
Cardenas et al. [32]	Subjects of all ages at U.S.- Mexico border	SAT	386	38.2

population studied. Tsukanov et al. [6] in one of the few studies from eastern Siberia recorded inordinately high rate of *H. pylori* infection, exceeding 90% for both ''Europoid'' (European descent) and ''Mongoloid'' (Asian descent) populations. Among selected subpopulations, Ullah et al. [7] reported a high *H. pylori* prevalence of 77.3% among a group of Bangladesh fish handlers, while Rahim et al. [8] in a study of aborigines in the Northeastern part of Malaysia reported a prevalence rate of 19%.

Pandeya et al. [9] in an Australian study of community controls of a nationwide study on esophageal cancer recorded a *H. pylori* prevalence rate of 15.5% in a study population of mainly white subjects. Fraser et al. [10] showed significant differences in *H. pylori* prevalence between Pacific Island (49.0%) vs. Maori (26.7%) and Asian (24.7%) vs. European adolescents (13.7%). Several studies on children and adolescents in Asia showed prevalence rates ranging from 20% to 84% [12–15]. Overall, as expected, the *H. pylori* prevalence rates from the Asia-Pacific region were high except among the white population of Australia and New Zealand. The prevalence of *H. pylori* infection was generally lower among children except for the one study from India [13] and another looking at African refugee children from resettlement in Western Australia [14].

Four studies were reported from Africa [16–19]. Studies from Africa recorded high *H. pylori* prevalence rates ranging from 41.3% to 91.3% [16–19]. There were seven studies that reported *H. pylori* prevalence from South America [20–26]. Four of these studies were on children [20–23]. The study by Dattoli et al. [20], a continuation of previous studies on diarrheal diseases in a town in northeastern Brazil, reported a *H. pylori* seroprevalence of 28.7%. Several risk factors for *H. pylori* infection were identified in the study and will be discussed in a later section. The other three studies on children [21–23] reported *H. pylori* prevalence rates ranging from 24.3% to 61.0%.

There were few studies from Europe [27,28] and North America [29–32]. In an important and interesting study from USA, Epplein et al. [29] reported a high *H. pylori* prevalence rate of 79.0% among a subpopulation of poor Americans (predominantly blacks) with a direct correlation of high *H. pylori* prevalence to the low, moderate, and high ''African'' ancestry. In contrast, Sonnenberg et al. [30] in a review of a huge database of all biopsies collected in a central laboratory in the USA reported a *H. pylori* prevalence of only 7.5%.

Several studies have focused on specific disease groups to determine the possible relationship with *H. pylori* infection [33–38] (Table 2). Kirchner et al. [33] did not find a significant difference in *H. pylori* seroprevalence between liver cirrhotic and noncirrhotic patients. Senbanjo et al. [34] compared the seroprevalence of *H. pylori* between children with and without sickle cell disease and found the prevalence to be high in both. High prevalence of *H. pylori* infection was seen among morbidly obese patients undergoing bariatric surgery (85.5%) [35] and patients with myelodysplasia (75.3%) [36]. On the other hand, an inverse relationship with HIV infection was noted in a study from Brazil [37]. This marked disparity has been observed previously [39–41], but the reason for it remains unclear. Schimke et al. [38] reported *H. pylori*

Table 2 *Helicobacter pylori* prevalence among special disease groups

Author	Population studied	Diagnostic test	Number of patients	*H. pylori* prevalence (%)
Kirchner et al. [33]	Cirrhotic patients and patients with chronic hepatitis without cirrhosis in Germany	Histology in cirrhotics serology in noncirrhotics	110 cirrhotics 44 noncirrhotics	69 63
Senbanjo et al. [34]	Children with sickle cell disease (SCD) and controls in Nigeria	Serology	118 SCD 118 controls	67.8 63.6
Al Akwaa [35]	Morbidly obese patients undergoing bariatric surgery in Saudi Arabia	Histology	62	85.5
Diamantidis et al. [36]	Patients with myelodysplastic syndromes in Greece	Serology, urea breath test, rapid urease test (RUT), histology	73	57.5–80.4
Fialho et al. [37]	HIV-positive patients and HIV-negative controls undergoing gastroscopy for dys pepsia in Northeastern Brazil	Histology, RUT	113 HIV-positive 141 HIV-negative	37.2 75.2
Schimke et al. [38]	Patients with type 2 diabetes mellitus in Australia	Serology	1179	62.0

seroprevalence of 62.0% among a cohort of patients with type 2 diabetes mellitus.

Two studies looked at time trend differences [31,42]. Nakajima et al. [42] studied subjects who went for annual health check at their hospital and reported a drop in *H. pylori* seroprevalence from 70% to 50% over a 17-year period (1988–2005) and along with this, a decline in the prevalence of peptic ulcer disease (PUD) and gastric cancer. In an endoscopy-based study from the USA with relatively small numbers, McJunkin et al. [31] also reported a dramatic drop in *H. pylori* prevalence (from 65.8% to 6.8%) and PUD (from 38.8% to 5.6%) over an 11-year period.

Incidence

There was only one study reporting on incidence of *H. pylori* infection. In this study by Muhsen et al. [43]., a cohort of Israeli Arab children at preschool age was tested for *H. pylori* infection using SAT and the test was repeated at school age. The prevalence of *H. pylori* infection was 49.7% and 58.9% at preschool age and school age, respectively. Among children tested in both examinations, there were fourteen new *H. pylori* infections among seventy previously uninfected children (20%) over a 4-year period, giving an annual incidence of 5%.

Transmission

Transmission of *H. pylori* is still not entirely clarified, but human-to-human spread through oral–oral or fecal–oral route is thought to be the most plausible.

Several studies looked at the spread of *H. pylori* infection between siblings [20,26,43–45]. Two of these were well-conducted cohort follow-up studies [43,44]. In the study by Muhsen et al. [43], Israeli Arab children aged 3–5 from three villages in northern Israel were followed up for 3–4 years. Having *H. pylori*-infected sibling was identified as an independent risk factor for both ''early'' and ''persistent'' *H. pylori* infection as well as late acquisition of the infection. In a second study, Cervantes et al. [44] reported that persistent *H. pylori* infection in older siblings always preceded infection in younger siblings and that the former was an important predictor of *H. pylori* infection in the latter, especially if the age difference was <3 years.

Other studies were basically cross-sectional studies and also showed infected siblings and mothers, overcrowding and poor social conditions as risk factors for *H. pylori* infection in children [20,26]. Siblings of young patients with gastric cancer were also found to have a higher prevalence of *H. pylori* infection than controls supporting spread between siblings [45]. Infected siblings appear to be an important reservoir of *H. pylori* infection in children.

Several studies showed the presence of *H. pylori* in saliva, dental plaques, oral cavity, and tonsillar tissue as well as in the esophagus [46–52]. These studies lend weight to an oral–oral route of spread of *H. pylori* infection. The presence of *H. pylori* in oral cavity is more frequent in seropositive subjects [46], and several studies from Brazil have consistently showed an association between gastric *H. pylori* infection and the presence of this bacterium in the oral cavity [47–49]. Moreover, the bacterium identified in the samples of the different sites within a given subject among all patients in one study [48] and in up to 89% in another study [49] were of identical genotype. The association is reinforced by a

recent meta-analysis [53] where the prevalence of *H. pylori* infection in the oral cavity in gastric *H. pylori*-positive patients was significantly higher (45.0%) than that in gastric *H. pylori*-negative patients (23.9%) (OR = 3.61, $p < 0.0001$). In addition, it was reported that the eradication rate of *H. pylori* from the stomach (85.8%) is much higher than from the oral cavity (5.7%) (OR = 55.59, $p < 0.00001$), raising concerns that *H. pylori* in the oral cavity could be a source of re-infection following successful gastric eradication.

A study reported the presence of *H. pylori* in tonsillar tissue of up to 48% of patients who underwent tonsillectomy [54]. However, this study utilized RUT which may yield false-positive results because of the presence of other urease-producing organisms in a polymicrobial environment such as the tonsillar tissues. In a separate study [55], *H. pylori* was not detected at all using fluorescence in situ hybridization and polymerase chain reaction–DNA hybridization assay (PCR–DEIA) in the adenotonsillar tissue of a cohort of children who underwent adenoidectomy or tonsillectomy with a *H. pylori* prevalence of 39%, suggesting that adenotonsillar tissue does not constitute an extragastric reservoir for *H. pylori*.

H. pylori could be cultured from rectal fluid and terminal ileal fluid in the setting of rapid intestinal transit supporting a fecal–oral route of transmission [56]. Al Sulami et al. [57] reported for the first time the occurrence of *H. pylori* in treated drinking water (2.0% of total isolates) in Basra, Iraq. In another study from Pakistan, Samra et al. [58], using a PCR assay targeting virulence genes found *H. pylori* in 40% of samples of drinking water. Linke et al. [59] introduced a highly sensitive and specific test for the detection of *H. pylori* in drinking water biofilms utilizing real-time PCR method. However, as detection of *H. pylori* DNA may not represent the presence of viable bacterium, the true significance of a positive test remains uncertain and requires further studies. Presence of viable *H. pylori* in drinking water, if confirmed, would be an important source of transmission, pointing to a fecal–oral route of spread.

Risk Factors

Poor Living Conditions

In a study from Brazil, Dattoli et al. [20] reported increased *H. pylori* infection with a larger number of siblings, nursery schooling, and housing in a street without paved roads and without flushed toilets indicating impoverished living conditions associated with poorer sanitation and overcrowding to be risk factors for *H. pylori* infection. Similarly, Fialho et al. [26] demonstrated the number of people per room and number of children in the household as independent risk factors for *H. pylori* infection. Using a statistical inference model, Strebel et al. [60] found ''more than three children living in the household'', ''more persons living per m^2 than average'', ''home situated at main road'' and ''using well water'' to be strongly associated with *H. pylori* infection.

Infected Siblings

Several studies [20,26,43–45] consistently supported infected siblings as a risk factor for *H. pylori* infection and these have been discussed earlier.

Race

Some studies examined the effect of race on *H. pylori* infection. Epplein et al. [29] recruited low-income African American and white patients into a large prospective study involving twelve southeastern states of the USA. Prevalence rates were inordinately high for both groups compared with known published prevalence rates among white Americans [61]. Interestingly, the amount of African ancestry using ''ancestry informative genetic markers'' predicted the prevalence of *H. pylori* with the highest African ancestry correlating with the highest *H. pylori* prevalence rates after adjustment for education, socioeconomic, and other environmental factors. This finding points to a possible genetic susceptibility to *H. pylori* infection. Fraser et al. [10] in a study on iron deficiency in New Zealand showed a difference in *H. pylori* prevalence according to ethnicity, being highest among Pacific Island students followed by Maori and Asian students, and lowest in European students. This confirms earlier observations made by Fraser et al. among different ethnic groups in New Zealand [62]. On the other hand, Muhsen et al. [43] found that among Arab Israelis living in three villages in northern Israel, *H. pylori* prevalence rate correlated with the socioeconomic status of the village, although ethnically they were all the same. Pandeya et al. [9] also observed differences in *H. pylori* prevalence between individuals born in Australia and New Zealand compared with those born overseas, the rate being lower in the former.

Public Health Implications

The epidemiological studies published in the past year support the evidence that *H. pylori* is most common in impoverished areas with overcrowding and poor sanitation. Transmission occurs during childhood through an

oral–oral or a fecal–oral route. Dattoli et al. [20]. demonstrated this very well in their study on risk factors, and Cervantes et al. [44], for example, identified early childhood with transmission between siblings as an important mode of transmission of infection. Public health measures should be targeted to alleviate poor living conditions which will in turn result in decreased transmission and reduction of the reservoir of infection.

There is conflicting data on the association of *H. pylori* infection with anemia. Some studies did not find any associations [22,24] while others did [10,63]. The association between *H. pylori* infection and anemia was addressed in recent review articles [64,65]. *H. pylori* infection has been reported to negatively impact child growth in one study [23], but overall data continue to show a lack of such association as pointed out in a review article [66]. Nevertheless, this is of great concern particularly in high prevalence areas as it may impact significantly on the well-being of a community or population.

There were two articles that looked at the outcome of *H. pylori* eradication and the development of gastric cancer, which is the most serious outcome of *H. pylori* infection. Kosunen et al. [67] in a large longitudinal cohort follow-up study for 10 years noted a marked decline in gastric cancer incidence following *H. pylori* eradication. In a second study from Japan, Take et al. [68] in another cohort follow-up study showed that gastric cancer developed at a rate of 0.30% per year even after *H. pylori* eradication. This indicates as we have known before that once pre-malignant changes have already developed, a ''point of no-return'' is reached.

In Japan, annual screening gastroscopy for gastric cancer has been implemented for a long time. Mizuno et al. [69] published an important paper which showed that pre-screening high-risk individuals in the population with serum pepsinogen and *H. pylori* serology can identify those with high risk of developing gastric cancer who can then undergo gastroscopy. In this population-based cohort study, participants were followed up for a total of 9 years and the incident cases of gastric cancer were recorded. Those with *H. pylori* and atrophy had an 11-fold increased risk of developing gastric cancer, but the highest risk was with those with absent *H. pylori* but presence of atrophic gastritis indicating a group with longstanding severe gastritis from which *H. pylori* disappeared.

Several review papers addressed the issue of prevention and elimination of gastric cancer in Japan. Asaka et al. [70] in a review paper on ''strategies on eliminating gastric cancer'' proposed gastric cancer screening by simultaneous measurement of serum pepsinogen and *H. pylori* antibody as described earlier by Mizuno et al., combined with eradication of *H. pylori* in all individuals at risk. He commented that the proposed strategy would prevent about 150,000 deaths from gastric cancer during the 5 years after its adoption and would probably reduce the incidence of gastric cancer by more than 80–90% within 10 years. In another review paper, Asaka et al. [71] reported on a study carried out by the Japan Gast Study Group which showed in a randomized study the effect of *H. pylori* eradication for prevention of recurrent gastric cancers following endoscopic mucosal resection. Shiota et al. [72]. discussed the most recent update on the Japanese Society for Helicobacter Research guidelines in 2009 [73] which has emphasized the importance of *H. pylori* eradication in preventing gastric cancer. The most important revision was the recommendation that all *H. pylori*-infected subjects be treated and eliminated regardless of clinical outcome. *H. pylori* eradication for all infected subjects will prevent not only *H. pylori* related diseases but also the spread of bacterium in future.

Harvey et al. [74] in the Bristol Helicobacter project found that the effect of *H. pylori* eradication was cost beneficial. Eradication of *H. pylori* infection in the community gives cumulative long-term benefit, with a continued reduction in the development of dyspepsia severe enough to require a consultation with a general practitioner up to at least 7 years. The cost savings resulting from this aspect of a community *H. pylori* eradication program, in addition to the other theoretical benefits, make such programs worthy of serious consideration, particularly in populations with a high prevalence of *H. pylori* infection.

Of public health interest too is a study by Feinstein et al. [75] who analyzed hospital discharge data from 1998–2005 in the USA using the Nationwide Inpatient Sample database. The overall peptic ulcer disease (PUD) hospitalization rate declined from 71.1 to 56.8 per 100,000 population from 1998 to 2005. At the same time, the *H. pylori*-related hospitalization rates also decreased from 35.9 to 19.2 per 100,000 population. The authors suggested that the decline in PUD hospitalization was because of the decline in *H. pylori* related complications.

Conflicts of Interest

The authors have declared no conflicts of interest.

References

1 Gong YH, Sun LP, Jin SG, Yuan Y. Comparative study of serology and histology based detection of *Helicobacter pylori* infections: a large population-based study of 7,241 subjects from China. *Eur J Clin Microbiol Infect Dis* 2010;29: 907–11.

2 Li Z, Zou D, Ma X, Chen J, Shi X, Gong Y, Man X, et al. Epidemiology of peptic ulcer disease: endoscopic results of the systematic investigation of gastrointestinal disease in China. *Am J Gastroenterol* 2010;105:2570–7.

3 Nam SY, Choi IJ, Ryu KH, Kim BC, Kim CG, Nam BH. Effect of *Helicobacter pylori* infection and its eradication on reflux esophagitis and reflux symptoms. *Am J Gastroenterol* 2010;105:2153–62.

4 Nguyen TL, Uchida T, Tsukamoto Y, Trinh DT, Ta L, Mai BH, et al. *Helicobacter pylori* infection and gastroduodenal diseases in Vietnam: a cross-sectional, hospital-based study. *BMC Gastroenterol* 2010;10:114.

5 Ozdil K, Sahin A, Kahraman R, Yuzbasioglu B, Demirdag H, Calhan T, et al. Current prevalence of intestinal metaplasia and *Helicobacter pylori* infection in dyspeptic adult patients from Turkey. *Hepatogastroenterology* 2010;57:1563–6.

6 Tsukanov VV, Butorin NN, Maady AS, Shtygasheva OV, Amelchugova OS, Tonkikh JL, et al. *Helicobacter pylori* Infection, Intestinal Metaplasia, and Gastric Cancer Risk in Eastern Siberia. *Helicobacter* 2011;16:107–12.

7 Ullah SS, Shamsuzzaman SM, Ara MN, Islam MN, Islam MS, Saha M, et al. Seropositivity of *Helicobacter Pylori* among the fish handlers. *Mymensingh Med J* 2010;19:219–24.

8 Rahim AA, Lee YY, Majid NA, Choo KE, Raj SM, Derakhshan MH, et al. *Helicobacter pylori* infection among Aborigines (the Orang Asli) in the northeastern region of Peninsular Malaysia. *Am J Trop Med Hyg* 2010;83:1119–22.

9 Pandeya N, Whiteman DC. Prevalence and determinants of *Helicobacter pylori* sero-positivity in the Australian adult community. *J Gastroenterol Hepatol* 2011; Mar 28. doi: 10.1111/j.1440-1746.2011.06726.x. [Epub ahead of print]

10 Fraser AG, Scragg R, Schaaf D, Metcalf P, Grant CC. *Helicobacter pylori* infection and iron deficiency in teenage females in New Zealand. *N Z Med J* 2010;123:38–45.

11 Al Faleh FZ, Ali S, Aljebreen AM, Alhammad E, Abdo AA. Seroprevalence rates of *Helicobacter pylori* and viral hepatitis A among adolescents in three regions of the Kingdom of Saudi Arabia: is there any correlation? *Helicobacter* 2010;15:532–7.

12 Ozen A, Furman A, Berber M, Karatepe HO, Mutlu N, Saricoban HE, et al. The effect of *Helicobacter pylori* and economic status on growth parameters and leptin, ghrelin, and insulin-like growth factor (IGF)-I concentrations in children. *Helicobacter* 2011;16:55–65.

13 Thankachan P, Muthayya S, Sierksma A, Eilander A, Thomas T, Duchateau GS, et al. *Helicobacter pylori* infection does not influence the efficacy of iron and vitamin B(12) fortification in marginally nourished Indian children. *Eur J Clin Nutr* 2010;64:1101–7.

14 Cherian S, Burgner DP, Cook AG, Sanfilippo FM, Forbes DA. Associations between *Helicobacter pylori* infection, co-morbid infections, gastrointestinal symptoms, and circulating cytokines in African children. *Helicobacter* 2010;15:88–97.

15 Abdollahi A, Morteza A, Khalilzadeh O, Zandieh A, Asgarshirazi M. The role of *Helicobacter pylori* infection in gastro-oesophageal reflux in Iranian children. *Ann Trop Paediatr* 2011;31:53–7.

16 Tanih NP, Okeleye BI, Ndip LM, Clarke AM, Naidoo N, Mkwetshana N, et al. *Helicobacter pylori* prevalence in dyspeptic patients in the Eastern Cape province - race and disease status. *S Afr Med J* 2010;100:734–7.

17 Joutei HA, Hilali A, Fechtali T, Rhallabi N, Benomar H. [*Helicobacter pylori* infection in 755 patients with digestive complaints: Pasteur Institute, Morocco, 1998–2007]. *East Mediterr Health J* 2010;16:778–82.

18 Aje AO, Otegbayo JA, Odaibo GN, Bojuwoye BJ. Comparative study of stool antigen test and serology for *Helicobacter pylor*i among Nigerian dyspeptic patients–a pilot study. *Niger J Clin Pract* 2010;13:120–4.

19 Hestvik E, Tylleskar T, Kaddu-Mulindwa DH, Ndeezi G, Grahnquist L, Olafsdottir E, et al. *Helicobacter pylori* in apparently healthy children aged 0-12 years in urban Kampala, Uganda: a community-based cross sectional survey. *BMC Gastroenterol* 2010;10:62.

20 Dattoli VC, Veiga RV, da Cunha SS, Pontes-de-Carvalho LC, Barreto ML, Alcantara-Neves NM. Seroprevalence and potential risk factors for *Helicobacter pylori* infection in Brazilian children. *Helicobacter* 2010;15:273–8.

21 Miranda AC, Machado RS, da Silva EM, Kawakami E. Seroprevalence of *Helicobacter pylori* infection among children of low socioeconomic level in Sao Paulo. *Sao Paulo Med J* 2010;128:187–91.

22 Janjetic MA, Goldman CG, Balcarce NE, Rua EC, Gonzalez AB, Fuda JA, et al. Iron, zinc, and copper nutritional status in children infected with *Helicobacter pylori*. *J Pediatr Gastroenterol Nutr* 2010;51:85–9.

23 Egorov AI, Sempertegui F, Estrella B, Egas J, Naumova EN, Griffiths JK. The effect of *Helicobacter pylori* infection on growth velocity in young children from poor urban communities in Ecuador. *Int J Infect Dis* 2010;14:e788–91.

24 Araf LN, Pereira CA, Machado RS, Raguza D, Kawakami E. *Helicobacter pylori* and iron-deficiency anemia in adolescents in Brazil. *J Pediatr Gastroenterol Nutr* 2010;51:477–80.

25 Ortega JP, Espino A, Calvo BA, Verdugo P, Pruyas M, Nilsen E, et al. [*Helicobacter pylori* infection in symptomatic patients with benign gastroduodenal diseases: analysis of 5.664 cases]. *Rev Med Chil* 2010;138:529–35.

26 Fialho AM, Braga AB, Braga Neto MB, Carneiro JG, Rocha AM, Rodrigues MN, et al. Younger siblings play a major role in *Helicobacter pylori* transmission among children from a low-income community in the Northeast of Brazil. *Helicobacter* 2010;15:491–6.

27 Vendt N, Kool P, Teesalu K, Lillemae K, Maaroos HI, Oona M. Iron deficiency and *Helicobacter pylori* infection in children. *Acta Paediatr* 2011; Mar 21. doi: 10.1111/j.1651-2227.2011.02281.x. [Epub ahead of print]

28 Katsanos KH, Tatsioni A, Tsakiris V, Christodoulou D, Tsianos EV. *Helicobacter pylori* is a major public health priority in western Balkans: an endoscopy referral center experience. *Eur J Intern Med* 2010;21:306–9.

29 Epplein M, Signorello LB, Zheng W, Peek RM Jr, Michel A, Williams SM, et al. Race, African ancestry, and *Helicobacter pylori* infection in a low-income United States population. *Cancer Epidemiol Biomarkers Prev* 2011;20:826–34.

30 Sonnenberg A, Lash RH, Genta RM. A national study of Helicobactor pylori infection in gastric biopsy specimens. *Gastroenterology* 2010;139:1894–901. e2; quiz e12.

31 McJunkin B, Sissoko M, Levien J, Upchurch J, Ahmed A. Dramatic Decline in Prevalence of *Helicobacter pylori* and Peptic Ulcer Disease in an Endoscopy-referral Population. *Am J Med* 2011;124:260–4.

32 Cardenas VM, Mena KD, Ortiz M, Karri S, Variyam E, Behravesh CB, et al. Hyperendemic *H. pylori* and tapeworm infections in a U.S.-Mexico border population. *Public Health Rep* 2010;125:441–7.

33 Kirchner GI, Beil W, Bleck JS, Manns MP, Wagner S. Prevalence of *Helicobacter pylori* and occurrence of gastroduodenal

lesions in patients with liver cirrhosis. *Int J Clin Exp Med* 2011;4:26–31.
34 Senbanjo I, Akinbami A, Diaku-Akinwumi I, Oshikoya K, Adeyemo T, Dada O, et al. *Helicobacter pylori* infection among a pediatric population with sickle cell disease. *J Natl Med Assoc* 2010;102:1095–9.
35 Al-Akwaa AM. Prevalence of *Helicobacter pylori* infection in a group of morbidly obese Saudi patients undergoing bariatric surgery: a preliminary report. *Saudi J Gastroenterol* 2010;16: 264–7.
36 Diamantidis MD, Ioannidou-Papagiannaki E, Kountouras J, Mandala E, Tsapournas G, Frida-Michailidou I, et al. High prevalence of *Helicobacter pylori* infection in Greek patients with myelodysplastic syndromes. *Acta Haematol* 2010;124:141–9.
37 Fialho AB, Braga-Neto MB, Guerra EJ, Fialho AM, Fernandes KC, Sun JL, et al. Low prevalence of *H. pylori* Infection in HIV-positive patients in the northeast of Brazil. *BMC Gastroenterol* 2011;11:13.
38 Schimke K, Chubb SA, Davis WA, Davis TM. *Helicobacter pylori* cytotoxin-associated gene-A antibodies do not predict complications or death in type 2 diabetes: the Fremantle Diabetes Study. *Atherosclerosis* 2010;212:321–6.
39 Werneck-Silva AL, Prado IB. Dyspepsia in HIV-infected patients under highly active antiretroviral therapy. *J Gastroenterol Hepatol* 2007;22:1712–6.
40 Chiu HM, Wu MS, Hung CC, Shun CT, Lin JT. Low prevalence of *Helicobacter pylori* but high prevalence of cytomegalovirus-associated peptic ulcer disease in AIDS patients: comparative study of symptomatic subjects evaluated by endoscopy and CD4 counts. *J Gastroenterol Hepatol* 2004;19:423–8.
41 Lv FJ, Luo XL, Meng X, Jin R, Ding HG, Zhang ST. A low prevalence of *H. pylori* and endoscopic findings in HIV-positive Chinese patients with gastrointestinal symptoms. *World J Gastroenterol* 2007;13:5492–6.
42 Nakajima S, Nishiyama Y, Yamaoka M, Yasuoka T, Cho E. Changes in the prevalence of *Helicobacter pylori* infection and gastrointestinal diseases in the past 17 years. *J Gastroenterol Hepatol* 2010;25(Suppl 1):S99–110.
43 Muhsen K, Athamna A, Bialik A, Alpert G, Cohen D. Presence of *Helicobacter pylori* in a sibling is associated with a long-term increased risk of *H. pylori* infection in Israeli Arab children. *Helicobacter* 2010;15:108–13.
44 Cervantes DT, Fischbach LA, Goodman KJ, Phillips CV, Chen S, Broussard CS. Exposure to *Helicobacter pylori*-positive siblings and persistence of *Helicobacter pylori* infection in early childhood. *J Pediatr Gastroenterol Nutr* 2010;50:481–5.
45 Nam JH, Choi IJ, Cho SJ, Kim CG, Lee JY, Nam SY, et al. *Helicobacter pylori* infection and histological changes in siblings of young gastric cancer patients. *J Gastroenterol Hepatol* 2011;26:1157–63.
46 Fernandez-Tilapa G, Axinecuilteco-Hilera J, Giono-Cerezo S, Martinez-Carrillo DN, Illades-Aguiar B, Roman-Roman A. *vac*A genotypes in oral cavity and *Helicobacter pylori* seropositivity among adults without dyspepsia. *Med Oral Patol Oral Cir Bucal* 2011;16:e175–80.
47 Rasmussen LT, Labio RW, Gatti LL, Silva LC, Queiroz VF, Smith Mde A, et al. *Helicobacter pylori* detection in gastric biopsies, saliva and dental plaque of Brazilian dyspeptic patients. *Mem Inst Oswaldo Cruz* 2010;105:326–30.
48 Silva DG, Tinoco EM, Rocha GA, Rocha AM, Guerra JB, Saraiva IE, et al. *Helicobacter pylori* transiently in the mouth may participate in the transmission of infection. *Mem Inst Oswaldo Cruz* 2010;105:657–60.
49 Assumpcao MB, Martins LC, Melo Barbosa HP, Barile KA, de Almeida SS, Assumpcao PP, et al. *Helicobacter pylori* in dental plaque and stomach of patients from Northern Brazil. *World J Gastroenterol* 2010;16:3033–9.
50 Cellini L, Grande R, Artese L, Marzio L. Detection of *Helicobacter pylori* in saliva and esophagus. *New Microbiol* 2010;33:351–7.
51 Silva DG, Stevens RH, Macedo JM, Albano RM, Falabella ME, Fischer RG, et al. Presence of *Helicobacter pylori* in supragingival dental plaque of individuals with periodontal disease and upper gastric diseases. *Arch Oral Biol* 2010;55:896–901.
52 Namiot DB, Leszczynska K, Namiot Z, Chilewicz M, Bucki R, Kemona A. The occurrence of *Helicobacter pylori* antigens in dental plaque; an association with oral health status and oral hygiene practices. *Adv Med Sci* 2010;55:167–71.
53 Zou QH, Li RQ. *Helicobacter pylori* in the oral cavity and gastric mucosa: a meta-analysis. *J Oral Pathol Med* 2011;40:317–24.
54 Lin HC, Wu PY, Friedman M, Chang HW, Wilson M. Difference of *Helicobacter pylori* colonization in recurrent inflammatory and simple hyperplastic tonsil tissues. *Arch Otolaryngol Head Neck Surg* 2010;136:468–70.
55 Vilarinho S, Guimaraes NM, Ferreira RM, Gomes B, Wen X, Vieira MJ, et al. *Helicobacter pylori* colonization of the adenotonsillar tissue: fact or fiction? *Int J Pediatr Otorhinolaryngol* 2010;74:807–11.
56 Kim do H, Jung HM, Hwang YJ, Ahn YS, Mun JS, Myoung BH, et al. [Culture and polymerase chain reaction of *Helicobacter pylori* from rectal and terminal ileal fluid after polyethylene glycol (colyte) ingestion in healthy adults with positive urea breath test]. *Korean J Gastroenterol* 2010;56:27–32.
57 Al-Sulami AA, Al-Taee AM, Juma'a MG. Isolation and identification of *Helicobacter pylori* from drinking water in Basra governorate, Iraq. *East Mediterr Health J* 2010;16:920–5.
58 Samra ZQ, Javaid U, Ghafoor S, Batool A, Dar N, Athar MA. PCR assay targeting virulence genes of *Helicobacter pylori* isolated from drinking water and clinical samples in Lahore metropolitan, Pakistan. *J Water Health* 2011;9:208–16.
59 Linke S, Lenz J, Gemein S, Exner M, Gebel J. Detection of *Helicobacter pylori* in biofilms by real-time PCR. *Int J Hyg Environ Health* 2010;213:176–82.
60 Strebel K, Rolle-Kampczyk U, Richter M, Kindler A, Richter T, Schlink U. A rigorous small area modelling-study for the *Helicobacter pylori* epidemiology. *Sci Total Environ* 2010;408:3931–42.
61 McQuillan GM, Kruszon-Moran D, Kottiri BJ, Curtin LR, Lucas JW, Kington RS. Racial and ethnic differences in the seroprevalence of 6 infectious diseases in the United States: data from NHANES III, 1988–1994. *Am J Public Health* 2004;94:1952–8.
62 Fraser AG, Scragg R, Metcalf P, McCullough S, Yeates NJ. Prevalence of *Helicobacter pylori* infection in different ethnic groups in New Zealand children and adults. *Aust N Z J Med* 1996;26:646–51.
63 Muhsen K, Barak M, Henig C, Alpert G, Ornoy A, Cohen D. Is the association between *Helicobacter pylori* infection and anemia age dependent? *Helicobacter* 2010;15:467–72.
64 Pacifico L, Anania C, Osborn JF, Ferraro F, Chiesa C. Consequences of *Helicobacter pylori* infection in children. *World J Gastroenterol* 2010;16:5181–94.
65 Malfertheiner P, Selgrad M. *Helicobacter pylori* infection and current clinical areas of contention. *Curr Opin Gastroenterol* 2010;26:618–23.
66 Mourad-Baars P, Hussey S, Jones NL. *Helicobacter pylori* infection and childhood. *Helicobacter* 2010;15(Suppl 1):53–9.

67 Kosunen TU, Pukkala E, Sarna S, Seppala K, Aromaa A, Knekt P, et al. Gastric cancers in Finnish patients after cure of *Helicobacter pylori* infection: a cohort study. *Int J Cancer* 2011;128:433–9.
68 Take S, Mizuno M, Ishiki K, Yoshida T, Ohara N, Yokota K, et al. The long-term risk of gastric cancer after the successful eradication of *Helicobacter pylori*. *J Gastroenterol* 2011;46:318–24.
69 Mizuno S, Miki I, Ishida T, Yoshida M, Onoyama M, Azuma T, et al. Prescreening of a high-risk group for gastric cancer by serologically determined *Helicobacter pylori* infection and atrophic gastritis. *Dig Dis Sci* 2010;55:3132–7.
70 Asaka M, Kato M, Graham DY. Strategy for eliminating gastric cancer in Japan. *Helicobacter* 2010;15:486–90.
71 Asaka M, Kato M, Graham DY. Prevention of gastric cancer by *Helicobacter pylori* eradication. *Intern Med* 2010;49:633–6.
72 Shiota S, Murakami K, Fujioka T, Yamaoka Y. Population-based strategies for *Helicobacter pylori*-associated disease management: a Japanese perspective. *Expert Rev Gastroenterol Hepatol* 2010;4:149–56.
73 Asaka M, Kato M, Takahashi S, Fukuda Y, Sugiyama T, Ota H, et al. Guidelines for the management of *Helicobacter pylori* infection in Japan: 2009 revised edition. *Helicobacter* 2010;15:1–20.
74 Harvey RF, Lane JA, Nair P, Egger M, Harvey I, Donovan J, et al. Clinical trial: prolonged beneficial effect of *Helicobacter pylori* eradication on dyspepsia consultations - the Bristol Helicobacter Project. *Aliment Pharmacol Ther* 2010;32:394–400.
75 Feinstein LB, Holman RC, Yorita Christensen KL, Steiner CA, Swerdlow DL. Trends in hospitalizations for peptic ulcer disease, United States, 1998–2005. *Emerg Infect Dis* 2010;16:1410–8.