3rd BRAZILIAN CONSENSUS ON *Helicobacter pylori*

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ABSTRACT - Significant progress has been obtained since the Second Brazilian Consensus Conference on *Helicobacter pylori* Infection held in 2004, in São Paulo, SP, Brazil, and justify a third meeting to establish updated guidelines on the current management of *H. pylori* infection. The Third Brazilian Consensus Conference on *H pylori* Infection was organized by the Brazilian Nucleus for the Study of Helicobacter, a Department of the Brazilian Federation of Gastroenterology and took place on April 12-15, 2011, in Bento Gonçalves, RS, Brazil. Thirty-one delegates coming from the five Brazilian regions and one international guest, including gastroenterologists, pathologists, epidemiologists, and pediatricians undertook the meeting. The participants were allocated in one of the five main topics of the meeting: *H pylori,* functional dyspepsia and diagnosis; *H pylori* and gastric cancer; *H pylori* and other associated disorders; *H pylori* treatment and retreatment; and, epidemiology of *H pylori* infection in Brazil. The results of each subgroup were submitted to a final consensus voting to all participants. Relevant data were presented, and the quality of evidence, strength of recommendation, and level of consensus were graded. Seventy per cent and more votes were considered as acceptance for the final statement. This article presents the main recommendations and conclusions to guide Brazilian doctors involved in the management of *H pylori* infection.

HEADINGS - *Helicobacter pylori.* Helicobacter infections. Dyspepsia. Consensus.

INTRODUCTION

Since its foundation in 1994, the Brazilian Helicobacter Study Nucleus, now also a Department of the Brazilian Federation of Gastroenterology has held two consensus conferences on *H pylori* infection[24, 31]. Almost 8 years after the 2nd Brazilian Consensus for Study of *Helicobacter pylori*, the Nucleus promoted its 3rd conference in Bento Gonçalves, RS, Brazil from 12 to 15 April 2012. Thirty-one delegates from all five Brazilian regions took part at the conference, including gastroenterologists, pathologists, epidemiologist, a pediatrician, and an international guest from the USA. Participants were invited for their knowledge and contribution to the study of *H pylori* infection. The meeting sought to re-examine the role of *H pylori* infection in dyspepsia, gastric cancer and extradigestive diseases, besides addressing therapeutic options for treating and retreating the infection in Brazil. Finally, it was sought to carry out a critical analysis of the epidemiological features of the infection in Brazil, with suggestions for possible interventions to reduce the prevalence of the infection and hence its clinical outcomes among us.

METHODOLOGY

The participants were divided into five groups according to their main area of interest/expertise, namely: *H pylori* and functional dyspepsia; *H pylori* and gastric cancer; *H pylori* and other associated disorders; *H pylori*, treatment and retreatment; and *H pylori* and epidemiological aspects. To each group was assigned a coordinator. Prior to the Consensus conference date, the coordinators held a meeting in São Paulo at which a questionnaire was drawn up with specific questions for each participant at the Consensus conference to answer. In Bento Gonçalves, participants were divided among the five groups. Each participant would make a 10 minute presentation to their group, containing in-depth analysis of the topic, citing the top 10 references on it, followed by extensive discussion, with modifications, additions and deletions. The strength of recommendations and levels of evidence adopted

Invited representatives from the Brazilian Nucleus for the Study of Helicobacter: [1] Departamento de Clínica Médica, Faculdade de Medicina, Universidade Federal de Minas Gerais, Belo Horizonte, MG.; [2] Departamento de Medicina Interna, Faculdade de Medicina, Universidade Federal do Rio Grande do Sul, Porto Alegre, RS.; [3] Presidente de Honra do Núcleo Brasileiro para Estudo do Helicobacter, São Paulo, SP.; [4] Universidade Federal do Piauí, Teresina, PI.; [5] Faculdade de Medicina, Universidade de São Paulo, São Paulo, SP, Brasil.
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were, wherever possible, those recommended by the Brazilian Medical Association[5] (Figure 1). The conclusions and recommendations from each group were then prepared and edited for the final plenary meeting, and were then presented to all participants for final voting, and those on which at least 70% of all participants agreed upon were adopted as consensual. The recommendations from these proceedings are reported here.

Recommendation grade	Evidence level	Study types
A	1A	Systematic review (with homogeneity) of randomized controlled trials
	1B	Randomized controlled trial with narrow confidence interval
	1C	Therapeutic results of the "all or nothing" type
B	2A	Systematic review (with homogeneity) of cohort studies
	2B	Cohort study (including a lower quality randomized clinical trial)
	2C	Observation of therapeutic results (outcomes research). Ecological study
	3A	Systematic review (with homogeneity) of case-control studies
	3B	Case-control study
C	4	Case reports (including cohort or lower quality case-control)
D	5	Opinion lacking critical evaluation or based on basic matters (physiological study or animal study)

Adapted from "Oxford Centre for Evidence-based Medicine". *Projeto Diretrizes - Associação Médica Brasileira e Conselho Federal de Medicina*. Updated in May 2001[5]

FIGURE 1. Recommendation grade and evidence level adopted at the 3rd Brazilian Consensus on *H pylori*

GROUP 1. *H PYLORI*, FUNCTIONAL DYSPEPSIA AND DIAGNOSIS

Statement 1:

The diagnosis of functional dyspepsia among us should be the one recommended by the Rome III Consensus, plus stool parasite testing or empiric use of antiparasitics

Agreement level: 100%; Recommendation grade: D; Evidence level: C

In accordance with the Rome III Consensus[42] the following criteria are required for diagnosis of functional dyspepsia: 1) dyspeptic complaints during the last 3 months, beginning at least 6 months prior; 2) the presence of one or more of the following symptoms is fundamental: a) postprandial fullness, b) early satiety c) epigastric pain d) epigastric burning, 3) absence of structural lesions (necessary to perform upper endoscopy) that may justify the symptoms.

Although variable, the prevalence of intestinal parasites in Brazil is still considered high in some regions, especially those caused by *Ascaris lumbricoides*, *Strongiloides stercoralis* and *Giardia lamblia*. In this context, the World Health Organization has considered valid the use of antiparasitic drugs at regular intervals for populations at high risk of contracting intestinal parasites[154]. Thus, the Consensus opted to adopt the concept of functional dyspepsia issued by the Rome III Consensus in addition to the performing of stool parasite testing or the empiric use of antiparasitics.

Statement 2:

When available, the urea breath test with ^{13}Carbon is the noninvasive method of choice for both diagnosis and confirmation of bacterial eradication

Agreement level: 100%; Recommendation grade: A; Evidence level: 1A

The ^{13}C-urea breath test is now universally accepted as the gold standard method for diagnosing and monitoring treatment of *H pylori* infection in adults and children over 6 years old, with sensitivity and specificity always higher than 95%[71]. The test was validated for adults in Brazil on 1999[26] and for adolescents and children on 2002[106]. Although highly accurate, simple and relatively cheap, the test has not yet been incorporated into daily gastroenterology practice, its use being restricted to large urban centers and for epidemiological studies. Difficulties in importing spectrometers and substrate (^{13}C-urea), in contrast to relatively low costs of endoscopy and its histopathology in Brazil, compared to North America and Europe, are factors that have hindered the spread of their employment among us.

Statement 3:

To perform the ^{13}C-urea breath test, antisecretory drugs and antimicrobials must be withdrawn at least 2 and 4 weeks, respectively, prior to examination date

Agreement level: 100%; Recommendation grade: A; Evidence level: 1A

Proton pump inhibitors and H_2 receptor antagonists, as well as antibiotics, may induce false-negative results, and it is recommended they be suspended 2 and 4 weeks, respectively, prior to testing[83]. False-positive results are seldom observed and may occur in patients undergoing surgery for gastric resection or individuals with oral flora rich in urease producing microorganisms retaining ingested urea in the oral cavity for a long time before swallowing[71].

Statement 4:

If the breath test is not available, fecal antigen test is the noninvasive method of choice for both diagnosis and confirmation of *H pylori* eradication, provided a monoclonal antibody is used

Agreement level: 100%; Recommendation grade: A; Evidence level: 1A

Although *H pylori* is seldom cultured in feces, the presence of antigens in fecal material can be determined by enzyme immunoassays using monoclonal antibodies in particular. The Maastricht IV Consensus acknowledged the role of testing for fecal antigens in diagnosing infection and their usefulness in cure control, but only in tests based on the ELISA format with a monoclonal antibody as reagent[132]. A Brazilian study showed that the test using monoclonal antigens is accurate for diagnosing infection in children under 7 years of age, although local validation is needed to determine the optimal cutoff point[163].

Quick, easy to perform, tests using immunochromatography in fecal samples in studies conducted in Europe and Asia, showed limited accuracy, especially because of their low positive predictive values[16, 184]. However, the predictive values of the tests depend on the sensitivity and specificity (inherent features of the tests), but also the prevalence of the disease in the population studied. A Brazilian study evaluating patients not undergoing treatment for *H pylori* infection found 88% (95% CI: 75.7 to 95.5) and positive predictive value of 87.5% (95% CI: 74.7 to 95.3) negative predictive value[189]. Further studies using the immune-chromatographic method, before and after treatment of *H pylori* infection, are needed to define its real accuracy among us. Difficulties in testing and collecting feces, moderately high cost and questionable acceptability by patients have hampered fecal antigen research in our midst.

Statement 5:

Serologic testing is reserved for epidemiological studies and in special situations and should always be locally validated

Agreement level: 100%; Recommendation grade: A; Evidence level: 2

Individuals infected by *H pylori* develop specific antibodies in the serum against this microorganism. In general, testing by ELISA is used the most. Although useful in epidemiological studies they are not useful for diagnosing an active infection, because patients who had the bacteria eradicated may remain seropositive for years. In a Brazilian study, 83/130 (64%) patients with a peptic ulcer were still seropositive 6.4 years after eradication of the microorganism[25]. In addition to epidemiological studies, serologic tests are recommended in situations where other tests have dubious results, such as recent use of antisecretors or antimicrobials, digestive bleeding, atrophy and gastric cancer[132]. The presence of specific anti-*H pylori* antibodies can also be demonstrated in other organic fluids such as urine and saliva.

The specificity of most serological tests is greater than 90%, but their sensitivity ranges from 60 to 90%, with accuracy being 80-84%. All serological tests must be locally validated[137, 186]. In Brazil, validation studies have been performed in Campinas and Belo Horizonte[146, 169]. Less used in daily practice, research on serum antibodies reactive to CagA protein can be used to detect samples of bacteria carrying the CagA gene. Commercially available in the early 2000, it was validated in Brazil in 2004[168] As anti-*H pylori* detected by immunoblotting, especially anti-CagA, can remain in plasma longer (even years after *H pylori* eradication) than those identified immunoenzymatically, they seem to be the most sensitive method for detecting past infection by *H pylori*[93].

Statement 6:

Upper endoscopy in dyspeptic patients, when indicated, should be accompanied by a collection of fragments for study. It is recommended that at least one sample of gastric antrum and corpus should be collected, and the urease test and/or histological examination be performed using H&E staining, and another, to better identify *H pylori* (Giemsa, for example). Wherever possible, antisecretory drugs (proton pump inhibitors and H_2 receptor antagonists) and antimicrobials must be suspended for two and four weeks, respectively.

Level of concordance: 93%-100%; Recommendation grade: A; Evidence level: 1A-1B

Digestive endoscopy in patients with dyspeptic complaints is usually indicated in those over 40 years of age or in the presence of alarm symptoms (weight loss, anemia, bleeding, dysphagia, visceral or abdominal masses, etc.). Endoscopy should always be accompanied by gastric biopsies. Although histological evaluation is ideally as that advocated by the updated Sydney system[41], the Consensus agrees that in order to identify *H pylori* in dyspeptic patients under practical circumstances, collecting at least one antrum and one gastric corpus sample is accepted. There is no specific staining for histological diagnosis for the presence of *H pylori*. Classical hematoxylin and eosin (H-E) staining used for the gastric histology study does not provide a good contrast between the bacterium and the gastric mucus. Therefore, using additional staining with acidophilic features capable of coloring the organism and not primarily the gastric mucus where it is found is recommended. Among the various existing stains, one of the most recommended because of its simplicity and low cost is Giemsa staining[52, 115, 169, 175]. Histological diagnosis and the urease test may show up to 95% sensitivity depending on the quality of material and expertise of the examiner[137, 197]. Antisecretory drugs (H_2 receptor antagonists of histamine and proton pump inhibitors) and/or previous use of bismuth or antibiotics, by reducing the bacterial load, affect the accuracy of the urease test, so, whenever possible, an interval of two and 4 weeks respectively between suspending the drugs and the test is recommended[83, 132]. Consensus held that with naïve anti-*H pylori* patients, where the use of antimicrobials and antisecretors can safely be discarded, a positive urease test is sufficient to diagnose infection. Meta-analysis and

systematic review have shown that the presence of active or recent gastrointestinal bleeding may interfere with the urease test, reducing its sensitivity[75].

Statement 7:

***H pylori* eradication is indicated for functional dyspepsia patients**

Agreement level: 93%; Recommendation grade: A; Evidence level: 1A

The benefits of eradicating *H pylori* for patients with functional dyspepsia symptoms are modest, with 60% to 80% of patients remaining symptomatic after treatment[87, 105, 145]. The most recent Cochrane meta-analysis on the subject examined 21 randomized controlled studies on the role of *H pylori* eradication in the development of dyspeptic symptoms. It was observed a 6% to 14% therapeutic gain, suggesting that eradication of the bacteria may be useful in patients with functional dyspepsia[143]. Among us, Mazzolene et al.[134], in a randomized clinical trial, analyzed 408 patients with functional dyspepsia, with improvement demonstrated in gastrointestinal symptoms (50%) with *H pylori* eradication in infected patients, compared with the group receiving a proton pump inhibitor in a single daily dose (37%). Cost/benefit analyses of this therapeutic option available today estimate the number needed to treat (NNT) as being between 8 and 14, i.e. 8-14 patients must be treated for a single one to benefit from improved symptoms, particularly epigastric pain[134, 143].

The long-term effects of eradicating *H pylori* in functional dyspepsia patients have also been evaluated. In a randomized controlled trial, 1,517 patients with functional dyspepsia were followed for up to 7 years after *H pylori* eradication. A cumulative gain over time was shown, with a 25% reduction in medical visits due to dyspeptic complaints in patients who had eradicated the bacteria[89]. *H pylori* eradication in patients with functional dyspepsia is now a consensus recommendation established by leading experts in different regions of the world[132, 141, 192, 207].

Statement 8:

Eradication of *H pylori* is the first therapeutic alternative in functional dyspepsia

Agreement level: 86.2%; Recommendation grade: A; Evidence level: 1A

Functional dyspepsia treatment is still unsatisfactory for many patients, with the different approaches providing little significant therapeutic gain. While *H pylori* eradication promotes an 8%-14% therapeutic gain, rates achieved using proton pump inhibitors vary between 7% and 10%. Less consistent data having similar results are also obtained using prokinetic agents, H_2 blocker antagonists, tricyclic antidepressants and serotonin reuptake inhibitors[112]. Recent evidence has demonstrated the long-term effects of *H pylori* eradication in reducing consultations for dyspeptic complaints[89, 129]. Cost-effectiveness analyses show variations in different regions of the world, depending on differing factors, with the best results obtained in regions where the infection is highly prevalent. Thus, studies in Asia and Brazil have shown benefit in the treatment of infection with NNT of 3.6 to 13 and 8 respectively[87, 105, 134, 145]. Additional advantages of this procedure include reduced transmission of the infection and its main clinical sequelae, peptic ulcer and gastric cancer.

Statement 9:

The test-and-treat strategy, using noninvasive testing and treating the infected individuals, should be considered in adults under 35 years of age, with no alarm signs and no family history of gastric cancer

Agreement level: 100%; Recommendation grade: A; Evidence level: 1B

Several strategies have been suggested for young patients up to 35 years of age with no alarm symptoms, nor a family history of gastric cancer. Patients' history and physical examination are neither sensitive nor specific enough to predict which patients' dyspeptic organic nosology will be detected y endoscopy[144, 200]. The low prevalence of cancer in this population and the high rate of irrelevant findings on endoscopy have encouraged the use of empirical treatment (*H pylori* eradication or a cycle with proton pump inhibitors) before performing an invasive and relatively costly procedure (upper endoscopy with biopsies). A Cochrane Collaboration review showed that, in the absence of alarm symptoms, the test-and-treat strategy is more effective than an initial endoscopy and empiric use of proton pump inhibitors[39]. The review also showed that the test-and-treat strategy was cheaper than the initial endoscopy. The non-invasive approach for initial diagnosis of *H pylori* infection can be performed using the labeled urea breath test, fecal antigen test or serology. Although serology is unable to define the presence of active infection, in areas where infection is highly prevalent its positivity has a high positive predictive value, and is considered an acceptable diagnostic alternative. The most commonly used serological tests are those performed by ELISA, as previously validated in Brazil[146, 169]. To control bacteria eradication in the test-and-treat strategy, only the labeled urea breath test and a fecal antigen survey are recommended, both of which have also been validated in Brazil already[26, 189].

Statement 10:

Eradication control should be done at least 4 weeks after treatment ends

Agreement level: 100%; Degree of recommendation: B; Evidence level: 2B

Infection cure control should be performed in no less than 4 weeks to avoid the occurrence of false-negatives[130]. The ^{13}C-urea breath test is the ideal noninvasive method for achieving eradication control. It is highly sensitive and specific, moderate cost, and is gradually becoming available in Brazil. Testing for fecal antigens has also been used with excellent results. If neither the breath test or fecal antigen

test is available, or an endoscopic evaluation is needed (gastric ulcer, MALT lymphoma, etc.), eradication control can be done by endoscopy, studying the bacteria in histological sections and with the urease test, using fragments of the antrum and gastric corpus in this situation. The quantitative serology is not an established method for confirming bacterial eradication.

Statement 11:

Eradication control should be done in patients with gastroduodenal ulcer, MALT lymphoma after an early gastric cancer resection and in patients with persistent symptoms after undergoing the test-and-treat strategy

Agreement level: 100; Recommendation grade: D; Evidence level: 5

Although from the pharmacological monitoring standpoint eradication control should be performed on all patients undergoing anti-*H pylori*, the Consensus held that eradication confirmation always be sought, at least in patients with gastroduodenal ulcer, MALT lymphoma after early gastric cancer resection and in those with persistent symptoms after undergoing the test-and-treat strategy.

GROUP 2. *H pylori*, GASTRIC ADENOCARCINOMA AND MALT LYMPHOMA

Statement 12:

***H pylori* is the single most relevant risk factor for gastric adenocarcinoma and MALT lymphoma**

Agreement level: 100%; Recommendation grade: A; Evidence level: 1A

Infection by *H pylori* is today the greatest risk factor for developing stomach adenocarcinoma and has, since 1994, been considered a type 1 carcinogen (defined) for developing gastric cancer in humans[100]. Current epidemiological evidence confers an 18.3 to 21 times higher risk in infected compared to uninfected individuals, especially in distal gastric cancer[7, 10, 46]. Experimental evidence and animal models have demonstrated a causal relationship between infection with *H pylori* and development of lesions leading to gastric cancer[88, 204]. It is accepted that the microorganism takes part in the development of gastric cancer through direct action by its virulent factors, with the most recognized among them being the CagA oncoprotein, or, indirectly, through the initiation and maintenance of chronic inflammation in the gastric mucosa. Despite the advancement of knowledge, there is no specific recommendation to search for the presence of bacterial virulence factors in daily practice. Recently, experimental studies in mice colonized with *H felis* have added other alternatives to the epithelial theory for gastric carcinogenesis. In this study, after becoming atrophic the infected gastric mucosa would be colonized by bone marrow stem cells that would differentiate into intestinal cells thus giving sequence to the intestinal metaplasia cascade, dysplasia and intraepithelial cancer[95].

Host factors also influence the risk of developing gastric adenocarcinoma, especially those related to the presence of cytokine polymorphisms. After initial studies involving increased risk of gastric atrophy and gastric cancer in patients with IL-1β polymorphisms, other genes have been implicated, especially IL-10, interferon-gamma, IL-8 and tumor necrosis factor[2, 48, 94]. However, from a clinical standpoint, so far no specific markers exist to be investigated in the search for increased risk of developing gastric cancer.

Nutritional and environmental factors also play a part in gastric cancer development, including smoking, alcohol consumption, salt, salty foods and N-nitroso compounds, among others. Increasing fruit and vegetable consumption continues to be considered a factor capable of lowering the risk of developing gastric cancer, although recent prospective studies have not been able to confirm this effect[81, 167]. Neither was vitamin supplementation in the diet also able to reduce the gastric cancer risk[6]. An important conclusion from recent extensive European study states that any nutritional effects on gastric cancer are strictly dependent on the presence of *H pylori* infection, and are minimal in its absence[11, 80].

The gastric MALT (mucosa-associated lymphoid tissue) lymphoma represents approximately 7% of all non-Hodgkin lymphoma and can stem from any extranodal region. At least one third of them present themselves as a gastric MALT lymphoma. Epidemiologic studies have shown its association with previous *H pylori* infection[157]. In vitro studies have shown that proliferation of low-grade MALT lymphomas, of stomach B cells, can be stimulated via T-lymphocytes and cytokines by specific strains of *H pylori*[208]. Because it is a rare disease, there are no prospective randomized trials to assess the effect of *H pylori* eradication in gastric MALT lymphoma remission. A recent systematic review evaluating 32 studies involving 1,408 patients with low-grade MALT lymphoma showed the presence of *H pylori* infection in 88.2% of cases and complete remission of the tumor just by eradicating the bacteria in over 75% of cases[214]. A recent consensus meeting acknowledges *H pylori* eradication to be a first line treatment for gastric MALT lymphoma[177].

Statement 13:

***H pylori* eradication reduces the risk of gastric cancer precursor lesions developing. Chronic active gastritis is reversed by *H pylori* eradication, whereas stopping Pelayo Correa's carcinogenic cascade.**

Agreement level: 100%; Recommendation grade: A; Evidence level: 1A

H pylori is the most important factor in the pathogenesis of chronic gastritis, which is considered an essential factor in up to 90% of cases of gastric cancer[41]. Different studies and meta-analysis, as well as trials on animals, have shown that, in the absence of more advanced changes (atrophic gastritis and intestinal metaplasia), *H pylori* eradication promotes remission of inflammatory lesions in the gastric mucosa in a variable period of time[65, 151, 206, 210].

Statement 14:

Does *H pylori* eradication reduce/regress gastric cancer precursor lesions?

YES, for atrophic gastritis of the corpus

Agreement level: 100%; Recommendation grade: B; Evidence level: 2A

The carcinogenetic *H pylori* infection sequence → chronic gastritis → glandular atrophy → intestinal metaplasia → dysplasia → intestinal-type adenocarcinoma, proposed by Pelayo Correa[33], provides the basis for initial studies on gastric adenocarcinoma prevention based on *H pylori* eradication. Atrophic gastritis and intestinal metaplasia observed in *H pylori* infected individuals are considered preneoplastic conditions indicating increased gastric cancer risk[90, 198]. A key issue in establishing gastric cancer prevention strategies is to define the exact point within the evolutionary cascade of chronic gastritis from which regression of histological changes after eradication of the microorganism is no longer observed. Although controversial, due to possible sampling errors, a recent meta-analysis suggests that atrophic gastritis of the corpus can reverse after *H pylori* eradication[203].

Statement 15:

Does *H pylori* eradication reduce/regress gastric cancer precursor lesions?

NOT for atrophic gastritis of the antrum

Agreement level: 100%; Recommendation grade: B; Evidence level: 2B

Pathologists often disagree over the diagnosis of atrophic antrum gastritis. This can be explained by the smaller number of gastric glands in the normal antral mucosa[18, 152]. The results of *H pylori* eradication on atrophic gastritis are often controversial[38, 102, 111, 203]. A recent meta-analysis study involving 12 trials analyzing 2,648 patients with atrophic gastritis of the antrum found no significant reversibility of atrophic changes in the antrum following *H pylori* eradication[203].

Statement 16:

Does *H pylori* eradication reduce/regress gastric cancer precursor lesions?

NOT for intestinal metaplasia

Agreement level: 100%; Recommendation grade: B; Evidence level: 2A

Intestinal metaplasia of the stomach refers to the gradual replacement of the gastric epithelium by an intestinal-type epithelium, that is, by a newly formed epithelium presenting morphological and biochemical features (under both optical and electron microscopy) of the intestinal epithelium, of either the small intestine or the colon. As such, the metaplastic epithelium may consist of different lineages of proper intestinal mucosal cells such as goblet cells, absorptive cells, Paneth cells and endocrine cells. These cells are easily identified in the gastric mucosa since they are not present in the normal gastric mucosa and their identification presents high inter-observer agreement[18]. Although it also presents discordant studies, different studies and meta-analysis have been unable to demonstrate intestinal metaplasia regression after *H pylori* eradication[113, 121, 153, 172, 203, 213].

Statement 17:

The optimal timing of *H pylori* eradication to prevent gastric cancer is before the appearance of preneoplastic conditions (atrophic gastritis and intestinal metaplasia)

Agreement level: 100%; Recommendation grade: A; Evidence level: 1A

Intervention studies conducted in Latin America and Asia and meta-analysis have shown that *H pylori* eradication is an effective step in preventing gastric cancer, particularly if treatment is performed on patients prior to development of precancerous conditions (atrophic gastritis and intestinal metaplasia)[65, 139, 193, 206, 210]. Studies using animal models have also confirmed that gastric cancer development can be prevented by early eradication of the microorganism[14, 151].

Statement 18:

Even with preneoplastic conditions already established, eradicating *H pylori* reduces the risk of gastric cancer

Agreement level: 100%; Recommendation grade: A; Evidence level: 1C

Randomized controlled trials conducted in Colombia and China have demonstrated a beneficial effect of eradicating the bacteria even in patients with precancerous conditions[34, 120, 139]. Even though the further advanced the existing preneoplastic condition is, the less likely it is that *H pylori* eradication will stop gastric cancer development[37, 59], a randomized study of patients undergoing *H pylori* eradication following early gastric cancer resection was able to demonstrate a reduction in the appearance of metachronous gastric cancer[66].

Statement 19:

In Brazil, surveying and treating the population as a measure to prevent gastric cancer is not indicated

Agreement level: 100%; Recommendation grade: D; Evidence level: 4

In 2008, the Asia-Pacific Consensus for Gastric Cancer Prevention recommended surveying and treating the entire populations for *H pylori* infection in high risk regions, defined as those where the incidence of gastric cancer in the population is higher than 20/100,000 inhabitants[59]. The recently published Maastricht IV Consensus believes that this approach should be considered in other high-risk areas in the world[132]. According to the Consensus, indication of treatment for the entire infected population is not currently recommended among us. Data on incidence and mortality of gastric cancer showed intermediate values (incidence of 13 cases to 100,000 in the male population and 7 cases per 100,000 inhabitants in the female population)[101]. Furthermore, epidemiological data on gastric cancer is incomplete in many regions, and non-invasive methods for diagnosing the infection are not widely available.

Statement 20:

Indications for eradication of *H pylori* as a measure to prevent gastric cancer:

First-degree relatives of gastric cancer carriers

Agreement level: 100%; Recommendation grade: A; Evidence level: 1B

After gastric resection, endoscopic or surgical adenocarcinoma

Agreement level: 100%; Recommendation grade: A; Evidence level: 1B

Patients with severe pangastritis, atrophic gastritis and/or intestinal metaplasia

Agreement level: 100%; Recommendation grade: B: Evidence level: 1B

Meta-analysis[173] and case-control studies conducted in Asia[188], Europe[47, 61] and Latin America[149], including Brazil[147], show that first-degree relatives of gastric cancer carriers have a 2 to 3 times higher risk of developing neoplasia, so search and eventual eradication of bacteria in this population is fully justified. Metachronous tumors in the gastric remnant have been described in up to 10% of patients undergoing gastric, endoscopic or surgical resection for early gastric cancer[182, 187, 194]. A recent randomized controlled trial from Japan showed that eradication of *H pylori* in patients undergoing endoscopic resection for early gastric cancer, followed for 3 years, was able to reduce the risk of developing metachronous gastric cancer from 4 per 100 persons per year to 1.4 per 100 persons per year in the eradicated group[66]. Also considered high-risk patients for development of gastric cancer are those undergoing gastric resections for benign diseases (peptic ulcer, for example) and patients carrying other gastric neoplasias such as adenoma and MALT lymphoma. Besides bacteria eradication, endoscopic monitoring at regular intervals in this population is recommended[17, 180, 190, 195].

One epidemiological study suggests that prolonged use (more than 1 year) of proton pump inhibitors might be associated with increased gastric cancer risk[159]. Prolonged use and high doses of antisecretories in an animal model has been capable of promoting adenocarcinoma development in *H pylori* infected animals, strengthening the recommendation for it to be eradicated as a measure of preventing gastric cancer in this group of individuals (see below)[88, 132].

Statement 21:

After eradication of *H pylori*, the follow-up of patients carrying precancerous conditions should be done with:

Endoscopic examinations with collection of two fragments from the gastric corpus and antrum

Agreement level: 100%; Recommendation grade: C; Evidence level: 2B

3-year interval between endoscopic examinations for patients with atrophy and/or extensive intestinal metaplasia in the gastric antrum and corpus

Agreement level: 100%; Recommendation grade: D; Evidence level: 4

The number and location of the biopsies to be taken during the endoscopic follow-up examination of patients with preneoplastic conditions is cause for major divergence, because of the lack of methodologically well-designed studies to support them. Even assuming that the technological progress of endoscopes and more comprehensive studies can substantially change this decision, the Consensus opted to follow the European recommendation to perform, at least, the removal of two fragments in the antrum and at least two fragments in the gastric corpus, in both small and large curvature[40]. It is also recommended that histological analysis of the fragments be made under the criteria established by the updated Sydney System[41] and, where possible, through it, to promote the atrophy and intestinal metaplasia graduation as recently described by systems, OLGA - Operative Link Assessment on Gastritis - and OLGIM - Operative Link on Gastritis by Intestinal Metaplasia[18, 176].

When atrophy and/or intestinal metaplasia is classified as mild or moderate and restricted to the antrum, the European group does not recommend follow-up, although the indication for *H pylori* eradication is formal, with a view to avoiding progression to dysplasia and cancer. Moreover, endoscopic surveillance is recommended for patients with extensive atrophy or extensive intestinal metaplasia (that is, extensive atrophy and/or extensive intestinal metaplasia in the gastric antrum and corpus); this follow-up should be done every 3 years[40].

GROUP 3. *H pylori* AND OTHER ASSOCIATED DISORDERS

Statement 22:

Epidemiologic and animal studies suggest an inverse relationship between *H pylori* infection and bronchial asthma or atopies

Agreement level: 100%; Recommendation grade: B; Evidence level: 2B

Epidemiological data indicate an increasing growth in bronchial asthma and atopies. The causes of this growth, although some correlations have been described, are not fully clarified[133, 191]. Recent publications point to an inverse association between *H pylori* infection in the childhood and the development of asthma and allergic diseases in the U.S., but not in Europe[22, 67, 165]. However, randomized controlled trials are needed to better establish and determine the causal relationship between asthma-atopy and *H pylori* infection.

Statement 23:

In upper gastrointestinal bleeding secondary to peptic ulcer, *H pylori* eradication is more effective than antisecretory treatment alone (with or without maintenance treatment) in preventing recurrent bleeding

Agreement level: 100%; Recommendation grade: A; Evidence level: 1A

Randomized studies and meta-analysis have demonstrated that, in patients carrying a peptic ulcer complicated with upper digestive bleeding, *H pylori* infection treatment was more effective than antisecretory treatment without eradication (with or without long-term antisecretory treatment) in preventing recurrent bleeding. Therefore all patients with peptic ulcer bleeding must be tested for *H pylori* and eradication treatment should be prescribed for infected patients[70, 125].

Statement 24:

Regarding the role of *H pylori* and the occurrence of upper gastrointestinal bleeding in users of NSAIDs and aspirin:

***H pylori* eradication reduces the risk of peptic ulceration and bleeding in patients on chronic use of NSAIDs and aspirin**

Agreement level: 100%; Recommendation grade: A; Evidence level: 2A

In patients on long-term use of NSAIDs, with a history of peptic ulcer disease, the mere eradication of *H pylori* is not sufficient to prevent recurrence of the ulcer and/or bleeding

Agreement level: 100%; Recommendation grade: A; Evidence level: 1B

Testing for and eradicating *H pylori* is indicated, prior to treatment with long-term aspirin in patients at high risk for peptic ulcer disease or complications

Agreement level: 100%; Recommendation grade: A; Evidence level: 2B

***H pylori* eradication reduces the risk of recurrent bleeding in patients taking aspirin long term and with a history of gastrointestinal peptic ulcer bleeding**

Agreement level: 100%; Recommendation grade: B; Evidence level: 1B

The relationship between *H pylori* infection and NSAID users and gastroduodenal pathology is complex, since both are risk factors for digestive bleeding. On its own, *H pylori* infection increases this risk 1.78 times and NSAID 4.89 times. The risk of a bleeding ulcer increases 6.13 times when both are present[97].

It is well established that the risk of association between NSAIDs and peptic disease and its complications, also depends on other risk factors inherent to the patient, including advanced age, presence of co-morbidities, concomitant drugs, smoking and a history of peptic ulcer disease and bleeding[126, 205]. The risk of NSAIDs causing ulceration and bleeding also varies with the toxicity, dosage and duration of the medication used[185].

For primary prevention of peptic ulcer and complications, *H pylori* eradication before starting NSAIDs significantly diminishes its occurrence as well as bleeding, despite concomitant use of proton pump inhibitors[20, 201].

In patients taking NSAIDs for a long time, merely eradicating *H pylori* is not sufficient to eliminate the risk of peptic ulceration and bleeding. In this scenario, using a proton pump inhibitor is better than simply eradicating the bacteria[19]. The best protection for the patient in these cases is to apply both, namely, the proton pump inhibitor and eradicating *H pylori*[20].

The risk of bleeding in patients taking aspirin is dose-related and irrespective of formulation[109]. Gastrointestinal bleeding risk in aspirin users is increased in *H pylori* infected patients (OR = 4.7) and those with a history of ulcers (OR = 15.2)[117, 158]. Eradicating *H pylori* as the primary prevention role prior to using aspirin is not well established in all patients, but it is reasonable and justifiable in patients with other risk factors for ulcers and digestive bleeding[118].

H pylori eradication in patients on long-term treatment with acetylsalicylic acid and with a history of ulcers and intestinal bleeding effectively reduces the risk of rebleeding. The best approach in these cases, besides eradicating *H pylori*, is to indicate the maintenance use of proton pump inhibitors[19, 114].

Statement 25:

***H pylori* should be eradicated in patients with idiopathic thrombocytopenic purpura**

Agreement level: 100%; Recommendation grade: B; Evidence level: 3A

Meta-analysis and systematic reviews have shown a 50% increase in platelet count in patients with idiopathic thrombocytopenic purpura who underwent *H pylori* eradication. The exact mechanism by which this response is achieved remains unknown[3, 62, 68].

Statement 26:

***H pylori* infection may be a risk factor for deficit hemoglobin, decreased levels of ferritin and iron deficiency anemia**

Agreement level: 100%; Recommendation grade: B; Evidence level: 2A

Studies suggest an association between *H pylori* and iron deficiency anemia, especially in risk groups with a relatively high demand for iron, such as children and adult women. *H pylori* eradication is recommended in these cases where the iron deficiency anemia etiology cannot be determined[98, 148, 161, 211].

Statement 27:

Eradication of *H pylori* does not favor the appearance of GERD

Agreement level: 100%; Recommendation grade: B; Evidence level: 1B

The *H pylori* treatment does not seem to worsen GERD symptoms, or induce erosive esophagitis. *H pylori* should be eradicated and searched in GERD patients who require chronic use of proton pump inhibitors[142, 178, 209].

GROUP 4. *H pylori*, TREATMENT AND RETREATMENT

Statement 28:

The conventional triple therapy (a proton pump inhibitor at standard dose, amoxicillin 1.0 g, and clarithromycin 0.5 g, administered twice daily for 7 days) is the first treatment option

Agreement level: 100%; Recommendation grade: A; Evidence level: 1A

The triple therapy is still the most used and recommended worldwide and also in Brazil[4, 13, 29, 31, 54, 68, 124, 134, 166, 207]. Its effectiveness basically depends on rates of resistance to clarithromycin and is not recommended in areas where these rates among the population are higher than 20%. The few Brazilian studies on clarithromycin resistance show rates below this value[45, 78, 123, 160]. While not outstanding, in the last 10 years this regimen has shown eradication rates close to 80% among us[29, 54, 134, 166]. Such results have also recently been described by a Spanish group while treating *H pylori* infection over 12 years[77]. A recent randomized trial, involving seven Latin American countries, including Chile and Colombia, achieved 82.2% *H pylori* eradication with the triple classic therapy scheme for 14 days[85]. Most of the recommendations by the consensus groups recommend a period of 7 days, especially because of the cost factor. In reality, meta-analysis studies have shown a 4% gain by extending to 10 days and 5% with 14 days[15, 60, 64, 91]. For patients with a possible or proven history of penicillin allergy to the scheme described above is recommended replacing amoxicillin with the furazolidone 200 mg twice a day[31, 35]. Other options include using metronidazole or levofloxacin instead of amoxicillin or adopting schemes employing tetracycline and metronidazole and bismuth salts[72, 73, 171]. Further studies evaluating the antimicrobial resistance profile of *H pylori* in the Brazilian population are urgently needed to better define future therapeutic strategies among us.

Statement 29:

Due to the absence of national validation studies, the alternative first-line regimens in eradicating *H pylori* such as the sequential therapy, concomitant scheme without bismuth, or those containing bismuth salts or levofloxacin are not routinely recommended in Brazil. In special situations, regimens containing furazolidone may be used

Agreement level: 86.2 to 89%; Recommendation grade: D; Evidence level: 5

Alternative regimens to classical triple therapy, recommended for situations where rates of resistance to clarithromycin are high, above 20%, have been increasingly employed in different countries. The sequential scheme, developed by Italian researchers, consists of administering a standard dose of proton pump inhibitor with 1.0 g of amoxicillin, twice daily for the 1st 5 days, followed by administering of the standard dose of proton pump inhibitor, 500 mg of clarithromycin and 500 mg of tinidazole administered twice daily for a further 5-day period. Although most studies are still restricted to a single country, the initial results show eradication rates around 90%[58, 104, 199, 216], with some Asian studies showing less significant results[23]. There is a lack of confirmatory studies as to the effectiveness of this scheme among us. In a recent randomized Latin American trial where 486 patients received the sequential regimen, *H pylori* eradication rates came to 76.5%[85]. The concomitant scheme (without bismuth) consisting of administering the standard dose of a proton pump inhibitor, amoxicillin, clarithromycin and metronidazole for 7 to 14 days has proven to be an effective, safe and well tolerated option for regions where no bismuth salts are available or efficacy of triple therapy is unacceptably low. Being less complex than sequential therapy, it encourages adherence to treatment. Recent meta-analysis demonstrated the superiority of concomitant therapy over triple therapy, with eradication rates per intention to treat analysis of 89.7% (95% CI: 86.8% to 92.1%)[127]. Although resistance to clarithromycin may reduce the efficacy of concomitant therapy, this seems to mean less impact on the eradication rates when compared with triple therapy. Studies with concomitant therapy without bismuth in patients with strains resistant to metronidazole are still limited. A recent randomized clinical trial, in Colombia, encountered similar eradication rates employing during 10 (85.3% eradication) or 14 (86.8%) days a combination of clarithromycin 500 mg twice daily, metronidazole 500 mg 3 times daily and amoxicillin 500 mg 3 times daily with or without a proton pump inhibitor[57].

The quadruple therapy containing proton pump inhibitor in standard dose + colloidal bismuth subcitrate 120 mg, 4 times daily + tetracycline hydrochloride 500 mg 4 times daily + metronidazole 250 mg 4 times a day for 7-10 days is a well established scheme in regions with high rates of resistance to clarithromycin. It has recently, been available in kits in the U.S. and Europe. A randomized clinical trial involving 39 centers in Europe, compared the classic triple therapy for 7 days with a quadruple therapy containing tetracycline, metronidazole and bismuth salt in a single formulation, and proton pump inhibitor, administered for 10 days on 440 patients undergoing anti-*H pylori* treatment for the first time. Eradication rates were 55% for the triple scheme and 80% for the quadruple scheme ($P<0.0001$). It is noteworthy that 70% of the strains were resistant to metronidazole and 20% to clarithromycin[131]. Recent meta-analysis showed that quadruple therapy provides eradication rates similar to those observed with classical triple therapy[127]. Its drawback is the need to ingest a large number of tablets per day, impairing adherence to the treatment. Although recommended by some studies as an option for first-line therapy, the use of levofloxacin is usually reserved for retreatment[21, 142].

Regimens employing furazolidone associated with an antimicrobial (amoxicillin, clarithromycin or tetracycline) as first-line treatment for *H. pylori* infection has been used in adults and children in Brazil, with eradication rates of 79.1% (95% CI: 74.1% to 84.2%). The treatment is performed

for 7 days, the doses of furazolidone used range from 100 mg (children) to 400 mg/day, with frequent adverse effects, particularly gastrointestinal[28, 35, 63, 107, 128]. A systematic review and meta-analysis of the effects of furazolidone and nitrofurantoinic derivatives in eradicating *H pylori* showed that schemes using such drugs had more frequent adverse effects and slightly less effective eradication rates when compared with the classic triple therapy[12].

Although some probiotics and prebiotics, when used as adjunctive therapy, show encouraging results in reducing adverse effects from using antibiotics[8, 196], the Consensus considered that its routine use in anti-*H pylori* therapy still needs further studies.

Statement 30:

Triple regimens containing proton pump inhibitor, levofloxacin, amoxicillin for 10 days* or proton pump inhibitor, levofloxacin and furazolidone for 7-10 days and quadruple regimens employing proton pump inhibitor, bismuth salt, tetracycline and furazolidonefor 10-14 days**, are recommended as second or third line therapy**

Agreement level: 89%; Recommendation grade: *A;**B; Evidence level:* 1A; **2C

Antibiotic resistance is the most important factor for lack of response to initial treatment. Indeed, *H pylori* eradication rates with classical triple therapy (proton pump inhibitor, amoxicillin and clarithromycin) are over 87% when the bacteria are sensitive to clarithromycin, against 17% when it is resistant[135]. Rates for secondary resistance, or that observed after failure of the first treatment, reaches 60% or more, which means that repeated treatment with clarithromycin should be avoided, unless antimicrobial susceptibility testing is available[92, 136, 150].

Regarding retreatment, this Consensus reiterated, with minor modifications, the recommendations of the previous Consensus[31]. Three meta-analysis confirm that associating a standard dose of proton pump inhibitor, twice a day, amoxicillin 1.0 g twice a day and levofloxacin 500 mg once daily for 10 days achieves eradication rates of around 80%[74,122,179]. Although widely used in Brazil there are no validation studies among us. National studies employing a standard dose of proton pump inhibitor, and furazolidone 400 mg and levofloxacin 500 mg, taken once daily for 10 days, or a standard dose of proton pump inhibitor associated with furazolidone 200 mg and levofloxacin 250 mg, administered twice daily for 7 days, have obtained eradication rates close to 80%[30, 44, 181].

The quadruple therapy employing a standard dose of proton pump inhibitor + colloidal bismuth subcitrate 120 mg 4 times daily + tetracycline hydrochloride 500 mg 4 times daily + metronidazole 250 mg 4 times a day for 10-14 days, is one of the most used regimens worldwide in retreating infection after the triple classical regimen has failed, with eradication rates of nearly 80%, according to European studies[75, 119, 174]. Due to high rates of primary resistance to metronidazole in Latin America, few studies exist[164]. Some studies, however, suggest that the primary resistance to imidazoles observed in vitro might be overcome by increasing the dose and/or duration of treatment[116, 127, 186]. One must also consider that the prevalence of metronidazole resistance tends to be overestimated when determined by the E-test[155].

Quadruple regimens where metronidazole is replaced by furazolidone have been used in Brazil and other countries in South America to treat patients who are refractory to classic triple therapy[43, 86, 181]. In Brazil, the quadruple regimen recommended for retreatment is to administer a standard dose of proton pump inhibitor, amoxicillin + 1.0 g (or doxycycline 100 mg) + furazolidone 200 mg + 240 mg colloidal bismuth subcitrate (2 comp.), administered twice a day (after lunch and dinner) for 10-14 days. A study employing this regimen achieved 80% eradication in Brazil[181]. The use of only two daily doses, as previously suggested by Graham et al.[84], appears to increase adherence and reduce the adverse effects of this regimen.

Using furazolidone in anti-*H. pylori* therapy regimens has been the subject of recent controversy. Available on the market for decades and it is recommended as an anti-*H. pylori* alternative drug by the *H. pylori* Consensus in Latin American in 2000[27], Brazil in 2005[31], China in 2008[96] and also by the World Gastroenterology Organization, in 2011[207]. Classified in 1997 by the International Agency for Research on Cancer (IARC) as a type 3 carcinogen (unclassifiable as a carcinogen in humans)[99], it is no longer available in North American and European markets because of possible genotoxic and carcinogenetic effects in animals[50, 51, 53]. It is still available in several Latin American countries, including Brazil, China and Iran, among others. While Zullo et al.[215], in a recent review suggest that patients who receive their prescription should be informed about its potential effects on animals, Graham and Lu[82], reviewing the processes that culminated in the withdrawal from U.S. trade, considered it to be an unfairly maligned and underused drug and particularly useful in areas where antibiotic resistance is widespread and multiple.

GROUP 5. EPIDEMIOLOGY OF INFECTION AND PROPOSALS FOR ACTION TO REDUCE ITS PREVALENCE AND IMPROVE FIGHTING IT IN BRAZIL

In general, *H pylori* infection is acquired early in childhood. In urban and rural Brazilian populations with a low socioeconomic status (SES) more than half the children are already colonized in the first 2-3 years of life, with numbers increasing until the 5th year, when the risk of acquiring the infection decreases. In populations with a higher SES, the risk of acquiring it also begins early, although more slowly, reaching significantly lower rates than those seen in populations with a low SES. Acquiring the infection during childhood may be decisive to the morbidity and mortality associated with chronic *H pylori* infection in the adult population[49, 140, 156, 162].

The prevalence of *H. pylori* infection in the adult population depends on the incidence in childhood, since infection

often persists throughout the life of the individual and it is seldom caught in adulthood. In Brazil, the prevalence is much higher than the average of the world population, with variability depending on the geographic area and the development level of the population surveyed. In populations with precarious SES, resident in urban and rural areas, the prevalence of infection may reach 70% of children at 5 years of age, reaching over 80% of individuals after the age of 20. Moreover, the improvement in the population's living conditions, characterized by higher household income, higher level of education and adequate health services, provides an impact on the prevalence of *H pylori* infection, with a drop in the prevalence of *H pylori* infection[1, 32, 103, 108, 138, 170, 183, 202, 212].

The primary risk factors for acquiring *H pylori* in Brazil are related to unfavorable living conditions experienced during childhood, including low family income, low education levels of the children's parents, lack of proper household sanitary facilities, household crowding or high density housing or in institutions; improper personal hygiene habits, presence of an infected family member, especially the mother, and deficient basic public health services such as supply of piped drinking water, household garbage collection and sewerage with treatment plants for collected waste[9, 36, 55, 56, 79, 110].

The group has listed a set of measures needed to reduce the risk of acquiring the infection (Figure 2), as well as suggestions for actions to be implemented by government agencies to reduce infection rates in Brazil (Figure 3).

1. Prophylactic measures should focus on protecting individuals in their early years of life, especially concerning personal hygiene precautions in order to avoid contact with vomit and human waste that can transmit *H pylori*.

2. Encourage and develop strategies with a view to improving the living conditions of the population, including: increasing family income; universal availability of proper sanitary system, including drinking water, collection and treatment of waste, piping and treatment of sewage, and sanitation of public areas; and increasing the population's levels of education.

3. Advise healthcare professionals about the potential risk of iatrogenic transmission of *H pylori*, as well as contamination of occupational health professionals themselves, especially regarding the possibility of contamination of endoscopes and medical instruments, which must undergo proper disinfection or sterilization.

4. Disseminate information among the Brazilian population about knowledge on *H pylori* infection, including modes of transmission, risk factors related to poor living conditions and hygiene and their association with the development of diseases.

FIGURE 2. Measures to reduce the risk of *H pylori* infection in Brazil

Create the Sector Chamber for *H pylori* at the Ministry of Health to develop the actions specified below, among others:

- Establish collaboration between the Ministry of Health, research institutions and the private sector to provide universal non-invasive methods to diagnose *H pylori* infection to be provided by the Unified National Health System
- Establish collaboration between the Ministry of Health and Ministry of Education to include the *H pylori* issue in the school syllabus for elementary and secondary education, in order to impart knowledge about this infection, including risk factors, its connection to poor living conditions and hygiene and its association with development of diseases.
- Assemble actions aimed at organizing knowledge and real prevalence of gastrointestinal diseases associated with *H pylori* infection by, characterizing geographic areas, risk factors and the age groups of the affected population.
- Create a clinical protocol, with the collaboration of the Brazilian Nucleus for the Study of Helicobacter, for treatment of *H pylori* and its dispensation by Unified National Health System at the various levels of health care.
- Encourage research institutions in establishing projects with a view to developing new therapeutic regimens and an anti-*H pylori* vaccine.
- Conduct educational campaigns and public awareness programs on *H pylori* infection stressing the preventive nature of all citizens' taking responsibility.
- Educate and train Family Health Strategy (FHS) professionals on *H pylori* infection stressing epidemiology, modes of transmission, associated diseases, preventive measures, and indication for treatment and recommended therapeutic schemes, making them the multipliers of such knowledge, with activities in communities, schools and organized civil society.

FIGURE 3. Suggestions by the Brazilian Center for studying *H pylori* to reduce *H pylori* infection rates in Brazil

DISCLOSURES

LG Coelho: consultant from Ache and Medley. I. Maguilnik: consultant from Medley. JPP Moraes-Filho: consultant from Medley, Reckitt Benckiser, and Takeda. JM Parente: consultant from Abbott Brasil and Janssen Brasil. MCF Passos: consultant from Abbott Brasil, Ache, Apsen, Janssen Brasil, Medley, and Takeda. S Zaterka: advisory board from Takeda.

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RESUMO - Os avanços significativos ocorridos desde o Segundo Consenso Brasileiro sobre *H. pylori* realizado em 2004, em São Paulo, justificam este terceiro consenso. O evento foi organizado pelo Núcleo Brasileiro para Estudo do Helicobacter, departamento da Federação Brasileira de Gastroenterologia, tendo sido realizado em Bento Gonçalves, RS, nos dias 12 a 15 de abril de 2011. Contou com a participação de 30 delegados provenientes das cinco regiões brasileiras e um convidado internacional, incluindo gastroenterologistas, patologistas, epidemiologistas e pediatras. Os participantes foram alocados em um dos cinco subgrupos do evento, a saber: *Helicobacter pylori,* dispepsia funcional e diagnóstico; *Helicobacter pylori* e câncer gástrico; *Helicobacter pylori* e afecções não-gastroduodenais; *Helicobacter pylori,* tratamento e retratamento, e, epidemiologia da infecção por *Helicobacter pylori* no Brasil. Após extensa discussão, todas as recomendações e conclusões emanadas tinham definidas a força da recomendações e seu grau de evidência científica. As conclusões de cada subgrupo foram referendadas em votação final com todos os participantes. Foi adotado como consensual as decisões que atingissem 70% ou mais de concordância entre os participantes. Este artigo apresenta as principais recomendações e conclusões para orientação aos profissionais brasileiros envolvidos com a infecção por *H. pylori*.

DESCRITORES - *Helicobacter pylori.* Infecções por Helicobacter. Dispepsia. Consenso.

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