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REVIEW ARTICLE

Periodontitis, Oral *Helicobacter pylori* Reservoirs, and Gastric Cancer: Implications for Adjunctive Periodontal Therapy

Michal Straka[1], Petra Borecová[1], Kamila Csóková[1], Erik Gerža[1], Isabella Julie James[2], Matej Straka[2]

1 Department of Dentistry, Faculty of Medicinae, Slovak Medical University, Bratislava, Slovakia, Limbova 14, 831 01 Bratislava, Slovakia
2 Private Praxis of Dentistry, Bratislava, Krížna 44, Slovakia, 831 08

Correspondence to: Michal Straka
Department of Dentistry, Faculty of Medicinae, Slovak Medical University, Bratislava, Slovakia, Limbova 14, 831 01 Bratislava, Slovakia
e-mail: michal.straka@szu.sk, mudrstraka@r3.roburnet.sk

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Abstract

In this review study, we address the epidemiological, causal, and clinical associations between the oral and gastric occurrence of *Helicobacter pylori* and its role in the etiopathogenesis of gastric cancer, gastritis, as well as peptic ulcer disease and dyspeptic disorders of the stomach and duodenum. We summarize and critically analyze numerous meta-analytical studies addressing the oral occurrence of *H. pylori* and its eradication from the stomach and oral cavity using conventional pharmacological eradication therapy. In the process of analysis, we examine whether the oral cavity can serve as a reservoir of *H. pylori* during reinfections of the gastric mucosa, while not all studies confirm the survival of *H. pylori* in the oral cavity. However, the majority of studies, including their meta-analytical outputs, conclude that *H. pylori* may survive in saliva and potentially persists in the oral cavity by exploiting the microaerophilic to anaerobic environment of periodontal pockets, as well as the structures of supra- and subgingival dental calculus and various locations of oral biofilms, which are inaccessible to both innate and adaptive immune defense mechanisms of the patient. While a minority of studies regard oral *H. pylori* as transient (Al-Ahmad, 2012), the weight of current evidence — particularly from PCR-based and co-culture studies (Scholz *et al.* 2025) — supports a biologically plausible reservoir role. The structures of periodontal pockets, oral biofilms, and dental calculi lack effective blood supply, moreover, these sites are not routinely accessible to home oral hygiene measures. For the removal and elimination of the mentioned structures, targeted periodontological treatment combined with various methodologies of professional oral hygiene is required. The elimination of *H. pylori* using these approaches has been confirmed by many studies, from which several clinically relevant therapeutic implications for clinical practice in dentistry and periodontology arise. These findings support a clinical recommendation, grounded in Cochrane-level meta-analytic evidence (OR 2.15, 95% CI 1.47–3.14; Ren *et al.* 2016), that dental practitioners

provide thorough periodontal treatment and eliminate the environment of periodontal pockets through comprehensive periodontal therapy combined with the removal of oral biofilms and dental calculi in patients with a diagnosed findingof *H. pylori* in the GIT who are undergoing pharmacological eradication treatment. In line with the observed improvement in gastric *H. pylori* eradication when periodontal therapy is added — with odds ratios of 2.15 (95% CI: 1.47–3.14) and 2.64–4.11 across independent meta-analyses — gastroenterologists, internists, and oncologists should systematically consider referring *H. pylori*-positive patients to dentists for periodontological and hygiene procedures, accompanied by regular recall appointments.

INTRODUCTION

More than 40 years ago, *Helicobacter pylori* was definitively identified as a main bacterial pathogen in the development of gastric cancer. In 1994, the International Agency for Research on Cancer (IARC/WHO) classified *H. pylori* as a **Group 1 carcinogen** for gastric cancer (Wroblewski *et al.* 2010). These findings clearly support the fact that for the treatment of gastric cancer, its elimination from the stomach and GIT is necessary. However, several studies confirm that the conventional medicinal triple-combination used for the eradication of *H. pylori* from the stomach does not remove its reservoirs in the oral cavity, which often leads to or may cause reinfection of the gastric mucosa during the swallowing of saliva and food. Although not all studies confirm oral survival — with Al-Ahmad (2012) characterising the presence as transient and attributable to PCR over-detection — the weight of current evidence, including viable co-culture data (Scholz *et al.* 2025), supports a biologically plausible reservoir role. Therefore, the aim of this review is to consolidate evidence on *H. pylori* survival in the oral microenvironments of periodontal pockets, biofilms, and dental calculi, and to formulate recommendations for its elimination through periodontal treatment in coordination with gastroenterological eradication therapy. Specifically, this review extends beyond the Cochrane analysis of Ren *et al.* (2016) and the meta-analysis of Öztürk (2021) by incorporating post-2021 co-culture viability data (Scholz *et al.* 2025), updated eradication prevention evidence (Ford *et al.* 2025), and a clinically actionable ≥4 mm pocket-depth referral threshold (Umeda *et al.* 2003) not foregrounded in prior syntheses.

Search strategy and study selection

A literature search was conducted in PubMed, Scopus, Web of Science covering publications from 1994 to 2025 using the following search terms: "*Helicobacter pylori*" AND "oral cavity" OR "periodontal" OR "dental plaque" AND "gastric cancer" OR "eradication" OR "reinfection". Studies were included if they reported on the association between oral *H. pylori*, periodontal disease, and gastric *H. pylori* infection or gastric cancer. Priority was given to meta-analyses, systematic reviews, and randomized controlled trials. Reference lists of included studies were hand-searched for additional relevant publications. A total of 47 references were included in the final review after screening; no formal PRISMA flow diagram was produced, consistent with the narrative review design.

EPIDEMIOLOGICAL ASSOCIATIONS

In an effort to detect mutual connections between periodontal diseases and gastric adenocarcinoma, several meta-analytical studies were carried out. Out of a total of 639 studies, 9 research papers were selected with a total number of 1,253 patients with gastric cancer in case-control studies and 1,631 in cohort studies with a number of 2,501 patients in the control sample. The conclusions of the study indicated that patients with periodontal disease had a 17% increased risk of gastric adenocarcinoma regardless of the diagnostic method for determining periodontal disease (RR = 1.17; 95% CI: 1.03–1.32). Upon the reported or confirmed occurrence of periodontal disease, the risk of stomach cancer rose to 34% (RR = 1.34; 95% CI: 1.06–1.69). The study states that the association between periodontal disease and the risk of developing gastric adenocarcinoma indicates that the infectious-inflammatory process involved in periodontitis may be related to the development of gastric cancer, and that further research into the oral-gastric microbiota and its role in gastric carcinogenesis is warranted (Aguiar *et al.* 2024). Another meta-analytical study compiled from 10 cohort papers stated that for periodontitis and gastrointestinal tract cancer, the risk ratio was 1.23 (95% CI: 1.10–1.37). Simultaneously, a meta-analysis of 9 cohort studies was performed, which found that periodontitis was associated with increased mortality from gastrointestinal tract cancer (HR = 1.59, 95% CI: 1.16–2.16), which means that patients with periodontitis have a 59% higher probability of death from GIT cancer (Zhang *et al.* 2020). Table 1.

Table 1 summarises the key meta-analytical and systematic evidence underpinning this review. For each study, the detection method used to identify *H. pylori* in oral and gastric compartments is specified, as these methods differ substantially in their sensitivity and biological interpretation: PCR-based methods detect bacterial DNA with high sensitivity but cannot distinguish viable from non-viable organisms, potentially overestimating true colonisation prevalence; culture-based methods confirm viability but are less sensitive and technically demanding; urea breath test (UBT) and histology serve as the standard clinical endpoints for gastric eradication. Effect sizes are reported as odds ratios (OR), relative risks (RR), or hazard ratios (HR) with 95% confidence intervals (CI). Footnotes (†, ‡, ►) flag results that require particular interpretive caution:

non-significant findings whose CIs cross 1.0, estimates affected by high between-study heterogeneity, and PCR-specific viability limitations. Readers are encouraged to consult the footnotes before drawing clinical inferences from individual rows.

GASTRIC CANCER

According to global data from 2020, gastric cancer accounts for 7.7% of all cancerrelated deaths. Out of 2.3 million new cancer cases in 2020, its incidence was 5.6% and it ranked fifth in the order of mortality, behind first breast cancer, second lung cancer, third colorectal carcinoma, and fourth prostate cancer (Sung *et al.* 2021). Gastric cancer is a multifactorial disease, in the etiology of which environmental as well as genetic factors are key, and which is often diagnosed only in its advanced stages (Carcas, 2014). Risk factors for the development of gastric cancer are obesity and increased intake of fats, nitrogen, and salt, genetic factors, premalignant lesions of the stomach, tobacco use, and alcoholism. Among genetic and familial predispositions, there were various stomach diseases such as polyps, gastric ulcers, stomach atrophies, and esophageal cancer (Yaghoobi *et al.* 2010). Familial occurrence of gastric cancer increases with the degree of relationship in the respective lineage or family. For example, a study from Turkey reported a 14% occurrence of cancer in siblings and a 12% occurrence in parents (Bakir *et al.* 2003).

A fundamental or breakthrough finding was the identification of the bacterium *Helicobacter pylori* as one of the main etiopathogenetic factors in the onset and course of this disease (Yusefi *et al.* 2018). *Helicobacter pylori* is a microaerophilic, Gram-negative, rod-shaped bacterium that resides beneath the gastric mucus layer on the surface of epithelial cells. Gastric infection by this organism causes inflammation of the gastric mucosa, which can lead to gastritis, duodenal or gastric ulcers, and in some subjects, to gastric carcinoma (Cześnikiewicz-Guzik *et al.* 2004). The connection between gastric cancer and the Gram-negative microaerophilic bacterium *Helicobacter pylori* has been confirmed by several independent studies, with Uemura *et al.* (2001) stating that gastric cancer occurred in 3% of subjects with *H. pylori*, compared to zero occurrence in the control group that was not infected with *H. pylori*. The human stomach is the natural source and reservoir of *Helicobacter pylori*, with which approximately half of the population is infected; however, its prevalence fell between 1980 and 2022 from approximately 55% to 43.9% (Wu & Liou, 2024). *H. pylori* infections usually occur in childhood through direct person-to-person contact or contaminated water, i.e., through oral-oral, fecal-oral, and gastric-oral transmission of bacteria (Duan *et al.* 2025). In the development of gastric cancer, a key role is played by its genetic makeup, particularly the presence of gene A, which is a cytotoxin-associated gene known by the abbreviation **CagA**. This protein penetrates the gastric mucosa and its epithelial cells, where it induces apoptosis, cytoskeletal remodeling, and subsequent phenotypic transformation associated with **epithelial-mesenchymal transition**, along with stimulation of proliferative cell growth (Duan *et al.* 2025). Cag is encoded by a DNA segment composed of 27 to 31 genes, and its expression associates with gastric ulcers and is known as **cag PAI or cag+**, while individual *H. pylori* strains are often divided into strains containing CagA and those not containing CagA. CagA-positive strains stimulate the onset of gastritis and carcinoma of the distal part of the stomach (Wroblewski *et al.* 2023).

ORAL OCCURRENCE OF *H. PYLORI*

Many studies suggest that the oral occurrence of *H. pylori* can be a source of primary infection, however,this was not confirmed by all studies (Liu *et al.* 2009; Silva *et al.* 2009; Payao *et al.* 2016). A pioneering study of great significance was the work of Japanese researchers who investigated whether the oral occurrence of *H. pylori* could adversely affect the result of *H. pylori* eradication therapy in the stomach. The conclusions were of a fundamental nature and confirmed that the success of bacterial eradication from the stomach was statistically significantly lower in subjects with oral occurrence of *H. pylori* than in patients with a negative finding in the mouth 1 month after treatment ($p = 0.0028$). Thus, the oral occurrence of *H. pylori* influenced the outcome of eradication therapy and is associated with the recurrence of gastric cancer. Oral detection of *H. pylori* through PCR can be considered a causal etiopathogenetic factor in recurrent or refractory forms of gastric carcinoma (Miyabayashi *et al.* 2000).

Helicobacter pylori has been detected in several oral microenvironments and, of course, also in saliva, while being co-cultured with several oral pathogenic and commensal bacteria: *Streptococcus mutans, Streptococcus oralis, Actinomyces naeslundii, Lacticaseibacillus casei*, and *Candida dubliniensis*. This study confirmed that *H. pylori* can survive in human saliva in the presence of certain oral bacteria (Scholz *et al.* 2025). Another study of Polish provenance found a 79% reduction of *H. pylori* after the frequently used triple-combination medicinal treatment of *H. pylori* in the stomach, but it did not affect the oral occurrence of this bacterium. Simultaneously, no relationship was found between gastric and oral *H. pylori* using genetic profiling by random amplification of polymorphic DNA (Czesnikiewicz-Guzik, 2007). The occurrence of *H. pylori* in oral environments is relatively dependent on different populations. Several studies found that in developed Western countries, *H. pylori* was not a reservoir in oral biofilms nor on the surfaces of dentures; however, its high occurrence in plaques was found in developing countries and was an important reservoir for

Tab. 1. Key meta-analytical evidence on oral *Helicobacter pylori*, periodontitis, and adjunctive periodontal treatment in *H. pylori* eradication.

Study (year)	Focus	Design / n	Detection method – oral / gastric	Main outcome measure	Key quantitative result	Interpretation
Navabi *et al.* 2011	Co-infection of gastric and dental plaque *H. pylori*	Systematic review & meta-analysis; 23 studies, 1,861 patients	**Oral:** PCR (primary method across pooled studies); culture in subset ► PCR may detect non-viable DNA / **Gastric:** urease test and/or histology (varied by primary study)	Prevalence of simultaneous gastric and dental plaque infection	Co-infection prevalence 49.7% (95% CI: 16–83.4%); agreement between dental and gastric status ≈82%	Nearly half of patients with gastric *H. pylori* also harbour the bacterium in dental plaque, supporting the oral reservoir hypothesis. Wide CI reflects high inter-study heterogeneity in detection methods.
Aguiar *et al.* 2024	Periodontal disease and gastric adenocarcinoma risk	Systematic review & meta-analysis; 9 case-control + cohort studies	**Oral:** Periodontal diagnosis (clinical; no *H. pylori* detection) / **Gastric:** Not applicable — outcome is cancer incidence, not bacterial detection	Relative risk (RR) of gastric adenocarcinoma	RR 1.17 (95% CI: 1.03–1.32) overall; RR 1.34 (95% CI: 1.06–1.69) when periodontal disease confirmed	Periodontal disease is associated with a 17–34% higher risk of gastric adenocarcinoma. *H. pylori* status not directly measured in this analysis.
Zhang *et al.* 2020	Periodontitis and GI cancer incidence/ mortality	Meta-analysis; 10 cohort (incidence), 9 cohort (mortality)	**Oral:** Periodontal diagnosis (clinical) / **Gastric:** Cancer registry / ICD coding — no *H. pylori* detection	RR for GI cancers; HR for GI cancer mortality	GI cancer incidence RR 1.23 (95% CI: 1.10–1.37); GI cancer mortality HR 1.59 (95% CI: 1.16–2.16)	Periodontitis associated with higher GI cancer incidence and ~59% higher GI cancer mortality. Indirect association — *H. pylori* not the measured mediator.
Tsimpiris *et al.* 2023	Periodontitis and *H. pylori* (oral and gastric)	Meta-analysis; 4 observational studies, 818 subjects	**Oral:** PCR and/or culture (mixed across 4 pooled studies) ► *Method inconsistency may contribute to non-significance* / **Gastric:** Urease breath test (UBT) and/or histology	OR for oral and gastric *H. pylori* in periodontitis	Oral *H. pylori*: OR 1.87 (95% CI: 0.85–4.10; ***p* = 0.12** †); gastric *H. pylori*: OR 1.80 (95% CI: 0.82–3.95; ***p* = 0.15** †)	Trends toward higher odds of *H. pylori* in periodontitis, but **results are not statistically significant** and CIs cross 1.0. Interpret as exploratory only.
Ren *et al.* 2016	Periodontal therapy + gastric eradication vs. eradication alone	Cochrane review; 7 RCTs, 691 participants	**Oral:** Post-treatment assessment by PCR or culture (varied by RCT) / **Gastric:** Urea breath test (UBT) as primary eradication endpoint across RCTs	OR for gastric eradication and non-recurrence	Gastric eradication OR 2.15 (95% CI: 1.47–3.14; $p < 0.0001$)	Adjunctive periodontal therapy more than doubles the odds of gastric *H. pylori* eradication. Highest-quality interventional evidence (Cochrane).
Öztürk 2021	Updated meta-analysis of periodontal therapy as adjunct	Meta-analysis; 6–10 RCTs, 541–909 participants	**Oral:** PCR or culture (primary RCT-level methods; heterogeneous) ‡ / **Gastric:** UBT (standard eradication endpoint across included RCTs)	OR for gastric eradication and non-recurrence	Fixed-effects OR 3.86 (95% CI: 2.55–5.84); random-effects OR **4.11** (95% CI: 1.91–8.87; $p = 0.01$) ‡; updated 10-study OR **2.64** ($p < 0.0001$) after excluding Chinese studies	Periodontal treatment plus systemic therapy improves gastric eradication odds ~2.5–4-fold. ‡ Significant between-study heterogeneity; random-effects estimate preferred.

Study (year)	Focus	Design / n	Detection method – oral / gastric	Main outcome measure	Key quantitative result	Interpretation
Inchingolo *et al.* 2025	Non-surgical periodontal treatment and oral *H. pylori*	Systematic review of 10 clinical studies	**Oral:** PCR and salivary sampling ► *Viability of detected organisms not confirmed in all studies* / **Gastric:** UBT and/or histology (varied by primary study)	Change in oral *H. pylori* levels; recurrence	Supra- and subgingival calculus removal plus mechanical debridement reduced salivary *H. pylori* and recurrence; benefit enhanced by antiseptic rinses	Mechanical periodontal therapy effectively reduces the oral reservoir and supports systemic eradication.
Ford *et al.* 2025	Gastric *H. pylori* eradication and gastric cancer prevention	Systematic review & meta-analysis; 11 RCTs	**Oral:** Not assessed / **Gastric:** UBT, stool antigen test, or histology (standard per individual RCT protocol)	RR of gastric cancer after eradication therapy	Eradication therapy significantly reduces gastric cancer incidence in *H. pylori*-positive individuals (consistent across designs)	Strengthens the rationale for maximising eradication success, including by addressing oral reservoirs.

† Tsimpiris et al. (2023): Both primary outcomes are non-significant ($p > 0.05$; 95% CIs cross 1.0). These results should be interpreted as trends only and do not independently justify clinical recommendations.
‡ Öztürk (2021): Considerable between-study heterogeneity reported; random-effects model (OR 4.11) is the appropriate estimate. The more conservative updated analysis excluding Chinese studies (OR 2.64, $p < 0.0001$) is preferred for generalisation beyond East Asian populations.
► PCR-based oral detection across multiple studies may identify non-viable *H. pylori* DNA, leading to overestimation of true colonisation prevalence. Culture-based confirmation of viable organisms is methodologically more stringent but was not uniformly applied (Limitations section; Al-Ahmad, 2012).

Helicobacter pylori. A Polish study of dyspeptic patients and patients with duodenal ulcers found that the oral cavity can act as a persistent reservoir of *H. pylori* and that successful eradication of *H. pylori* from the stomach by systemic therapy fails in the sense of the persistence of. *H. pylori* in the oral cavity, which could be a potential source of gastric reinfection in these patients (Pytko-Polonczyk *et al.* 1996). While analyzing samples of the stomach and saliva from 400 symptomatic patients in the Indian state of Hyderabad, oral-oral transmission of *H. pylori* was detected, but also through food prepared in unhygienic conditions as well as transmission through municipal water (Ahmed *et al.* 2006). The aim of the study by Gebara *et al.* (2004) was to evaluate the prevalence of PCR-diagnosed *H. pylori* in the oral cavity of patients with gingivitis and periodontitis with a positive test for this bacterium in the stomach. The study found that a high percentage of patients harbored *H. pylori* in the mouth. The bacterium was identified by the PCR method in saliva, supragingival and subgingival plaque, which suggests that these sites can be considered reservoirs for *H. pylori* in patients positive for the urease test, while 43.3% of patients harbored *H. pylori* in the oral cavity (Gebara *et al.* 2004). Despite all the mentioned findings regarding the presence of *H. pylori* in the oral cavity, there is no unified opinion among gastroenterologists regarding its infectivity and role in the GIT, and several questions still remain unanswered. The main question remains: How does gastric infection occur? Does *H. pylori* reside in the oral cavity and then reach the stomach via other GIT organs? What role does the oral environment play in this process? Is the oral cavity a primary or permanent source of *H. pylori* or is it merely a secondary site of colonization? In principle, if the route of *H. pylori* infection into the stomach cannot be uncovered, medicine will find it difficult to deal with this infection (Yee, 2017). In the next subchapter, we can seek answers to these questions, while the attention of researchers focuses on patients with periodontitis and periodontal pockets deeper than 5 mm, which formally and realistically provide *H. pylori* with a perfect anaerobic or microaerophilic environment isolated from the surroundings.

ASSOCIATIONS BETWEEN *HELICOBACTER PYLORI* GENOTYPES IN GASTRIC AND ORAL LOCATIONS

The subject of several studies was to identify whether gastric and oral findings are genetically related or, respectively, whether they are caused by identical homologous strains. In a study by authors Román-Román

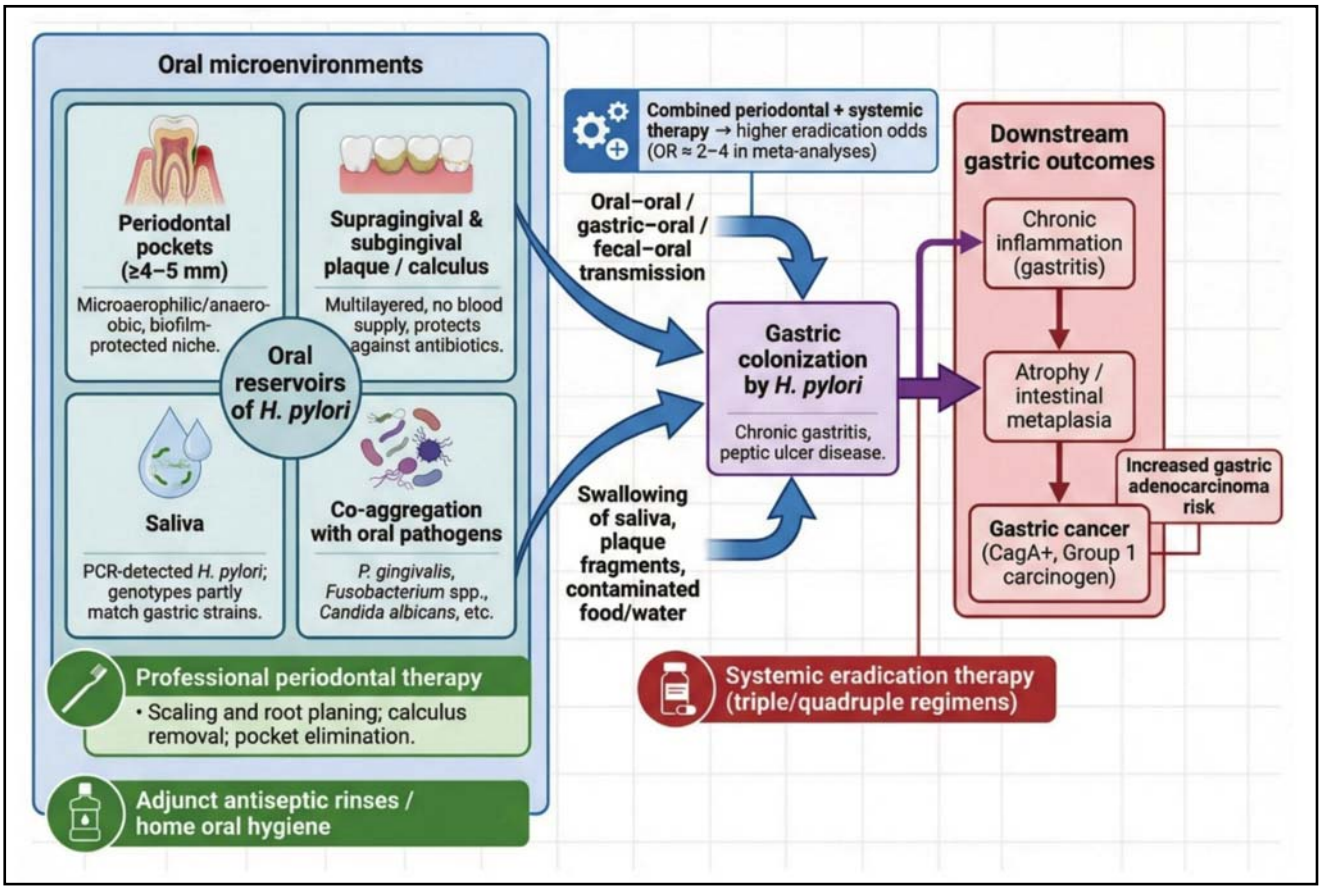

Fig. 1. Proposed oral–gastric pathway of *Helicobacter pylori* and points of intervention by periodontal therapy.
Arrows indicate three established transmission routes: oral-oral, fecal-oral, and gastro-oral (Duan et al., 2025). Periodontal therapy intervention points include: (1) supra- and subgingival calculus removal; (2) scaling and root planing of periodontal pockets ≥4 mm; (3) antiseptic oral rinses; (4) structured home oral hygiene. Adjunctive periodontal therapy at these sites improves gastric H. pylori eradication odds by 2.15–4.11-fold compared to pharmacological treatment alone (Ren et al., 2016; Öztürk, 2021).
Note: The pathway depicted represents a synthesis of current evidence and is proposed rather than definitively established; the role of the oral cavity as a primary versus secondary colonisation site remains under investigation (Al-Ahmad, 2012; Yee, 2017).

et al. (2013), *vacA* genotypes of *Helicobacter pylori* in saliva and biopsies from the gastric mucosa in patients with gastric ulcers and chronic gastritis were examined. A total of 162 patients with chronic gastritis and 34 with gastric ulcers were examined, and saliva samples and biopsies were collected from each patient. *H. pylori* DNA was identified by conventional PCR, and nested PCR was used for *vacA* genotyping. In one or both genotypes, *H. pylori vacAs1m1* or *s1m2* were detected in saliva in 41.5% of patients with chronic gastritis. Genotypes found in the saliva and biopsy of the same patient had a 51.1% agreement. Genotypes *s1m1/s1m2*, alone or together, are found simultaneously in the saliva and gastric biopsy of the same patient. These results suggest that *H. pylori* reaches the oral cavity in various ways and that saliva may be a transmitting and reinfection vector (Román-Román *et al.* 2013).

A more extensive study of 300 bioptic samples of the stomach, saliva, dental plaque, and stool examined the common genotypes of *H. pylori* in each patient. The prevalence of *H. pylori* among patients with gastric cancer was 80%, in patients with peptic ulcers it was 90.47%, and in patients with dyspeptic ulcer disorder 74.13%. The evaluation of vacA and cagA genotypes showed 6 differences between stomach biopsies and saliva samples and 11 differences between stomach and stool samples, while high pathogenicity of *H. pylori* was confirmed in 94.42% of patients who were cagA positive. The high similarity of samples from the stomach and stool, as well as saliva, supports the thesis that the main transmission route lies in the fecal-oral transmission of *H. pylori* and its presence in saliva can serve as a reservoir for reinfection. Furthermore, multiple genotypes of *H. pylori* may coexist within a single patient (Momtaz *et al.* 2012). Figure 1.

ASSOCIATIONS BETWEEN PERIODONTITIS AND THE ORAL OCCURRENCE OF *H. PYLORI*

Helicobacter pylori is transmitted by oral-oral, gastro-oral, and fecal-oral routes, and in 1994 it was classified by IARC as a **Group 1 carcinogen**, and oral *H. pylori* is considered a risk factor for the reoccurrence of *H. pylori*

infection in the stomach. Some studies have demonstrated that *H. pylori* in the oral cavity could adversely affect the clinical outcome of eradication therapy (Miyabayashi *et al.* 2000; Zhang *et al.* 2022). A certain progress in the issue was brought by a meta-analytical study compiled from 1,861 patients in 23 studies, which confirmed the infection rate in the stomach and in the oral biofilm in almost half of the patients (49.7%) (Navabi *et al.* 2011). However, some studies presented the occurrence of *H. pylori* in the oral cavity without direct correlations with gastric infection (Aksit Bicak *et al.* 2017). In conclusion, the majority of studies report positive findings of *H. pylori* in the oral environment. However, molecular biology evidence suggests that these findings do not directly reflect the survival ability of the microbial pathogen in the oral environment. Some studies have established factors of potential survival in the oral cavity such that *H. pylori* can "hide" in oral biofilms, carious cavities, and in the environment of periodontal pockets and thus be the cause of reinfection after its eradication from the stomach (Zhang *et al.* 2022). Several studies have also confirmed synergistic and symbiotic relationships with other oral pathogens such as *Porphyromonas gingivalis* (Kadota *et al.* 2020), *Fusobacterium gingivalis* (Andersen *et al.* 1998), or *Candida albicans* (Palencia *et al.* 2022). Some studies state a connection between the occurrence of *H. pylori* in the stomach and in the oral cavity (Oshowo *et al.* 1998; Parsonnet *et al.* 1999), although the study by authors Song *et al.* (2000) summarized that the oral occurrence of *H. pylori* in 97% of tested patients with a characteristic distribution was independent of gastric *H. pylori* infection.

Various studies inform that periodontal pockets are, or may be, a significant extra-gastric source or reservoir of *H. pylori* after eradication treatment. The conclusions of the study state that the oral cavity is an extra-gastric reservoir of *H. pylori* when it is affected by periodontal disease, and that periodontal disease correlates with gastric *H. pylori* infection (Azzi *et al.* 2017). Another study found, through PCR testing in the oral cavity, a high prevalence of *H. pylori* in 35.1% of patients, and patients with periodontitis and infection in the GIT had a *H. pylori* prevalence of 46.6%.

Critically, among patients with confirmed gastric or duodenal *H. pylori* infection, 41.2% had periodontal pockets ≥4 mm, compared to only 9.1% in those without pockets — a 4.5-fold difference (Umeda *et al.* 2003). This threshold of ≥4 mm is consistent with the clinical definition of periodontitis and identifies the specific patient subgroup in whom oral *H. pylori* reservoirs are most likely to undermine systemic eradication therapy. These data provide the most direct empirical basis for the referral recommendation stated in the Conclusions: gastroenterologists treating *H. pylori*-positive patients should prioritize those with periodontal pocket depths ≥4 mm for urgent periodontal evaluation. The subsequent meta-analytical evidence (Tsimpiris *et al.* 2023; Ren *et al.* 2016; Öztürk, 2021) further supports this clinical pathway, though with varying levels of statistical certainty.

TREATMENT AND TREATMENT STRATEGIES FOR GASTRIC CANCER

Gastric cancer represents a serious, incompletely addressed or resolved clinical problem with an incidence of more than 1 million on a global scale. A significant portion of patients with gastric cancer is associated with various pathogens such as *Helicobacter pylori* and Epstein-Barr virus (EBV). In its treatment, therapeutic strategies for prevention, prophylaxis, and the elimination of gastric cancer development are important, such as the eradication of *H. pylori*, which has helped alleviate or prevent the massive and rapid progression of cancerous growth. In Stage IA and IB, after surgical and complex treatment, the 5-year survival rate is 60 to 80% of subjects, which, however, is not the case for Stage III disease, where the survival rate is only 15 to 50% of treated patients (Sexton *et al.* 2020). Complex treatment of gastric cancer includes, and in practice also applies, several molecular and anti-infection treatment strategies, some of which, such as the eradication of *Helicobacter pylori* in the organism and the oral cavity, is also a matter of dentistry. These new findings, measures, and treatment strategies will subsequently be analyzed and reviewed.

One of the main strategies for the treatment of gastric cancer is eradication therapy for *Helicobacter pylori* through a classic medicinal triple-combination or newer quadruple-combinations of drugs. In a meta-analytical study consisting of 11 randomized controlled trials, the influence of medicinal eradication on the incidence of gastric cancer was monitored in adults with a positive test for *H. pylori* without gastric neoplasia at the beginning of treatment or in patients with a positive test for *H. pylori* with gastric neoplasia. The control group received placebo or no eradication. The results of the study provided further evidence that the administration of eradication therapy prevents gastric cancer in individuals with a positive test for *H. pylori*, while the results are consistent even among studies of different designs (Ford *et al.* 2025).

The issue of the necessity of eradicating *Helicobacter pylori* from the oral cavity and from its various environments or oral structures directly concerns dentists, and in the near future, we can expect increased demands and requirements for the introduction of *H. pylori* eradication in clinical dental practice. Currently, there is no consensus, or definitive conclusions have not been formulated as to whether oral *H. pylori* infection exists and whether its presence in the oral cavity is decisive for the further course of the disease. In clinical practice, the established methodology is that negative results of the urea breath test indicate the cure of *H. pylori* infection. However, some studies provide compelling

Tab. 2. Oral microenvironments harboring *Helicobacter pylori*, supporting evidence, and implications for periodontal therapy

Oral site / factor	Supporting evidence (examples from article)	Key findings (as described)	Clinical implications you already state
Supragingival and subgingival plaque	Gebara *et al.* 2004; Umeda *et al.* 2003; Pytko-Polonczyk *et al.* 1996; Navabi *et al.* 2011	PCR-detected *H. pylori* in saliva, supra and subgingival plaque; 43.3% oral positivity in ureasepositive patients; higher prevalence in patients with periodontal pockets ≥4 mm; coinfection stomach–plaque in ~50% of patients	Professional supra and subgingival calculus removal plus scaling/ root planing is required; systemic therapy alone does not clear plaque reservoirs.
Periodontal pockets (≥4–5 mm)	Umeda *et al.* 2003; Azzi *et al.* 2017; Tsimpiris *et al.* 2023	Periodontal pockets provide microaerophilic/anaerobic, biofilmprotected niche; 41.2% of patients with gastric/duodenal infection had pockets ≥4 mm vs. 9.1% without pockets; odds of oral and gastric *H. pylori* higher in chronic periodontitis (OR 1.87 and 1.80, though not statistically significant)	Elimination of active pockets is a core target; periodontal debridement disrupts the protected niche that systemic antibiotics cannot reach.
Dental calculus (supra and subgingival)	Pytko-Polonczyk *et al.* 1996; Zhang *et al.* 2022; Inchingolo *et al.* 2025	Calculus and biofilm structures lack blood supply, are multilayered, and shield bacteria from host defenses and systemic drugs; calculus removal shown to reduce salivary *H. pylori* and recurrence	Complete removal of calculus is essential during gastric eradication therapy; supportive periodontal treatment (scaling, deep scaling, root planing) reduces oral reservoir and gastric reinfection risk.
Saliva	Momtaz *et al.* 2012; Scholz *et al.* 2025; Ahmed *et al.* 2006; Román-Román *et al.* 2013	*H. pylori* DNA found in saliva; coculture studies show survival in saliva with oral species (*Streptococcus, Actinomyces, Candida*); saliva genotypes show ~51% concordance with gastric strains; fecal–oral and oral–oral transmission routes documented	Emphasizes need for wholemouth hygiene (toothbrushing technique, tongue cleaning, antiseptic rinses) when coordinating with medical eradication regimes.
Coaggregation with oral pathogens	Kadota *et al.* 2020; Andersen *et al.* 1998; Palencia *et al.* 2021; Zhang *et al.* 2022	*H. pylori* coaggregates with *P. gingivalis*, *Fusobacterium* spp., and *Candida albicans*; synergistic/ symbiotic relationships in biofilms; potential impact on virulence and persistence	Periodontal therapy targeting key periodontopathogens (e.g., P. gingivalis) may also indirectly reduce *H. pylori* survival in subgingival biofilms.
Oral hygiene and adjunctive treatment	Yuksel Sert *et al.* 2019; Ren *et al.* 2016; Öztürk 2021; Inchingolo *et al.* 2025	Combined periodontal + systemic therapy improves gastric eradication odds (OR ≈ 2.15–4.11) and lowers recurrence; better outcomes when plaque control is maintained	Strongly supports your recommendations for simultaneous medical eradication and professional plus home oral hygiene, including structured recall.

evidence that a negative urea breath test may still be associated with the presence of *H. pylori* in the oral cavity. These conclusions are based on studies in which *H. pylori* was detected in the oral cavity of patients with a negative **urea breath test (UBT)** result who showed no evidence of gastric reflux of *H. pylori* (Yee, 2016; Wang *et al.* 2014). These findings support the notion that successful eradication of gastric *H. pylori* infection, as indicated by a negative urea breath test, does not necessarily guarantee the prevention of reinfection. However, the results of some studies question the relevance of oral *H. pylori* in relation to gastric infection and challenge the potentially misleading assumption that *H. pylori* is located in the human oral cavity, suggesting that this bacterium should be regarded as transient and independent of oral health status, and they conclude that, to date, positive PCR results for *H. pylori* in the oral cavity may have been overestimated and insufficiently critically interpreted in the literature (Al-Ahmad, 2012). In contrast, opposing views based on studies from several reputable research centers argue against these conclusions, criticizing what they describe as premature assertion that "the oral cavity is not a site of colonization." These studies also highlight

the limitations of conventional culture-based methods for isolating *H. pylori* from the oral cavity, which may have reached their methodological limits (Yee, 2016).

Despite ongoing uncertainties and the unresolved nature of the issue regarding the occurrence of *H. pylori* in the oral cavity, more recent treatment procedures recommend simultaneous eradication from both the stomach and the oral cavity, which may more effectively eliminate *H. pylori* infection (Abadi *et al.* 2014). The hypothesis that oral eradication provides a significant beneficial effect on gastric *H. pylori* eradication is supported by several dozen studies, from which selected results are presented. Regarding the issue of oral *H. pylori* eradication, several clinical studies have been conducted investigating and evaluating various oral-depurative and disinfectant agents and methods. In a clinical study with 98 patients, the beneficial effect of periodontological treatment on the rate of *H. pylori* eradication in the stomach was confirmed, which improved if adequate plaque control was maintained ($p = 0.02$). Triple-combination therapy combined with periodontal treatment yielded a 64.7% eradication rate versus 51.1% with triple therapy alone ($p = 0.17$). **The $p = 0.02$ finding reflects a within-group subgroup analysis (adequate vs. inadequate plaque control) and should not be interpreted as a between-group treatment effect.** Within the combined-treatment group, patients maintaining adequate plaque control achieved significantly higher eradication rates ($p = 0.02$), indicating that efficacy is contingent on patient compliance

In a meta-analytical study including 7 smaller RCT studies with 691 subjects, it was found that periodontological depurative treatment combined with *H. pylori* eradication therapy increased the rate of gastric *H. pylori* eradication compared to eradication therapy alone with the following results (OR = 2.15; 95% CI: 1.47 to 3.14; $p < 0.0001$). This indicates that combined oral and gastric eradication more than doubled the odds of eradicating *H. pylori* from the stomach (approximately a 115% increase in odds). (Ren *et al.* 2016). These results represent good motivational prerequisites for simultaneous gastric and oral periodontological eradication of *H. pylori*.

A meta-analytical study with 10 included papers evaluated the benefits of non-surgical periodontal treatment for the eradication of *Helicobacter pylori* in the oral cavity. Supportive periodontological treatment included procedures for the removal of dental calculus and plaque, mechanical and depurative treatment of the root surface (scaling, deep scaling, root planing), and oral rinses. The study conclusions indicated that simultaneous conservative periodontal therapy combined with pharmacological treatment of *H. pylori* reduces bacterial recurrence. Supra- and subgingival removal of dental calculus was demonstrated to be the most effective periodontal intervention, as it reduced salivary *H. pylori* levels and minimized the oral reservoir, which represents a key factor in reinfection. Favorable outcomes of mechanical debridement were further enhanced by adjunctive therapies, including oral rinses with antiseptic solutions (Inchingolo *et al.* 2025).

Another meta-analytical study provided relevant data on the effect of professional periodontal therapy on the systemic eradication of *H. pylori* in the stomach. The study demonstrated that simultaneous periodontal treatment procedures added to conventional systemic eradication significantly improved gastric *H. pylori* eradication. The resulting statistical processing indicated that the combined OR with the fixed-effects model was 3.86 (95% CI [2.55; 5.84]) and with the random-effects model 4.11 ([1.91; 8.87 p-value = 0.01]). These two types of models were used due to the considerable heterogeneity between studies, where it is better to apply the random-effects model. Due to considerable between-study heterogeneity, the random-effects model is the preferred estimate (OR 4.11; 95% CI: 1.91–8.87; $p = 0.01$, 6 studies). The updated analysis excluding Chinese studies yielded a more conservative but still highly significant estimate (OR 2.64; $p < 0.0001$, 10 studies), which is the recommended figure for generalization beyond East Asian populations, indicating that the odds of successful gastric *H. pylori* eradication were approximately four times higher when concurrent periodontal treatment was provided. The updated study, after excluding Chinese studies, demonstrated for 10 studies the following results of. *H. pylori* eradication in the stomach: (OR 2.64, p-value < 0.0001). That is, the odds of successful gastric eradication were 2.64 times higher with adjunctive periodontal treatment (OR = 2.64, $p < 0.0001$). The general conclusions of the mentioned studies suggest that conventional pharmacological treatment of *H. pylori* is not effective against *H. pylori* in dental plaque, which is multi-layered and without blood supply, and the bacteria contained within it are protected against exogenous sources, against immunity, and medicinal therapy. Only its mechanical removal by means of professional and home hygiene can eliminate the occurrence of *H. pylori* from the oral cavity.

Table 2. Each row represents a distinct oral site or biological factor in which *H. pylori* has been detected or shown to survive; the supporting evidence column cites only studies already reviewed in this article. The "Key findings" column summarises the data as reported by those studies; the "Clinical implications" column maps each finding to the corresponding therapeutic action described in the Conclusions. The Tsimpiris *et al.* (2023) data in row 2 (periodontal pockets) carry non-significant p-values (0.12 and 0.15) and should be interpreted as exploratory trends only; the therapeutic rationale for targeting pockets ≥4 mm rests primarily on the mechanistic evidence (Umeda *et al.* 2003) and the interventional meta-analyses (Ren *et al.* 2016; Öztürk, 2021).

Limitations

This narrative review has several limitations. First, as a non-systematic review, the selection of studies may be subject to selection bias. Second, the meta-analyses summarized herein exhibit considerable heterogeneity, as noted by Öztürk (2021), who reported significant between-study heterogeneity necessitating random-effects modeling. Third, although current evidence for the periodontitis–*H. pylori* association is suggestive rather than definitive (Tsimpiris *et al.* 2023: OR 1.87 and 1.80, $p > 0.05$), the mechanistic rationale and therapeutic benefit data (OR 2.15–4.11) support eliminating active pockets as part of the eradication strategy; the detection of oral *H. pylori* varied across studies — PCR-based methods (used in Gebara *et al.* 2004; Umeda *et al.* 2003; Román-Román *et al.* 2013) have higher sensitivity but may detect non-viable DNA, while culture-based methods (highlighted by Al-Ahmad, 2012) have lower sensitivity but confirm viable organisms. This methodological discrepancy may account for divergent prevalence estimates (ranging from 35% to 97% across the studies reviewed). Fourth, the Tsimpiris *et al.* (2023) meta-analysis — a central reference for the periodontitis–*H. pylori* link — reported non-significant p-values (0.12 and 0.15), and the confidence intervals for both oral and gastric associations crossed 1.0, warranting cautious interpretation. Finally, geographic and socioeconomic confounders may influence the periodontitis–gastric cancer association independently of *H. pylori*, as the manuscript acknowledges differing oral reservoir prevalence between developed and developing countries

CONCLUSIONS FOR CLINICAL PRACTICE

1. Based on the findings of the above-mentioned studies, **current meta-analytic evidence supports close interdisciplinary collaboration** between dentists and periodontists with gastroenterologists, oncologists, internists, and general practitioners in the management of patients with dyspeptic syndrome, gastritis, gastric and duodenal ulcers, and gastric and duodenal cancer. This position is consistent with Cochrane-level data (OR 2.15; Ren *et al.* 2016) and is further corroborated by the conservative cross-population estimate of OR 2.64 (Öztürk, 2021).
2. During pharmacological eradication therapy of *Helicobacter pylori* from the GIT, simultaneous professional comprehensive conservative dental treatment should be ensured in cooperation with dental practitioners. This includes complete removal of dental calculus, infected root cementum, and oral biofilms, along with the implementation of targeted home oral hygiene measures.
3. In patients with inflammatory periodontal diseases, effective periodontal therapy should be instituted to eliminate active periodontal pockets. Combined periodontal treatment should ensure disruption of the subgingival microaerophilic and anaerobic microenvironment that enables the survival of *H. pylori* in the oral cavity.
4. In this patient population, a long-term regimen of regular professional and home oral hygiene should be implemented

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