PERIODONTAL INFLAMMATION AND GASTRIC PATHOLOGY: MICROBIAL, IMMUNE, AND CLINICAL CONNECTIONS

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Abstract

Background: Periodontitis is a chronic, dysbiosis-driven inflammatory disease with systemic immune and inflammatory footprints. Major gastric diseases—including *Helicobacter pylori*–associated gastritis, peptic ulcer disease, and gastric cancer—also evolve within an inflammation-shaped mucosal ecosystem. Objective: To summarize current evidence connecting periodontal inflammation with gastric outcomes and to identify clinically actionable signals and research gaps. Results: Observational studies and meta-analyses generally report higher odds of gastric *H. pylori* infection in individuals with periodontitis, while oral detection of *H. pylori* (especially in dental plaque) is frequent but method-dependent and does not prove viable colonization. Systematic reviews of randomized trials suggest that adjunctive non-surgical periodontal therapy delivered alongside eradication regimens can increase eradication success and may reduce recurrence, supporting (but not confirming) an oral reservoir contribution in selected patients. Periodontal assessment should complement, not replace, guideline-based eradication and test-of-cure, and may be prioritized in practice after repeated treatment failure episodes. Evidence linking periodontitis with chronic gastritis, atrophic changes, or peptic ulcer disease is less robust and is dominated by cross-sectional designs with incomplete control of NSAID exposure, smoking, socioeconomic position, and metabolic comorbidity. For gastric cancer, pooled observational data indicate small risk elevations with substantial heterogeneity and potential reverse causality; emerging genetic approaches have reported null or inconclusive causal signals. Conclusions: The oral–gastric connection is biologically plausible and most consistently supported for *H. pylori*–related endpoints, whereas causality for broader gastric outcomes remains unproven. Standardized periodontal phenotyping, guideline-consistent gastric endpoints, and contemporary multicenter trials are needed to define which high-risk subgroups benefit from integrated dental–gastroenterology management.

Keywords: periodontitis; *Helicobacter pylori*; gastritis; peptic ulcer disease; gastric cancer

1. Introduction

Periodontitis is a chronic, biofilm-related inflammatory disease marked by the progressive destruction of the tissues supporting the teeth and, ultimately, tooth loss [1]. Beyond its local effects, periodontitis is increasingly seen as a dysbiosis-driven condition where a permissive inflammatory environment sustains microbial imbalance and worsens tissue damage, with potential systemic effects through inflammatory mediators and intermittent bacteremia [2]. From a public health standpoint, its impact is significant: current Global Burden of Disease estimates report around 1.1 billion cases of severe periodontitis worldwide in 2019, with numbers continuing to rise over recent decades [3]. Simultaneously, gastric diseases—especially *Helicobacter pylori*–related gastritis, peptic ulcer disease, and gastric adenocarcinoma—remain leading causes of illness and death worldwide, emphasizing the importance of prevention and long-term risk reduction [4, 5].

H. pylori infection acts as a key biological link between oral and gastric diseases. Although the overall prevalence appears to be decreasing globally, combined estimates indicate that a

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significant proportion of the world's population carries *H. pylori*, with notable differences across regions and socioeconomic groups [6]. In clinical settings, successful eradication is increasingly difficult due to rising antibiotic resistance, and guidelines emphasize the importance of carefully selecting treatment regimens and implementing strategies to boost eradication rates and reduce the risk of reinfection [4]. Meanwhile, gastric cancer development is often described as a multistep process where chronic inflammation leads to atrophic changes, intestinal metaplasia, dysplasia, and eventually invasive cancer—the "precancerous cascade" that forms the basis of many prevention strategies [7]. Any factor that prolongs or repeats gastric infection and inflammation—whether microbial, immune-related, or behavioral—likely has relevant implications for the pathways leading to gastric disease.

The oral cavity, especially dental plaque and periodontal pockets, has been proposed as an extragastric niche that may harbor *H. pylori* and contribute to stomach recolonization after treatment [8]. This idea is supported by the broader understanding that structured biofilms can protect microbes from antibiotics and host defenses, allowing persistence and reseeding of distant mucosal sites under favorable conditions. In this context, periodontitis is not merely a coincidental comorbidity; it may represent a permissive ecological state in which complex biofilm communities and chronic gingival inflammation promote microbial persistence, immune activation, and altered mucosal communication [2]. Consistent with this reasoning, observational studies have reported a link between *H. pylori* infection and periodontal diseases, while noting significant variation in study design, diagnostic methods, and control of confounding factors [9, 10].

Converging clinical data also indicate that periodontal health may impact gastric outcomes important to patients and healthcare systems. In particular, adjunctive periodontal treatments have been studied as complementary options alongside standard pharmacologic eradication protocols, based on the idea that lowering oral biofilm could reduce the risk of persistence or recurrence [11, 12]. Although the extent and direction of benefits vary across studies and settings, this research has shifted the focus from purely associative links to testable, intervention-based questions. At the same time, the relationship is likely bidirectional. Gastric disease and its treatments can plausibly influence periodontal health through changes in diet, micronutrient absorption, medications—including antibiotics and acid suppressants—and systemic inflammation—factors that may alter oral ecology and host response. These reciprocal influences are clinically plausible, though they remain incompletely understood in well-controlled longitudinal studies.

Beyond infection-focused endpoints, interest has expanded to long-term gastric outcomes, including neoplasia. Epidemiologic studies have long used tooth loss and periodontal disease as proxies for cumulative oral inflammatory burden, and more recent systematic assessments have specifically examined gastric adenocarcinoma risk in relation to periodontal disease [13]. Such associations, even when modest, are biologically meaningful given the high baseline incidence and mortality of gastric cancer worldwide and the established role of chronic inflammation in gastric carcinogenesis [5, 7]. However, interpretation requires caution: shared risk factors—smoking, diet, socioeconomic status, metabolic disease, healthcare access, and health behaviors—can confound observed associations, and exposure misclassification is common when periodontal status is self-reported or inferred solely from tooth loss [1, 13].

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Against this backdrop, a focused narrative review is timely for three reasons. First, the evidence base has expanded to include not only cross-sectional associations but also meta-analyses on oral reservoirs and interventional periodontal approaches in the context of *H. pylori* eradication [8, 12]. Second, modern frameworks for periodontitis classification (staging and grading) emphasize the heterogeneity of periodontal disease, encouraging more precise phenotyping when evaluating systemic links [1]. Third, current gastric guidelines increasingly acknowledge microbiome-related considerations and the broader clinical implications of eradication strategies in an era of antibiotic resistance [4]. Incorporating these developments can clarify what is currently supported by evidence, what remains speculative, and where clinical translation may be justified.

Therefore, the aim of this narrative review is to synthesize current knowledge on the relationship between periodontal inflammation and gastric pathology, focusing on microbial and immune mechanisms, the idea of the oral cavity as an extragastric reservoir for *H. pylori*, and the clinical evidence linking periodontitis to *H. pylori*–related disease and gastric cancer. We also highlight important methodological limitations—especially confounding factors, differences in diagnostic methods, and limited long-term data—and outline priorities for future research and integrated dental–gastroenterology care pathways.

2. Overview of gastric diseases

The possible connections between periodontal inflammation and gastric disease are best understood within the context of major disease categories where *H. pylori* (or broader chronic mucosal inflammation) plays a key causal role. The conditions outlined below—gastritis, peptic ulcer disease, and gastric cancer—form a biologically connected spectrum in many patients, with infection-driven inflammation serving as a common initial cause (Malfertheiner, 2022; Chey, 2024). This spectrum is also where the hypothesized links between oral and gastric health (such as microbial seeding, immune priming, and shared inflammatory susceptibility) are most likely to be examined.

2.1 Gastritis and *H. pylori* infection

Gastritis is a histopathologic diagnosis characterized by inflammatory cell infiltrates in the gastric mucosa. It can be acute or chronic, focal or diffuse, and may occur with or without gland loss (atrophy). In modern practice, chronic gastritis is most often examined through an etiologic perspective, with *H. pylori*–associated gastritis being the most common infectious type worldwide [14]. *H. pylori* colonizes the mucus layer and attaches to the gastric epithelium, using urease activity and niche adaptation to survive despite the acidic environment. The host response typically involves neutrophilic activity, mononuclear infiltrates, and a cytokine milieu that can persist for decades, suggesting incomplete bacterial clearance and immune tolerance [14].

Clinically significant trajectories develop when chronic inflammation advances beyond superficial mucosal damage. Long-term *H. pylori* gastritis can progress toward multifocal atrophic gastritis, intestinal metaplasia, dysplasia, and ultimately adenocarcinoma—typically described as a stepwise cascade [7]. Importantly, not all infected individuals follow this pathway; progression depends on bacterial virulence factors, host genetic and immune characteristics, and environmental exposures (such as dietary salt and smoking). This variability is important for oral–gastric hypotheses: if periodontal inflammation influences systemic immune activation or alters microbial ecology, its effects are likely to

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be most observable in vulnerable subgroups rather than across all infected populations [4].

From a causal perspective, *H. pylori* is classified as carcinogenic to humans, supporting its role as a trigger for serious gastric outcomes when chronic infection persists [15]. Current guidelines, therefore, consider *H. pylori* infection a clinically significant condition, even in the absence of obvious ulcer disease, and focus on eradication and confirmation of cure after treatment [4].

2.2 Peptic ulcer disease

Peptic ulcer disease (PUD) involves mucosal ulceration—most often in the stomach or proximal duodenum—caused when aggressive factors such as acid, pepsin, infection, or medications surpass mucosal defenses, including the mucus–bicarbonate barrier, epithelial restitution, perfusion, and prostaglandin-mediated protection. In current populations, the main causes are still *H. pylori* and nonsteroidal anti-inflammatory drugs (NSAIDs), with other contributing factors like aspirin, anticoagulants/antiplatelet agents, smoking, and critical illness in specific cases [16, 17].

The *H. pylori*–ulcer axis involves both direct and indirect mechanisms: bacterial-induced inflammation alters gastrin–somatostatin signaling, impacts acid production (especially in duodenal ulcer types), and damages epithelial integrity through inflammatory mediators. In NSAID-related disease, cyclooxygenase inhibition decreases prostaglandin production, impairing mucosal blood flow, bicarbonate secretion, and epithelial repair. Clinically, these pathways come together: exposure to both *H. pylori* and NSAIDs increases ulcer risk, and the individual roles of each factor differ across populations and prescribing patterns [17].

PUD is also a serious condition because complications—such as upper gastrointestinal bleeding, perforation, and gastric outlet obstruction—contribute to morbidity and mortality. Acid suppression, usually with proton pump inhibitors, helps promote healing, but preventing recurrence depends on addressing the underlying cause: eradicating *H. pylori* significantly lowers ulcer relapse, while strategies such as dose reduction, switching medications, or using gastroprotective agents to mitigate NSAID-related risks help reduce recurrent injury [16]. In the context of periodontal–gastric links, PUD serves as a "hard endpoint" that indicates ongoing mucosal vulnerability, and factors such as systemic inflammation, medication use, and microbial persistence can be assessed as interacting risks.

2.3 Gastric cancer

Gastric cancer remains a leading cause of cancer globally, with notable geographic differences that reflect variations in infection rates, environmental exposures, screening practices, and sociodemographic factors [5]. Adenocarcinoma is the main histology, often categorized into two main types: intestinal-type, which typically follows a recognizable precancerous sequence, and diffuse-type, which can develop without the usual metaplasia–dysplasia steps and is more strongly associated with host factors in some cases.

The most well-established inflammation-driven model is the precancerous cascade described by Correa: chronic non-atrophic gastritis advances to multifocal atrophic gastritis, intestinal metaplasia, dysplasia, and invasive carcinoma [7]. *H. pylori* infection is usually the initial trigger in this pathway and has long been regarded as a carcinogenic exposure in humans [15]. A central mechanistic theme is the cumulative impact of persistent inflammation—oxidative stress, epithelial turnover, DNA damage, and remodeling of the mucosal microenvironment—rather than a single discrete injury event.

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While *H. pylori* is central, there is increasing interest in the wider gastric microbiome and its potential role in carcinogenesis, especially in cases of atrophy and hypochlorhydria, where the stomach's acidic environment is less restrictive. During preneoplastic stages, microbial diversity and composition may change, possibly promoting inflammatory signals or producing carcinogenic metabolites; whether these alterations are driving factors, incidental, or both, is still being studied [18].

This expanded microbial perspective is relevant to periodontal hypotheses because it suggests ways oral bacteria can impact the gastric environment—through direct translocation, swallowed biofilm fragments, or immune-mediated changes—particularly when gastric defenses are weakened.

2.4 GERD and functional dyspepsia

Gastroesophageal reflux disease (GERD) is mainly an esophageal disorder marked by the reflux of gastric contents, leading to symptoms and/or mucosal damage. Its underlying mechanisms focus on the competence of the lower esophageal sphincter, reflux volume, and esophageal clearance rather than on primary gastric mucosal inflammation. Current guidelines emphasize symptom-based assessment, targeted endoscopy, and a stepwise treatment approach that includes proton pump inhibitors, lifestyle changes, and certain procedural interventions [19]. GERD can still be an important factor to consider in oral–gastric research because prolonged acid suppression may alter the microbial environment in the upper gastrointestinal tract, and reflux symptoms may affect diet, oral hygiene practices, and healthcare utilization [19].

Functional dyspepsia, characterized by troublesome epigastric symptoms without an underlying structural disease, represents a distinct framework emphasizing visceral hypersensitivity, motility issues, mucosal immune activation, and brain–gut interactions [20]. Consensus guidelines for uninvestigated dyspepsia typically focus on age and risk-based evaluation, *H. pylori* testing and treatment when suitable, and empiric acid suppression in select patients [21]. Since functional dyspepsia is not inherently an "organic gastric disease," it will be considered peripheral to the mechanistic core of this review, but it remains important for interpreting symptom-based outcomes.

3. Biological rationale for an oral–gastric connection

The plausibility of a link between periodontal inflammation and gastric disease depends on a few interconnected mechanisms: (i) the oral cavity acting as a niche that can host gastric-related microbes, including *H. pylori*, within hardy biofilms; (ii) repeated delivery of microbes to the upper gastrointestinal tract through swallowing and, in certain cases, aspiration; (iii) systemic inflammatory and immune signals produced by periodontitis that may affect the stomach's defense and inflammatory response; and (iv) a shared set of exposures that can confuse or influence observed links. Importantly, these pathways are not mutually exclusive and may function differently across clinical types, such as untreated severe periodontitis, acid suppression, atrophic gastritis, or older age [2, 22].

3.1 Oral microbiome as a reservoir

The oral cavity hosts various structured microbial niches—including supragingival plaque, subgingival biofilms within periodontal pockets, and the tongue dorsum—that can support ongoing colonization and complex community interactions. Periodontitis causes an ecological shift marked by deeper anaerobic environments, increased gingival crevicular fluid, and persistent

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inflammation, all of which help stabilize dysbiotic biofilms and hinder clearance [2] In this context, the proposed "oral reservoir" hypothesis suggests that *H. pylori* can persist in oral biofilms (often detected by molecular methods) and contribute to gastric recolonization after eradication therapy [23].

Evidence supporting an oral reservoir is mixed, partly because detection depends on the method used, and the microbial load in the mouth might be low. However, recent reviews suggest that oral *H. pylori* detection—especially in dental plaque—tends to occur alongside gastric infection more often than by chance alone, supporting a model of a reservoir or shared exposure [8, 24]. In a 2025 systematic review and meta-analysis, the presence of *H. pylori* in dental plaque was associated with a higher risk of gastric *H. pylori* infection, and the authors explicitly discussed dental plaque as an extragastric reservoir with possible implications for treatment [8]. Additional overviews highlight that oral cavity detection occurs frequently enough to warrant mechanistic research, while also recognizing variability in sampling methods (plaque vs saliva vs tongue), diagnostic tests (PCR, rapid urease tests, culture), and contamination control [23].

Clinical interventional data indirectly support the reservoir hypothesis. If oral biofilms contribute to persistence or recurrence, then lowering subgingival biofilm levels could improve eradication success. An updated meta-analysis of clinical trials found that adjunctive periodontal treatment was associated with better gastric *H. pylori* eradication outcomes than eradication therapy alone [12]. Individual studies have also shown lower recurrence rates when periodontal therapy accompanies eradication protocols, although differences in follow-up, regional reinfection risk, and eradication approaches make direct comparisons difficult [25]. Overall, these findings do not confirm that the mouth is a true reservoir for all patients but support the biological possibility that oral biofilm management can influence important gastric outcomes in some cases [23].

3.2 Aspiration/swallowing pathways and microbial translocation

A second mechanistic pathway involves the repeated delivery of oral microbes to the stomach through swallowing. Humans continuously swallow saliva; estimates commonly cited in recent oral–gut axis reviews range from 1 to 1.5 liters per day, which carry microbes and biofilm fragments downstream [26]. Under healthy conditions, gastric acidity and bile create strong ecological barriers, and the gut microbiota offers colonization resistance. Consistent with this, an analysis using strain-level techniques reported no evidence of stable colonization of the distal gut by oral bacteria in healthy adults, indicating that oral-to-gut transmission is limited in healthy individuals [27].

However, barrier strength varies among individuals. Conditions that reduce gastric acidity—such as chronic proton pump inhibitor use and atrophic gastritis—alter motility or disrupt microbial colonization resistance, increasing the likelihood that swallowed oral taxa survive transit and temporarily (or permanently) influence downstream communities [28]. Reviews focusing on the oral–gut microbiota relationship describe situations in which oral taxa are more often detected in the gut—especially when chemical barriers are weakened or inflammation alters niches—supporting a context-dependent translocation model rather than a universal one [28, 29]. While most oral microbes may not establish permanent gastric colonization, repeated exposure could still be biologically significant at the level of mucosal immune activation, microbial metabolite signaling, or competitive interactions with *H. pylori* and other gastric microbes.

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In addition to swallowing, microaspiration can introduce oral bacteria into the upper aerodigestive tract, especially in older adults or those with impaired airway protective reflexes. Although aspiration is more often discussed in respiratory disease, the broader point remains relevant: periodontal dysbiosis can increase the microbial burden available for spread to nearby or downstream mucosal surfaces, particularly when host defenses are weakened [28].

3.3 Systemic inflammation and immune crosstalk

Periodontitis is increasingly recognized as a chronic inflammatory condition with systemic effects, including elevated circulating inflammatory biomarkers and changes in immune cell behavior [2]. Meta-analyses show that individuals with periodontitis have higher serum C-reactive protein (CRP) levels than controls, supporting the idea of low-grade systemic inflammation [30]. Further interventional studies report that periodontal therapy reduces serum CRP levels over follow-up periods of up to about six months, which is consistent with (though does not prove) a causal role of periodontal inflammation in systemic inflammation [31].

These systemic signals are relevant for gastric disease because gastric mucosal homeostasis relies on tightly regulated innate and adaptive immune responses, epithelial barrier function, and proper resolution of inflammation. Periodontitis-associated cytokines (including IL-6-driven acute phase signaling) and oxidative stress pathways could, in principle, trigger mucosal immune responses or lower the threshold for inflammatory amplification when the gastric mucosa encounters *H. pylori*, NSAIDs, or other injuries [2, 32]. Oral–gut axis frameworks also suggest that oral dysbiosis can influence immune trafficking patterns (e.g., Th17-skewed responses) that might affect distant mucosal sites, although the extent to which these mechanisms operate specifically in the stomach is less directly tested than in intestinal models [28, 33].

A practical implication of this immune crosstalk model is effect modification: if systemic inflammation contributes significantly, the strongest periodontal–gastric links would be expected in individuals with severe or uncontrolled periodontitis (higher inflammatory load) and those with reduced gastric defenses (atrophy, hypochlorhydria, chronic acid suppression), rather than across all patients uniformly.

3.4 Shared risk factors and confounding

Any discussion of mechanisms must be paired with careful attention to shared exposures that can generate false associations or conceal true effects. Smoking is a strong risk factor for periodontitis and is independently linked to major gastric outcomes; meta-analyses support a significantly higher incidence of periodontitis among smokers [34]. Socioeconomic status influences both periodontal and gastric disease risk through access to care, health behaviors, diet, crowding, and early-life exposures; long-term studies show that lower socioeconomic status throughout life is linked to worse periodontal outcomes [35].

Diabetes and metabolic dysfunction are especially important confounders and potential mediators. Diabetes increases the risk of periodontitis, and periodontal inflammation can negatively affect glycemic control, creating a bidirectional relationship that complicates causal inference in observational studies [36]. Diet, oral hygiene, and age can affect both oral inflammatory status and susceptibility to gastric disease. Medications also play a key role: antibiotics can alter oral microbial communities and inflammatory markers, while proton pump inhibitors can change the microbial ecology

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of the upper gastrointestinal tract and possibly influence the survival of swallowed oral bacteria [37]. Without proper adjustment and stratification, these shared factors can be mistaken for a direct biological link between periodontal and gastric conditions.

3.5 Reverse pathway: gastric disease affecting the periodontium

Bidirectionality is plausible not only in immune responses but also through nutritional and pharmacologic pathways. Chronic atrophic gastritis—whether caused by *H. pylori* or autoimmunity—can impair the absorption of micronutrients essential for blood and epithelial health. Clinical guidance and expert reviews indicate that atrophic gastritis is associated with iron and vitamin B12 deficiency (due to impaired acid-dependent nutrient release and reduced intrinsic factor in autoimmune cases), with subsequent effects including anemia and neurologic issues [38, 39]. Nutritional deficiencies and anemia can plausibly impact periodontal tissue strength, wound healing, and immune function in the host, potentially worsening periodontal outcomes in vulnerable individuals.

Gastric disease management can also impact oral ecology. Proton pump inhibitors, often used for symptom relief and stomach protection, are increasingly linked to changes in the oral–gut microbiota; mechanistic reviews suggest that hypochlorhydria may shift microbial selection pressures along the aerodigestive tract and alter patterns of oral-to-gut microbial transit [40].

Antibiotic use during *H. pylori* eradication can cause short- and medium-term disruptions in microbiota; experimental and clinical studies indicate that systemic antibiotics can change oral microbiota composition and immune responses, with possible effects on periodontal inflammation [37]. Additionally, chronic dyspeptic symptoms, stress, dietary restrictions, and changes in self-care behaviors may indirectly influence oral hygiene routines and periodontal health—behavioral pathways that are difficult to quantify but have clinical significance.

4. Evidence linking periodontitis to specific gastric outcomes

4.1 Periodontitis and *H. pylori* infection (presence, load, eradication failure)

A consistent finding across observational studies is that periodontitis is associated with higher odds of *H. pylori* detection, both in the stomach and, to a lesser extent, in oral niches sampled in parallel. In an updated meta-analysis of observational studies, periodontal disease was associated with increased odds of *H. pylori* infection overall [9] (Table 1).

Interpretation heavily depends on how *H. pylori* is detected and where it is sampled. Oral detection has used inconsistent methods—PCR-based tests (including target and primer selection), rapid urease tests on plaque or tongue samples, antigen-based assays, and (less often) culture—each with different risks of false positives or negatives and limited comparability across studies [10]. A related issue is that detecting *H. pylori* DNA in plaque does not always indicate the presence of live bacteria or a stable oral reservoir. Additionally, sampling often misses deep periodontal pockets or tongue dorsum biofilms, where biomass and microbial diversity vary.

The most clinically relevant part of this literature concerns eradication outcomes. A Cochrane review of randomized trials concluded that adding periodontal therapy to standard eradication regimens increased short-term eradication success and also improved longer-term non-recurrence rates [11]. While these findings align with the “oral reservoir” hypothesis discussed earlier, the underlying trials were generally small, varied in

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periodontal protocols, and were conducted in relatively limited geographic settings; therefore, generalizability to modern eradication regimens (in an era of rising antibiotic resistance) remains uncertain.

4.2 Periodontitis and gastritis / atrophic gastritis

Evidence linking periodontitis with gastritis is primarily based on cross-sectional studies. In a large Korean population dataset, self-reported periodontitis was associated with higher odds of chronic gastritis after multivariable adjustment [41]. This type of analysis demonstrates large-scale correlation but cannot determine directionality (periodontitis → gastritis, gastritis → periodontitis, or shared factors).

For atrophic gastritis and intestinal metaplasia, data are more limited but suggest that periodontal inflammatory burden may be associated with precancerous mucosal changes. In an endoscopy-based cross-sectional study with clinical oral examinations, bleeding on probing—a marker of active gingival inflammation—was associated with a higher odds of gastric precancerous lesions (including chronic atrophic gastritis and intestinal metaplasia) [42]. The study's biopsy-confirmed outcomes strengthen phenotyping, but the sample size and cross-sectional design limit causal conclusions, and residual confounding factors (such as dietary patterns, smoking intensity, and socioeconomic status) remain a concern.

4.3 Periodontitis and peptic ulcer disease

Observational studies have shown modest links between periodontitis and peptic ulcer disease, although controlling for smoking and NSAID use remains challenging. In the KoGES cross-sectional analysis, periodontitis was linked to a history of peptic ulcers after adjustment [41].

A recent systematic review and meta-analysis pooling multiple study designs found that periodontitis was associated with peptic ulcer disease overall, with stronger signals for duodenal ulcer than for gastric ulcer [43].

Even in adjusted models, interpretation remains cautious because (i) ulcer outcomes are often clinically coded rather than endoscopically verified, (ii) NSAID/aspirin exposure is incompletely captured in many datasets, and (iii) periodontitis may act as a proxy for broader health behaviors that also influence ulcer risk.

Table 1. Evidence linking periodontitis to specific gastric outcomes

Gastric outcome	Main evidence types	Direction/size of association (typical findings)	Key limitations / interpretation notes
H. pylori infection (presence/positivity)	Observational studies; meta-analyses	Higher odds of *H. pylori* in periodontal disease in pooled analyses [9]	Heterogeneous detection methods; oral PCR does not establish viability; variable control of confounding
H. pylori eradication failure / recurrence	Randomized trials synthesized in systematic reviews	Adjunctive periodontal therapy improves eradication and non-recurrence in pooled trial data [11]	Small/older trials; periodontal protocols vary; applicability to current eradication regimens uncertain
Chronic gastritis / atrophic gastritis	Large cross-sectional datasets; smaller endoscopy-based studies	Positive association in population data (Byun, 2020); inflammatory indices linked with precancerous lesions [42]	Cross-sectional design; self-report in some datasets; residual confounding

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Peptic ulcer disease	Observational studies; meta-analysis	Increased risk in pooled adjusted analyses; stronger for duodenal than gastric ulcer in one meta-analysis [43]	NSAID exposure and smoking often incompletely captured; outcome misclassification
Gastric cancer / adenocarcinoma	Cohort/case-control studies; meta-analyses; emerging Mendelian randomization	Small increased risk in pooled estimates [13, 44]; MR may show null causal signal [45]	Confounding (smoking/diet/SES), reverse causality; heterogeneous exposure definitions

4.4 Periodontitis and gastric cancer (risk and precancerous lesions)

The literature on periodontitis and gastric cancer often uses proxies like periodontal diagnoses, tooth loss, or combined "poor oral health" indices. A systematic review and meta-analysis focusing on gastric adenocarcinoma reported a pooled association with a higher risk among those with periodontal disease, with differences depending on region and exposure measurement [13].

Another meta-analysis examining oral health and gastric cancer incidence similarly found that periodontitis slightly but significantly increased the risk of gastric cancer, while several other oral-health indicators showed weaker or inconsistent links [44].

These pooled results are reasonable considering chronic inflammation and microbial factors, but they remain susceptible to residual confounding (such as smoking, diet, socioeconomic factors, and healthcare use) and reverse causality (where preclinical cancer affects nutrition, immunity, oral hygiene, and dental visits).

Genetic epidemiology has started to test causality more directly, with at least one bidirectional Mendelian randomization analysis reporting no clear causal effect in either direction [45]. Such findings do not definitively disprove causality—instrument strength, phenotype definition (periodontitis case definition), ancestry structure, and pleiotropy can all weaken signals—but they highlight that observational associations should not be taken as proof of a causal relationship.

4.5 Summarize evidence quality (consistency, temporality, dose-response, plausibility, confounding)

Across outcomes, consistency is strongest for associations between periodontitis and *H. pylori*–related endpoints, supported by multiple meta-analyses and reinforced by interventional data for eradication success [9]. Temporality is weakest overall because many datasets are cross-sectional or rely on self-report or diagnosis history [41]. Dose–response is inconsistently examined; when clinical indices are used, signals often align better with inflammatory activity markers than with crude exposure proxies [42]. Biological plausibility is strong, given microbial and inflammatory pathways, but residual confounding remains a key limitation, especially for ulcer and cancer outcomes where smoking, NSAIDs, diet, and socioeconomic factors overlap with periodontal risk.

5. Interventional evidence and clinical relevance

5.1 Periodontal treatment as an adjunct to gastric disease management

Most interventional research at the oral–gastric interface has focused on *H. pylori* eradication, exploring whether periodontal debridement and enhanced oral hygiene—administered alongside standard antibiotic treatments—can improve eradication rates and reduce the risk of future recurrence. In randomized trials, the

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"periodontal" component usually involves scaling and root planing combined with oral hygiene education, sometimes supplemented with antiseptic mouthrinses, given either before or during eradication therapy. The basic clinical idea is practical: if dental plaque or periodontal pockets serve as protected microbial environments, reducing biofilm may lessen persistence or reseeding after systemic treatment.

A Cochrane review concluded that adjunctive periodontal therapy may increase eradication rates and reduce recurrence compared with eradication therapy alone, while noting that the number and quality of available trials are limited and that larger, well-designed multicenter studies are necessary [11].

An updated meta-analysis of clinical trials similarly reported improved eradication outcomes when periodontal treatment was added, suggesting that periodontal care is a potentially useful supportive strategy amid rising antibiotic resistance [12]. A more recent systematic review focused on non-surgical periodontal treatment (NSPT) also examined this question and reflects ongoing interest in whether periodontal intervention significantly enhances eradication success in modern protocols [46].

At the individual study level, trials have assessed both initial eradication and recurrence after apparent cure. For example, a randomized study reported that adjunctive periodontal therapy improved eradication success and decreased recurrence compared to eradication alone, supporting the clinical plausibility of a modifiable oral contribution in some patient groups [25].

However, the overall evidence remains heterogeneous: follow-up periods vary from weeks to a year or more, recurrence definitions differ—distinguishing between true reinfection and recrudescence is rarely possible without strain typing—and eradication protocols have changed over time. These issues limit the ability to generalize pooled effect sizes across different settings.

From a clinical perspective, the most justifiable implication is not that periodontal therapy should be universally included as part of initial *H. pylori* treatment, but that periodontal assessment and biofilm management are reasonable adjunctive options in specific situations—especially in patients with active periodontitis and repeated eradication failures or suspected recurrence—where the potential benefits are significant and the intervention offers inherent oral health advantages. The evidence supporting effects on dyspepsia symptom scores or gastric inflammatory biomarkers is relatively limited, and most studies focus on microbiological cure rather than mechanistic gastric outcomes (Table 2).

Table 2. Interventional evidence and clinical relevance at the oral–gastric interface

Design / setting	**Population**	**Periodontal exposure/ intervention**	**Gastric intervention / comparator**	**Key outcomes reported**	**Main takeaway**	**Major limitations**
Systematic review (Cochrane) of RCTs [11]	*H. pylori*-infected participants in included trials	Periodontal therapy as adjunct (typically scaling/root planing + oral hygiene)	Standard eradication therapy ± adjunct periodontal therapy	Eradication efficiency; non-recurrence	Adjunct periodontal therapy may improve eradication and non-recurrence vs eradication alone	Limited number/quality of trials; heterogeneity in periodontal protocols and follow-up; older regimens in some trials
Updated meta-analysis of	6 studies; pooled sample reported as	Periodontal treatment adjunct to eradication	Eradication therapy ± periodontal treatment	Eradication rate	Pooled trial evidence supports higher eradication rates	Small pooled samples; differences in regimens,

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clinical trials [12]	541 participants				when periodontal treatment is added	adherence, periodontal definitions; recurrence outcomes less consistently reported
Prospective randomized trial [25]	698 gastric *H. pylori*-infected patients (approx. 347 eradication alone vs 342 eradication + periodontal therapy)	Periodontal therapy added to eradication arm	Eradication therapy alone vs eradication + periodontal therapy	Eradication; recurrence (follow-up reported in article)	Suggests adjunct periodontal therapy can improve eradication and reduce recurrence in a large single-country RCT	Single setting; recurrence vs reinfection not strain-typed; periodontal protocols and adherence details may limit transferability
Systematic review [46]	Studies evaluating NSPT and *H. pylori* endpoints	NSPT-focused periodontal intervention	Eradication regimens ± NSPT	Eradication outcomes	Confirms ongoing evidence base assessing NSPT as adjunct; conclusions depend on included-study heterogeneity	Limited number of eligible trials; protocol variability; need for contemporary, multicenter RCTs
Narrative/mechanistic synthesis [23]	—	Discusses oral *H. pylori* detection methods and reservoir concept	—	Methodologic interpretation (PCR vs culture/urease; sampling sites)	Highlights that oral detection ≠ viable reservoir, and assay/sampling choices drive heterogeneity	Not interventional; supports interpretation rather than effect estimation

5.2 Gastric disease management and periodontal outcomes

The reverse clinical pathway—gastric disease management affecting periodontal health—is biologically plausible and increasingly discussed, but the evidence for direct outcomes is less developed. *H. pylori* eradication regimens involve multi-drug antibiotic exposure that can disrupt microbial communities beyond the stomach. A recent review noted that eradication therapy affects not only the gut microbiome but also the oral microbiome, with reports of shifts toward potentially unfavorable oral community patterns after treatment [47]. Whether these compositional shifts lead to clinically significant periodontal deterioration—or, conversely, transient improvement due to suppression of periodontal pathogens—is not consistently confirmed across controlled studies.

More broadly, systemic antibiotics can alter the host–microbe immune balance in ways relevant to periodontal inflammation. Experimental studies have demonstrated that prolonged systemic antibiotic use can cause dysbiosis and accelerate periodontitis through immune imbalance pathways in model systems, reinforcing the idea that antibiotic-driven ecosystem changes could affect periodontal outcomes in susceptible individuals [37]. In real-world care, the effect's direction is likely context-dependent—based on baseline periodontal health, oral hygiene habits, antibiotic type and duration, and the ecological rebound after treatment.

Acid suppression, especially with proton pump inhibitors (PPIs), is a common factor in upper gastrointestinal care that

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may impact periodontal outcomes. Mechanistic reviews suggest that PPIs can alter aerodigestive microbial selection through hypochlorhydria and subsequent alterations in the microbiota, potentially affecting oral–gut microbial interactions [40]. Clinically, a systematic review until April 2024 examined whether PPI use correlates with the severity of periodontal disease and peri-implantitis, highlighting increasing interest in possible periodontal effects or confounding factors in observational data [48]. Currently, these findings should be approached with caution: medication use is linked to underlying disease severity, healthcare utilization, and lifestyle factors that can also influence periodontal health.

Overall, the interventional and exposure-based literature supports two practical messages. First, periodontal therapy seems capable of affecting clinically meaningful gastric outcomes (eradication and recurrence) in some settings, although the strength and applicability of these effects need more robust contemporary trials [11, 12]. Second, common gastric treatments (antibiotics and PPIs) are likely to affect oral ecology, but well-controlled longitudinal studies linking these exposures to standardized periodontal outcomes remain essential [47, 48].

6. Methodological issues and gaps

Interpreting the periodontal–gastric literature is less limited by a lack of plausible mechanisms than by significant methodological differences. Several recurring issues prevent cross-study comparison and make causal inference more difficult.

Variability in defining periodontitis cases is a major challenge. Many studies—especially those using older cohorts and large administrative datasets—use outdated periodontal categories or proxies, such as tooth loss, that don’t align with current staging and grading standards. The 2017 World Workshop framework (commonly implemented through the staging/grading case definition) focuses on severity, complexity, and risk of progression, which are not captured by labels like "chronic vs aggressive" or self-reported periodontitis [1]. As a result, combining data from different studies often mixes biologically distinct phenotypes, which can dilute or make the true effects seem inconsistent.

Various methods are used to detect *H. pylori* and sample sites. Gastric infection status is evaluated using noninvasive tests such as urea breath tests and stool antigens, along with biopsy-based approaches, all of which are influenced by recent antibiotics, bismuth, and acid suppressants. Current recommendations favor test-of-cure with urea breath tests, stool antigen tests, or biopsy after at least 4 weeks post-therapy [14]. Consensus also states that serology cannot distinguish between active and past infections and should not be used to confirm eradication [4]. In oral studies, variability is even higher: samples from plaque, saliva, the tongue dorsum, or subgingival areas are tested via PCR, rapid urease tests, antigen assays, or, occasionally, culture, with important differences in how “positivity” is defined. Reviews note that estimates of oral *H. pylori* prevalence vary widely, and differences in sampling and detection methods hinder comparisons across studies [23, 29].

Limited longitudinal cohort data and prevalence of cross-sectional studies. Much of the evidence linking periodontitis with gastritis, peptic ulcer disease, or *H. pylori* infection depends on cross-sectional designs, which cannot determine causality and are susceptible to reverse causation. An example from a large population-based study is the KoGES analysis, which reports associations between periodontitis and chronic gastritis and peptic ulcer. However, the cross-

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sectional nature of this study limits causal inference, even after multivariable adjustment [41]. Longitudinal cohorts involving repeated periodontal assessments and validated gastric endpoints remain relatively rare.

Confounder control is inconsistent and often incomplete. Smoking, socioeconomic status, and diabetes/metabolic dysfunction are strong determinants of periodontitis and are also relevant to gastric outcomes; inadequate measurement or adjustment can lead to false associations. For example, smoking is linked to a significantly higher incidence of periodontitis in pooled analyses [34], socioeconomic disadvantage shows a life-course relationship with poorer periodontal outcomes [35], and diabetes is bidirectionally connected with periodontitis and systemic inflammatory burden [36]. Studies also differ in how they account for oral hygiene behaviors, diet, medication use (PPIs, antibiotics), healthcare access, and dental attendance—variables that may confound or influence the observed periodontal–gastric relationships.

Publication bias and geographic clustering. The oral *H. pylori* field, in particular, is vulnerable to selective publication because small studies using various assays and sampling protocols can yield differing results. Additionally, study populations are often drawn from regions with high background *H. pylori* prevalence or from symptomatic endoscopy cohorts, which may overestimate effects and limit applicability to lower-prevalence settings [29]. Systematic reviews frequently highlight heterogeneity and methodological differences as major limitations, emphasizing the need for standardized approaches [24].

Need for standardized outcomes and harmonized reporting. Progress will require greater alignment of both periodontal and gastric endpoints. On the gastric side, standardized definitions of eradication success—including timing and choice of test-of-cure—consistent with guidelines are essential [4]. On the periodontal side, adopting staging and grading, along with uniform clinical parameters—such as probing depth, clinical attachment loss, bleeding on probing, and radiographic bone loss—would improve comparability [1]. When testing the oral reservoir hypothesis, studies should predefine sampling sites (plaque, tongue, or subgingival pockets), use assays that distinguish viability when feasible, apply contamination controls, and incorporate microbial profiling (e.g., metagenomics) with standardized bioinformatics pipelines. Finally, interventional trials should report not only eradication rates but also recurrence definitions, adherence, periodontal response, and (when possible) gastric inflammation biomarkers; the Cochrane synthesis explicitly underscores the need for larger, well-designed multicenter RCTs [11].

7. Future directions

Prospective cohorts should include standardized periodontal and gastric phenotyping. The next generation of observational studies needs to go beyond simple proxies (such as self-reported periodontitis, tooth loss, and "poor oral health") and adopt modern periodontal staging and grading that use calibrated full-mouth measurements. This approach will enable stratified analysis by severity and progression risk [1]. On the gastric side, cohorts should employ guideline-consistent definitions of active *H. pylori* infection and eradication, including test-of-cure with validated methods, appropriate timing, and careful documentation of recent PPIs and antibiotics [4]. A significant gap exists in understanding temporality: longitudinal studies with repeated oral and gastric assessments could clarify whether periodontal inflammation precedes infection persistence or recurrence, or whether gastric disease and its treatments drive periodontal deterioration. When

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evaluating recurrence, strain typing—when feasible—would help distinguish recrudescence from reinfection.

Interventional RCTs are aligned with modern eradication regimens. While previous syntheses suggest that adding periodontal therapy to eradication regimens can improve success rates and reduce recurrence, heterogeneity among trials limits their generalizability. Future RCTs should be adequately powered, multicenter, and standardized in both periodontal interventions (e.g., reproducible steps of non-surgical periodontal therapy with objective response metrics) and gastric therapy, using current first-line regimens that align with guidelines and consider local resistance patterns [14]. Beyond simply determining "eradication yes/no," trials should also report adherence, adverse effects, periodontal endpoint trajectories (probing depth, clinical attachment level, bleeding on probing), and clearly define recurrence windows.

Multi-omics approaches are used to examine the oral–gastric (and oral–gut) axis. Progress in understanding mechanisms will likely come from paired sampling across different compartments and integrated analyses, rather than studies focusing on a single site or assay. Emerging research shows how multi-omics can link changes in microbial communities with functional outcomes (metagenomics) and metabolic signatures (metabolomics) across oral and intestinal environments in periodontitis and after periodontal therapy [49]. Applying this framework to gastric outcomes would involve coordinated sampling of periodontal sites (e.g., subgingival plaque, tongue dorsum, saliva) alongside gastric tests (preferably with standardized infection confirmation) and host measurements (e.g., systemic inflammatory markers and targeted cytokine panels). Reviews of the oral–gut/systemic axis increasingly highlight that immune profiling (including Th17/Treg-related signatures) and markers of barrier function can serve as biologically meaningful links between dysbiosis and distant mucosal inflammation [50].

Clinical pathways and integrated dental–gastroenterology strategies. A practical translational goal is to identify who may benefit most from cross-disciplinary care. Current *H. pylori* guidelines emphasize risk groups relevant to prevention efforts (e.g., individuals at higher gastric cancer risk, including certain immigrant populations from high-incidence regions, and those with additional risk factors) [14]. Within these groups, it is sensible to test integrated approaches that include (i) periodontal screening and biofilm control during eradication therapy—especially in patients with recurrent or resistant infections—and (ii) referral systems where gastroenterology clinics can identify severe periodontal inflammation as a potentially modifiable comorbidity. The success, feasibility, and cost of such pathways should be assessed using implementation science outcomes (uptake, adherence, recurrence reduction, patient-reported benefits), rather than solely microbiologic endpoints.

8. Clinical implications

Clinical translation of the periodontal–gastric literature should remain cautious because much of the evidence is associative and methodologically diverse. Nonetheless, several practical implications can be considered without assuming causality.

Consider conducting a periodontal evaluation in patients with recurrent or failed *H. pylori* eradication. For those with persistent infection after guideline-recommended treatment or suspected recurrence, assessing periodontal health—and reinforcing professional biofilm control—can be a reasonable part of a broader review of modifiable factors. This approach is indirectly supported by meta-analyses of randomized trials that

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suggest that adjunctive periodontal therapy may enhance eradication success and reduce recurrence compared with eradication therapy alone, although the evidence's certainty is limited and protocols differ [11]. Importantly, current guidelines emphasize optimized eradication regimens and systematic confirmation of cure ("test-of-cure"), so periodontal care—when performed—should serve as an adjunct rather than a replacement for evidence-based pharmacologic treatment [4].

Emphasize oral hygiene and periodontal care as part of overall efforts to reduce inflammation risk. Regardless of any direct gastric benefits, diagnosing and managing periodontitis remains crucial for lowering local inflammatory levels and preventing tooth loss. Given possible links among periodontal inflammation, systemic inflammatory markers, and mucosal immune regulation, effective periodontal management can be presented as a general risk-reduction approach—especially for patients with chronic inflammatory conditions—without overstating disease-specific prevention benefits.

For patients with gastric disease who have malabsorption or anemia, consider an oral or periodontal assessment. Atrophic gastritis, including autoimmune types and *H. pylori*–related corpus-predominant atrophy, is associated with iron and vitamin B12 deficiency, and expert guidance recommends screening for these deficiencies in such patients [38]. In cases where patients present with iron deficiency anemia, B12 deficiency, or nutritional mucosal vulnerability, a periodontal exam may be clinically beneficial, as oral inflammation can worsen nutritional intake, and impaired hematologic status may harm mucosal health and tissue repair. In practice, a low threshold for integrated management—involving primary care, gastroenterology, and dentistry— is advised when anemia, chronic gastritis or atrophy, and poor oral health are present together.

9. Conclusions

Current evidence indicates a biologically plausible link between periodontitis and gastric conditions, strongest for *Helicobacter pylori*–related outcomes. The idea of the oral cavity—especially dental plaque and periodontal pockets—as a microbial niche, along with periodontitis-related systemic inflammation, provides coherent mechanisms connecting oral and gastric diseases. Interventional data suggest that adjunctive periodontal therapy may enhance *H. pylori* eradication and lower recurrence in some cases, but variability in trial protocols and changing eradication methods limit broad application.

Associations have been reported between gastritis, peptic ulcer disease, and gastric cancer. However, establishing causality is limited by the predominance of cross-sectional studies, inconsistent periodontal definitions, and residual confounding factors—particularly smoking, socioeconomic status, metabolic disease, and medication use. Therefore, periodontal care should be considered an evidence-based priority for oral health with potential secondary benefits for the stomach, rather than a proven preventive measure for gastric disease. Future research should focus on standardized phenotyping, guideline-aligned gastric endpoints, and modern multicenter RCTs to identify which patient groups, if any, may gain meaningful gastric benefits from integrated periodontal–gastroenterology management.

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