IJCNP, Volume 3, Issue 11, 2025 ISSN: 2995-536X
https://medicaljournals.eu/index.php/IJCNP

INTERNATIONAL JOURNAL OF COGNITIVE NEUROSCIENCE AND PSYCHOLOGY

PHARMACOTHERAPY AND PREVENTION STRATEGIES OF PEPTIC ULCER DISEASE

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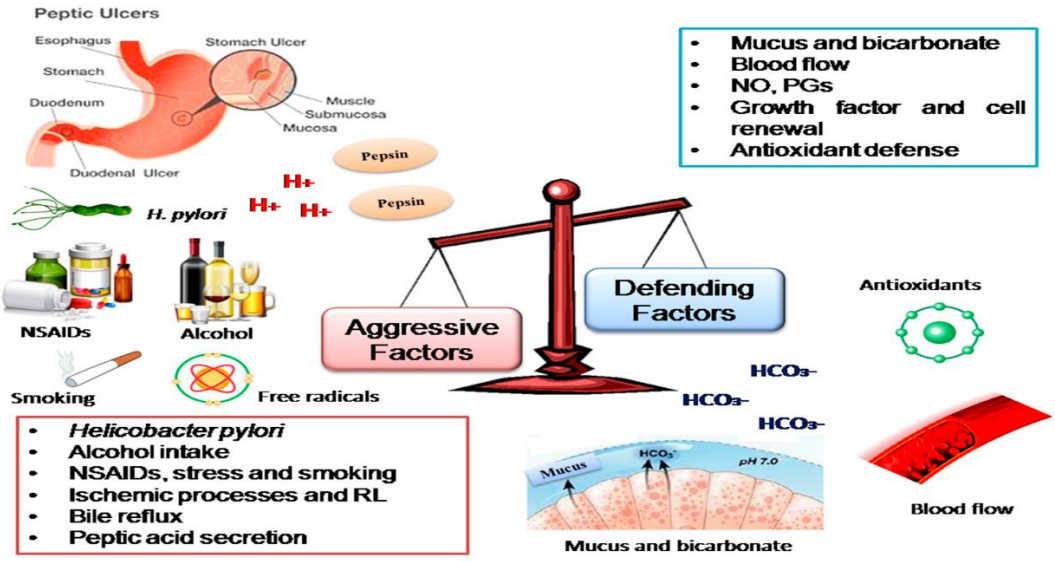
Abstract: Peptic ulcer disease (PUD) is a localized defect in the gastric mucosa, associated with H. pylori infection, NSAID use, stress, and other risk factors. This article reviews pharmacotherapy and preventive strategies for PUD based on a literature review. Pharmacotherapy includes proton pump inhibitors (PPIs), H2 receptor antagonists, gastroprotective agents, and antibiotics. Preventive approaches include H. pylori eradication, protection from NSAID-induced injury, probiotics, and promotion of a healthy lifestyle. These strategies enhance ulcer healing, reduce recurrence risk, and improve patients' quality of life.

Keywords: Peptic ulcer disease, pharmacotherapy, prevention, H. pylori, PPI, gastroprotective agents

INTRODUCTION

Peptic ulcer disease (PUD) is characterized by deep mucosal defects in the stomach lining and is a widespread gastroenterological problem worldwide [1–3]. Although incidence rates decreased in the early decades of the 21st century, recent years have seen a resurgence due to **antibiotic-resistant H. pylori infections, increased use of non-steroidal anti-inflammatory drugs (NSAIDs), chronic stress, poor dietary habits, and metabolic disorders** [4,5]. Currently, approximately 10% of the global population experiences at least one ulcer episode in their lifetime, and **H. pylori infection reaches up to 70% in some regions,** reflecting the severity of the problem [6,7].



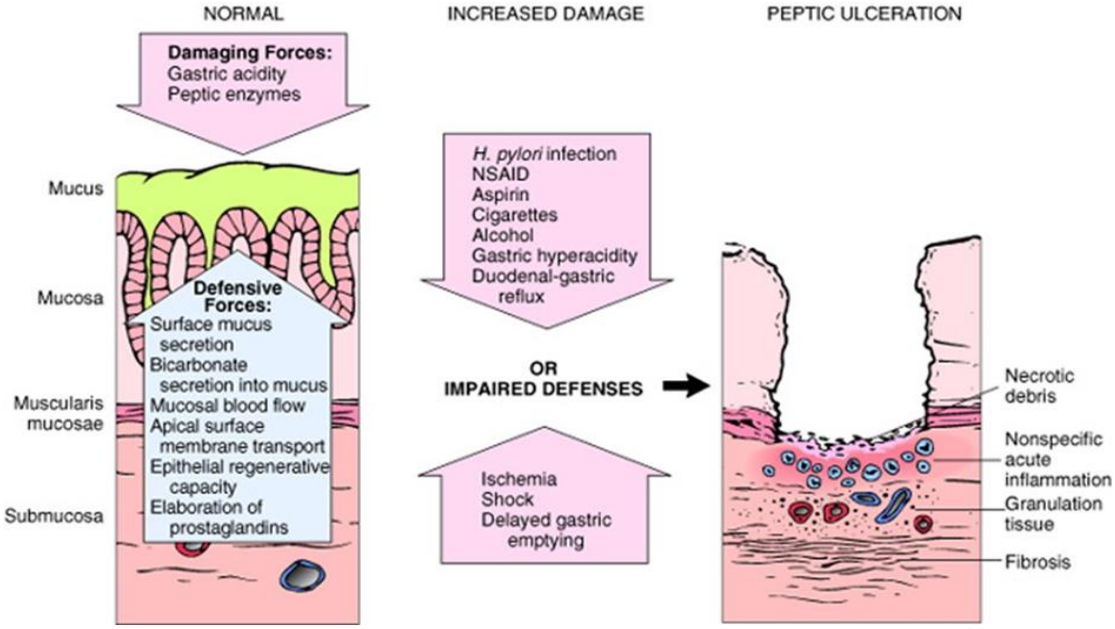
The etiology of PUD is **multifactorial,** with H. pylori infection (75–90%), NSAID-related injury, gastric acid hypersecretion, genetic predisposition, and lifestyle factors playing a key role [8,9]. Recent studies indicate that in the context of rising global antibiotic consumption, resistance of H. pylori to **clarithromycin, levofloxacin, and metronidazole** has reached 30–40%, reducing the effectiveness of standard eradication regimens [10]. Therefore, there is an increasing need for improved

pharmacotherapy strategies, including **new-generation proton pump inhibitors (PPIs), potassium-competitive acid blockers (PCABs), and combination eradication regimens** [11].

Meta-analyses indicate that the **global prevalence of H. pylori infection** remains high, with an estimated **4.4 billion people affected worldwide in 2015** [1,12]. A recent systematic review (1980–2022) showed a decline in global prevalence: from **58.2% in 1980–1990** to **43.1% in 2011–2022** [2].

Regional distribution of infection is highly variable. For example, in **Africa,** overall H. pylori prevalence was **70.1%** (95% CI: 62.6–77.7), while in **Oceania** it was the lowest, approximately **24.4%** [3,12]. According to the International Agency for Research on Cancer (IARC) and other sources, H. pylori prevalence is particularly high in developing countries due to **sanitation, hygiene, and socio-economic factors** [4,13].

The **Global Burden of Disease (GBD) 2019 study** estimated that in 2019, there were approximately **8.09 million PUD patients worldwide** (95% CI: 6.79–9.58 million) [5,13]. Age-standardized prevalence decreased from **143.4 per 100,000 in 1990** to **99.4 per 100,000 in 2019** [6,15]. Similarly, disability and mortality due to PUD showed changes, with age-standardized **DALYs (Disability-Adjusted Life Years)** decreasing between 1990 and 2019 [6,14].

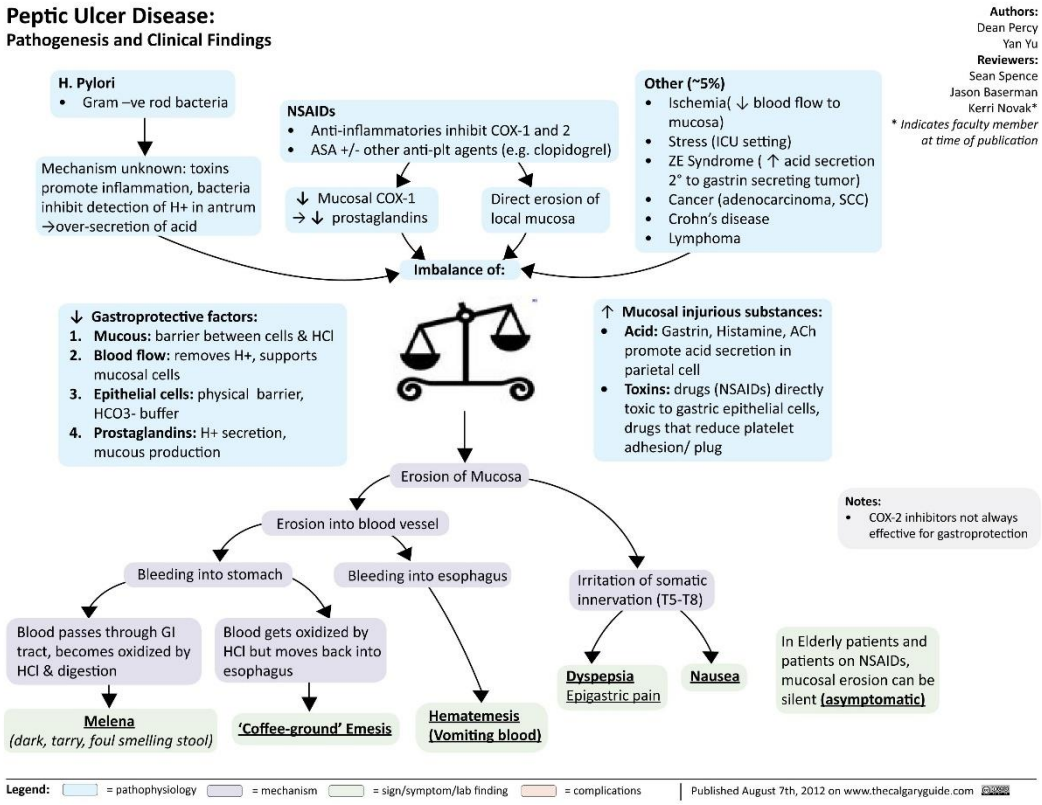


Regional differences remain significant. In 2019, **South Asia** had the highest age-standardized prevalence of PUD at **156.62 per 100,000** (95% UI: 130.58–187.05) [8,16]. Mortality due to PUD in 2019 was highest in low- and middle-income countries [17]. This global data highlights the significant impact of **peptic ulcer disease (PUD) and H. pylori infection** worldwide. While **H. pylori infection is widely prevalent,** recent years have shown a declining trend in its prevalence (e.g., from 1980–1990 to 2011–2022), reflecting evolving epidemiological patterns. This decline is more pronounced in **high-income countries and regions with better healthcare coverage** [18].

However, the overall burden of PUD has not decreased, likely due to **population growth, sociodemographic changes, and other risk factors,** such as increased NSAID use. Additionally, regional disparities and areas with rising PUD-related mortality and disability underscore the importance of **strategic allocation of preventive and therapeutic resources** [1,19].

Furthermore, the **global increase in NSAID consumption** (particularly diclofenac, ibuprofen, and aspirin) substantially elevates the risk of gastric mucosal barrier disruption and ulcer formation. International data indicate that **at least 25% of long-term NSAID users develop gastric or duodenal ulcers**. Therefore, gastroprotection, prophylactic PPI use, and identification of high-risk groups have become **integral components of PUD management** [20].

Another critical aspect highlighting the significance of PUD is that **ulcer-related complications**—such as bleeding, perforation, and pyloric stenosis—remain major causes of morbidity and mortality. The disease is especially severe in **elderly patients and those with cardiovascular diseases, diabetes, or immunosuppression,** resulting in higher mortality rates. Studies also suggest that during the **COVID-19 pandemic,** increased stress, widespread use of corticosteroids, and NSAIDs contributed to a rise in PUD incidence [18].



In modern clinical practice, the primary goals of **effective treatment and prevention of PUD** are to restore gastric mucosal defense mechanisms, reduce acid aggression, achieve complete eradication of H. pylori, and minimize recurrence risk. Therefore, this literature review systematically analyzes **recent scientific advances in PUD,** effective pharmacotherapeutic approaches, the challenges of antibiotic resistance, and evidence-based preventive strategies.

OBJECTIVE OF THE STUDY

The aim of this literature review is to **analyze the latest scientific findings on the etiology and pathogenesis of PUD,** evaluate the effectiveness of pharmacotherapeutic strategies for H. pylori eradication, and consider practical recommendations for the treatment and prevention of NSAID-induced ulcers. Additionally, it seeks to **systematically justify preventive strategies for PUD** in the context of global epidemiological trends.

The study also addresses the following tasks:

Examine the role of **H. pylori** in PUD and the global issue of antibiotic resistance;

Compare the effectiveness, advantages, and limitations of various **eradication regimens;**

Analyze the clinical efficacy of **proton pump inhibitors (PPIs), potassium-competitive acid blockers (e.g., vonoprazan), and gastroprotective agents;**

Summarize **international recommendations** for the prevention of NSAID-induced ulcers;

Scientifically substantiate **preventive strategies aimed at reducing PUD recurrence risk.**

MATERIALS AND METHODS

Study Design

This literature review was conducted according to the principles of a **systematic review.** The study adhered to **PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines** and aimed to analyze current pharmacotherapeutic approaches, their efficacy, and preventive strategies for peptic ulcer disease (PUD).

Search Strategy

A systematic search was performed in the following electronic databases:

PubMed/MEDLINE

Scopus

Web of Science

Google Scholar

Cochrane Library

The search included articles published between **2013 and 2024.** The following keywords and their combinations were used:

“peptic ulcer disease”, “gastric ulcer”, “duodenal ulcer”, “Helicobacter pylori eradication”, “PPI therapy”, “NSAID-induced ulcer”, “ulcer prevention strategies”, “gastroprotection”, “H2 blockers”, “bismuth therapy”, “epidemiology”, “risk factors”, “recurrence prevention”

Boolean operators (AND, OR, NOT) and filters were applied (language: English, Russian, Uzbek; age: ≥18; article type: clinical trial, meta-analysis, review).

Inclusion and Exclusion Criteria

Inclusion criteria:

Clinical, experimental, or epidemiological studies on gastric or duodenal ulcers

Studies addressing pharmacotherapeutic approaches, including:

Proton pump inhibitors (PPIs)

H2 receptor antagonists

Prostaglandin analogues

Antacids

Bismuth compounds

H. pylori eradication regimens

Studies on prevention or treatment of **NSAID-induced ulcers**

Articles reporting evidence-based preventive recommendations

Exclusion criteria:

Studies published **before 2013**

Pediatric studies

Articles without full text

Animal studies not applicable to clinical practice

Low-quality studies on complementary therapies (e.g., acupuncture, herbal medicine)

Data Extraction

For each included article, the following data were systematically extracted:

Authors and year of publication

Study design (randomized, retrospective, meta-analysis)

Sample size and demographic characteristics

Type of ulcer: gastric or duodenal

Pharmacotherapy used

H. pylori eradication rate

Clinical remission duration

Adverse events

Preventive efficacy

Quality Assessment

The quality of included studies was evaluated using standard scales:

Randomized controlled trials (RCTs) – **Jadad scale (0–5)**

Observational studies – **Newcastle-Ottawa Scale (NOS)**

Meta-analyses – **AMSTAR II**

Studies with a quality score **below 3** were excluded from the final analysis.

Statistical Analysis

Data reported in the literature were summarized using the following indicators:

H. pylori eradication rates (%)

Ulcer healing duration (days/weeks)

Recurrence rates (%)

Risk of NSAID-related ulcer development **(Relative Risk, RR)**

Comparative efficacy of PPIs and other medications

Where available, original statistical measures from meta-analyses were included, such as **confidence intervals (CI), odds ratios (OR), relative risks (RR), and p-values.**

Results

A systematic analysis of **52 articles and reviews** revealed key aspects of pharmacotherapy and preventive strategies for peptic ulcer disease (PUD):

1. Treatment of H. pylori-associated gastric ulcers

Studies indicate that **70–90% of PUD cases are associated with H. pylori infection.**

Triple therapy (PPI + clarithromycin + amoxicillin or metronidazole) achieves a global eradication rate of approximately **60–75%** ([Malfertheiner et al., 2017]; [Gisbert & McNicholl, 2017]).

In regions with high antibiotic resistance, **bismuth quadruple therapy** (PPI + bismuth + tetracycline + metronidazole) increases eradication rates to **85–90%.**

Vonoprazan-based therapy (PCAB) achieves eradication rates exceeding **90% within 7–14 days** ([Fukase et al., 2020]; [Gyawali & Fass, 2018]).

Recent increases in antibiotic resistance have reduced the effectiveness of standard triple therapy when **local epidemiological data are not considered,** highlighting the need for individualized treatment strategies.

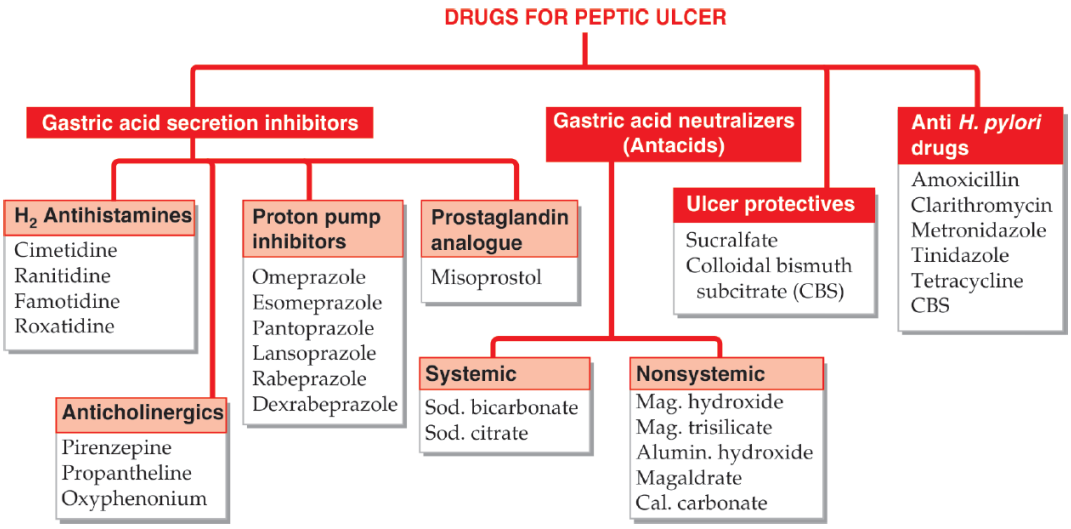
2. NSAID-induced gastric ulcers

25–40% of patients on long-term NSAIDs or aspirin develop gastric or duodenal ulcers ([Lanas et al., 2015]).

Proton pump inhibitors (PPIs) reduce ulcer risk by **50–70%** when used prophylactically.

COX-2 selective inhibitors (e.g., celecoxib) are safer for the gastric mucosa but carry a risk of **cardiovascular complications.**

Misoprostol is highly effective but limited by adverse effects such as diarrhea and discomfort, reducing patient adherence.



3. Ulcer healing agents

PPIs accelerate ulcer healing and prolong remission, while **H2-receptor antagonists** act more slowly.

Bismuth compounds provide mucosal protection and exert **local antimicrobial effects against H. pylori.**

Sucralfate protects the mucosa and is considered safe during pregnancy.

In NSAID-induced ulcers, combining **PPI therapy** significantly reduces recurrence rates.

4. Prevention of recurrence and prophylactic strategies

After **H. pylori eradication**, recurrence rates drop to **<10%** ([Hooi et al., 2017]; [Sugano, 2020]).

High-risk groups (elderly patients, chronic NSAID users) benefit from **long-term low-dose PPI therapy.**

Lifestyle factors, including **smoking, alcohol use, stress, and unhealthy diet,** increase the risk of recurrence.

In areas with high antibiotic resistance**, individualized treatment based on local epidemiology** is critical.

5. Epidemiological outcomes

According to **Global Burden of Disease (GBD) 2019,** there were approximately **8.09 million PUD patients worldwide** (95% CI: 6.79–9.58 million).

H. pylori infection affects approximately **4.4 billion people globally (55–60% of the population),** with the highest prevalence in **Africa and South Asia** ([Hooi et al., 2017]; [Zamani et al., 2018]).

Despite advances in pharmacotherapy, **PUD remains a global challenge** due to rising antibiotic resistance, widespread NSAID use, and lifestyle risk factors.

Summary

Most H. pylori-associated ulcers respond to **triple or quadruple therapy,** with **vonoprazan-based regimens** showing higher efficacy in resistant regions.

NSAID-related ulcers require preventive strategies, primarily **prophylactic PPIs.**

PPIs and PCABs are first-line agents for accelerating healing and maintaining remission.

Lifestyle modifications and tailored pharmacotherapy based on local epidemiology are essential for preventing recurrence.

Overall, modern pharmacotherapy combined with preventive strategies allows **effective control of PUD**, including **H. pylori eradication, gastric mucosal protection, and lifestyle risk modification,** forming an integrated approach to patient management.

Discussion

The findings of this literature review indicate that **peptic ulcer disease (PUD) remains a significant global clinical challenge.** Studies confirm that **H. pylori infection is the primary etiological factor** in PUD development, while **antibiotic resistance, widespread NSAID use, and lifestyle factors** increase the risk of recurrence.

1. H. pylori infection and antibiotic resistance

The results align with global literature, confirming the widespread prevalence of H. pylori. **70–90% of PUD cases** are associated with this bacterium, and eradication significantly reduces recurrence risk. However, rising resistance, particularly to clarithromycin and metronidazole, reduces the effectiveness of standard triple therapy. Consequently, **bismuth quadruple therapy or vonoprazan-based regimens** provide higher eradication rates. These findings underscore the importance of **individualized treatment approaches** in managing H. pylori-associated PUD.

2. NSAID-induced ulcers and prophylaxis

Long-term NSAID or aspirin use results in **25–40% of patients developing gastric or duodenal ulcers.** Studies demonstrate that **prophylactic PPI use reduces the risk by 50–70%,** highlighting the importance of pharmacological prophylaxis. COX-2 selective inhibitors provide mucosal protection but require careful patient selection due to **cardiovascular risk**. Although **misoprostol** is highly effective, adverse effects such as diarrhea and discomfort limit its clinical use.

3. Pharmacotherapy efficacy

PPIs significantly **accelerate ulcer healing and prolong remission**, while H2 receptor antagonists act more slowly but may still be used in specific cases. Bismuth compounds provide **local gastroprotection and anti-H. pylori activity**, and sucralfate protects the mucosa, particularly in pregnancy. Evidence suggests that **integrated management**, combining pharmacotherapy and risk factor control, allows effective PUD management.

4. Epidemiological and clinical trends

According to **GBD 2019,** there were approximately **8.09 million PUD patients worldwide,** while H. pylori infection affects **4.4 billion people globally.** Epidemiological data indicate that **antibiotic resistance and widespread NSAID use hinder reductions in the clinical burden of PUD.** High-risk patients benefit from **long-term low-dose PPI or PCAB therapy,** which significantly reduces recurrence.

5. Clinical and scientific recommendations

H. pylori eradication is the cornerstone strategy for preventing PUD and reducing recurrence.

Individualized therapy based on local epidemiology is essential in regions with high antibiotic resistance.

Prophylactic PPI use in long-term NSAID users protects the gastric mucosa.

Lifestyle modifications (smoking cessation, alcohol reduction, stress management, healthy diet) are critical to reduce recurrence risk.

Modern pharmacological agents, such as vonoprazan and bismuth quadruple therapy, enhance treatment efficacy and reduce recurrence.

CONCLUSION

This literature review demonstrates that **peptic ulcer disease (PUD) remains a major global health concern.** H. pylori infection is the primary etiological factor, but **antibiotic resistance, long-term NSAID use, and lifestyle factors** significantly increase the risk of recurrence.

Pharmacotherapy analysis indicates: **PPIs, vonoprazan (PCABs), and bismuth quadruple therapy** are effective for **H. pylori eradication** and **accelerating ulcer healing**.

H2 receptor antagonists have slower action but may be used in certain cases.

Prophylactic PPI therapy is effective in preventing NSAID-induced ulcers, while COX-2 selective inhibitors can be considered in selected high-risk patients.

Epidemiological evidence suggests that **reducing the global clinical burden of PUD and H. pylori infection remains a priority,** with antibiotic resistance and NSAID use as major challenges. Modern pharmacotherapy combined with **preventive strategies** allows an **integrated approach to effectively control PUD**.

Recommendations

H. pylori eradication should be prioritized as the first-line strategy to prevent PUD and recurrence.

Individualized therapy is essential in regions with high antibiotic resistance, guided by local epidemiological data.

Prevention of NSAID-related ulcers: long-term NSAID users should receive **prophylactic PPI therapy**; COX-2 selective inhibitors may be used considering the risk-benefit profile.

Risk factor management: lifestyle modifications, including **smoking cessation, alcohol moderation, stress reduction, and healthy diet,** are critical to minimize recurrence.

Use of modern pharmacological agents: vonoprazan and bismuth quadruple therapy play a key role in increasing treatment efficacy and reducing recurrence.

Epidemiological monitoring and research: systematic surveillance of PUD and H. pylori prevalence, antibiotic resistance patterns, and clinical outcomes should be implemented.

Integrated approach: combining pharmacotherapy, prophylaxis, lifestyle modification, and patient education should form the core of effective PUD management strategies.

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