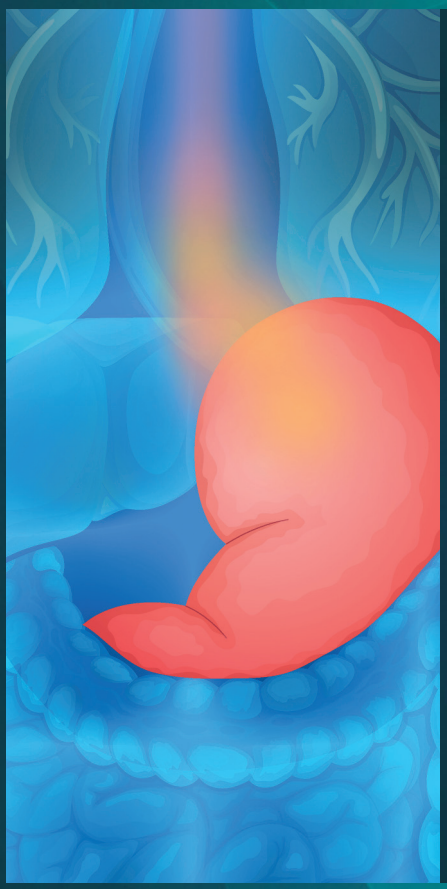
ISSN 0120-9957
ISSN 2500-7440 (Online)
DOI: https://doi.org/10.22516/issn.2500-7440

40 YEARS

RCG Revista Colombiana de Gastroenterología

Supplement 3 - Volume 40
2025

www.revistagastrocol.com
www.gastrocol.com · www.scielo.org.co



CLINICAL PRACTICE GUIDELINE FOR THE DIAGNOSIS AND TREATMENT OF GASTROESOPHAGEAL REFLUX DISEASE (GERD) IN ADULTS: 2025 UPDATE

GUIDES COMMITTEE

Luis Carlos Sabbagh
William Otero Regino
Raúl Cañadas
Diego Mauricio Aponte
Juan David Linares
Alejandro Concha

ASOCIACION COLOMBIANA DE GASTROENTEROLOGIA
1947

RCG Revista Colombiana de Gastroenterología

Editorial

Presentation of the Clinical Practice Guideline for the Diagnosis and Treatment of Gastroesophageal Reflux Disease (GERD) in Adults: 2025 Update 1

David B. Páramo-Hernández.

Supplement

Clinical Practice Guideline for the Diagnosis and Treatment of Gastroesophageal Reflux Disease (GERD) in Adults: 2025 Update 3

Albis Cecilia Hani de Ardila, Raúl Antonio Cañadas-Garrido, Diego Mauricio Aponte-Martín, Angie Ximena Ortiz-Chamorro, José Bareño-Silva, Jaime Andrés Ibarra-Burgos, María Carolina Ardila-Hani, Juan David Linares-Ramírez, William Alberto Otero-Regino, Alejandro Concha-Mejía, Luis Carlos Sabbagh.

https://doi.org/10.22516/25007440.1474

Supplement

Presentation of the Clinical Practice Guideline for the Diagnosis and Treatment of Gastroesophageal Reflux Disease (GERD) in Adults: 2025 Update

David B. Páramo-Hernández.[1]

OPEN ACCESS

Citation:
Páramo-Hernández D. Presentation of the Clinical Practice Guideline for the Diagnosis and Treatment of Gastroesophageal Reflux Disease (GERD) in Adults: 2025 Update. Revista. colomb. Gastroenterol. 2025;40(Supl 3):1-2. https://doi.org/10.22516/25007440.1474

[1] Gastroenterologist and Clinical Epidemiologist. Digestive Health Institute, GutMédica. Director and Editor, Revista Colombiana de Gastroenterología. Bogotá, Colombia.

***Correspondence:** David B. Páramo Hernández. paramo.david@gmail.com

Received: 06/10/2025
Accepted: 07/10/2025

CC BY NC ND

With this volume, Revista Colombiana de Gastroenterología celebrates 40 years of continuous publication and editorial work. For this reason, the 2024–2025 Board of Directors of the Colombian Association of Gastroenterology, chaired by Dr. Diego Mauricio Aponte Martín, together with the Journal's Editorial Committee, have decided to commemorate this milestone through the publication of three supplements containing updated versions of the most relevant clinical practice guidelines (CPGs).

In this supplement, we present the updated version of the Clinical Practice Guideline for the Diagnosis and Treatment of Gastroesophageal Reflux Disease (GERD) in Adults: 2025 Update. This initiative originated from the Association's presidency and brought together a CPG Committee led by Drs. Luis Carlos Sabbagh, William Otero Regino, Raúl Cañadas, Diego Aponte, Alejandro Concha Mejía, and Juan David Linares. The guideline, coordinated by Dr. Albis Hani, was developed under strict methodological standards with the support of epidemiology experts from Universidad CES and the collaboration of specialized subject matter experts. We formulated clinically relevant questions and conducted a search for national and international guidelines in specialized databases. The Universidad CES team carried out a systematic review of the literature. We used the GRADE methodology and evidence-to-decision (EtD) frameworks, based on systematic searches of international guidelines, systematic reviews, and meta-analyses published between 2015 and 2025. The final consensus was reached through a multidisciplinary panel of experts, considering factors such as applicability, resources, and equity within the Colombian health system. The methodological process and technical appendices are available in the digital version of the guideline, along with its complete supplements, at: www.gastrocol.com.

Based on the Methodological Guide for the Adoption and Adaptation of Evidence-Based Clinical Practice Guidelines (2017), developed by the Colombian Ministry of Health and Social Protection and the Institute for Technological Health Assessment (IETS) (currently in force)[(1)], we adopted and adapted an evidence-based methodological approach for the CPG. Accordingly, we adopted recommendations from existing guidelines when these aligned with the national context, taking into account time and resource limitations for the development of a *de novo* CPG, and recognizing that this guideline constitutes an update of the 2015 version[(2)].

Undoubtedly, this document serves as a key reference for consultation, implementation, and adoption by health professionals, public and private health institutions, health administrators, insurers, and policymakers who seek the support and guidance provided by this updated clinical practice guideline.

REFERENCES

1. Pérez Gómez AV, Gómez Espitia LM, Yepes-Núñez JJ, Rodríguez Moreno JH, Flórez ID. Guía metodológica para la adopción - adaptación de guías de práctica clínica basadas en evidencia [Internet]. 1.ª edición. Bogotá: Ministerio de Salud y Protección Social; 2017. Disponible en: https://www.iets.org.co/Archivos/79/Guia_de_Adopcion_VF.pdf
2. Hani AC, Galindo A, Leguizamo A, Maldonado C, Páramo D, Costa V, et al. Guía de práctica clínica para la enfermedad por reflujo gastroesofágico. Rev Col Gastroenterol. 2015;30(Suppl 1):1-8.

https://doi.org/10.22516/25007440.1450

Supplement

Clinical Practice Guideline for the Diagnosis and Treatment of Gastroesophageal Reflux Disease (GERD) in Adults: 2025 Update

Albis Cecilia Hani de Ardila,[1*] Raúl Antonio Cañadas-Garrido,[2] Diego Mauricio Aponte-Martín,[3] Angie Ximena Ortiz-Chamorro,[4] José Bareño-Silva,[5] Jaime Andrés Ibarra-Burgos,[6] María Carolina Ardila-Hani,[7] Juan David Linares-Ramírez,[8] William Alberto Otero-Regino,[9] Alejandro Concha-Mejía,[10] Luis Carlos Sabbagh.[11]

OPEN ACCESS

Citation:
Hani de Ardila AC, Cañadas-Garrido RA, Aponte-Martín DM, Ortiz-Chamorro AX, Bareño-Silva J, Ibarra-Burgos JA, Ardila-Hani MC, Linares-Ramírez JD, Otero-Regino WA, Concha-Mejía A, Sabbagh LC. Clinical Practice Guideline for the Diagnosis and Treatment of Gastroesophageal Reflux Disease (GERD) in Adults: 2025 Update. Revista. colomb. Gastroenterol. 2025;40(Supl 3):3-31. https://doi.org/10.22516/25007440.1450

[1] Gastroenterologist. Full Professor, Hospital San Ignacio, Pontificia Universidad Javeriana. Bogotá, Colombia.
[2] Gastroenterologist. Associate Professor of Medicine, Department of Internal Medicine, Pontificia Universidad Javeriana; Head, Gastroenterology Unit, Hospital Universitario San Ignacio. Bogotá, Colombia.
[3] Internist, Epidemiologist, and Gastroenterologist. Head of the Gastroenterology Postgraduate Program, Fundación Universitaria Sanitas. Clínica Reina Sofía. President, Colombian Association of Gastroenterology. Bogotá, Colombia.
[4] Physician, Epidemiologist. Research Professor, School of Health Sciences, Universidad CES. Medellín, Colombia.
[5] Physician, Epidemiologist. Research Professor, School of Health Sciences, Universidad CES. Medellín, Colombia.
[6] Internist, Clinical Epidemiologist. School of Health Sciences, Universidad CES. Medellín, Colombia.
[7] Gastroenterologist, Clinical Epidemiologist. Clínica Colsanitas. Bogotá, Colombia.
[8] Gastroenterologist. Organización Sanitas Internacional. Bogotá, Colombia.
[9] MD, FAGA, FASGE, FACP. Gastroenterologist, Full Professor of Medicine, Universidad Nacional de Colombia. Centro de Gastroenterología y Endoscopia. Bogotá, Colombia.
[10] Internist, Gastroenterologist, Endoscopist, and Epidemiologist. Clínica del Country, Clínica La Colina, and Clínica Shaio. Bogotá, Colombia.
[11] MD, FASGE. Head of the Gastroenterology Department, Clínica Reina Sofía and Clínica Universitaria Colombia. Director of the Gastroenterology Postgraduate Program, Fundación Universitaria Sanitas. Director of the World Gastroenterology Organization (WGO) Training Center, Bogotá, Colombia.

***Correspondence:** Albis Cecilia Hani de Ardila
albishani@gmail.com

Received: 16/09/2025
Accepted: 25/09/2025

Abstract

Objective: To provide an evidence-based clinical practice guideline for the diagnosis and treatment of gastroesophageal reflux disease (GERD), addressing the effectiveness and safety of interventions, and aimed at healthcare professionals managing gastrointestinal disorders in any clinical setting in Colombia. **Materials and Methods:** This guideline was developed by a multidisciplinary team with support from the Colombian Association of Gastroenterology and Universidad CES. Relevant clinical questions were formulated, and searches were conducted in databases of national and international guidelines. The retrieved guidelines were assessed for quality and applicability; five met criteria for adoption or adaptation. Additional evidence-based documents were considered during drafting. The Universidad CES research group performed a systematic literature review. The GRADE methodology and Evidence-to-Decision (EtD) frameworks were applied, based on guidelines, systematic reviews, and meta-analyses published between 2015 and 2025. Consensus was reached through a multidisciplinary panel, considering applicability, resource availability, and equity within the Colombian healthcare system. The complete methodology and technical appendices are available in the full version at www.gastrocol.com. **Results:** A clinical practice guideline was developed for the diagnosis and management of patients with GERD in Colombia, addressing six core clinical questions, with 39 evidence-based recommendations and 18 good practice points. Previous evidence was updated, new recommendations on diagnosis and management were added, and a section dedicated to pregnant patients was included. **Conclusions:** This update incorporates new recommendations and establishes a quality standard for the timely diagnosis and management of GERD, contributing to the reduction of disease burden and offering clear criteria for diagnostic evaluation, treatment, and follow-up.

Keywords

Gastroesophageal Reflux Disease, Clinical Practice Guidelines, Barrett's Esophagus.

INTRODUCTION

Gastroesophageal reflux disease (GERD) represents an increasing public health challenge due to the growing number of prevalent and incident cases and the associated years lived with disability (YLDs). To address this condition, we must understand changes in global and regional epidemiological trends and the burden it imposes on policymakers and other stakeholders[1]. This makes it essential to identify diagnostic and therapeutic methods that are both effective and affordable[2].

Reported prevalence rates for this disease are 23% in South America, 18.1–27.8% in North America, 11.6% in Australia, 8.8–25.9% in Europe, 8.7–33.1% in the Middle East, and 7.8% in East Asia[3]. In Latin America, one systematic review assessed several prevalence studies in the region (one in Argentina, five in Brazil, and two in Mexico) and identified rates ranging from 3% to 11.9%, similar to estimates from Europe and North America and higher than those reported in Asia[4].

In Colombia, the estimated prevalence of reflux symptoms is around 12%. These data come from a population-based survey on gastroesophageal reflux symptoms and associated factors conducted in major Colombian cities (Bogotá, Cali, Medellín, and Barranquilla). A total of 6,842 questionnaires were collected, revealing an estimated overall prevalence of reflux symptoms of 11.98% (95% confidence interval [CI]: 11.05–12.97), similar to reports from other Latin American countries. Among cities, Barranquilla showed the highest frequency (16.22%; 95% CI: 14.58–18.01), while Bogotá had the lowest (10.75%; 95% CI: 9.30–12.38). According to the GERDQ questionnaire, the estimated prevalence by symptom was as follows: heartburn, 13.6% (95% CI: 12.50–14.60); regurgitation, 16.9% (95% CI: 15.74–17.99); epigastric pain, 16.67% (95% CI: 15.54–17.80); nausea, 11.4% (95% CI: 10.46–12.35); sleep disturbance due to heartburn or regurgitation, 8.17% (95% CI: 7.36–8.97); and use of additional nonprescribed medications, 6.68% (95% CI: 6.01–7.35). Female sex, residence in Barranquilla or Medellín, and the presence of comorbidities were statistically associated with reflux symptoms[5].

In 2015, the Colombian Association of Gastroenterology, with support from the Clinical Research Institute of the Universidad Nacional de Colombia, developed the *Evidence-Based Clinical Practice Guideline for the Diagnosis and Treatment of Gastroesophageal Reflux Disease in Adult Patients*. Since that publication, new therapeutic alternatives and evolving concepts regarding treatment goals have emerged. For this reason, we considered it necessary to update the guideline in 2025, incorporating new recommendations for diagnostic and therapeutic approaches within the Colombian context.

Through this updated clinical practice guideline (CPG), we aim to provide recommendations grounded in the best available evidence and national epidemiological data[5], to optimize the diagnosis, treatment, and follow-up of GERD in Colombia. Furthermore, we seek to support healthcare professionals in clinical decision-making, promote the rational use of pharmacological and nonpharmacological treatments, address extradigestive manifestations, include specific considerations during pregnancy and lactation, and contribute to the prevention and monitoring of complications such as Barrett's esophagus and esophageal adenocarcinoma.

OBJECTIVES OF THE CLINICAL PRACTICE GUIDELINE

- Provide healthcare professionals who treat patients with GERD a foundation for diagnostic assessment, treatment, and follow-up.
- Offer different treatment options for GERD in cases of inadequate response to initial management.
- Guide the timely diagnostic and therapeutic approach for patients with GERD, ensuring referral for specialized evaluation in difficult-to-manage or treatment-refractory cases.
- Ensure appropriate follow-up and management of complications associated with GERD.

SCOPE OF THE CLINICAL PRACTICE GUIDELINE

The purpose of this clinical practice guideline (CPG) is to provide the healthcare community with the most recent evidence on the effectiveness and safety of different strategies for the management of GERD. It is intended for healthcare professionals who manage gastrointestinal diseases at any level of care across the country—especially those treating patients with GERD—and indirectly for decision-makers in healthcare delivery, insurance entities, healthcare payers, and health policymakers.

USERS OF THE CLINICAL PRACTICE GUIDELINE

This guideline is addressed to general practitioners, internists, family physicians, gastroenterologists, surgeons, otorhinolaryngologists, healthcare administrators, public health specialists, and surgeons working in outpatient settings, emergency departments, general hospitalization wards, or intensive care units.

TARGET POPULATION

- Adult patients (aged 18 years and older) diagnosed with GERD, regardless of disease duration or clinical status.

- Pregnant or breastfeeding patients with gastroesophageal reflux.

This guideline is not designed for patients with systemic diseases that may cause GERD-like symptoms, nor for pediatric populations.

HEALTHCARE SETTINGS

This guideline aims to support decision-making in the diagnosis, treatment, and follow-up of patients with GERD from the first level of care through referral to specialized centers in clinical gastroenterology. It provides healthcare professionals with the necessary information for early detection and timely diagnosis of the disease, including criteria for referral to gastroenterology specialists.

CLINICAL ASPECTS ADDRESSED BY THE GUIDELINE

This CPG covers the diagnosis, treatment, and follow-up of patients with GERD. Specifically, it addresses the following clinical aspects:

- Diagnosis
- Pharmacological and nonpharmacological treatment
- Monitoring and management of complications
- Management of extradigestive manifestations
- Considerations during pregnancy and lactation

COMPOSITION OF THE GUIDELINE DEVELOPMENT GROUP

The group included expert gastroenterologists, internists, general practitioners, and epidemiologists. All participants submitted conflict of interest declarations. Full information is available in the extended version of the CPG.

DECLARATION OF CONFLICT OF INTEREST

All members of the development group and expert panel, as well as individuals participating in the external review, signed a conflict of interest disclosure form. Conflicts were analyzed, and decisions regarding full participation, partial participation, or exclusion from the guideline development process were made accordingly. The detailed analysis is included in the full version of the guideline, available at www.gastrocol.com.

DECISION ON THE UPDATE

The Colombian Association of Gastroenterology, Grupo Cochrane ITS, and the Clinical Research Institute of Universidad Nacional de Colombia developed the Evidence-Based Guideline for Gastroesophageal Reflux Disease in Adult Patients in 2015. The development group reached a consensus to update this guideline, taking into account the evidence published over the past 10 years on key aspects such as diagnosis, management, follow-up, and special populations, including pregnant women.

METHODOLOGY FOR UPDATING THE CLINICAL PRACTICE GUIDELINE

Updating the Clinical Questions of the Guideline

The process and reporting followed the CheckUp recommendations for updating clinical practice guidelines (CPGs) [6]. During this process, we reviewed the scope, target population, users, objectives, and clinical questions from the 2015 version of the CPG. A comparison and justification of the changes can be consulted in the supplementary material. Additionally, the panel developed new clinical questions for inclusion in the 2025 version of the guideline. In total, six questions were included: one was retained from the 2015 version, four were modified, and one new question was added. Regarding clinically relevant outcomes, we maintained those considered in the 2015 version concerning appropriate diagnosis, treatment, and follow-up.

The review and update of clinical practice recommendations and good practice points were based on the evidence identified in existing CPGs and, in some cases, complemented by systematic literature reviews (SLRs). These were appraised using the GRADE methodology (Grading of Recommendations, Assessment, Development, and Evaluation), considering the quality of evidence and the strength of recommendations (**Table 1**).

Certainty Rating of the Evidence

For the evidence synthesis, we considered the studies selected and referenced within the adopted clinical practice guidelines (CPGs) and verified their corresponding GRADE assessments. Using this approach, we generated the respective evidence profiles and determined the confidence in effect estimates according to the overall quality of the evidence. The GRADE system[7] establishes four levels of evidence, which are shown in **Table 1**.

Contextualization of the Evidence

We developed evidence-to-recommendation tables presenting the value judgments that guided the formulation of the recommendations. The evidence-to-decision (EtD) tables, available as supplementary material, outline the rationale behind each recommendation, including judgments about

Table 1. GRADE criteria for strength of recommendation and quality of evidence

Dimension	Meaning
Strength of Recommendation	
Strong in favor	The desirable consequences clearly outweigh the undesirable ones. **It is recommended to do it.**
Conditional in favor	The desirable consequences probably outweigh the undesirable ones. **It is suggested to do it.**
Conditional against	The undesirable consequences probably outweigh the desirable ones. **It is suggested not to do it.**
Strong against	The undesirable consequences clearly outweigh the desirable ones. **It is recommended not to do it.**
Quality of Evidence	
High	It is very unlikely that new studies will change our confidence in the estimated effect.
Moderate	It is likely that new studies will have an important impact on our confidence in the estimated effect and may change it.
Low	It is very likely that new studies will have an important impact on our confidence in the estimated effect and may change it.
Very low	Any estimated effect is very uncertain.
Good practice point*	Recommended practice based on the clinical experience of the CPG Development Group.

*Not included in the GRADE system. Author's own research.

desirable and undesirable effects, certainty of evidence, variability, balance of risks and benefits, resource use, cost-effectiveness, equity, acceptability, and feasibility.

Methodology for Adoption/Adaptation of the Clinical Practice Guideline

Following the *Methodological Guide for the Adoption and Adaptation of Evidence-Based Clinical Practice Guidelines* (2017), currently in force, by the Colombian Ministry of Health and Social Protection and the Institute for Technological Health Assessment (IETS), we applied the corresponding methodology for the adoption and adaptation of evidence-based CPGs[8]. Complete traceability of the process is available in the full version of the guideline.

Below, we present the clinical questions, followed by their respective recommendations or good practice points.

QUESTION 1: WHAT TESTS ARE USEFUL FOR DIAGNOSING GERD IN ADULTS?

Recommendation 1

We recommend a thorough clinical history that evaluates the presence of typical GERD symptoms such as heartburn, regurgitation, and non-cardiac chest pain, as well as the identification of possible extradigestive manifestations, including cough, laryngitis, sleep disturbances, or others.
Certainty Level: Very low
Strength of Recommendation: Strong in favor

Evidence Summary

Among the evidence adopted from previous guidelines, a systematic review by Moayyedi et al. (AMSTAR-2 rating: low to moderate certainty) included 15 studies that assessed the diagnostic accuracy of clinical judgment for GERD across a total of 11,366 patients, of whom 4,817 (42%) were classified as having GERD. The studies evaluated general practitioners, specialists, and a computer model. For primary care physicians, four studies comprising 1,459 patients reported diagnostic accuracy data: 579 patients (40%) were diagnosed with GERD. The sensitivity of primary care physicians ranged from 67% to 95%, and specificity from 25% to 52%. The pooled positive likelihood ratio (LR+) was 1.3 (95% CI: 1.2–1.4; $p = 0.39$), and the negative likelihood ratio (LR–) was 0.66 (95% CI: 0.55–0.79; $p = 0.23$). One study reported an LR– of 0.21, classifying 82% of GERD patients, with a sensitivity of 95% but a specificity of only 23%[9].

A systematic review from Latin America by Salis (AMSTAR-2 rating: critically low), which aimed to estimate the prevalence and incidence of GERD and identify

risk factors and potential comorbidities, included eight studies from Latin American countries (Brazil [n = 5], Mexico [n = 2], and Argentina [n = 1]). Reported prevalence of heartburn or regurgitation ranged from 11.9% to 31.3% for symptoms occurring at least weekly, and 25% to 35% in studies that did not specify symptom frequency[4].

Recommendation 2

We recommend not using clinical interviews or symptom questionnaires (such as the GerdQ) as the sole tools for establishing a GERD diagnosis.
Certainty Level: Low
Strength of Recommendation: Strong against

Evidence Summary

We reviewed two recent meta-analyses that evaluated the diagnostic performance of the GerdQ questionnaire for GERD. The first, by Zhang et al.[10], included 40 studies and concluded that GerdQ has limited sensitivity and specificity compared with diagnostic tests such as pH monitoring, esophageal impedance, and endoscopy. Although it is a widely used screening tool due to its ease of application, its ability to confirm or rule out GERD is poor, limiting its usefulness as a stand-alone diagnostic method. The second meta-analysis, by Simadibrata et al.[11], included more than 11,000 participants and found that GerdQ has moderate sensitivity and specificity, with an area under the curve (AUC) of 0.705. While it cannot be considered a definitive diagnostic test, it retains value as an initial screening tool—particularly in contexts where more precise tests are unavailable or contraindicated. Therefore, we recommend using the GerdQ to support the initial clinical evaluation but always complemented with objective diagnostic tests according to the clinical scenario.

Recommendation 3

For patients with classic GERD symptoms, such as heartburn and regurgitation, who do not present alarm symptoms, we may recommend a therapeutic trial with a proton pump inhibitor (PPI) once daily before meals for eight weeks.
Certainty Level: Moderate
Strength of Recommendation: Strong in favor

Evidence Summary

The meta-analysis by Ghoneim et al. (AMSTAR-2 rating: moderate certainty) included 19 studies with a total of 1,691 patients. For GERD, the PPI trial demonstrated a pooled sensitivity of 79% (95% CI: 72%–84%) and a pooled specificity of 45% (95% CI: 40%–49%). This indicates that the PPI test has good sensitivity for GERD but suboptimal specificity. The test performed best in cases of non-cardiac chest pain associated with GERD[12]. Thus, a PPI trial provides symptomatic relief and acceptable sensitivity to guide initial management of typical, non-alarm symptoms; however, its limited specificity means that it does not confirm GERD. Therefore, if there is no response or if red flags are present, we should proceed with endoscopy and/or pH-impedance testing, in accordance with the current diagnostic framework.

Recommendation 4

We do not recommend a proton pump inhibitor (PPI) trial to diagnose extraesophageal GERD in patients with concomitant typical GERD symptoms (heartburn, regurgitation).
Certainty Level: Low
Strength of Recommendation: Strong against

Evidence Summary

The Latin American Consensus Expert Panel (2024) addressed the question: *Is a proton pump inhibitor trial recommended to diagnose extraesophageal GERD (dysphonia, cough, asthma) in patients with typical GERD symptoms (heartburn, regurgitation)?* Based on the available evidence, the panel concluded that a PPI trial is not a useful first step for diagnosing GERD in patients presenting with extraesophageal manifestations, even when typical symptoms are present. However, it may be useful for managing the concomitant typical symptoms[13]. Symptoms such as chronic cough, dysphonia, and throat clearing may suggest an extraesophageal reflux syndrome (EERS)[14,15]. However, the correlation between EERS and GERD remains uncertain and difficult to establish[16]. This uncertainty contributes to substantial healthcare costs—the evaluation and management of patients with extraesophageal reflux syndrome are estimated to be five times more expensive than those of GERD with typical symptoms.

Recommendation 5

We do not recommend a PPI trial to diagnose extraesophageal GERD in patients without concomitant typical GERD symptoms (heartburn, regurgitation) or chest pain.
Certainty Level: Low
Strength of Recommendation: Strong against

Evidence Summary

In clinical practice, extraesophageal symptoms are often attributed to GERD—even in the absence of concomitant typical symptoms, despite a lack of response to PPI therapy or negative reflux monitoring results[17]. Moreover, studies including patients with extraesophageal reflux syndrome—

with and without typical GERD symptoms—have reported sensitivity ranging from 52% to 86% and specificity from 41% to 58%. These studies generally had small sample sizes and heterogeneous designs, resulting in limited diagnostic validity of the PPI trial for extraesophageal GERD[18–20].

Recommendation 6

In patients with GERD symptoms and alarm features such as dysphagia, odynophagia, weight loss, gastrointestinal bleeding, persistent vomiting, or unexplained iron-deficiency anemia, we recommend performing an upper gastrointestinal endoscopy.
Certainty Level: Moderate
Strength of Recommendation: Strong in favor

Evidence Summary

No randomized controlled trials (RCTs) are feasible in this context—it would be unethical to randomize patients with dysphagia or hematemesis to a "no endoscopy" group. Therefore, the available evidence derives from observational studies, large cohorts, and diagnostic studies in dyspepsia and GERD, which consistently show that alarm symptoms are associated with a higher prevalence of malignancy or serious complications. The 2015 CPG cited the systematic review by Ford et al. on alarm symptoms in dyspepsia, which included several prospective and retrospective studies. The review reported a sensitivity of 51.9% (95% CI: 50.4–53.4) and specificity of 85.1% (95% CI: 84.9–85.3) of alarm symptoms for detecting organic disease. The rate of cancer detected was 1.3% among patients with dyspepsia undergoing esophagogastroduodenoscopy. These findings can serve as indirect evidence in patients with dyspepsia to assess the predictive value of alarm symptoms[53].

Recommendation 7

In patients with typical GERD symptoms, we recommend careful endoscopic evaluation, comprehensive reporting, and photographic documentation of the following aspects to improve patient care and clinical outcomes:

- Objective findings of GERD, when present: erosive esophagitis (classified according to the Los Angeles system), Barrett's esophagus (using the Prague classification), and peptic strictures.
- Landmarks and integrity of the gastroesophageal junction: hiatal hernia dimensions (using the Hill classification or the American Foregut Society classification in both frontal and retroflexed views); position of the upper gastric folds, Z-line, and diaphragmatic impression; and description of any existing fundoplication (if present).

Certainty Level: Very low
Strength of Recommendation: Strong in favor

Evidence Summary

We identified a retrospective observational study by Boys et al., which reviewed 100 esophagogastroduodenoscopy (EGD) reports from 100 different endoscopists in distinct patients. Esophagitis was observed in 33 patients but classified in only 14 (42%). Hiatal hernia was reported in 61 patients (57%), measured in 31 (51%), and classified in only 26% of cases[21]. The certainty of the evidence was low due to the absence of substantial studies and the limited data available from a single, low-power observational study. We conducted an updated search to identify prospective evidence published after the Clinical Practice Guideline (CPG) of the American Society for Gastrointestinal Endoscopy (ASGE) (2025). However, we did not find additional studies that contributed significantly to the recommendation or the certainty of the evidence; therefore, we adopted the recommendation.

Recommendation 8

In patients with reflux symptoms (symptomatic GERD) following peroral endoscopic myotomy (POEM), we suggest performing an upper endoscopic evaluation.
Certainty Level: Very low
Strength of Recommendation: Conditional in favor

Evidence Summary

In a meta-analysis by Vishnu et al. (AMSTAR-2: moderate-quality evidence) that included nine studies with 1,226 patients (540 with full-thickness and 686 with modified myotomy), patients who underwent POEM—particularly with the full-thickness technique—showed a higher risk of symptomatic reflux. The odds ratio (OR) for reflux with full-thickness versus modified techniques was 1.58 (95% CI: 1.12–2.23). Therefore, in patients with post-POEM reflux symptoms (either full-thickness or similar techniques), we suggest performing upper endoscopy, given the low certainty of evidence and conditional recommendation strength. However, this meta-analysis has limitations, as it included observational studies and presented methodological heterogeneity[22].

Recommendation 9

We recommend diagnostic endoscopy after discontinuing PPI therapy for two to four weeks in patients whose typical GERD symptoms do not adequately respond to an 8-week empirical PPI trial or whose symptoms recur after discontinuation.

Certainty Level: Low
Strength of Recommendation: Strong in favor

Evidence Summary

A small prospective study by Dubar et al. involving 12 patients with Los Angeles (LA) grade C esophagitis in remission showed that discontinuation of PPI therapy led to recurrence of esophagitis after only one week in 10 patients, and five patients presented recurrent grade C esophagitis after two weeks. However, these results may not be generalizable to lower-grade esophagitis[23]. Therefore, to ensure accurate phenotyping of GERD, we recommend performing endoscopy after at least two weeks—preferably four—of PPI withdrawal[24].

Recommendation 10

In patients with chest pain without heartburn who have undergone appropriate evaluation to rule out coronary artery disease, we recommend objective testing to confirm or exclude GERD (endoscopy, reflux monitoring, or high-resolution esophageal manometry to rule out motility disorders).
Certainty Level: Low
Strength of Recommendation: Conditional in favor

Evidence Summary

According to the American College of Gastroenterology (ACG) Clinical Practice Guideline for the diagnosis and management of GERD, in patients with chest pain without heartburn, once cardiac causes have been excluded, we should perform objective testing to confirm or rule out GERD[25].

Endoscopy is frequently used to evaluate classic GERD symptoms such as heartburn and regurgitation, but its role in assessing extraesophageal symptoms remains less defined. In patients with extraesophageal manifestations of GERD, reported rates of erosive esophagitis range from 18% to 52%. However, the presence of erosive esophagitis does not confirm GERD as the cause of extraesophageal symptoms, since erosive esophagitis has been found in 16% of asymptomatic individuals undergoing routine health checkups[26]. Nonetheless, if Los Angeles grade C or D erosive esophagitis is present, this establishes a diagnosis of severe GERD and justifies a therapeutic PPI trial.

Recommendation 11

We recommend 24-hour impedance-pH monitoring (pH-metry) off therapy in patients with a low pretest probability of GERD, in those who do not respond to PPI treatment and have normal upper endoscopy findings with reflux symptoms, in patients being evaluated prior to antireflux surgery, and in those with extradigestive manifestations of reflux.
Certainty Level: Low
Strength of Recommendation: Conditional in favor

Evidence Summary

The 2022 ACG guideline states that the choice of test and whether it should be performed on or off PPI therapy depends on the clinical question. If the patient has never had an objective diagnosis of GERD (only empirical treatment), if the pretest probability is low, or if antireflux surgery is being considered, we should perform testing off PPI therapy (including 24-hour impedance-pH monitoring). The guideline also recommends considering pH or impedance-pH monitoring off PPI therapy when there is no prior objective evidence of GERD (e.g., LA grade C/D esophagitis, Barrett's esophagus, or positive pH monitoring).

Likewise, the Lyon Consensus 2.0 (2024) states that when there is no conclusive evidence of GERD (unproven GERD), testing should be performed to establish or refute the diagnosis. Ambulatory reflux monitoring should therefore be performed off antisecretory therapy. Wireless pH monitoring or catheter-based pH or impedance-pH monitoring are acceptable alternatives depending on local feasibility, availability, and cost. Conclusive GERD evidence and borderline findings supported by complementary metrics, as defined by the Lyon Consensus, serve to confirm the diagnosis of GERD[24].

Recommendation 12

We recommend not performing 24-hour pH monitoring off PPI therapy solely as a diagnostic test for GERD in patients with endoscopic evidence of reflux esophagitis grade B, C, or D according to the Los Angeles classification, or in patients with long-segment Barrett's esophagus.
Certainty Level: Moderate
Strength of Recommendation: Strong against

Evidence Summary

A multicenter study by Visaggi et al. (n = 155) provides recent data supporting this position regarding grade B disease. The authors found that 100% of patients with grade B esophagitis had objective evidence of GERD on pH-impedance monitoring (acid exposure time [AET] >6% or AET 4%–6% with altered physiological indices). In contrast, only 17.6% of patients with grade A esophagitis had objective confirmation, while 75% of those with grade C did (the remainder already confirmed by endoscopic findings). The clinical response to PPI therapy was comparable between grades B and C (74% and 70%, respectively) but significantly lower in grade A (39%). This indicates that

grade B behaves as objective evidence of GERD, similar to grade C, and that performing pH monitoring off PPI therapy in these cases adds no clinical value while generating additional costs and patient discomfort[27].

Recommendation 13

We recommend using the total number of reflux episodes measured by pH-impedance monitoring as one of the parameters to diagnose GERD. The diagnosis of GERD based on multichannel intraluminal impedance-pH (MII-pH) monitoring does not depend solely on the total number of reflux episodes but also considers acid exposure time and nocturnal baseline impedance, among other metrics.
Certainty Level: Low
Strength of Recommendation: Weak in favor

Evidence Summary

In a study by Nikolic et al., 67 patients with weakly acidic reflux (defined on 24-hour pH-impedance monitoring performed off PPI therapy as esophageal acid exposure time <4.2% and >40 total reflux episodes) underwent magnetic sphincter augmentation, resulting in significant improvement in GERD-related symptoms and quality of life[28]. In a study by Horton and Clayton, 72 patients with GERD symptoms underwent 24-hour pH-impedance monitoring performed off PPI therapy. Using abnormal esophageal acid exposure time as the reference parameter for GERD diagnosis, the area under the curve (AUC) analysis showed that a threshold of ≥41 total reflux episodes was optimally sensitive and specific for identifying GERD (sensitivity: 69.6%, specificity: 80.7%, AUC: 0.83; 95% CI: 0.73–0.92), although this finding does not identify the number of reflux episodes as an independent predictor of GERD[29].

Recommendation 14

We suggest using multichannel intraluminal impedance-pH (MII-pH) monitoring off PPI therapy instead of conventional pH monitoring to guide therapeutic decisions in patients with unconfirmed GERD and PPI-refractory heartburn.
Certainty Level: Low
Strength of Recommendation: Conditional in favor

Evidence Summary

Quantitative analysis from the Latin American consensus was based on a single study showing that MII-pH monitoring off PPI therapy provided higher diagnostic yield and led to treatment modifications more frequently than conventional pH monitoring (relative risk [RR]: 1.31; 95% CI: 1.02–1.70)[30]. However, the study did not assess treatment outcomes based on reflux monitoring, so it remains uncertain whether these findings truly translate into changes in therapeutic management. Importantly, MII-pH also allows for the measurement of additional parameters that can be useful in cases of diagnostic uncertainty, such as the post-reflux swallow-induced peristaltic wave index (PSPW-I) and mean nocturnal baseline impedance (MNBI).

Recommendation 15

In patients in whom rumination is suspected as a confounding factor, we recommend performing high-resolution esophageal manometry with impedance.
Certainty Level: Low
Strength of Recommendation: Weak in favor of high-resolution esophageal manometry with impedance

Evidence Summary

Behavioral disorders such as supragastric belching and rumination syndrome may act as confounding factors in GERD evaluation. In patients with suspected rumination, although pH-impedance monitoring may suggest rumination, it does not provide conclusive evidence. Impedance-manometry with postprandial monitoring remains the reference standard for confirmation[31].

Persistent postprandial regurgitation despite PPI therapy may be due to ongoing GERD but may also result from rumination—a functional gastrointestinal disorder characterized by repetitive regurgitation of recently ingested food into the mouth in the absence of structural abnormalities. Objective testing can help differentiate GERD from rumination; however, overlap may occur in some patients[32,33]. High-resolution esophageal manometry with impedance (HRM-IMP) combined with postprandial testing is currently one of the most widely used methods to evaluate rumination. In patients with suspected PPI-refractory GERD symptoms, MII-pH monitoring is often used to confirm or rule out GERD and can also assist in identifying rumination[13].

Recommendation 16

In patients with symptoms refractory to PPI therapy and suspected supragastric belching as a confounding factor, we recommend using multichannel intraluminal impedance-pH (MII-pH) monitoring.
Certainty Level: Low
Strength of Recommendation: Strong in favor

Evidence Summary

Quantitative analysis from the Latin American consensus included one study with 50 patients (low-quality evidence)

that did not specifically address PPI-refractory GERD symptoms but evaluated the ability of MII-pH to identify supragastric belching perceived by patients as troublesome in the context of reflux symptoms. The study reported a sensitivity of 60% and specificity of 64%, concluding that supragastric belching is more frequent in patients with typical reflux symptoms than in healthy controls. These belches often occur in close association with episodes of acid and weakly acidic reflux[34].

Recommendation 17

We do not recommend using a barium esophagram study as the sole diagnostic test for GERD.
Certainty Level: Low
Strength of Recommendation: Conditional against using the barium esophagram study as the only test for GERD.

Evidence Summary

The quantitative analysis conducted by the Latin American consensus included two studies: one comparative study by Johnston et al. involving 125 patients who underwent barium radiography and esophageal pH monitoring[35], and another by Serna et al. involving 65 patients. These studies reported a sensitivity of 50% (95% CI: 32–68) and a specificity of 64% (95% CI: 45–80) for the esophagram in diagnosing GERD[36]. The expert panel of the Latin American consensus recommended not performing the esophagram to diagnose GERD, with a 100% level of agreement[13].

A retrospective cohort study by Richa Bhardwaj, including 182 adult patients who underwent ambulatory reflux monitoring without antisecretory treatment and a barium esophagram between 2018 and 2023, found that, in patients with symptoms suggestive of reflux disease, reflux observed on barium esophagography had suboptimal characteristics for predicting conclusive GERD. Sixty-one patients underwent barium studies (GERB) and 101 underwent esophageal physiological tests (GERpH), while 58 presented neither GERB nor GERpH[37].

QUESTION 2: WHAT ARE THE MOST APPROPRIATE PHARMACOLOGICAL TREATMENTS FOR THE MANAGEMENT AND PREVENTION OF RECURRENCES IN GERD?

Good Practice Point 1

In patients with GERD, alginate provides benefits as a rescue medication for symptom control (particularly postprandial and nocturnal) and can be used alone or in combination with an acid suppressant.

Recommendation 18

We suggest the use of alginate for the control of symptoms (heartburn and regurgitation) in patients with GERD.
Certainty Level: Very low
Strength of Recommendation: Conditional in favor

Evidence Summary

This recommendation was adopted from the Brazilian CPG, whose authors selected 117 articles, of which 27 were included; seven specifically compared alginate with PPIs or placebo[38]. The patients studied were refractory or not to conventional treatment, generally with PPIs. The analyzed outcomes included symptom resolution or improvement (heartburn or regurgitation) and the occurrence of adverse events. In this analysis, 897 patients with non-erosive GERD were treated with PPIs combined with alginate or with alginate alone, and were compared with 929 patients on maintenance therapy with PPIs or placebo. A 14% increase (95% CI: 2–25) in symptom control (heartburn and regurgitation) was observed compared with the pooled result for PPIs alone and placebo[39-41].

Recommendation 19

In patients with symptomatic and confirmed GERD with predominant heartburn, we recommend medical treatment with PPIs at the lowest possible dose and for the shortest possible duration while initiating a discussion about long-term treatment options.
Certainty Level: Moderate
Strength of Recommendation: Strong in favor

Evidence Summary

To assess symptom remission, we reference an existing network meta-analysis by Zhang et al.[42] with high overall AMSTAR-2 confidence, which examined 98 RCTs comparing PPIs, H_2 blockers, and placebo, including a total of 45,964 participants. Twenty-two RCTs assessed various PPIs at different dose strengths (n = 41,373) compared with placebo (n = 5037) for symptom remission. Patients with GERD taking PPIs were four times more likely to experience symptom relief than those taking placebo, with a pooled OR of 4.2 (95% CI: 3.25–5.48; $p < 0.01$).

The most recent evidence synthesis for maintenance strategy comes from the systematic review and meta-analysis by Kang et al. (11 studies)[43] with low overall AMSTAR-2 confidence. On-demand versus continuous PPI therapy showed comparable overall therapeutic failure (RR: 1.26; 95% CI: 0.76–2.07), and results remained similar for NERD/mild ERD (RR: 1.48; 95% CI: 0.39–5.63). The

degree of esophagitis modified the effect: in studies of severe erosive esophagitis, continuous therapy was more effective (β: 0.127; 95% CI: 0.066–0.188; $p < 0.001$). Moreover, daily PPI consumption was approximately 50% lower with on-demand PPI use (RD: −0.52 tablets/day; 95% CI: −0.62 to −0.42), with no differences in satisfaction (RR: 0.97; 95% CI: 0.93–1.01) or adverse events.

Recommendation 20

We recommend treatment with PPIs rather than H_2 receptor antagonists (H_2RAs) for the healing of erosive esophagitis.
Certainty Level: High
Strength of Recommendation: Strong in favor of PPIs

Evidence Summary

Meta-analyses suggest that overall symptom relief in GERD and healing rates differ little among the seven available PPIs, although some studies show variations in pH control. A meta-analysis with low overall AMSTAR-2 confidence that examined the efficacy of different PPIs for healing erosive esophagitis included 10 studies with a total of 15,316 patients. After eight weeks, there was a 5% relative increase in the probability of healing with esomeprazole (RR: 1.05; 95% CI: 1.02–1.08), representing an absolute risk reduction of 4% and a number needed to treat (NNT) of 25—a figure likely not clinically significant[44].

Recommendation 21

We recommend treatment with PPIs rather than H_2 receptor antagonists (H_2RAs) for the maintenance of healing in erosive esophagitis.
Certainty Level: Moderate
Strength of Recommendation: Conditional in favor

Evidence Summary

This recommendation, adopted from the ACG guideline, issues a strong recommendation in favor of PPIs over H_2RAs with a moderate level of certainty. It is based on randomized clinical trials and systematic reviews that demonstrated the superior efficacy of PPIs in preventing endoscopic recurrence of erosive esophagitis, with significantly lower relapse rates and more sustained acid suppression, as mentioned in Recommendations 2 and 3. Additionally, the systematic literature review and meta-analysis by Kang (comparing PPI maintenance strategies) showed that while on-demand use may be comparable to continuous maintenance in NERD/mild ERD, in studies including severe esophagitis, continuous therapy was more effective (β: 0.127; 95% CI: 0.066–0.188; $p < 0.001$), and daily PPI consumption was approximately 50% lower with on-demand use. These data support the premise that greater disease severity requires more consistent suppression, in line with PPIs being the cornerstone of maintenance therapy in erosive esophagitis[43].

Recommendation 22

We recommend administering PPIs 30 to 60 minutes before meals to control GERD symptoms.
Certainty Level: Moderate
Strength of Recommendation: Strong in favor

Evidence Summary

The classic pharmacodynamic study cited by the ACG, *Proton pump inhibitors: better acid suppression when taken before a meal than without a meal*, concluded that acid suppression (pH-metry) is superior when a PPI is taken before eating rather than without food—direct evidence supporting preprandial dosing. The guideline uses this study to reinforce the rationale that active proton pumps are stimulated by meals[25,45].

Similarly, the Brazilian CPG indicates that for patients refractory to PPIs, the first intervention is optimization of use—ensuring daily intake 30–60 minutes before the first meal (or before breakfast and dinner if taken twice daily). With this optimization, symptomatic improvement exceeding 50% is observed in 11%–35% of patients, highlighting the clinical importance of administration timing[38].

Recommendation 23

In patients with GERD who do not have erosive esophagitis or Barrett's esophagus, and whose symptoms have resolved with PPI therapy, we suggest attempting discontinuation or switching to an on-demand regimen in which PPIs are taken only when symptoms appear and stopped when symptoms resolve.
Certainty Level: Low
Strength of Recommendation: Conditional in favor

Evidence Summary

The systematic literature review and meta-analysis by Kang, including 11 randomized controlled trials, compared on-demand versus continuous therapy. Overall, there was a small increase in the risk of "treatment failure" with on-demand management (RR: 1.26; 95% CI: 1.04–1.54), with imprecise effects when restricted to NERD/mild EE (RR: 1.48; 95% CI: 0.39–5.63). Symptom control was similar, with a slight advantage for continuous therapy (RR: 1.09; 95% CI: 1.01–1.18). Regarding safety, there were no significant differences in adverse events. A key finding was the ~50% reduction in PPI exposure with the

on-demand strategy (risk difference: −0.52; 95% CI: −0.62 to −0.42), suggesting resource savings and reduced medication burden[43].

Good Practice Point 2

In patients with GERD who require maintenance therapy with PPIs, we suggest administering the minimum dose that effectively controls symptoms and maintains healing of reflux esophagitis; however, treatment should be tailored to each case.

Good Practice Point 3

We recommend maintenance therapy with PPIs for patients with esophagitis grades B, C, and D (Los Angeles classification). Antireflux surgery may be considered in selected cases, such as young patients who prefer to avoid long-term medication or in those with predominant regurgitation.

Complementary Evidence Summary

The ACG guideline (2022) provides a strong recommendation, supported by moderate-quality evidence, for PPI use in grade C and D esophagitis because of the high rates of endoscopic and symptomatic relapse upon treatment withdrawal. Maintenance PPI therapy is recommended for patients with GERD complications, including severe erosive esophagitis (Los Angeles grades C or D) and Barrett's esophagus[46]. Recurrence of erosive esophagitis after discontinuation may occur within as little as one to two weeks, particularly in patients with prior LA grade C erosive esophagitis[23]. Patients with LA grade C or D esophagitis should remain on long-term PPI therapy to maintain healing.

For grade B, recent studies have provided additional evidence, such as the multicenter study by Visaggi et al.[27], which demonstrated that 100% of patients with grade B esophagitis showed objective evidence of GERD by pH-impedance monitoring. Clinical response to PPIs was comparable to that of grade C (74% compared to 70%). Moreover, the Lyon Consensus 2.0 (Gyawali et al.) updated GERD diagnostic criteria and officially recognized grade B esophagitis as conclusive evidence of GERD, together with grades C and D—eliminating the prior classification of grade B as "inconclusive" evidence[24].

Recommendation 24

We suggest on-demand or intermittent PPI therapy for controlling heartburn symptoms in patients with non-erosive reflux disease.
Certainty Level: Low
Strength of Recommendation: Conditional in favor

Evidence Summary

A recent meta-analysis by Kang et al., with low overall AMSTAR-2 confidence, included 11 parallel-design randomized controlled trials. Compared with continuous PPI therapy, on-demand therapy yielded similar results for treatment failure (RR: 1.26; 95% CI: 0.76–2.07), particularly in the group with non-erosive gastroesophageal reflux disease and mild erosive reflux disease (RR: 1.48; 95% CI: 0.39–5.63). In studies including patients with severe esophagitis, continuous maintenance treatment with PPIs was more effective (β: 0.127; 95% CI: 0.066–0.188; $p < 0.001$). The severity of esophagitis was associated with greater efficacy of continuous maintenance therapy. Daily PPI use was approximately half in the on-demand group compared with the continuous group (RD: −0.52; 95% CI: −0.62 to −0.42).

Recommendation 25

We recommend continuous PPI therapy in patients with Barrett's esophagus to control symptoms and prevent progression to dysplasia or esophageal adenocarcinoma.
Certainty Level: Moderate
Strength of Recommendation: Strong in favor

Evidence Summary

The systematic review and meta-analysis by Eusebi et al., with moderate AMSTAR-2 confidence and including 26 studies and more than 100,000 patients, showed that the risk of developing Barrett's esophagus in patients with GERD is significantly higher compared with those without GERD (OR: 2.42; 95% CI: 1.59–3.68). This risk increases markedly in patients with long-segment Barrett's (OR: 6.30; 95% CI: 4.56–8.70), while it is not significant in short segments[47]. Consistently, the global meta-analysis by Saha et al., also with moderate AMSTAR-2 confidence, found that the prevalence of Barrett's esophagus in patients with GERD reaches 7% compared with 2.2% in those without reflux, corresponding to an OR of 2.91 (95% CI: 2.33–3.64). This risk is even higher for long segments (OR: 4.17; 95% CI: 2.22–7.82). These findings reinforce the biological plausibility that sustained acid exposure is a key factor in extensive metaplasia and its progression to neoplastic lesions[48].

Recommendation 26

We suggest considering PPI therapy (standard dose divided twice daily for 8–12 weeks) in patients with extraesophageal manifestations and GERD symptoms, or in those with objective evidence of GERD.
Certainty Level: Low
Strength of Recommendation: Conditional in favor

Evidence Summary

The efficacy of PPIs in laryngopharyngeal reflux (LPR) remains uncertain because two meta-analyses found no significant benefit from PPIs[49,50], while two others found some benefit[51,52]. In a meta-analysis of 10 RCTs evaluating PPI treatment for LPR, with critically low overall AMSTAR-2 confidence, the pooled RR for improvement with any PPI therapy was 1.31, with a stronger effect observed in studies that excluded dietary management of LPR (RR: 1.42)[51]. Another meta-analysis with AMSTAR-2 confidence found symptom improvement in LPR patients treated with PPIs compared with placebo, though no significant improvement in the reflux finding score (RFS) on laryngoscopy[52]. These analyses showed substantial heterogeneity in diagnostic criteria for LPR, as well as in clinical outcomes, treatment regimens, and treatment duration, which limits our ability to make firm recommendations regarding PPI use in LPR[56].

Recommendation 27

We recommend the use of any available PPI, as no significant differences have been found among PPI groups in their therapeutic effect for GERD.
Certainty Level: Moderate
Strength of Recommendation: Strong in favor

Evidence Summary

Comparisons among different PPIs show no significant differences in therapeutic effect for GERD treatment. PPI therapy (omeprazole, lansoprazole, pantoprazole, rabeprazole, esomeprazole, or dexlansoprazole) is significantly more effective than placebo, and clinical response differences among PPIs are not significant[38].

The 2023 Brazilian CPG, from which this recommendation is adopted, reports that analyses have shown PPIs to be the most prescribed drug class, with consistent therapeutic efficacy in controlling typical symptoms (heartburn and regurgitation) and healing esophagitis compared with placebo. This analysis included 11 randomized controlled trials[54–58] involving 5,396 patients—2,944 treated with PPIs and 2,452 with placebo. PPI treatment increased the symptom-resolution rate by 22% (95% CI: 19–26%) compared with placebo.

A meta-analysis with low overall AMSTAR-2 confidence, evaluating PPI efficacy in 15,316 patients for erosive esophagitis healing, found a 5% relative increase in healing probability at week 8 with esomeprazole (RR: 1.05; 95% CI: 1.02–1.08), resulting in a 4% absolute risk reduction and an NNT of 25—values that are likely not clinically significant[44]. Notably, this analysis did not include dexlansoprazole, the only dual-release PPI, which is absorbed first in the duodenum and later in the ileum. Owing to this property, dexlansoprazole has been shown to provide comparable heartburn control when administered at different times of day[59,60].

Recommendation 28

We suggest paying special attention to patients at higher risk of bone, kidney, or nutritional disorders (iron, vitamin D, vitamin B_{12}, magnesium) during long-term PPI use, since—although a definitive causal relationship has not been established—there is clinical concern regarding the potential for adverse events.
Certainty Level: Very low
Strength of Recommendation: Conditional in favor

Evidence Summary

Long-term PPI therapy has been associated with observational studies subject to bias, which cannot be considered definitive for determining causality. In a randomized, double-blind, placebo-controlled trial that included 17,598 patients, administration of pantoprazole 40 mg/day for three years was associated with a small but significant increase in the incidence of enteric infections, though not with other adverse events[61].

The same applies to the possibility of hypomagnesemia in these cases[62]. A meta-analysis by Srinutta et al., with low overall AMSTAR-2 confidence, included observational studies examining the association between PPI use and the development of hypomagnesemia. It identified 16 observational studies—13 cross-sectional, 2 case-control, and 1 cohort—comprising a total of 131,507 patients. The pooled percentage of PPI users was 43.6% (95% CI: 25.0%–64.0%). Among PPI users, 19.4% (95% CI: 13.8%–26.5%) had hypomagnesemia, compared with 13.5% (95% CI: 7.9%–22.2%) among non-users. Using a meta-analysis with low overall AMSTAR-2 confidence, PPI use was significantly associated with hypomagnesemia, with an unadjusted pooled OR of 1.83 (95% CI: 1.26–2.67; $p = 0.002$) and an adjusted pooled OR of 1.71 (95% CI: 1.33–2.19; $p < 0.001$). In subgroup analyses, high-dose PPI use was associated with higher odds of hypomagnesemia compared with low-dose PPI use (adjusted pooled OR: 2.13; 95% CI: 1.26–3.59; $p = 0.005$)[63].

Recommendation 29

PPIs and potassium-competitive acid blockers (PCABs) are recommended as the drugs of choice for the treatment of acid reflux.
Certainty Level: Moderate
Strength of Recommendation: Strong in favor

Evidence Summary

PPIs remain the first-line medications for the treatment of acid reflux, and in recent years, PCABs have emerged as alternatives with comparable or superior efficacy in some outcomes[38]. The main therapeutic goal in GERD is a satisfactory symptom response to therapy, which should be achieved with a standard once-daily PPI dose administered for four to eight weeks[64,65]. The systematic literature review by Sigterman et al., with high overall AMSTAR-2 confidence, included 34 trials (1,314 participants): 15 empirical-treatment studies, 15 non-erosive reflux disease studies, and four covering both. In empirical GERD treatment, the risk ratio for heartburn remission (the primary efficacy variable) in placebo-controlled trials was 0.37 (two trials, 95% CI: 0.32–0.44) for PPIs, 0.77 (two trials, 95% CI: 0.60–0.99) for H_2RAs, and 0.86 (one trial, 95% CI: 0.73–1.01) for prokinetics[64].

Good Practice Point 4

We recommend that maintenance treatment for GERD successfully managed with PPIs or PCABs consist of continuous PPI or PCAB administration, followed by gradual dose reduction until transitioning to on-demand use for symptom recurrence. This strategy should be tailored to each case and guided by clinical follow-up.

Recommendation 30

We suggest using PCABs as an appropriate therapeutic option for the treatment of erosive GERD.
Certainty Level: Moderate
Strength of Recommendation: Conditional in favor

Evidence Summary

The Brazilian CPG, from which this recommendation is adopted, reported that 442 studies were reviewed, of which six randomized controlled trials were included to support the evidence synthesis[66–71]. In patients with GERD, treatment with vonoprazan 10 mg or 20 mg for four to eight weeks was not inferior to PPIs in relieving heartburn or in the risk of treatment-related adverse events. A meta-analysis by Cheng et al., with low overall AMSTAR-2 confidence, directly comparing efficacy, found vonoprazan yielded an RR of 1.06 (95% CI: 0.99–1.13) for efficacy and 1.08 (95% CI: 0.96–1.22) for adverse events compared with PPIs[72].

The meta-analysis by Chandan et al., with critically low overall AMSTAR-2 confidence, comparing vonoprazan 20 mg with lansoprazole 30 mg, found that in patients with severe erosive esophagitis (Los Angeles grades C and D), vonoprazan achieved significantly higher rates of endoscopic healing at two, four, and eight weeks. Among the overall population with erosive esophagitis, vonoprazan showed significantly higher healing rates at two and eight weeks, and comparable rates at four weeks[73].

Recommendation 31

We do not recommend treating GERD with a prokinetic agent unless there is objective evidence of gastroparesis.
Certainty Level: Low
Strength of Recommendation: Strong against

Evidence Summary

Another meta-analysis of randomized controlled trials by Zamani et al., with moderate overall AMSTAR-2 confidence, evaluated domperidone + PPI versus PPI alone (11 RCTs; n = 841). The addition of domperidone to PPI therapy showed improvement in global symptom scores, though with considerable heterogeneity, and only modest improvements in specific domains (e.g., heartburn), with a mean difference (MD) of −1.73 (95% CI: −2.03 to −1.43) and high heterogeneity (inconsistency index [I^2]: 90.7%). Regarding physiological parameters, esophageal pH increased (MD: +1.68; 95% CI: 1.33–2.03; $I^2 = 0\%$), while reflux time (MD: −1.82; 95% CI: −2.17 to −1.48) and frequency of reflux episodes (MD: −7.42; 95% CI: −8.24 to −6.59) were reduced; however, these outcomes are not equivalent to mucosal healing or to long-term patient-centered results. In terms of safety, total adverse events did not differ significantly compared with PPI alone (OR: 1.18; 95% CI: 0.72–1.94), nor did cardiac events (OR: 0.99; 95% CI: 0.40–2.45). In conclusion, while patients with GERD responded well to domperidone + PPI therapy, there was no statistically significant difference between combination therapy and monotherapy with respect to adverse effects[74].

Good Practice Point 5

We do not recommend sucralfate for the treatment of GERD (except during pregnancy).

Note: This recommendation is presented as a good practice point because the available evidence is indirect, fragmented, and of low methodological quality, and the clinical decision relies more on expert consensus and safety considerations than on clinical trial results. Classifying this statement as a good practice point ensures methodological coherence within the guideline while advising clinicians on the prudent use of sucralfate, preventing it from being interpreted as a formal recommendation supported by high-certainty evidence.

Recommendation 32

We recommend, as therapeutic options for patients with refractory GERD, increasing the PPI dose, switching to another PPI within the same therapeutic class, using PCABs, or considering antireflux surgery (which may be an option in selected patients).
Certainty Level: Moderate
Strength of Recommendation: Strong in favor

Evidence Summary

The Brazilian CPG, from which this recommendation is adopted[38], references 11 randomized controlled trials supporting the evidence synthesis[75–80]. Between 19% and 44% of patients with reflux symptoms report a partial or absent response to PPI therapy. In these patients, objective improvement was observed with vonoprazan therapy, which demonstrated 24-hour inhibition of gastric acid secretion and resulted in healing of erosive esophagitis in 60% of patients with PPI-refractory GERD[76]. Several mechanisms may explain PPI refractoriness, including: (a) incorrect dosing or timing of drug administration; (b) non-acid or bile reflux; (c) mutations in the hepatic cytochrome P-450 enzyme; (d) esophageal hypersensitivity to physiological reflux; and (e) functional heartburn[38].

In a meta-analysis by Chandan et al. (four RCTs; n = 2,208), vonoprazan 20 mg achieved higher rates of endoscopic healing at two weeks (RR: 1.10; $p < 0.001$) and eight weeks (RR: 1.04; $p = 0.03$) compared with lansoprazole 30 mg. In patients with severe erosive esophagitis (Los Angeles classification grades C and D), this advantage was consistent at two, four, and eight weeks ($p \leq 0.009$). Safety was comparable, with no increase in serious adverse events; the authors rated the overall certainty of evidence as high for the main outcomes.

QUESTION 3: WHAT ARE THE MOST APPROPRIATE NON-PHARMACOLOGICAL TREATMENTS FOR MANAGING GERD?

Good Practice Point 6

Patients with GERD symptoms and unequivocal evidence of reflux esophagitis of grade B or higher, who are not taking PPIs, may be good candidates for antireflux surgery.

Recommendation 33

We recommend antireflux surgery performed by an experienced surgeon as a long-term treatment option for patients with objective evidence of GERD—particularly those with severe reflux esophagitis (Los Angeles classification grades C or D), large hiatal hernias (symptomatic, >5 cm), adverse reactions to PPIs, objectively confirmed weakly acidic reflux in selected cases with clear symptom association, regurgitation as the predominant symptom, or patient preference.
Certainty Level: Moderate
Strength of Recommendation: Strong in favor

Evidence Summary

Studies, including retrospective analyses, have demonstrated that reflux esophagitis classified as LA grade B is comparable to grades C and D in terms of acid suppression response rates, esophageal motility, and reflux burden (based on MII–pH parameters), and significantly different from patients without reflux esophagitis. These findings supported LA grade B esophagitis as conclusive diagnostic evidence of GERD. The study included 401 patients: 254 without reflux esophagitis, 51 with LA grade A, 44 with LA grade B, and 52 with LA grades C or D. Patients with LA grade B and LA grades C/D esophagitis showed significantly higher response rates to acid suppression compared with those without reflux esophagitis ($p < 0.05$), while no significant difference was found between patients with LA grade A esophagitis and those without reflux esophagitis (no reflux esophagitis LA grade A vs. LA grade B vs. LA grades C/D: 52.4% vs. 70.6% vs. 75.0% vs. 82.7%)[81].

Recommendation 34

In patients with GERD symptoms, we recommend lifestyle modifications: weight loss for those who are overweight or obese, smoking cessation, elevation of the head of the bed, and avoiding meals within three hours before bedtime.
Certainty Level: Low
Strength of Recommendation: Strong in favor

Evidence Summary

The ASGE conducted a systematic literature search to assess the role of various lifestyle modifications (e.g., weight loss, smoking cessation, head-of-bed elevation, late meals) in reducing GERD symptoms. Three randomized controlled trials showed that weight loss was associated with a decrease in GERD symptoms and acid exposure time[82–84], as well as an improvement in reflux disease questionnaire scores in one RCT[85]. Large population-based studies demonstrated a linear relationship between body mass index and GERD symptoms[86,87]. Smoking cessation was associated with a reduction in reflux symptoms[88,89]. Elevating the head of the bed was linked to fewer reflux episodes and reduced acid exposure[90]. Moreover, late-night meals have been associated with increased reflux[91]. By contrast, no data have shown that abstaining from alcohol

improves GERD symptoms sufficiently to support a formal recommendation.

Good Practice Point 7

We recommend the left lateral decubitus position to improve nocturnal esophageal acid exposure. In addition, patients should avoid foods they personally identify as symptom triggers. Evidence on dietary restriction in GERD remains limited, although avoiding foods (fatty or spicy meals, tomato, dark beverages such as chocolate and coffee, and alcohol) that consistently and predictably worsen symptoms should be considered.

FOLLOW-UP

QUESTION 4: IN PATIENTS WITH GERD AFTER SLEEVE GASTRECTOMY, SHOULD SCREENING ENDOSCOPY BE PERFORMED TO PREVENT BARRETT'S ESOPHAGUS AND ESOPHAGEAL ADENOCARCINOMA?

Recommendation 35

In patients with reflux symptoms after sleeve gastrectomy, we suggest an endoscopic evaluation. In asymptomatic patients following sleeve gastrectomy, we suggest screening endoscopy three years after the procedure and every five years thereafter. If Barrett's esophagus is detected in this population, we recommend follow-up according to current guidelines for Barrett's esophagus surveillance.
Certainty Level: Very low quality
Strength of Recommendation: Conditional in favor

Evidence Summary

In the meta-analysis by Qumseya et al., with low to critically low overall AMSTAR-2 confidence, the incidence of *de novo* GERD, GERD-related esophagitis, and Barrett's esophagus after sleeve gastrectomy was compared with baseline rates (when reported). Overall, 680 patients from 10 observational studies who had undergone esophagogastroduodenoscopy (EGD) between six months and 10 years after sleeve gastrectomy were analyzed. The pooled prevalence of Barrett's esophagus was 11.6% (95% CI: 8.1%–16.4%; $p < 0.001$; $I^2 = 28.7\%$). In the logistic meta-regression analysis, no significant association was found between Barrett's esophagus and postoperative GERD prevalence ($\beta = 3.5$; 95% CI: −18 to 25; $p = 0.75$). A linear relationship was observed between time to postoperative EGD and the rate of esophagitis ($\beta = 0.13$; 95% CI: 0.06–0.20; $p = 0.0005$); the risk of esophagitis increased by 13% for each year after sleeve gastrectomy[92]. The ASGE expert panel identified that this risk of Barrett's esophagus exceeds the 10% threshold established by prior guidelines, and therefore suggested screening in this patient population, starting at three years postoperatively—regardless of GERD symptoms—and continuing every five years thereafter. If Barrett's esophagus is detected, surveillance should follow the recommendations of the previous ASGE guideline.

Recommendation 36

In patients with GERD symptoms but without alarm features, we suggest endoscopic evaluation in those with risk factors for Barrett's esophagus (family history of Barrett's esophagus or esophageal adenocarcinoma; GERD plus at least one other risk factor [≥50 years of age, male sex, White race, smoking, or obesity]).
Certainty Level: Very low
Strength of Recommendation: Conditional in favor

Evidence Summary

For this recommendation, the 2025 ASGE clinical practice guideline drew on the consensus of its prior 2015[93] and 2019[94] guidelines, as well as its own systematic review and meta-analysis[90]. The guidelines recommend screening endoscopy in at-risk patients—defined as individuals with a family history of Barrett's esophagus or esophageal adenocarcinoma, or patients with GERD plus at least one additional risk factor—since early detection and surveillance are beneficial for cancer prevention[93,94].

Because the existing guidelines provided a conditional recommendation for endoscopy in this population, the panel likewise supported a conditional recommendation. Additionally, EGD is often performed as part of the preoperative assessment in patients being considered for antireflux surgery or for the placement of wireless esophageal pH monitoring devices, and is inherently part of several endoscopic antireflux procedures. The expert panel endorsed these established recommendations and incorporated them into the existing indications for endoscopy in GERD[90].

QUESTION 5: WHAT ARE THE MOST APPROPRIATE MANAGEMENT STRATEGIES FOR PATIENTS WITH GERD WHO PRESENT WITH EXTRADIGESTIVE MANIFESTATIONS?

Recommendation 37

We suggest that patients with extraesophageal manifestations of GERD but without typical symptoms (heartburn, regurgitation) undergo reflux testing for evaluation before initiating PPI therapy.
Certainty Level: Low
Strength of Recommendation: Conditional in favor

Evidence Summary

The limitations of an empirical PPI trial for diagnosing extraesophageal reflux (EER) lie in the inconsistent therapeutic response of EER-associated syndromes to PPI therapy. A meta-analysis by Numans et al., with low AMSTAR-2 confidence, demonstrated a sensitivity of 71%–78% and a specificity of 41%–54% for an empirical PPI trial (compared with esophagitis on endoscopy or ambulatory pH monitoring) in patients with classic reflux symptoms of heartburn and regurgitation[95].

Good Practice Point 8

Patients with extraesophageal symptoms should not receive PPI or PCAB treatment unless GERD has been objectively confirmed. We recommend performing upper gastrointestinal endoscopy or pH monitoring with impedance.

Good Practice Point 9

We suggest using upper endoscopy to evaluate mucosal integrity and complications in patients with asthma, chronic cough, or laryngopharyngeal reflux associated with GERD symptoms. It should not be used as a standalone diagnostic test to attribute extraesophageal symptoms to GERD and, when normal, should be followed by reflux monitoring (24-hour pH impedance monitoring).

Note: The 2022 ACG guideline explicitly states: "We suggest that upper endoscopy not be used to establish the diagnosis of asthma, chronic cough, or laryngopharyngeal reflux related to GERD" (conditional; low-certainty evidence). Upper endoscopy may document GERD if erosive esophagitis (e.g., LA classification grades C or D) or complications are present, but it does not prove causality for the extraesophageal symptom. If endoscopy is normal, reflux monitoring should be performed to confirm or rule out GERD. The 2023 AGA guideline also highlights the limited role of EGD/laryngoscopy and proposes considering reflux testing in these patients.

Good Practice Point 10

Demonstrating erosive esophagitis on endoscopy establishes the diagnosis of GERD but does not confirm that GERD is the cause of the extraesophageal symptoms.

Recommendation 38

We suggest not using laryngoscopic findings as a standalone diagnostic tool to attribute laryngopharyngeal or extraesophageal symptoms to GERD.
Certainty Level: Low
Strength of Recommendation: Strong against

Evidence Summary

Laryngoscopic findings associated with reflux include hypertrophy of the posterior commissure, laryngeal and arytenoid inflammation, vocal fold edema, and endolaryngeal mucus. However, the correlation between symptoms, laryngoscopic findings, and other objective tests such as pH monitoring or pH-impedance monitoring is weak. A systematic review by Lechien et al., with critically low overall AMSTAR-2 confidence, evaluated different reported signs of laryngopharyngeal reflux and relevant clinical outcomes. The authors examined 29 different laryngopharyngeal reflux signs and multiple scoring systems. Laryngoscopic findings of laryngopharyngeal reflux were found to have low specificity, with validation hindered by the lack of a reference standard for diagnosis[96].

Recommendation 39

In patients treated for GERD, surgical or endoscopic antireflux procedures are recommended only for those with objective evidence of reflux.
Certainty Level: Low
Strength of Recommendation: Conditional in favor

Evidence Summary

Two systematic reviews, by Iqbal et al.[97] and Sidwa et al.[98], found that the outcomes of antireflux surgery for extraesophageal GERD symptoms are inferior to those achieved in patients with typical GERD symptoms. These reviews—comprising primarily small, retrospective, and uncontrolled studies—reported wide variability in the improvement of extraesophageal symptoms, with rates ranging from 15% to 95%.

QUESTION 6: HOW SHOULD GERD BE DIAGNOSED AND TREATED DURING PREGNANCY AND LACTATION, CONSIDERING THE EFFICACY AND SAFETY OF DIFFERENT THERAPEUTIC OPTIONS?

Gastroesophageal reflux disease (GERD) during pregnancy—reported in up to 66% of cases—can develop in any trimester, even among mothers with no prior history of GERD, and typically resolves after delivery. Significant weight gain may be a predictor of persistent GERD one year postpartum. The use of standard GERD medications may be limited in pregnant patients (for example, to sucralfate only).

Reviews and guidelines such as Pregnancy Review 2022 (Evidence-Based Treatment Recommendations for Gastroesophageal Reflux Disease During Pregnancy)[99], ACG 2022[25], and the 2025 Latin American Expert Good Practice Recommendations[100] recommend a stepwise therapeutic approach, beginning with lifestyle modifications as the first-line measure.

When non-pharmacological interventions fail to control symptoms, treatment should advance progressively. Calcium-containing antacids are considered the preferred first-line pharmacologic option, with an established safety profile during pregnancy. In patients with persistent symptoms, sucralfate (1 g three times daily) may be added, followed by H_2 receptor blockers, all classified as category B by the U.S. Food and Drug Administration (FDA), indicating a low risk of fetal harm. In cases where symptom control with H_2 blockers and antacids is insufficient, proton pump inhibitors (PPIs)—also classified as category B during pregnancy, except omeprazole, which is category C—may be considered[25,99].

The ACG 2022[25] and Mexico Good Practice Recommendations 2025[100] also highlight the use of alginates and sucralfate as safe first-line options, particularly when initial lifestyle measures fail. None of these guidelines provide specific recommendations for lactation, though they imply continuity of a safety-based pharmacological approach.

Good Practice Point 11

Lifestyle and dietary modifications should be considered the first-line treatment during pregnancy; however, if heartburn is sufficiently severe, pharmacologic therapy should be initiated after medical consultation.

Good Practice Point 12

Lifestyle modification measures include elevating the head of the bed and lying on the left lateral side, reducing or avoiding foods that may trigger reflux (e.g., fatty or spicy foods, citrus fruits, carbonated beverages, alcohol), and avoiding lying down within three hours after eating.

Good Practice Point 13

If symptom relief is not achieved through lifestyle modification, pharmacologic therapy may be initiated, beginning with antacids. Calcium-, aluminum-, and magnesium-based antacids are recommended as needed as second-line treatment for GERD during pregnancy.

Good Practice Point 14

The preferred antacids are those containing calcium in normal therapeutic doses, given the additional benefit of this treatment in preventing hypertension and preeclampsia.

Good Practice Point 15

Antacids containing bicarbonate or magnesium trisilicate are not recommended during pregnancy.

Good Practice Point 16

In patients who continue to experience GERD symptoms while taking antacids or alginates, sucralfate may be the next pharmacologic option (1 g oral tablet, three times daily).

Good Practice Point 17

If symptoms persist with antacids alone, H_2 receptor blockers may be combined with antacids. The combination of H_2 receptor blockers and antacids should be considered the third-line treatment for GERD during pregnancy.

Good Practice Point 18

If the combination of H_2 receptor blockers and antacids does not adequately control symptom severity, PPIs should be used in conjunction with antacids as rescue medication for GERD.

Copyright

According to Section 20 of Law 23 of 1982, the proprietary rights of this work belong to the Colombian Association of Gastroenterology (the institution that provided financial support and supervised its execution), without prejudice to the moral rights recognized under Section 30 of the same law.

Conflict of Interest

The contributors and participants involved in developing the recommendations of this guideline declare that they have no conflicts of interest, are not involved as researchers in ongoing clinical trials on the topic, have not received donations or benefits from groups with vested interests in the recommendations, and are not part of professional organizations with conflicts of interest. The preparation, development, and publication of these recommendations were exclusively funded by the Colombian Association of Gastroenterology, which also holds the copyright.

Funding Sources

The development of this updated guideline was financed by the Colombian Association of Gastroenterology through its 2025 contract with Universidad CES.

Declaration of Editorial Independence

The funding and executing entities did not influence the content of this document. All work was conducted independently by the authors.

ANNEX SUMMARY OF RECOMMENDATIONS

Question 1: What tests are useful for diagnosing gastroesophageal reflux disease (GERD) in adults?

Recommendation 1

We recommend a thorough clinical history that evaluates the presence of typical GERD symptoms such as heartburn, regurgitation, and non-cardiac chest pain, as well as the identification of possible extradigestive manifestations, including cough, laryngitis, sleep disturbances, or others.

Certainty Level: Very low

Strength of Recommendation: Strong in favor

Recommendation 2

We recommend not using clinical interviews or symptom questionnaires (such as the GerdQ) as the sole tools for establishing a gastroesophageal reflux disease GERD diagnosis.

Certainty Level: Low

Strength of Recommendation: Strong against

Recommendation 3

For patients with classic GERD symptoms such as heartburn and regurgitation, without alarm symptoms, we may recommend an 8-week empirical or therapeutic trial with a once-daily PPI taken before meals.

Certainty Level: Moderate

Strength of Recommendation: Strong in favor

Recommendation 4

We do not recommend a proton pump inhibitor (PPI) trial to diagnose extraesophageal GERD in patients who have concomitant typical GERD symptoms (heartburn, regurgitation).

Certainty Level: Low

Strength of Recommendation: Strong against

Recommendation 5

We do not recommend a PPI trial to diagnose extraesophageal GERD in patients without concomitant typical GERD symptoms (heartburn, regurgitation) and chest pain.

Certainty Level: Low

Strength of Recommendation: Strong against

Recommendation 6

In patients with GERD symptoms and alarm features such as dysphagia, odynophagia, weight loss, gastrointestinal bleeding, persistent vomiting, or unexplained iron-deficiency anemia, we recommend performing an upper gastrointestinal endoscopy.

Certainty Level: Moderate

Strength of Recommendation: Strong in favor

Recommendation 7

In patients with typical GERD symptoms, we recommend careful endoscopic evaluation, comprehensive reporting, and photographic documentation of the following aspects to improve patient care and clinical outcomes:

- Objective findings of GERD, when present: erosive esophagitis (classified according to the Los Angeles system), Barrett's esophagus (using the Prague classification), and peptic strictures.
- Landmarks and integrity of the gastroesophageal junction: hiatal hernia dimensions (using the Hill classification or the American Foregut Society classification in both frontal and retroflexed views); position of the upper gastric folds, Z-line, and diaphragmatic impression; and description of any existing fundoplication (if present).

Certainty Level: Very low

Strength of Recommendation: Strong in favor

Recommendation 8

In patients with reflux symptoms (symptomatic GERD) following peroral endoscopic myotomy (POEM), we suggest performing an upper endoscopic evaluation.

Certainty Level: Very low

Strength of Recommendation: Conditional in favor

Recommendation 9

We recommend diagnostic endoscopy after discontinuing PPI therapy for two to four weeks in patients whose typical GERD symptoms do not adequately respond to an 8-week empirical PPI trial or whose symptoms recur after discontinuation.

Certainty Level: Low

Strength of Recommendation: Strong in favor

Recommendation 10

In patients with chest pain without heartburn who have undergone appropriate evaluation to rule out coronary artery disease, we recommend objective testing to confirm or exclude GERD (endoscopy, reflux monitoring, or high-resolution esophageal manometry to rule out motility disorders).

Certainty Level: Low

Strength of Recommendation: Conditional in favor

Recommendation 11

We recommend 24-hour impedance-pH monitoring (pH-metry) off therapy in patients with a low pretest probability of GERD, in those who do not respond to PPI treatment and have normal upper endoscopy findings with reflux symptoms, in patients being evaluated prior to antireflux surgery, and in those with extradigestive manifestations of reflux.

Certainty Level: Low

Strength of Recommendation: Conditional in favor

Recommendation 12

We recommend not performing 24-hour pH monitoring off PPI therapy solely as a diagnostic test for GERD in patients with endoscopic evidence of reflux esophagitis grade B, C, or D according to the Los Angeles classification, or in patients with long-segment Barrett's esophagus.

Certainty Level: Moderate

Strength of Recommendation: Strong against

Recommendation 13

We recommend using the total number of reflux episodes measured by pH-impedance monitoring as one of the parameters to diagnose GERD. The diagnosis of GERD based on multichannel intraluminal impedance-pH (MII-pH) monitoring does not depend solely on the total number of reflux episodes but also considers acid exposure time and nocturnal baseline impedance, among other metrics.

Certainty Level: Low

Strength of Recommendation: Weak in favor

Recommendation 14

We suggest using multichannel intraluminal impedance-pH (MII-pH) monitoring off PPI therapy instead of conventional pH monitoring to guide therapeutic decisions in patients with unconfirmed GERD and PPI-refractory heartburn.

Certainty Level: Low

Strength of Recommendation: Conditional in favor

Recommendation 15

In patients in whom rumination is suspected as a confounding factor, we recommend performing high-resolution esophageal manometry with impedance.

Certainty Level: Low

Strength of Recommendation: Weak in favor of high-resolution esophageal manometry (HRM) with impedance

Recommendation 16

In patients with symptoms refractory to PPI therapy and suspected supragastric belching as a confounding factor, we recommend using multichannel intraluminal impedance-pH (MII-pH) monitoring.

Certainty Level: Low

Strength of Recommendation: Strong in favor

Recommendation 17

We do not recommend using a barium esophagram study as the sole diagnostic test for GERD.

Certainty Level: Low

Strength of Recommendation: Conditional against

Question 2: What are the most appropriate pharmacological treatments for the management and prevention of recurrences in GERD?

Recommendation 18

We suggest the use of alginate for the control of symptoms (heartburn and regurgitation) in patients with GERD.

Certainty Level: Very low

Strength of Recommendation: Conditional in favor

Good Practice Point 1

In patients with GERD, alginate provides benefits as a rescue medication for symptom control (particularly postprandial and nocturnal) and can be used alone or in combination with an acid suppressant.

Recommendation 19

In patients with symptomatic and confirmed GERD with predominant heartburn, we recommend medical treatment with PPIs at the lowest possible dose and for the shortest possible duration while initiating a discussion about long-term treatment options.

Certainty Level: Moderate

Strength of Recommendation: Strong in favor

Recommendation 20

We recommend PPI therapy rather than histamine-2 receptor antagonists (H_2RAs) for the healing of erosive esophagitis.

Certainty Level: High

Strength of Recommendation: Strong in favor of PPIs

Recommendation 21

We recommend treatment with PPIs rather than H_2 receptor antagonists (H_2RAs) for the maintenance of healing in erosive esophagitis.

Certainty Level: Moderate

Strength of Recommendation: Conditional in favor

Recommendation 22

We recommend administering PPIs 30 to 60 minutes before meals to control GERD symptoms.

Certainty Level: Moderate

Strength of Recommendation: Strong in favor

Recommendation 23

In patients with GERD who do not have erosive esophagitis or Barrett's esophagus, and whose symptoms have resolved with PPI therapy, we suggest attempting discontinuation or switching to an on-demand regimen in which PPIs are taken only when symptoms appear and stopped when symptoms resolve.

Certainty Level: Low

Strength of Recommendation: Conditional in favor

Good Practice Point 2

In patients with GERD who require maintenance therapy with PPIs, we suggest administering the minimum dose that effectively controls symptoms and maintains healing of reflux esophagitis; however, treatment should be tailored to each case.

Good Practice Point 3

We recommend maintenance therapy with PPIs for patients with esophagitis grades B, C, and D (Los Angeles classification). Antireflux surgery may be considered in selected cases, such as young patients who prefer to avoid long-term medication or in those with predominant regurgitation.

Recommendation 24

We suggest on-demand or intermittent PPI therapy for controlling heartburn symptoms in patients with non-erosive reflux disease.

Certainty Level: Low

Strength of Recommendation: Conditional in favor

Recommendation 25

We recommend continuous PPI therapy in patients with Barrett's esophagus to control symptoms and prevent progression to dysplasia or esophageal adenocarcinoma.

Certainty Level: Moderate

Strength of Recommendation: Strong in favor

Recommendation 26

We suggest considering PPI therapy (standard dose divided twice daily for 8–12 weeks) in patients with extraesophageal manifestations and GERD symptoms, or in those with objective evidence of GERD.

Certainty Level: Low

Strength of Recommendation: Conditional in favor

Recommendation 27

We recommend the use of any available PPI, as no significant differences have been found among PPI groups in their therapeutic effect for GERD.

Certainty Level: Moderate

Strength of Recommendation: Strong in favor

Recommendation 28

We suggest paying special attention to patients at higher risk of bone, kidney, or nutritional disorders (iron, vitamin D, vitamin B_{12}, magnesium) during long-term PPI use, since—although a definitive causal relationship has not been established—there is clinical concern regarding the potential for adverse events.

Certainty Level: Very low

Strength of Recommendation: Conditional in favor

Recommendation 29

PPIs and potassium-competitive acid blockers (PCABs) are recommended as the drugs of choice for the treatment of acid reflux.

Certainty Level: Moderate

Strength of Recommendation: Strong in favor

Good Practice Point 4

We recommend that maintenance treatment for GERD successfully managed with PPIs or PCABs consist of continuous PPI or PCAB administration, followed by gradual dose reduction until transitioning to on-demand use for symptom recurrence. This strategy should be tailored to each case and guided by clinical follow-up.

Recommendation 30

We suggest using PCABs as an appropriate therapeutic option for the treatment of erosive GERD.

Certainty Level: Moderate

Strength of Recommendation: Conditional in favor

Recommendation 31

We do not recommend treating GERD with a prokinetic agent unless there is objective evidence of gastroparesis.

Certainty Level: Low

Strength of Recommendation: Strong against

Good Practice Point 5

We do not recommend sucralfate for the treatment of GERD (except during pregnancy).

Recommendation 32

We recommend, as therapeutic options for patients with refractory GERD, increasing the PPI dose, switching to another PPI within the same therapeutic class, using PCABs, or considering antireflux surgery (which may be an option in selected patients).

Certainty Level: Moderate

Strength of Recommendation: Strong in favor

Question 3: What are the most appropriate non-pharmacological treatments for managing GERD?

Good Practice Point 6

Patients with GERD symptoms and unequivocal evidence of reflux esophagitis of grade B or higher, who are not taking PPIs, may be good candidates for antireflux surgery.

Recommendation 33

We recommend antireflux surgery performed by an experienced surgeon as a long-term treatment option for patients with objective evidence of GERD—particularly those with severe reflux esophagitis (Los Angeles classification grades C or D), large hiatal hernias (symptomatic, >5 cm), adverse reactions to PPIs, objectively confirmed weakly acidic reflux in selected cases with clear symptom association, regurgitation as the predominant symptom, or patient preference.

Certainty Level: Moderate

Strength of Recommendation: Strong in favor

Recommendation 34

In patients with GERD symptoms, we recommend lifestyle modifications: weight loss for those who are overweight or obese, smoking cessation, elevation of the head of the bed, and avoiding meals within three hours before bedtime.

Certainty Level: Low

Strength of Recommendation: Strong in favor

Good Practice Point 7

We recommend the left lateral decubitus position to improve nocturnal esophageal acid exposure. In addition, patients should avoid foods they personally identify as symptom triggers. Evidence on dietary restriction in GERD remains limited, although avoiding foods (fatty or spicy meals, tomato, dark beverages such as chocolate and coffee, and alcohol) that consistently and predictably worsen symptoms should be considered.

Question 4: In patients with GERD after sleeve gastrectomy, should screening endoscopy be performed to prevent Barrett's esophagus and esophageal adenocarcinoma?

Recommendation 35

In patients with reflux symptoms after sleeve gastrectomy, we suggest an endoscopic evaluation. In asymptomatic patients following sleeve gastrectomy, we suggest screening endoscopy three years after the procedure and every five years thereafter. If Barrett's esophagus is detected in this population, we recommend follow-up according to current guidelines for Barrett's esophagus surveillance.

Certainty Level: Very low

Strength of Recommendation: Conditional in favor

Recommendation 36

In patients with GERD symptoms but without alarm features, we suggest endoscopic evaluation in those with risk factors for Barrett's esophagus (family history of Barrett's esophagus or esophageal adenocarcinoma; GERD plus at least one other risk factor [≥50 years of age, male sex, White race, smoking, or obesity]).

Certainty Level: Very low quality

Strength of Recommendation: Conditional in favor

Question 5: What are the most appropriate management strategies for patients with GERD who present with extradigestive manifestations?

Recommendation 37

We suggest that patients with extraesophageal manifestations of GERD but without typical symptoms (heartburn, regurgitation) undergo reflux testing for evaluation before initiating PPI therapy.

Certainty Level: Low

Strength of Recommendation: Conditional in favor

Good Practice Point 8

Patients with extraesophageal symptoms should not receive PPI or PCAB treatment unless GERD has been objectively confirmed. We recommend performing upper gastrointestinal endoscopy or pH monitoring with impedance.

Good Practice Point 9

We suggest using upper gastrointestinal endoscopy to assess mucosal integrity and complications in patients with asthma, chronic cough, or laryngopharyngeal reflux associated with GERD symptoms. It should not be used as a standalone diagnostic test to attribute extraesophageal symptoms to GERD, and when normal, it should be complemented by reflux monitoring (24-hour pH monitoring with impedance).

Good Practice Point 10

Demonstrating erosive esophagitis on endoscopy establishes the diagnosis of GERD but does not confirm that GERD is the cause of the extraesophageal symptoms.

Recommendation 38

We suggest not using laryngoscopic findings as a standalone diagnostic tool to attribute laryngopharyngeal or extraesophageal symptoms to GERD.

Certainty Level: Low

Strength of Recommendation: Strong against

Recommendation 39

In patients treated for GERD, surgical or endoscopic antireflux procedures are recommended only for those with objective evidence of reflux.

Certainty Level: Low

Strength of Recommendation: Conditional in favor

Question 6: How should GERD be diagnosed and treated during pregnancy and lactation, considering the efficacy and safety of different therapeutic options?

Good Practice Point 11

Lifestyle and dietary modifications should be considered the first-line treatment during pregnancy; however, if heartburn is sufficiently severe, pharmacologic therapy should be initiated after medical consultation.

Good Practice Point 12

Lifestyle modification measures include elevating the head of the bed and lying on the left lateral side, reducing or avoiding foods that may trigger reflux (e.g., fatty or spicy foods, citrus fruits, carbonated beverages, alcohol), and avoiding lying down within three hours after eating.

Good Practice Point 13

If symptom relief is not achieved through lifestyle modification, pharmacologic therapy may be initiated, beginning with antacids. Calcium-, aluminum-, and magnesium-based antacids are recommended as needed as second-line treatment for GERD during pregnancy.

Good Practice Point 14

The preferred antacids are those containing calcium in normal therapeutic doses, given the additional benefit of this treatment in preventing hypertension and preeclampsia.

Good Practice Point 15

Antacids containing bicarbonate or magnesium trisilicate are not recommended during pregnancy.

Good Practice Point 16

In patients who continue to experience GERD symptoms while taking antacids or alginates, sucralfate may be the next pharmacologic option (1 g oral tablet, three times daily).

Good Practice Point 17

If symptoms persist with antacids alone, H_2 receptor blockers may be combined with antacids. The combination of H_2 receptor blockers and antacids should be considered the third-line treatment for GERD during pregnancy.

Good Practice Point 18

If the combination of H_2 receptor blockers and antacids does not adequately control symptom severity, PPIs should be used in conjunction with antacids as rescue medication for GERD.

REFERENCES

1. Zhang D, Liu S, Li Z, Wang R. Global, regional and national burden of gastroesophageal reflux disease, 1990-2019: update from the GBD 2019 study. Ann Med. 54(1):1372-84. https://doi.org/10.1080/07853890.2022.2074535
2. Tabaeian SP, Moeini S, Rezapour A, Afshari S, Souresrafil A, Barzegar M. Economic evaluation of proton pump inhibitors in patients with gastro-oesophageal reflux disease: a systematic review. BMJ Open Gastroenterol. 2024;11(1):e001465. https://doi.org/10.1136/bmjgast-2024-001465
3. El-Serag HB, Sweet S, Winchester CC, Dent J. Update on the epidemiology of gastro-oesophageal reflux disease: a systematic review. Gut. 2014;63(6):871-80. https://doi.org/10.1136/gutjnl-2012-304269
4. Salis G. Systematic review: Epidemiology of gastroesophageal reflux disease in Latin America. Acta Gastroenterol Latinoam. 2011;41(1):60-9.
5. Páramo Hernández DB, Albis R, Galiano MT, Molano BM de, Rincón R, Ovalle LFP, et al. Prevalencia de síntomas del reflujo gastroesofágico y factores asociados: una encuesta poblacional en las principales ciudades de Colombia. Rev Colomb Gastroenterol. 2016;31(4):337-46. https://doi.org/10.22516/25007440.108
6. Chen Y, Yang K, Marušic A, Qaseem A, Meerpohl JJ, Flottorp S, et al. A Reporting Tool for Practice Guidelines in Health Care: The RIGHT Statement. Ann Intern Med. 2017;166(2):128-32. https://doi.org/10.1016/j.energy.2016.12.127
7. Mustafa RA, Santesso N, Brozek J, Akl EA, Walter SD, Norman G, et al. The GRADE approach is reproducible in assessing the quality of evidence of quantitative evidence syntheses. J Clin Epidemiol. 2013;66(7):736-742.e5. https://doi.org/10.1016/j.jclinepi.2013.02.004
8. Ministerio de Salud y Protección Social, IETS. Guía metodológica Adopción - Adaptación de Guías de Práctica Clínica Basadas en Evidencia [Internet]. Ministerio de Salud y Protección Social, IETS; 2017 [consultado el 8 de septiembre de 2025]. Disponible en: https://www.iets.org.co/Archivos/79/Guia_de_Adopcion_VF.pdf
9. Moayyedi P, Talley NJ, Fennerty MB, Vakil N. Can the Clinical History Distinguish Between Organic and Functional Dyspepsia? JAMA. 2006;295(13):1566-76. https://doi.org/10.1001/jama.295.13.1566
10. Zhang M, Pandolfino JE, Zhou X, Tan N, Li Y, Chen M, et al. Assessing different diagnostic tests for gastroesophageal reflux disease: a systematic review and network meta-analysis. Ther Adv Gastroenterol. 2019;12:1756284819890537. https://doi.org/10.1177/1756284819890537
11. Simadibrata DM, Ngadiono E, Sinuraya FAG, Damara I, Fass R, Simadibrata M. Diagnostic accuracy of gastroesophageal reflux disease questionnaire for gastroesophageal reflux disease: A systematic review and meta-analysis. Neurogastroenterol Motil. 2023;35(12). https://doi.org/10.1111/nmo.14619
12. Ghoneim S, Wang J, El Hage Chehade N, Ganocy SJ, Chitsaz E, Fass R. Diagnostic Accuracy of the Proton Pump Inhibitor Test in Gastroesophageal Reflux Disease and Noncardiac Chest Pain: A Systematic Review and Meta-analysis. J Clin Gastroenterol. 2023;57(4):380-8. https://doi.org/10.1097/MCG.0000000000001686
13. Olmos JA, Pandolfino JE, Piskorz MM, Zamora N, Díaz MAV, Troche JMR, et al. Latin American consensus on diagnosis of gastroesophageal reflux disease. Neurogastroenterol Motil. 2024;36(3):e14735. https://doi.org/10.1111/nmo.14735
14. Vakil N, van Zanten SV, Kahrilas P, Dent J, Jones R, Global Consensus Group. The Montreal definition and classification of gastroesophageal reflux disease: a global evidence-based consensus. Am J Gastroenterol. 2006;101(8):1900-20. https://doi.org/10.1111/j.1572-0241.2006.00630.x
15. O'Hara J, Stocken DD, Watson GC, Fouweather T, McGlashan J, MacKenzie K, et al. Use of proton pump inhibitors to treat persistent throat symptoms: multicentre, double blind, randomised, placebo controlled trial. The BMJ. 2021;372:m4903. https://doi.org/10.1136/bmj.m4903
16. Vaezi MF, Katzka D, Zerbib F. Extraesophageal Symptoms and Diseases Attributed to GERD: Where is the Pendulum Swinging Now? Clin Gastroenterol Hepatol Off Clin Pract J Am Gastroenterol Assoc. 2018;16(7):1018-29. https://doi.org/10.1016/j.cgh.2018.02.001
17. de Bortoli N, Nacci A, Savarino E, Martinucci I, Bellini M, Fattori B, et al. How many cases of laryngopharyngeal reflux suspected by laryngoscopy are gastroesophageal reflux disease-related? World J Gastroenterol. 2012;18(32):4363-70. https://doi.org/10.3748/wjg.v18.i32.4363
18. Metz DC, Childs ML, Ruiz C, Weinstein GS. Pilot study of the oral omeprazole test for reflux laryngitis. Otolaryngol--Head Neck Surg Off J Am Acad Otolaryngol-Head Neck Surg. 1997;116(1):41-6. https://doi.org/10.1016/S0194-59989770350-4

19. Siupsinskiene N, Adamonis K. Diagnostic test with omeprazole in patients with posterior laryngitis. Med Kaunas Lith. 2003;39(1):47-55.
20. Park W, Hicks DM, Khandwala F, Richter JE, Abelson TI, Milstein C, et al. Laryngopharyngeal reflux: prospective cohort study evaluating optimal dose of proton-pump inhibitor therapy and pretherapy predictors of response. The Laryngoscope. 2005;115(7):1230-8. https://doi.org/10.1097/01.MLG.0000163746.81766.45
21. Boys JA, Azadgoli B, Martinez M, Oh DS, Hagen JA, DeMeester SR. Adequacy of EGD Reporting: a Review of 100 Reports from 100 Endoscopists. J Gastrointest Surg Off J Soc Surg Aliment Tract. 2021;25(5):1117-23. https://doi.org/10.1007/s11605-020-04634-2
22. Suresh Kumar VC, Singh S, Moond V, Pannala SS, Bidani K, Mohan BP, et al. Comparison of the safety, efficacy, and rates of GERD between full-thickness versus modified peroral endoscopic myotomy for achalasia: a systematic review and meta-analysis. Gastrointest Endosc. 2025;S0016-5107(25)01837-1. https://doi.org/10.1016/j.gie.2025.07.017
23. Dunbar KB, Agoston AT, Odze RD, Huo X, Pham TH, Cipher DJ, et al. Association of Acute Gastroesophageal Reflux Disease With Esophageal Histologic Changes. JAMA. 2016;315(19):2104-12. https://doi.org/10.1001/jama.2016.5657
24. Gyawali CP, Yadlapati R, Fass R, Katzka D, Pandolfino J, Savarino E, et al. Updates to the modern diagnosis of GERD: Lyon consensus 2.0. Gut. 2024;73(2):361-71. https://doi.org/10.1136/gutjnl-2023-330616
25. Katz PO, Dunbar K, Schnoll-Sussman FH, Greer KB, Yadlapati R, Spechler SJ. ACG Clinical Guideline: Guidelines for the Diagnosis and Management of Gastroesophageal Reflux Disease. Am J Gastroenterol. 2022;117(1):27-56. https://doi.org/10.14309/ajg.0000000000001538
26. Lei WY, Yu HC, Wen SH, Liu TT, Yi CH, Wang CC, et al. Predictive factors of silent reflux in subjects with erosive esophagitis. Dig Liver Dis Off J Ital Soc Gastroenterol Ital Assoc Study Liver. 2015;47(1):24-9. https://doi.org/10.1016/j.dld.2014.09.017
27. Visaggi P, Del Corso G, Gyawali CP, Ghisa M, Baiano Svizzero F, Stefani Donati D, et al. Ambulatory pH-Impedance Findings Confirm That Grade B Esophagitis Provides Objective Diagnosis of Gastroesophageal Reflux Disease. Am J Gastroenterol. 2023;118(5):794-801. https://doi.org/10.14309/ajg.0000000000002173
28. Nikolic M, Matic A, Feka J, Gensthaler L, Kristo I, Osmokrovic B, et al. Expanded Indication for Magnetic Sphincter Augmentation: Outcomes in Weakly Acidic Reflux Compared to Standard GERD Patients. J Gastrointest Surg Off J Soc Surg Aliment Tract. 2022;26(3):532-41. https://doi.org/10.1007/s11605-021-05152-5
29. Horton AJ, Clayton SB. Optimization of impedance-measured reflux events in GORD utilizing acid exposure time. BMC Gastroenterol. 2020;20(1):179. https://doi.org/10.1186/s12876-020-01321-z
30. Bredenoord AJ, Weusten BLAM, Timmer R, Conchillo JM, Smout AJPM. Addition of esophageal impedance monitoring to pH monitoring increases the yield of symptom association analysis in patients off PPI therapy. Am J Gastroenterol. 2006;101(3):453-9. https://doi.org/10.1111/j.1572-0241.2006.00427.x
31. Zerbib F, Bredenoord AJ, Fass R, Kahrilas PJ, Roman S, Savarino E, et al. ESNM/ANMS consensus paper: Diagnosis and management of refractory gastroesophageal reflux disease. Neurogastroenterol Motil. 2021;33(4):e14075. https://doi.org/10.1111/nmo.14075
32. Nakagawa K, Sawada A, Hoshikawa Y, Nikaki K, Sonmez S, Woodland P, et al. Persistent Postprandial Regurgitation vs Rumination in Patients With Refractory Gastroesophageal Reflux Disease Symptoms: Identification of a Distinct Rumination Pattern Using Ambulatory Impedance-pH Monitoring. Am J Gastroenterol. 2019;114(8):1248-55. https://doi.org/10.14309/ajg.0000000000000295
33. Halland M, Pandolfino J, Barba E. Diagnosis and Treatment of Rumination Syndrome. Clin Gastroenterol Hepatol. 2018;16(10):1549-55. https://doi.org/10.1016/j.cgh.2018.05.049
34. Hemmink GJM, Bredenoord AJ, Weusten BLAM, Timmer R, Smout AJPM. Supragastric belching in patients with reflux symptoms. Am J Gastroenterol. agosto de 2009;104(8):1992-7. https://doi.org/10.1038/ajg.2009.203
35. Johnston BT, Troshinsky MB, Castell JA, Castell DO. Comparison of barium radiology with esophageal pH monitoring in the diagnosis of gastroesophageal reflux disease. Am J Gastroenterol. 1996;91(6):1181-5.
36. Serna-Gallegos D, Basseri B, Bairamian V, Pimentel M, Soukiasian HJ. Gastroesophageal reflux reported on esophagram does not correlate with pH monitoring and high-resolution esophageal manometry. Am Surg. 2014;80(10):1026-9. https://doi.org/10.1177/000313481408001025
37. Bhardwaj R, Davis TA, Franz A, Kem D, Edds S, Rogers B, et al. Reflux Seen on a Barium Swallow is Not a Substitute For Ambulatory Reflux Monitoring in Symptomatic Patients. J Clin Gastroenterol. 2025. https://doi.org/10.1097/MCG.0000000000002133
38. Moraes-Filho JPP, Domingues G, Chinzon D. Brazilian clinical guideline for the therapeutic management of gastroesophageal reflux disease (Brazilian Federation Of Gastroenterology, FBG). Arq Gastroenterol. 2024;61:e23154. https://doi.org/10.1590/s0004-2803.24612023-154
39. Reimer C, Lødrup AB, Smith G, Wilkinson J, Bytzer P. Randomised clinical trial: alginate (Gaviscon Advance) vs. placebo as add-on therapy in reflux patients with inadequate response to a once daily proton pump inhibitor. Aliment Pharmacol Ther. 2016;43(8):899-909. https://doi.org/10.1111/apt.13567

40. Kim JH, Lee YC, Kim EH, Park JC, Shin SK, Lee SK, et al. The Clinical Efficacy of a Pure Alginate Formulation (Lamina G) for Controlling Symptoms in Individuals with Reflux Symptoms: A Randomized Clinical Study. Gut Liver. 2019;13(6):642-8. https://doi.org/10.5009/gnl18378
41. Thomas E, Wade A, Crawford G, Jenner B, Levinson N, Wilkinson J. Randomised clinical trial: relief of upper gastrointestinal symptoms by an acid pocket-targeting alginate-antacid (Gaviscon Double Action) - a double-blind, placebo-controlled, pilot study in gastro-oesophageal reflux disease. Aliment Pharmacol Ther. 2014;39(6):595-602. https://doi.org/10.1111/apt.12640
42. Zhang C, Kwong JSW, Yuan RX, Chen H, Xu C, Wang YP, et al. Effectiveness and Tolerability of Different Recommended Doses of PPIs and H2RAs in GERD: Network Meta-Analysis and GRADE system. Sci Rep. 2017;7:41021. https://doi.org/10.1038/srep41021
43. Kang SJ, Jung HK, Tae CH, Kim SY, Lee KJ. On-demand Versus Continuous Maintenance Treatment of Gastroesophageal Reflux Disease With Proton Pump Inhibitors: A Systematic Review and Meta-analysis. J Neurogastroenterol Motil. 2022;28(1):5-14. https://doi.org/10.5056/jnm21095
44. Gralnek IM, Dulai GS, Fennerty MB, Spiegel BMR. Esomeprazole versus other proton pump inhibitors in erosive esophagitis: a meta-analysis of randomized clinical trials. Clin Gastroenterol Hepatol Off Clin Pract J Am Gastroenterol Assoc. 2006;4(12):1452-8. https://doi.org/10.1016/j.cgh.2006.09.013
45. Hatlebakk JG, Katz PO, Camacho-Lobato L, Castell DO. Proton pump inhibitors: better acid suppression when taken before a meal than without a meal. Aliment Pharmacol Ther. 2000;14(10):1267-72. https://doi.org/10.1046/j.1365-2036.2000.00829.x
46. Savarino V, Marabotto E, Zentilin P, Furnari M, Bodini G, De Maria C, et al. Pathophysiology, diagnosis, and pharmacological treatment of gastro-esophageal reflux disease. Expert Rev Clin Pharmacol. 2020;13(4):437-49. https://doi.org/10.1080/17512433.2020.1752664
47. Eusebi LH, Telese A, Cirota GG, Haidry R, Zagari RM, Bazzoli F, et al. Effect of gastro-esophageal reflux symptoms on the risk of Barrett's esophagus: A systematic review and meta-analysis. J Gastroenterol Hepatol. 2022;37(8):1507-16. https://doi.org/10.1111/jgh.15902
48. Saha B, Vantanasiri K, Mohan BP, Goyal R, Garg N, Gerberi D, et al. Prevalence of Barrett's Esophagus and Adenocarcinoma With and Without Gastroesophageal Reflux: A Systematic Review and Meta-Analysis. Clin Gastroenterol Hepatol Off Clin Pract J Am Gastroenterol Assoc. 2024;22(7):1381-1394.e7. https://doi.org/10.1016/j.cgh.2023.10.006
49. Megwalu UC. A systematic review of proton-pump inhibitor therapy for laryngopharyngeal reflux. Ear Nose Throat J. 2013;92(8):364-71. https://doi.org/10.1177/014556131309200811
50. Qadeer MA, Phillips CO, Lopez AR, Steward DL, Noordzij JP, Wo JM, et al. Proton pump inhibitor therapy for suspected GERD-related chronic laryngitis: a meta-analysis of randomized controlled trials. Am J Gastroenterol. 2006;101(11):2646-54. https://doi.org/10.1111/j.1572-0241.2006.00844.x
51. Lechien JR, Saussez S, Schindler A, Karkos PD, Hamdan AL, Harmegnies B, et al. Clinical outcomes of laryngopharyngeal reflux treatment: A systematic review and meta-analysis. The Laryngoscope. 2019;129(5):1174-87. https://doi.org/10.1002/lary.27591
52. Guo H, Ma H, Wang J. Proton Pump Inhibitor Therapy for the Treatment of Laryngopharyngeal Reflux: A Meta-Analysis of Randomized Controlled Trials. J Clin Gastroenterol. 2016;50(4):295-300. https://doi.org/10.1097/MCG.0000000000000324
53. Karkos PD, Wilson JA. Empiric treatment of laryngopharyngeal reflux with proton pump inhibitors: a systematic review. The Laryngoscope. 2006;116(1):144-8. https://doi.org/10.1097/01.mlg.0000191463.67692.36
54. Cho YK, Choi MG, Park H, Kim JW, Lee DH, Ko KH, et al. Efficacy of S-pantoprazole 10 mg in the Symptom Control of Non-erosive Reflux Disease: A Phase III Placebo-controlled Trial. J Neurogastroenterol Motil. 2021;27(2):223-30. https://doi.org/10.5056/jnm19053
55. Peura DA, Le Moigne A, Wassel H, Pollack C. Sustained efficacy following resolution of frequent heartburn with an over-the-counter regimen of esomeprazole 20 mg or placebo for 14 days: two randomized trials. BMC Gastroenterol. 2018;18:69. https://doi.org/10.1186/s12876-018-0790-2
56. Katz PO, Le Moigne A, Pollack C. Analysis of 2-Week Data from Two Randomized, Controlled Trials Conducted in Subjects with Frequent Heartburn Treated with Esomeprazole 20 mg. Clin Ther. 2017;39(5):960-70. https://doi.org/10.1016/j.clinthera.2017.03.015
57. Tan VPY, Wong WM, Cheung TK, Lai KC, Hung IFN, Chan P, et al. Treatment of non-erosive reflux disease with a proton pump inhibitor in Chinese patients: a randomized controlled trial. J Gastroenterol. 2011;46(7):906-12. https://doi.org/10.1007/s00535-011-0402-1
58. Zheng RN. Comparative study of omeprazole, lansoprazole, pantoprazole and esomeprazole for symptom relief in patients with reflux esophagitis. World J Gastroenterol. 2009;15(8):990-5. https://doi.org/10.3748/wjg.15.990
59. Graham DY, Tansel A. Interchangeable Use of Proton Pump Inhibitors Based on Relative Potency. Clin Gastroenterol Hepatol Off Clin Pract J Am Gastroenterol Assoc. 2018;16(6):800-808.e7. https://doi.org/10.1016/j.cgh.2017.09.033
60. Lee RD, Mulford D, Wu J, Atkinson SN. The effect of time-of-day dosing on the pharmacokinetics and pharmacodynamics of dexlansoprazole MR: evidence for dosing flexibility with a Dual Delayed Release proton pump inhibitor.

Aliment Pharmacol Ther. 2010;31(9):1001-11. https://doi.org/10.1111/j.1365-2036.2010.04272.x
61. Moayyedi P, Eikelboom JW, Bosch J, Connolly SJ, Dyal L, Shestakovska O, et al. Safety of Proton Pump Inhibitors Based on a Large, Multi-Year, Randomized Trial of Patients Receiving Rivaroxaban or Aspirin. Gastroenterology. 2019;157(3):682-691.e2.
62. Castellana C, Pecere S, Furnari M, Telese A, Matteo MV, Haidry R, et al. Side effects of long-term use of proton pump inhibitors: practical considerations. Pol Arch Intern Med. 2021;131(6):541-9. https://doi.org/10.20452/pamw.15997
63. Srinutta T, Chewcharat A, Takkavatakarn K, Praditpornsilpa K, Eiam-Ong S, Jaber BL, et al. Proton pump inhibitors and hypomagnesemia: A meta-analysis of observational studies. Medicine (Baltimore). 2019;98(44):e17788. https://doi.org/10.1097/MD.0000000000017788
64. Sigterman KE, van Pinxteren B, Bonis PA, Lau J, Numans ME. Short-term treatment with proton pump inhibitors, H2-receptor antagonists and prokinetics for gastro-oesophageal reflux disease-like symptoms and endoscopy negative reflux disease. Cochrane Database Syst Rev. 2013;2013(5):CD002095. https://doi.org/10.1002/14651858.CD002095.pub5
65. Modlin IM, Hunt RH, Malfertheiner P, Moayyedi P, Quigley EM, Tytgat GNJ, et al. Diagnosis and management of non-erosive reflux disease--the Vevey NERD Consensus Group. Digestion. 2009;80(2):74-88. https://doi.org/10.1159/000219365
66. Dent J, El-Serag HB, Wallander MA, Johansson S. Epidemiology of gastro-oesophageal reflux disease: a systematic review. Gut. 2005;54(5):710-7. https://doi.org/10.1136/gut.2004.051821
67. Kinoshita Y, Sakurai Y, Shiino M, Kudou K, Nishimura A, Miyagi T, et al. Evaluation of the Efficacy and Safety of Vonoprazan in Patients with Nonerosive Gastroesophageal Reflux Disease: A Phase III, Randomized, Double-Blind, Placebo-Controlled, Multicenter Study. Curr Ther Res Clin Exp. 2016;81-82:1-7. https://doi.org/10.1016/j.curtheres.2016.12.001
68. Xiao Y, Zhang S, Dai N, Fei G, Goh KL, Chun HJ, et al. Phase III, randomised, double-blind, multicentre study to evaluate the efficacy and safety of vonoprazan compared with lansoprazole in Asian patients with erosive oesophagitis. Gut. 2020;69(2):224-30. https://doi.org/10.1136/gutjnl-2019-318365
69. Sakurai K, Suda H, Fujie S, Takeichi T, Okuda A, Murao T, et al. Short-Term Symptomatic Relief in Gastroesophageal Reflux Disease: A Comparative Study of Esomeprazole and Vonoprazan. Dig Dis Sci. 2019;64(3):815-22. https://doi.org/10.1007/s10620-018-5365-0
70. Ashida K, Sakurai Y, Hori T, Kudou K, Nishimura A, Hiramatsu N, et al. Randomised clinical trial: vonoprazan, a novel potassium-competitive acid blocker, vs. lansoprazole for the healing of erosive oesophagitis. Aliment Pharmacol Ther. 2016;43(2):240-51. https://doi.org/10.1111/apt.13461
71. Kinoshita Y, Sakurai Y, Takabayashi N, Kudou K, Araki T, Miyagi T, et al. Efficacy and Safety of Vonoprazan in Patients With Nonerosive Gastroesophageal Reflux Disease: A Randomized, Placebo-Controlled, Phase 3 Study. Clin Transl Gastroenterol. 2019;10(11):e00101. https://doi.org/10.14309/ctg.0000000000000101
72. Cheng Y, Liu J, Tan X, Dai Y, Xie C, Li X, et al. Direct Comparison of the Efficacy and Safety of Vonoprazan Versus Proton-Pump Inhibitors for Gastroesophageal Reflux Disease: A Systematic Review and Meta-Analysis. Dig Dis Sci. 2021;66(1):19-28. https://doi.org/10.1007/s10620-020-06141-5
73. Chandan S, Deliwala S, Mohan BP, Ramai D, Dhindsa B, Bapaye J, et al. Vonoprazan versus lansoprazole in erosive esophagitis - A systematic review and meta-analysis of randomized controlled trials. Indian J Gastroenterol Off J Indian Soc Gastroenterol. 2023;42(4):475-84. https://doi.org/10.1007/s12664-023-01384-2
74. Zamani NF, Sjahid AS, Tuan Kamauzaman TH, Lee YY, Islam MA. Efficacy and Safety of Domperidone in Combination with Proton Pump Inhibitors in Gastroesophageal Reflux Disease: A Systematic Review and Meta-Analysis of Randomised Controlled Trials. J Clin Med. 2022;11(18):5268. https://doi.org/10.3390/jcm11185268
75. Spechler SJ, Hunter JG, Jones KM, Lee R, Smith BR, Mashimo H, et al. Randomized Trial of Medical versus Surgical Treatment for Refractory Heartburn. N Engl J Med. 2019;381(16):1513-23. https://doi.org/10.1056/NEJMoa1811424
76. Iwakiri K, Sakurai Y, Shiino M, Okamoto H, Kudou K, Nishimura A, et al. A randomized, double-blind study to evaluate the acid-inhibitory effect of vonoprazan (20 mg and 40 mg) in patients with proton-pump inhibitor-resistant erosive esophagitis. Ther Adv Gastroenterol. 2017;10(6):439-51. https://doi.org/10.1177/1756283X17705329
77. Mizuki A, Tatemichi M, Sakakibara T, Miura Y, Zeki S, Ohata M, et al. A Multicenter, Randomized, Open-Label Trial: Efficacy of Once-Daily Versus Twice-Daily Double-Dose Rabeprazole on Refractory Gastroesophageal Reflux Disease-Related Symptoms and Quality of Life. Curr Ther Res Clin Exp. 2016;79:1-7. https://doi.org/10.1016/j.curtheres.2016.11.002
78. Fass R, Murthy U, Hayden CW, Malagon IB, Pulliam G, Wendel C, et al. Omeprazole 40 mg once a day is equally effective as lansoprazole 30 mg twice a day in symptom control of patients with gastro-oesophageal reflux disease (GERD) who are resistant to conventional-dose lansoprazole therapy-a prospective, randomized, multi-centre study. Aliment Pharmacol Ther. 2000;14(12):1595-603. https://doi.org/10.1046/j.1365-2036.2000.00882.x
79. Rivière P, Vauquelin B, Rolland E, Melchior C, Roman S, Bruley des Varannes S, et al. Low FODMAPs diet or usual

dietary advice for the treatment of refractory gastroesophageal reflux disease: An open-labeled randomized trial. Neurogastroenterol Motil. 2021;33(9):e14181. https://doi.org/10.1111/nmo.14181
80. Pauwels A, Raymenants K, Geeraerts A, Boecxstaens V, Masuy I, Broers C, et al. Clinical trial: a controlled trial of baclofen add-on therapy in PPI-refractory gastro-oesophageal reflux symptoms. Aliment Pharmacol Ther. 2022;56(2):231-9. https://doi.org/10.1111/apt.17068
81. Chen J, Dong P, Chen S, Zhuang Q, Zhang M, Sun K, et al. The Los Angeles-B esophagitis is a conclusive diagnostic evidence for gastroesophageal reflux disease: the validation of Lyon Consensus 2.0. Gastroenterol Rep. 2025;13:goaf004. https://doi.org/10.1093/gastro/goaf004
82. Mathus-Vliegen EMH, van Weeren M, van Eerten PV. Loss function and obesity: the impact of untreated obesity, weight loss, and chronic gastric balloon distension. Digestion. 2003;68(2-3):161-8. https://doi.org/10.1159/000075525
83. Mathus-Vliegen EMH, Tygat GNJ. Gastro-oesophageal reflux in obese subjects: influence of overweight, weight loss and chronic gastric balloon distension. Scand J Gastroenterol. 2002;37(11):1246-52. https://doi.org/10.1080/003655202761020498
84. Mathus-Vliegen LM, Tytgat GN. Twenty-four-hour pH measurements in morbid obesity: effects of massive overweight, weight loss and gastric distension. Eur J Gastroenterol Hepatol. 1996;8(7):635-40.
85. Singh S, Garg SK, Singh PP, Iyer PG, El-Serag HB. Acid-suppressive medications and risk of oesophageal adenocarcinoma in patients with Barrett's oesophagus: a systematic review and meta-analysis. Gut. 2014;63(8):1229-37. https://doi.org/10.1136/gutjnl-2013-305997
86. Ness-Jensen E, Lindam A, Lagergren J, Hveem K. Weight loss and reduction in gastroesophageal reflux. A prospective population-based cohort study: the HUNT study. Am J Gastroenterol. 2013;108(3):376-82. https://doi.org/10.1038/ajg.2012.466
87. Jacobson BC, Somers SC, Fuchs CS, Kelly CP, Camargo CA. Body-mass index and symptoms of gastroesophageal reflux in women. N Engl J Med. 2006;354(22):2340-8. https://doi.org/10.1056/NEJMoa054391
88. Ness-Jensen E, Lindam A, Lagergren J, Hveem K. Tobacco smoking cessation and improved gastroesophageal reflux: a prospective population-based cohort study: the HUNT study. Am J Gastroenterol. 2014;109(2):171-7. https://doi.org/10.1038/ajg.2013.414
89. Kohata Y, Fujiwara Y, Watanabe T, Kobayashi M, Takemoto Y, Kamata N, et al. Long-Term Benefits of Smoking Cessation on Gastroesophageal Reflux Disease and Health-Related Quality of Life. Plos One. 2016;11(2):e0147860. https://doi.org/10.1371/journal.pone.0147860
90. Desai M, Ruan W, Thosani NC, Amaris M, Scott JS, Saeed A, et al. American Society for Gastrointestinal Endoscopy guideline on the diagnosis and management of GERD: summary and recommendations. Gastrointest Endosc. 2025;101(2):267-84. https://doi.org/10.1016/j.gie.2024.10.008
91. Piesman M, Hwang I, Maydonovitch C, Wong RKH. Nocturnal reflux episodes following the administration of a standardized meal. Does timing matter? Am J Gastroenterol. 2007;102(10):2128-34. https://doi.org/10.1111/j.1572-0241.2007.01348.x
92. Qumseya BJ, Qumsiyeh Y, Ponniah SA, Estores D, Yang D, Johnson-Mann CN, et al. Barrett's esophagus after sleeve gastrectomy: a systematic review and meta-analysis. Gastrointest Endosc. 2021;93(2):343-352.e2. https://doi.org/10.1016/j.gie.2020.08.008
93. Muthusamy VR, Lightdale JR, Acosta RD, Chandrasekhara V, Chathadi KV, Eloubeidi MA, et al. The role of endoscopy in the management of GERD. Gastrointest Endosc. 2015;81(6):1305-10. https://doi.org/10.1016/j.gie.2015.02.021
94. Qumseya B, Sultan S, Bain P, Jamil L, Jacobson B, Anandasabapathy S, et al. ASGE guideline on screening and surveillance of Barrett's esophagus. Gastrointest Endosc. 2019;90(3):335-359.e2. https://doi.org/10.1016/j.gie.2019.05.012
95. Numans ME, Lau J, de Wit NJ, Bonis PA. Short-term treatment with proton-pump inhibitors as a test for gastroesophageal reflux disease: a meta-analysis of diagnostic test characteristics. Ann Intern Med. 2004;140(7):518-27. https://doi.org/10.7326/0003-4819-140-7-200404060-00011
96. Lechien JR, Schindler A, De Marrez LG, Hamdan AL, Karkos PD, Harmegnies B, et al. Instruments evaluating the clinical findings of laryngopharyngeal reflux: A systematic review. The Laryngoscope. 2019;129(3):720-36. https://doi.org/10.1002/lary.27537
97. Iqbal M, Batch AJ, Spychal RT, Cooper BT. Outcome of surgical fundoplication for extraesophageal (atypical) manifestations of gastroesophageal reflux disease in adults: a systematic review. J Laparoendosc Adv Surg Tech A. 2008;18(6):789-96. https://doi.org/10.1089/lap.2007.0165
98. Sidwa F, Moore AL, Alligood E, Fisichella PM. Surgical Treatment of Extraesophageal Manifestations of Gastroesophageal Reflux Disease. World J Surg. 2017;41(10):2566-71. https://doi.org/10.1007/s00268-017-4058-8
99. Altuwaijri M. Evidence-based treatment recommendations for gastroesophageal reflux disease during pregnancy: A review. Medicine (Baltimore). 2022;101(35):e30487. https://doi.org/10.1097/MD.0000000000030487
100. Valdovinos-Díaz MA, Hani A, Defilippi-Guerra C, Fernando-Pineda L, Remes-Troche JM, Riquelme A, et al. Recomendaciones de buena práctica clínica para el manejo de la enfermedad por reflujo gastroesofágico. Revisión por expertos latinoamericanos. Rev Gastroenterol México. 2025;90(2):288-308. https://doi.org/10.1016/j.rgmx.2025.02.001