GASTRO-OESOPHAGEAL REFLUX DISEASE

CHI Formulary Development Project

INDICATION UPDATE

ADDENDUM- August 2023

To the CHI Original Gastro-esophageal reflux disease Clinical Guidance- Issued November 2019

Contents

List of Figures

List of Tables

Related Documents

Related SOPs

- IDF-FR-P-02-01-IndicationsReview&IDFUpdates
- IDF-FR-P-05-01-UpdatedIndicationReview&IDFUpdates

Related WI:

- IDF-FR-WI-01-01SearchMethodologyGuideForNewIndications

Abbreviations

ACG	American College of Gastroenterology
AGA	American Gastroenterological Association
BE	Barrett's Esophagus
CHI	Council of Health Insurance
COPD	Chronic Obstructive Pulmonary Disease
CPG	Clinical Practice Guideline
EAC	Esophageal Adenocarcinoma
EET	Endoscopic Eradication Therapy
EoE	Eosinophilic Esophagitis
FDA	Food and Drug Administration
GERD	Gastro-Esophageal Reflux Disease
H2RA	H2 Receptor Antagonists
HGD	High-Grade Dysplasia
IDF	CHI Drug Formulary
IPF	Idiopathic Pulmonary Fibrosis
LGD	Low-Grade Dysplasia
NDBE	Non-dysplastic Barrett's esophagus
NERD	Nonerosive Reflux Disease
OSAHS	Obstructive Sleep Apnea Hypopnea Syndrome
PAAEs	PPI-Associated Adverse Events
PPI	Proton Pump Inhibitor
RYGB	Roux-en-Y Gastric Bypass
SFDA	Saudi Food and Drug Authority
TIF	Transoral Incisionless Fundoplication

Executive Summary

Gastroesophageal reflux disease (GERD) is characterized by bothersome symptoms that are significant enough to hinder an individual's overall well-being. It can also involve injury or complications that arise from the backward flow of stomach contents into the esophagus, oropharynx, and/or respiratory tract. Symptoms caused by reflux, the presence of erosive esophagitis, and long-term complications can severely impact daily activities, work efficiency, sleep patterns, and overall quality of life in a detrimental manner[1].

The global pooled prevalence of GERD was 13.98% and varied greatly according to region (12.88% in Latin America and the Caribbean to 19.55% in North America) and country (4.16% in China to 22.40% in Turkey). Using the United Nations 2017 Revision of World Population Prospects, the estimated number of individuals suffering from GERD globally is 1.03 billion[2].

In Saudi Arabia, based on two studies conducted in the west region and Riyadh using the GERDQ questionnaire with a score of ≥ 8 as the diagnostic criteria of GERD, the prevalence range of GERD was 23.47% - 45.4%[3].

Failure to receive appropriate treatment or incorrect treatment of this condition can result in the development of complications. The current medical approach involves the utilization of medications, such as proton pump inhibitors (PPIs), which function by reducing the production of stomach acid. Additionally, surgical interventions are employed with the objective of increasing pressure in the lower esophageal sphincter to prevent reflux[4]. Treatment also includes simple antacids and H2 blockers.

There are certain preventive measures that can assist in reducing the discomfort associated with GERD. These include avoiding food and beverages that can trigger the burning sensation, quitting smoking, and maintaining a healthy weight. Making lifestyle changes can also help alleviate symptoms. These changes may involve refraining from lying down immediately after eating, consuming meals 2-3 hours before bedtime, opting for smaller and spaced-out meals throughout the day, avoiding tight-fitting clothing, and elevating the head of the bed by 15-20 centimeters[5].

All recommendations are well supported by reference guidelines, Grade of Recommendation (GoR), Level of Evidence (LoE) and Strength of Agreement (SoA) reflecting specific drug class role in the management of GERD.

This report functions as an addendum to the prior CHI Gastro-esophageal reflux disease report and seeks to offer guidance for the effective management of GERD.

Regarding the management of GERD, there were no additions of new drugs recommended in the guidelines, there were no new drugs approved by the FDA. As for the delisted medications, ranitidine is no longer SFDA registered as the FDA has issued a request to withdraw the drug from the market in April 2020[6]. Some changes concerning prior authorization and age limit were addressed in this report.

Below is a table summarizing the major changes based on the different GERD guidelines used to issue this report:

Table 1. General Recommendations for the Management of Gastroesophageal Reflux Disease (GERD)

Management of GERD		
General Recommendations	**Level of Evidence/Grade of Recommendation**	**Reference**
For patients with GERD who do not have EE or Barrett's esophagus, and whose symptoms have resolved with PPI therapy, an attempt should be made to discontinue PPIs or to switch to on-demand therapy in which PPIs are taken only when symptoms occur and discontinued when they are relieved.	Conditional recommendation, low level of evidence	2022 ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease[7]
The guideline does not recommend baclofen in the absence of objective evidence of GERD.	Strong recommendation, moderate level of evidence.	2022 ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease[7]
The guideline recommends against treatment with a prokinetic agent of any kind for GERD therapy unless there is objective evidence of gastroparesis.	Strong recommendation, low level of evidence.	2022 ACG Clinical Guideline for the Diagnosis and Management of

		Gastroesophageal Reflux Disease[7]
The guideline does not recommend sucralfate for GERD therapy except during **pregnancy**.	Strong recommendation, low level of evidence.	2022 ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease[7]
The guideline suggests on-demand or intermittent PPI therapy for heartburn symptom control in patients with **NERD**.	Conditional recommendation, low level of evidence.	2022 ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease[7]
For patients who have both **extra**esophageal and typical GERD symptoms, the guideline suggests considering a trial of twice-daily PPI therapy for 8–12 weeks before additional testing.	Conditional recommendation, low level of evidence.	2022 ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease[7]
For patients who have regurgitation as their primary PPI-**refractory** symptom and who have had abnormal gastroesophageal reflux documented by objective testing, we suggest consideration of antireflux surgery or TIF.	Conditional recommendation, low level of evidence.	2022 ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease[7]
The guideline suggests consideration of Roux-en-Y gastric bypass (RYGB) as an option to treat GERD in **obese** patients who are candidates for this procedure and who are willing to accept its risks and requirements for lifestyle alterations.	Conditional recommendation, low level of evidence.	2022 ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease[7]
1. Surgical (fundoplication) versus medical (PPI) management in adult and pediatric patients with chronic or refractory GERD	Conditional recommendation based on very low certainty in the evidence of effects	2021 Guidelines for the Surgical Treatment of Gastroesophageal Reflux (GERD)[8]

1a. The panel suggests managing adult patients with confirmed chronic or chronic refractory gastroesophageal reflux with surgical fundoplication rather than continued medical treatment. 1b. No recommendation was made regarding pediatric patients.		
Testing can be considered for those with an established objective diagnosis of GERD who do not respond to high doses of acid suppression. Testing can include pH-impedance monitoring while on acid suppression to evaluate the role of ongoing acid or non-acid reflux.	Not graded	2023 AGA Clinical Practice Update on the Diagnosis and Management of Extraesophageal Gastroesophageal Reflux Disease[9]
All patients with BE should be placed on at least daily proton pump inhibitor therapy.	Not graded	2022 AGA Clinical Practice Update on New Technology and Innovation for Surveillance and Screening in Barrett's Esophagus: Expert Review[10]
Most patients with an indication for chronic PPI use who take twice-daily dosing should be considered for step down to once-daily PPI.	Not graded	2022 AGA Clinical Practice Update on De-Prescribing of Proton Pump Inhibitors: Expert Review[12]
Patients with complicated GERD, such as those with a history of severe erosive esophagitis, esophageal ulcer, or peptic stricture, should generally not be considered for PPI discontinuation.	Not graded	2022 AGA Clinical Practice Update on De-Prescribing of Proton Pump Inhibitors: Expert Review[12]

Patients with known Barrett's esophagus, eosinophilic esophagitis, or idiopathic pulmonary fibrosis should generally not be considered for a trial of de-prescribing.	Not graded	2022 AGA Clinical Practice Update on De-Prescribing of Proton Pump Inhibitors: Expert Review[12]
In patients with proven GERD, Roux-en-Y gastric bypass is an effective primary anti-reflux intervention in obese patients, and a salvage option in non-obese patients, whereas sleeve gastrectomy has potential to worsen GERD.	Not graded	2022 AGA Clinical Practice Update on the Personalized Approach to the Evaluation and Management of GERD: Expert Review[13]
Clinicians should provide patients presenting with troublesome heartburn, regurgitation, and/ or non-cardiac chest pain without alarm symptoms a 4- to 8-week trial of single-dose PPI therapy. With inadequate response, dosing can be increased to twice a day or switched to a more effective acid suppressive agent once a day. When there is adequate response, PPI should be tapered to the lowest effective dose.	Not graded	2022 AGA Clinical Practice Update on the Personalized Approach to the Evaluation and Management of GERD: Expert Review[13]

Section 3 lists the key recommendations synthesis for GERD treatment.

Section 1.0 Summary of Reviewed Clinical Guidelines & Evidence

This section is divided into two parts: one part includes recommendations from **updated versions of guidelines** mentioned in the previous CHI GERD report, and one part includes **newly added guidelines** that have helped generate this report.

Table 2. Guidelines Requiring Revision

Guidelines requiring revision	
Old versions	**Updated versions**
American College of Gastroenterology Guidelines for the Diagnosis and Management of Gastroesophageal Reflux Disease	ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease 2022[7]
NICE Guidelines on Managing gastro-esophageal reflux disease in adults 2019	N/A*
European Association of Endoscopic Surgery Guidelines for the management of gastroesophageal reflux disease 2014	N/A*
World Gastroenterology Organization Global Guidelines 2017	N/A*

*: *No updated version available* (the existing version is the most recent one and no further updates or revisions have been made or released)

1.1 Revised guidelines

This part contains the updated versions of the guidelines mentioned in the 2019 CHI GERD Report and the corresponding recommendations.

1.1.1 ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease 2022

(Please refer to section 1.1 of the 2019 CHI report on GERD)

The 2022 American College of Gastroenterology (ACG) Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease listed the recommendations below[7]:

Table 3. 2022 ACG Guideline Recommendations

Indication	Recommendation	Class of Evidence
GERD	A recently approved device for evaluation of GERD uses a catheter-based balloon lined by sensors that measure mucosal impedance during endoscopy. This technique has shown promise for differentiating GERD from EoE and may develop to be a useful adjunct to endoscopy in the diagnosis of GERD.	Not graded
GERD	The guideline suggests avoiding meals within 2–3 hours of bedtime.	Conditional recommendation, low level of evidence.
GERD	For patients with GERD who do not have EE or Barrett's esophagus, and whose symptoms have resolved with PPI therapy, an attempt should be made to discontinue PPIs or to switch to on-demand therapy in which PPIs are taken only when symptoms occur and discontinued when they are relieved.	Conditional recommendation, low level of evidence.
GERD	The guideline recommends maintenance PPI therapy indefinitely or antireflux surgery for patients with LA grade C or D esophagitis.	Strong recommendation, moderate level of evidence.
GERD	The guideline does not recommend baclofen in the absence of objective evidence of GERD.	Strong recommendation, moderate level of evidence.
GERD	The guideline recommends against treatment with a prokinetic agent of any kind for GERD therapy unless there is objective evidence of gastroparesis.	Strong recommendation, low level of evidence.
GERD	Antacids are used exclusively for on-demand symptom relief with little evidence to favor 1 type over another. Studies with an alginic acid preparation manufactured in the United Kingdom suggest potential efficacy in	Not graded.

	symptom relief compared with other products, but alginate content of preparations sold in other countries is variable.	
GERD	The guideline does not recommend sucralfate for GERD therapy except during pregnancy.	Strong recommendation, low level of evidence.
GERD	The guideline suggests on-demand or intermittent PPI therapy for heartburn symptom control in patients with NERD.	Conditional recommendation, low level of evidence.
Extra-esophageal GERD	The guideline recommends that patients who have extraesophageal manifestations of GERD without typical GERD symptoms (e.g., heartburn and regurgitation) undergo reflux testing for evaluation before PPI therapy.	Strong recommendation, moderate level of evidence.
Extra-esophageal GERD	For patients who have both extraesophageal and typical GERD symptoms, the guideline suggests considering a trial of twice-daily PPI therapy for 8–12 weeks before additional testing.	Conditional recommendation, low level of evidence.
Extra-esophageal GERD	In patients treated for extraesophageal reflux disease, surgical or endoscopic antireflux procedures are only recommended in patients with objective evidence of reflux.	Conditional recommendation, low level of evidence.
Refractory GERD	The guideline recommends optimization of PPI therapy as the first step in management of refractory GERD.	Strong recommendation, moderate level of evidence.
Refractory GERD	For patients who have regurgitation as their primary PPI-refractory symptom and who have had abnormal gastroesophageal reflux documented by objective testing, we suggest consideration of antireflux surgery or TIF.	Conditional recommendation, low level of evidence.
Surgical and endoscopic options for GERD	The guideline suggests consideration of TIF for patients with troublesome regurgitation or heartburn who do not wish to undergo antireflux surgery and who do not have severe	Conditional recommendation, low level of evidence.

	reflux esophagitis (LA grade C or D) or hiatal hernias > 2 cm.	
Surgical and endoscopic options for GERD	The guideline suggests consideration of Roux-en-Y gastric bypass (RYGB) as an option to treat GERD in obese patients who are candidates for this procedure and who are willing to accept its risks and requirements for lifestyle alterations.	Conditional recommendation, low level of evidence.
Surgical and endoscopic options for GERD	The guideline recommends antireflux surgery performed by an experienced surgeon as an option for long-term treatment of patients with objective evidence of GERD, especially those who have severe reflux esophagitis (LA grade C or D), large hiatal hernias, and/or persistent, troublesome GERD symptoms.	Strong recommendation, moderate level of evidence.

Figure 1 details the algorithm for the diagnosis of **GERD**[7].

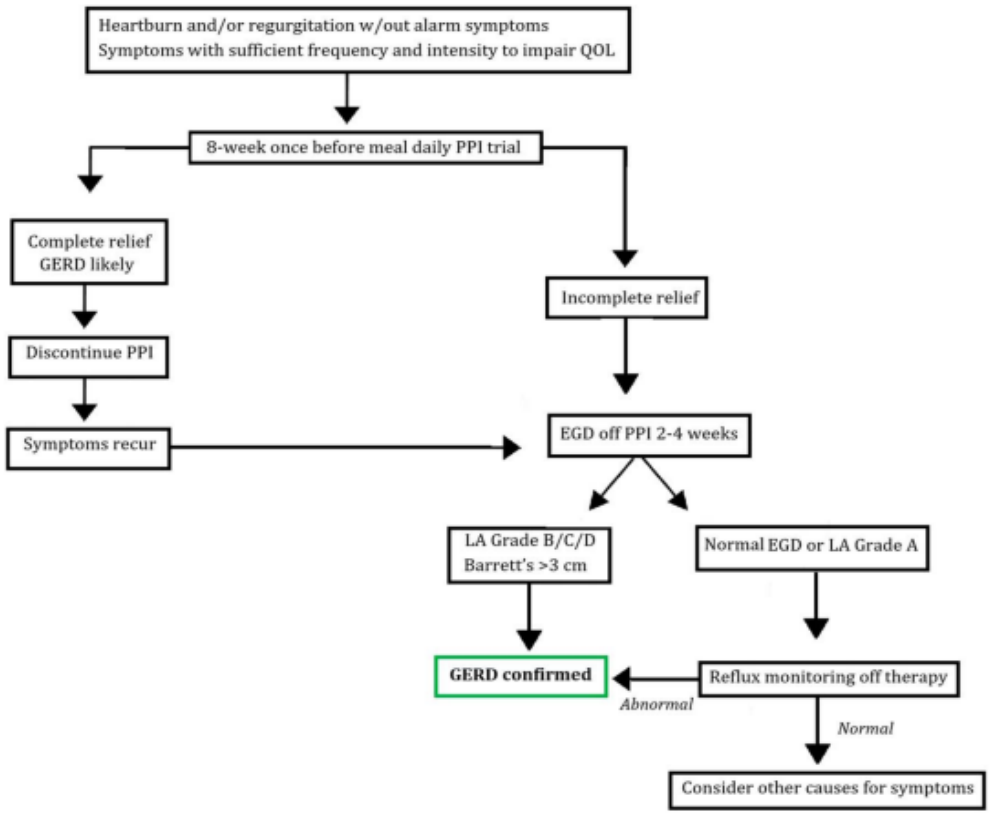

Figure 1. Diagnosis of GERD. Adapted from Katz PO, Dunbar KB, Schnoll-Sussman FH, Greer KB, Yadlapati R, Spechler SJ. ACG Clinical Guideline for the Diagnosis and Management of

Gastroesophageal Reflux Disease. American Journal of Gastroenterology. 2022;117(1):27-56. doi:10.14309/ajg.0000000000001538.

Figure 2 represents the steps for the diagnosis of **extraesophageal** reflux disease[7].

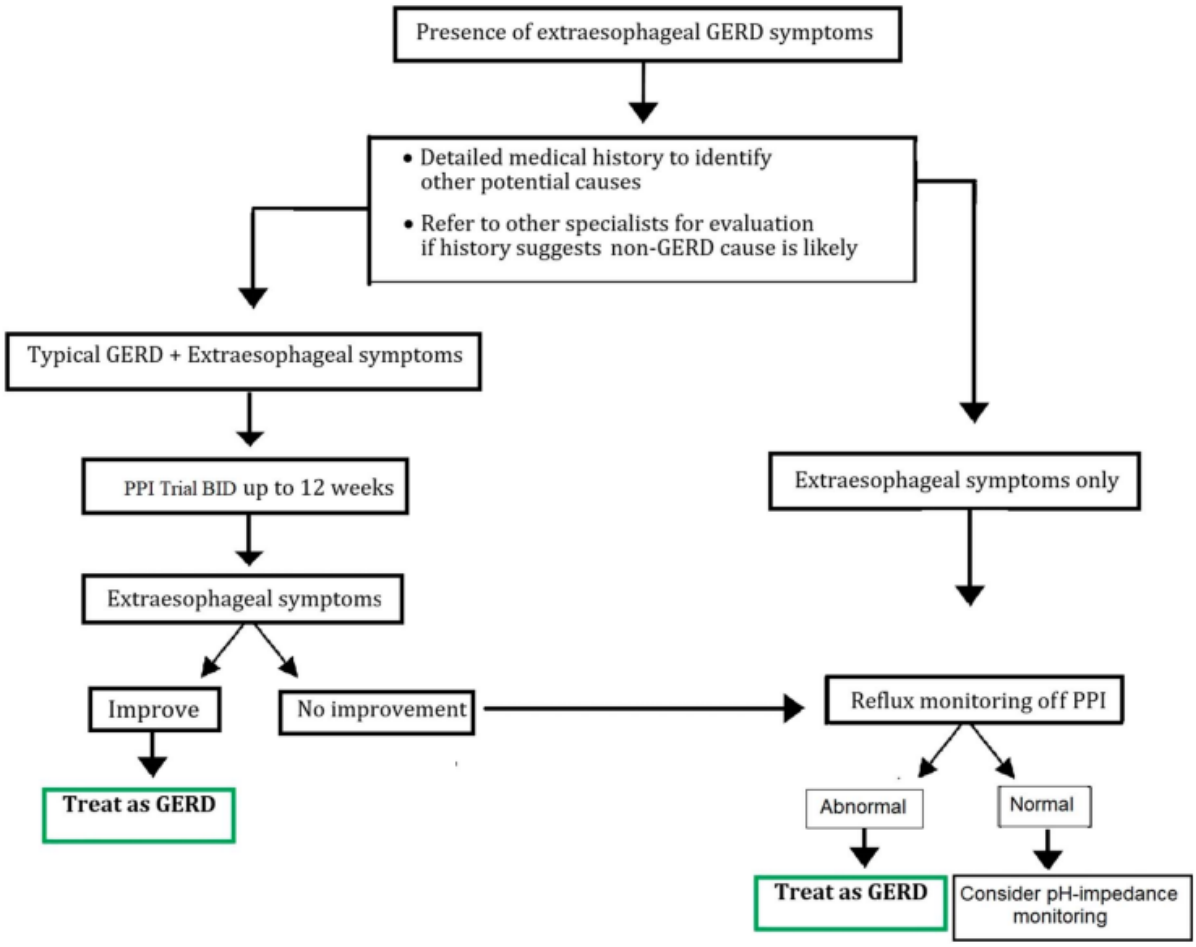

Figure 2. Diagnostic Algorithm for Extraesophageal GERD. Adapted from Katz PO, Dunbar KB, Schnoll-Sussman FH, Greer KB, Yadlapati R, Spechler SJ. ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease. American Journal of Gastroenterology. 2022;117(1):27-56. doi:10.14309/ajg.0000000000001538

1.2 Additional Guidelines

This part includes the added guidelines to the previous CHI GERD report, along with their recommendations.

Table 4. List of Additional Guidelines

Additional Guidelines
2021 SAGES Guidelines for the Surgical Treatment of Gastroesophageal Reflux (GERD)[8]
2023 AGA Clinical Practice Update on the Diagnosis and Management of Extraesophageal Gastroesophageal Reflux Disease: Expert Review[9]
2022 AGA Clinical Practice Update on New Technology and Innovation for Surveillance and Screening in Barrett's Esophagus: Expert Review[10]
2022 AGA Clinical Practice Update on De-Prescribing of Proton Pump Inhibitors: Expert Review[12]
2022 AGA Clinical Practice Update on the Personalized Approach to the Evaluation and Management of GERD: Expert Review[13]
2022 ACG Guidelines on the Diagnosis and Management of Barrett's Esophagus[14]

1.2.1 2021 SAGES Guidelines for the Surgical Treatment of Gastroesophageal Reflux (GERD)

The Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) published in 2021 their clinical guidelines for the surgical treatment of gastroesophageal reflux (GERD). The main recommendations are detailed below[8]:

1- **Surgical (fundoplication) versus medical (PPI) management in adult and pediatric patients with chronic or refractory GERD**

1a. The panel suggests managing adult patients with confirmed chronic or chronic refractory gastroesophageal reflux with surgical fundoplication rather than continued medical treatment (conditional recommendation based on very low certainty in the evidence of effects).

1b. No recommendation was made regarding pediatric patients.

2- **Robotic versus laparoscopic fundoplication in adult and pediatric patients with GERD requiring surgery.**

2a. The panel suggests that adult patients with gastroesophageal reflux who are candidates for surgery be treated with either robotic or laparoscopic fundoplication based on surgeon and patient's shared decision-making (conditional recommendation based on low certainty in the evidence of effects).

2b. The panel suggests that children with gastroesophageal reflux who are candidates for surgery be treated with either robotic or laparoscopic fundoplication based on surgeon and patient's shared decision-making and feasibility (conditional recommendation based on very low certainty in the evidence of effects).

3- **Complete versus partial fundoplication in adult and pediatric patients with GERD who are candidates for surgery.**

3a. The panel suggests that adult patients with GERD who are candidates for surgery be treated with either partial or complete fundoplication based on patients' values (conditional recommendations based on low certainty in the evidence of effects).

3b. For pediatric patients without large hiatal hernia, the panel suggests either partial or complete fundoplication approaches guided by shared surgeon-patient decision-making (conditional recommendations based on low certainty in the evidence of effects).

1.2.2 2023 AGA Clinical Practice Update on the Diagnosis and Management of Extraesophageal Gastroesophageal Reflux Disease

The recommendations of 2023 AGA Clinical Practice Update on the Diagnosis and Management of Extraesophageal Gastroesophageal Reflux Disease: Expert Review are listed below[9]:

- Initial testing to evaluate reflux should be tailored to patients' clinical presentation and can include upper endoscopy and ambulatory reflux monitoring studies of acid suppressive therapy.

- Testing can be considered for those with an established objective diagnosis of GERD who do not respond to high doses of acid suppression. Testing can include pH-impedance monitoring while on acid suppression to evaluate the role of ongoing acid or non-acid reflux.

- Alternative treatment methods to acid suppressive therapy (e.g., lifestyle modifications, alginate containing antacids, external upper esophageal sphincter compression device, cognitive behavioral therapy, neuromodulators) may serve a role in management of EER symptoms.

1.2.3 2022 AGA Clinical Practice Update on New Technology and Innovation for Surveillance and Screening in Barrett's Esophagus

The recommendations of 2022 AGA Clinical Practice Update on New Technology and Innovation for Surveillance and Screening in Barrett's Esophagus: Expert Review are listed below[10]:

- All patients with BE should be placed on at least daily proton pump inhibitor therapy.

- Patients with nondysplastic BE should undergo surveillance endoscopy in 3 to 5 years.

- In patients undergoing surveillance after endoscopic eradication therapy, random biopsies should be taken of the esophagogastric junction, gastric cardia, and the distal 2 cm of the neo squamous epithelium as well as from all visible lesions, independent of the length of the original BE segment.

1.2.4 2022 AGA Clinical Practice Update on De-Prescribing of Proton Pump Inhibitors

The recommendations of 2022 AGA Clinical Practice Update on De-Prescribing of Proton Pump Inhibitors are listed below[12]:

- Most patients with an indication for chronic PPI use who take twice-daily dosing should be considered for step down to once-daily PPI.

- Patients with complicated GERD, such as those with a history of severe erosive esophagitis, esophageal ulcer, or peptic stricture, should generally not be considered for PPI discontinuation.

- Patients with known Barrett's esophagus, eosinophilic esophagitis, or idiopathic pulmonary fibrosis should generally not be considered for a trial of de-prescribing.

- PPI users should be assessed for upper GI bleeding risk using an evidence-based strategy before de-prescribing.

- Patients at high risk for upper GI bleeding should not be considered for PPI deprescribing.

- Patients who discontinue long-term PPI therapy should be advised that they may develop transient upper GI symptoms due to rebound acid hypersecretion.

- When de-prescribing PPIs, either dose tapering, or abrupt discontinuation can be considered.

- The decision to discontinue PPIs should be based solely on the lack of an indication for PPI use, and not because of concern for PPI associated adverse events (PAAEs). The presence of a PAAE or a history of a PAAE in a current PPI user is not an independent indication for PPI withdrawal. Similarly, the presence of underlying risk factors for the development of an adverse event associated with PPI use should also not be an independent indication for PPI withdrawal.

1.2.5 2022 AGA Clinical Practice Update on the Personalized Approach to the Evaluation and Management of GERD

The recommendations of 2022 AGA Clinical Practice Update on the Personalized Approach to the Evaluation and Management of GERD are listed below[13]:

- In patients with proven GERD, Roux-en-Y gastric bypass is an effective primary anti-reflux intervention in obese patients, and a salvage option in non-obese patients, whereas sleeve gastrectomy has potential to worsen GERD.

- In patients with proven GERD, laparoscopic fundoplication and magnetic sphincter augmentation are effective surgical options, and transoral incisionless fundoplication is an effective endoscopic option in carefully selected patients.

- Clinicians should personalize adjunctive pharmacotherapy to the GERD phenotype, in contrast to empiric use of these agents. Adjunctive agents include alginate antacids for breakthrough symptoms, nighttime H2 receptor antagonists for nocturnal symptoms, baclofen for regurgitation or belch predominant symptoms, and prokinetics for coexistent gastroparesis.

- Clinicians should provide patients presenting with troublesome heartburn, regurgitation, and/ or non-cardiac chest pain without alarm symptoms a 4- to 8-week trial of single-dose PPI therapy. With inadequate response, dosing can be increased to twice a day or switched to a more effective acid suppressive

agent once a day. When there is adequate response, PPI should be tapered to the lowest effective dose.

1.2.6 2022 ACG Guidelines on the Diagnosis and Management of Barrett's Esophagus

The recommendations of the 2022 ACG guidelines on the diagnosis and management of Barrett's esophagus (BE) are listed below:[14]

Table 5. Level. of Evidence

GRADE	Explanation
High	Further research is very unlikely to change our confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very low	Any estimate of effect is very uncertain

Table 6. Grades of Recommendation

GRADE	Explanation
Strong	The desirable effects of an intervention clearly outweigh the undesirable effects or clearly do not.
Weak/conditional	The tradeoffs are less certain between the desirable and undesirable effects of an intervention.

Screening of BE:

- The guideline suggests a single screening endoscopy for patients with chronic GERD symptoms and 3 or more additional risk factors for BE, including male sex, age > 50 years, White race, tobacco smoking, obesity, and family history of BE or esophageal adenocarcinoma (EAC) in a first-degree relative (strength of recommendation: conditional; quality of evidence: very low).
- The guideline suggests that a swallowable, nonendoscopic capsule sponge device combined with a biomarker is an acceptable alternative to endoscopy for screening for BE in those with chronic reflux symptoms and other risk

factors (strength of recommendation: conditional; quality of evidence: very low).

- Repeat endoscopic screening in patients who have undergone an initial negative screening examination by endoscopy is not recommended (strength of recommendation: conditional; quality of evidence: low).

Management of BE with low grade dysplasia vs high grade dysplasia:

- The guideline recommends that length of the non-dysplastic Barrett's esophagus (NDBE) segment be considered when assigning surveillance intervals such that longer segments of BE (≥3 cm) are surveyed on a 3-year interval and shorter segments of BE (< 3cm) are surveyed on a 5-year interval (quality of evidence: moderate; strength of recommendation: strong).

Non endoscopic treatment of BE:

- The guideline suggests at least once-a-day PPI therapy in patients with BE without allergy or other contraindication to PPI use (strength of recommendation: conditional; quality of evidence: very low).
- The use of antireflux surgery as an antineoplastic measure in patients with BE is not recommended (strength of recommendation: conditional; quality of evidence: low).
- The guideline could not make a recommendation on combination therapy with ASA and PPI in patients with BE to reduce the risk of progression to HGD/EAC.

Endoscopic treatment of BE:

- The guideline recommends endoscopic eradication therapy (EET) compared with esophagectomy in patients with BE with high-grade dysplasia (HGD) (strength of recommendation: strong; quality of evidence: moderate).
- The guideline suggests endoscopic therapy in patients with BE with confirmed low-grade dysplasia (LGD) to reduce the risk of progression to HGD/EAC, with endoscopic surveillance of confirmed LGD as an acceptable alternative (strength of recommendation: conditional; quality of evidence: moderate).
- The guideline recommends an endoscopic surveillance program in patients with BE who have completed successful EET (strength of recommendation: strong; quality of evidence: moderate).

Section 2.0 Drug Therapy

This section comprises three subsections: the first one contains the newly recommended drugs, the second one covers drug modifications, and the third one outlines the drugs that have been withdrawn from the market.

2.1 Additions

After November 2019, there are no new drugs added to the treatment of GERD. The drugs used for the management of GERD are still the same.

2.2 Modifications

Some modifications were made from the previous 2019 CHI report.

Please refer to section 2.1.7 in the previous report to highlight these modifications:

- Metoclopramide does not need prior authorization (PA) as a prescribing edit: it is an old drug, not expensive; tardive dyskinesia as a serious side effect should be monitored[15].

- Metoclopramide age limits are not to be used in less than 1 year old, however, it is also not recommended to be used in patients older than 60years of age[15].

Please refer to section 2.2.6 in the previous 2019 CHI report:

- Cimetidine, famotidine and nizatidine do not need prior authorization (PA): they are drugs that have been on the market since decades and used as a second-line treatment option with concurrent use of PPI if symptoms are still present.

Please refer to section 2.7.7 in the previous 2019 CHI report:

- Domperidone does not need PA: it is a drug that has been on the market for decades, and it is only used if a patient has gastroparesis and did not improve while using metoclopramide[16].

- Domperidone has an age limit: efficacy has not been demonstrated; use is not recommended in infants and children < 12 years[16].

2.3 Delisting

Ranitidine was withdrawn from the market after a request by the FDA in April 2020, and it is no longer registered by the SFDA. The withdrawal was due to the presence of a contaminant known as N-Nitroso dimethylamine (NDMA) in ranitidine medications. NDMA is a probable human carcinogen[6].

Section 3.0 Key Recommendations Synthesis

GERD diagnosis:

- In patients with chest pain who have had adequate evaluation to exclude heart disease, objective testing for GERD (endoscopy and/or reflux monitoring) is recommended. (Conditional recommendation, low level of evidence)
- Endoscopy is recommended as the first test for evaluation of patients presenting with dysphagia or other alarm symptoms (weight loss and GI bleeding) and for patients with multiple risk factors for Barrett's esophagus. (Strong recommendation, low level of evidence)
- In patients for whom the diagnosis of GERD is suspected but not clear, and endoscopy shows no objective evidence of GERD, guidelines recommend reflux monitoring be performed off therapy to establish the diagnosis. (Strong recommendation, low level of evidence)

GERD management:

- Treatment with PPIs is recommended over H2RA for maintenance of healing for EE. (Strong recommendation, moderate level of evidence)
- Maintenance PPI therapy is recommended indefinitely or antireflux surgery for patients with LA grade C or D Moderate Strong esophagitis. (Strong recommendation, moderate level of evidence)
- Baclofen is not recommended in the absence of objective evidence of GERD. (Strong recommendation, moderate level of evidence.)
- Treatment with a prokinetic agent is not recommended for any kind for GERD therapy unless there is objective evidence of gastroparesis. (Strong recommendation, low level of evidence.)
- Sucralfate is only recommended in pregnancy GERD. (Strong recommendation, low level of evidence.
- For patients with GERD who do not have EE or Barrett's esophagus, and whose symptoms have resolved with PPI therapy, an attempt should be made to discontinue PPIs or to switch to on-demand therapy in which PPIs are

taken only when symptoms occur and discontinued when they are relieved. (Conditional recommendation, low level of evidence)

Extraesophageal GERD symptoms:

- Evaluation for non-GERD causes in patients with possible extraesophageal manifestations is recommended before ascribing symptoms to GERD. (Strong recommendation, moderate level of evidence.)
- For patients who have extraesophageal manifestations of GERD without typical GERD symptoms (e.g., heartburn and regurgitation) the guidelines recommend undergoing reflux testing for evaluation before PPI therapy. Strong recommendation, moderate level of evidence.)
- For patients who have both extraesophageal and typical GERD symptoms, the guideline suggests considering a trial of twice-daily PPI therapy for 8–12 weeks before additional testing. (Conditional recommendation, low level of evidence)

Refractory GERD:

- Optimization of PPI therapy is recommended as the first step in management of refractory GERD. Strong recommendation, moderate level of evidence.)
- Esophageal pH monitoring (Bravo, catheter-based, or combined impedance-pH monitoring) performed OFF PPIs is recommended if the diagnosis of GERD has not been established by a previous pH monitoring study or an endoscopy showing long-segment Barrett's esophagus or severe reflux esophagitis (LA grade C or D). (Conditional recommendation, low level of evidence)
- Esophageal impedance-pH monitoring performed ON PPIs is recommended for patients with an established diagnosis of GERD whose symptoms have not responded adequately to twice-daily PPI therapy. (Conditional recommendation, low level of evidence).
- For patients who have regurgitation as their primary PPI-refractory symptom and who have had abnormal gastroesophageal reflux documented by objective testing, we suggest consideration of antireflux surgery or TIF. (Conditional recommendation, low level of evidence)

Surgical and endoscopic options for GERD:

- Antireflux surgery performed by an experienced surgeon is recommended as an option for long-term treatment of patients with objective evidence of GERD. Those who have severe reflux esophagitis (LA grade C or D), large hiatal hernias, and/or persistent, troublesome GERD symptoms, are likely to benefit most from surgery. (Strong recommendation, moderate level of evidence).

- The guidelines recommend consideration of MSA (magnetic sphincter augmentation) as an alternative to laparoscopic fundoplication for patients with regurgitation who fail medical management. (Strong recommendation, moderate level of evidence).
- The guidelines suggest consideration of Roux-en-Y gastric bypass (RYGB) as an option to treat GERD in obese patients who are candidates for this procedure and who are willing to accept its risks and requirements for lifestyle alterations. (Conditional recommendation, low level of evidence)
- The guidelines suggest consideration of TIF for patients with troublesome regurgitation or heartburn who do not wish to undergo antireflux surgery and who do not have severe reflux esophagitis (LA grade C or D) or hiatal hernias >2 cm. (Conditional recommendation, low level of evidence)

Section 4.0 Conclusion

This report serves as **an annex to the previous CHI GERD report** and aims to provide recommendations to aid in the management of gastro-esophageal reflux disease. It is important to note that these recommendations should be utilized to support clinical decision-making and not replace it in the management of individual patients with GERD. Health professionals are expected to consider this guidance alongside the specific needs, preferences, and values of their patients when exercising their judgment.

Section 5.0 References

1. The World Gastroenterology Organisation (WGO). definition of GERD. Accessed June 20, 2023. https://www.worldgastroenterology.org/guidelines/gastroesophageal-reflux-disease
2. Jorabar Singh Nirwan, Muhammad Usman Ghori. Prevalence of GERD worldwide. Published online 2020. Accessed June 20, 2023. https://pubmed.ncbi.nlm.nih.gov/32242117/
3. Obaidallah Buraykan Alsuwat, Mohammad Eid Mahmoud Mahfouz. prevalence of GERD in Saudi Arabia.
4. Spechler SJ, Lee E. Goals of GERD . Accessed June 20, 2023. https://aboutgerd.org/treatment/long-term-treatments/#:~:text=If%20untreated%20or%20treated%20incorrectly,esophageal%20sphincter%20and%20prevent%20reflux
5. Ministry of health of Saudi Arabia. Prevention ways to decrease GERD symptoms. . Published online 2019. Accessed June 20, 2023. https://www.moh.gov.sa/en/awarenessplateform/VariousTopics/Pages/GERD.aspx
6. FDA Requests Removal of All Ranitidine Products (Zantac) from the Market. Published April 1, 2020. Accessed August 11, 2023. https://www.fda.gov/news-events/press-announcements/fda-requests-removal-all-ranitidine-products-zantac-market
7. Katz PO, Dunbar KB, Schnoll-Sussman FH, Greer KB, Yadlapati R, Spechler SJ. ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease. *American Journal of Gastroenterology*. 2022;117(1):27-56. doi:10.14309/ajg.0000000000001538
8. Slater BJ, Dirks RC, Mckinley SK, et al. *Guidelines for the Surgical Treatment of Gastroesophageal Reflux (GERD) Sages.Org/Publications/Guidelines/Guidelines-for-the-Surgical-Treatment-of-Gastroesophageal-Reflux-Gerd AUTHORS*.
9. Chen JW, Vela MF, Peterson KA, Carlson DA. AGA Clinical Practice Update on the Diagnosis and Management of Extraesophageal Gastroesophageal Reflux Disease: Expert Review. *Clin Gastroenterol Hepatol*. Published online April 13, 2023. doi:10.1016/j.cgh.2023.01.040
10. Muthusamy VR, Wani S, Gyawali CP, et al. AGA Clinical Practice Update on New Technology and Innovation for Surveillance and Screening in Barrett's Esophagus: Expert Review. *Clinical Gastroenterology and Hepatology*. 2022;20(12):2696-2706.e1. doi:10.1016/j.cgh.2022.06.003

11. Drug VL, Antoniu S, Bărboi OB, et al. Romanian Guidelines for the Diagnosis and Treatment of GERDinduced Respiratory Manifestations. *Journal of Gastrointestinal and Liver Diseases*. 2022;31(1):119-142. doi:10.15403/jgld-4196

12. Targownik LE, Fisher DA, Saini SD. AGA Clinical Practice Update on De-Prescribing of Proton Pump Inhibitors: Expert Review. *Gastroenterology*. 2022;162(4):1334-1342. doi:10.1053/j.gastro.2021.12.247

13. Yadlapati R, Gyawali CP, Pandolfino JE, et al. AGA Clinical Practice Update on the Personalized Approach to the Evaluation and Management of GERD: Expert Review. *Clinical Gastroenterology and Hepatology*. 2022;20(5):984-994.e1. doi:10.1016/j.cgh.2022.01.025

14. Shaheen NJ, Falk GW, Iyer PG, et al. Diagnosis and Management of Barrett's Esophagus: An Updated ACG Guideline. *American Journal of Gastroenterology*. 2022;117(4):559-587. doi:10.14309/ajg.0000000000001680

15. lexicomp. metoclopramide. Published online 2023. Accessed June 23, 2023. https://online-lexi-com.ezproxy.lau.edu.lb:2443/lco/action/doc/retrieve/docid/multinat_f/4669125?cesid=84MWNPuZvVR&searchUrl=%2Flco%2Faction%2Fsearch%3Fq%3Dmetoclopramide%26t%3Dname%26acs%3Dfalse%26acq%3Dmetoclopramide

16. Lexicomp. domperidone . Published online 2023. Accessed June 23, 2023. https://online-lexi-com.ezproxy.lau.edu.lb:2443/lco/action/doc/retrieve/docid/multinat_f/4668235?cesid=aWBfb7RDp2u&searchUrl=%2Flco%2Faction%2Fsearch%3Fq%3Ddomperidone%26t%3Dname%26acs%3Dfalse%26acq%3Ddomperidone#doe

Section 6.0 Appendices

Appendix 1. Supplementary Appendix

I. Prescribing Edits

Some covered drugs may have additional requirements, rules or limits on coverage. These requirements and limits may include:

Prescribing edits Tools	Description
AGE (Age):	Coverage may depend on patient age
CU (Concurrent Use):	Coverage may depend upon concurrent use of another drug
G (Gender):	Coverage may depend on patient gender
MD (Physician Specialty):	Coverage may depend on prescribing physician's specialty or board certification
PA (Prior Authorization):	Requires specific physician request process
QL (Quantity Limits):	Coverage may be limited to specific quantities per prescription and/or time period
ST (Step Therapy):	Coverage may depend on previous use of another drug
EU (Emergency Use only):	This drug status on Formulary is only for emergency use
PE (Protocol Edit):	Use of drug is dependent on protocol combination, doses, and sequence of therapy

Table 7: Indications for Proton Pump Inhibitors

This table from the AGA Clinical Practice Update on De-Prescribing of Proton Pump Inhibitors summarizes the indications for PPI: [12]

Indications					
Definitely indicated for long-term use (>8 wk)	Conditionally indicated for long-term use	Not indicated for long-term use	Definitely indicated for acute/short-term use (≤8 wk)	Conditionally indicated for acute/short-term use	Not indicated for acute/ short-term use
Barrett's esophagus Clinically significant (LA Classification grade C/D) erosive esophagitis Esophageal strictures from GERD (ie, peptic strictures) Zollinger-Ellison syndrome Eosinophilic esophagitis Gastroprotection in users of ASA/nonsteroidal anti-inflammatory drug at high risk for GI bleeding Prevention of progression of idiopathic pulmonary fibrosis	PPI-responsive endoscopy-negative reflux disease, with recurrence on PPI cessation PPI-responsive functional dyspepsia, with recurrence on PPI cessation PPI-responsive upper airway symptoms ascribed to laryngopharyngeal reflux, with recurrence on PPI cessation Refractory steatorrhea in chronic pancreatic insufficiency with enzyme replacement Secondary prevention of gastric and duodenal peptic ulcers with no concomitant antiplatelet drugs	Symptoms of nonerosive reflux disease with no sustained response to high-dose PPI therapy Functional dyspepsia with no sustained response to PPI therapy Steroid therapy in the absence of ASA/ nonsteroidal anti-inflammatory drug therapy Prevention of recurrent upper GI bleeding from causes other than: Peptic ulcer disease, including gastric and duodenal erosions Erosive esophagitis	*Helicobacter pylori* eradication Stress ulcer prophylaxis for ICU patients with risk factors Uninvestigated GERD/ dyspepsia Treatment of NSAID-related gastric and duodenal peptic ulcers	Initial or on-demand treatment of endoscopy-negative reflux disease Initial treatment of functional dyspepsia Uninvestigated dyspepsia Ulcer prevention after sclerotherapy or band ligation treatment of esophageal varices Prevention of rebleeding from Mallory-Weiss tears	Empiric treatment of laryngopharyngeal symptomatology Acute undifferentiated abdominal pain Acute nausea and vomiting not believed to be related to GERD/esophagitis Any isolated lower GI symptomatology

Table 8: Lifestyle Modifications for the Management of GERD

This table from the ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease 2022 represents the lifestyle modifications that alleviate the symptoms of GERD: [7]

Lifestyle modification	Strength of scientific evidence	Pathophysiologically conclusive?	Recommendable?
Avoid fatty meals	Equivocal	Equivocal	Yes
Avoid carbonated beverages	Moderate	Yes	Yes
Select decaffeinated beverages	Equivocal	Equivocal	Not generally
Avoid citrus	Weak	Yes	Yes, if citrus triggers symptoms
Eat smaller meals	Weak	Yes	Yes
Lose weight	Equivocal	Equivocal	Yes[a]
Avoid alcoholic beverages	Weak	Mechanisms not understood; different alcoholic beverages have different effects	Not generally
Stop smoking	Weak	Yes	Yes[a]
Avoid excessive exercise	Weak	Yes	Yes
Sleep with head elevated	Equivocal	Equivocal	Yes
Sleep on the left side	Unequivocal	Yes	Yes

[a]Obesity and smoking seem to be risk factors for cancer of the distal esophagus.

Appendix 2. Scope Review

Section	Rationale/Updates
Section 1.1 American College of Gastroenterology Guidelines for the Diagnosis and Management of Gastroesophageal Reflux Disease	**2022 ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease** [7] <u>Updated recommendations:</u> • A recently approved device for evaluation of GERD uses a catheter-based balloon lined by sensors that measure mucosal impedance during endoscopy. This technique has shown promise for differentiating GERD from EoE and may develop to be a useful adjunct to endoscopy in the diagnosis of GERD. • The guideline suggests avoiding meals within 2–3 hours of bedtime (conditional recommendation, low level of evidence). • The guideline recommends treatment with PPIs over treatment with histamine-2-receptor antagonists (H2RA) for healing EE (strong recommendation, high level of evidence). • The guideline recommends PPI administration 30–60 minutes before a meal rather than at bedtime for GERD symptom control (strong recommendation, moderate level of evidence). • For patients with GERD who do not have EE or Barrett's esophagus, and whose symptoms have resolved with PPI therapy, an attempt should be made to discontinue PPIs or to switch to on-demand therapy in which PPIs are taken only when symptoms occur and discontinued when they are relieved (conditional recommendation, low level of evidence). • For patients with GERD who require maintenance therapy with PPIs, the PPIs

	should be administered in the lowest dose that effectively controls GERD symptoms and maintains healing of reflux esophagitis (conditional recommendation, low level of evidence). • The guideline recommends maintenance PPI therapy indefinitely or antireflux surgery for patients with LA grade C or D esophagitis (strong recommendation, moderate level of evidence). • The guideline does not recommend baclofen in the absence of objective evidence of GERD (strong recommendation, moderate level of evidence). • The guideline recommends against treatment with a prokinetic agent of any kind for GERD therapy unless there is objective evidence of gastroparesis (strong recommendation, low level of evidence). • The guideline does not recommend sucralfate for GERD therapy except during pregnancy (strong recommendation, low level of evidence). • The guideline suggests on-demand or intermittent PPI therapy for heartburn symptom control in patients with NERD (conditional recommendation, low level of evidence). • Antacids are used exclusively for on-demand symptom relief with little evidence to favor 1 type over another. Studies with an alginic acid preparation manufactured in the United Kingdom suggest potential efficacy in symptom relief compared with other products, but alginate content of preparations sold in other countries is variable. <u>Extraesophageal GERD:</u> We recommend evaluation for non-GERD causes in patients with possible extraesophageal manifestations before ascribing symptoms to GERD (strong

	recommendation, moderate level of evidence) The guideline recommends that patients who have extraesophageal manifestations of GERD without typical GERD symptoms (e.g., heartburn and regurgitation) undergo reflux testing for evaluation before PPI therapy (strong recommendation, moderate level of evidence) For patients who have both extraesophageal and typical GERD symptoms, the guideline suggests considering a trial of twice-daily PPI therapy for 8–12 weeks before additional testing (conditional recommendation, low level of evidence) In patients treated for extraesophageal reflux disease, surgical or endoscopic antireflux procedures are only recommended in patients with objective evidence of reflux (conditional recommendation, low level of evidence). <u>Refractory GERD:</u> The guideline recommends optimization of PPI therapy as the first step in management of refractory GERD (strong recommendation, moderate level of evidence) For patients who have regurgitation as their primary PPI-refractory symptom and who have had abnormal gastroesophageal reflux documented by objective testing, we suggest consideration of antireflux surgery or TIF (conditional recommendation, low level of evidence). <u>Surgical and endoscopic options for GERD:</u> 1- We recommend antireflux surgery performed by an experienced surgeon as an option for long-term treatment of patients with objective evidence of GERD, especially those who have severe reflux esophagitis (LA grade C or D), large hiatal hernias, and/or persistent, troublesome GERD symptoms (strong recommendation, moderate level of evidence) 2- The guideline suggests consideration of Roux-en-Y gastric bypass (RYGB) as an option to treat GERD in obese patients who are candidates for this procedure and who are willing to accept its risks and

	requirements for lifestyle alterations (conditional recommendation, low level of evidence). 3- The guideline suggests consideration of TIF for patients with troublesome regurgitation or heartburn who do not wish to undergo antireflux surgery and who do not have severe reflux esophagitis (LA grade C or D) or hiatal hernias 2 cm (conditional recommendation, low level of evidence).
N/A	**2021 Guidelines for the Surgical Treatment of Gastroesophageal Reflux (GERD)** [8] <u>Missed guidelines:</u> **4- Surgical (fundoplication) versus medical (PPI) management in adult and pediatric patients with chronic or refractory GERD** 1a. The panel suggests managing adult patients with confirmed chronic or chronic refractory gastroesophageal reflux with surgical fundoplication rather than continued medical treatment (conditional recommendation based on very low certainty in the evidence of effects). 1b. No recommendation was made regarding pediatric patients. **5- Robotic versus laparoscopic fundoplication in adult and pediatric patients with GERD requiring surgery.** 2a. The panel suggests that adult patients with gastroesophageal reflux who are candidates for surgery be treated with either robotic or laparoscopic fundoplication based on surgeon and patient's shared decision-making (conditional recommendation based on low certainty in the evidence of effects). 2b. The panel suggests that children with gastroesophageal reflux who are candidates for surgery be treated with either robotic or laparoscopic fundoplication based on surgeon and patient's shared decision-making and feasibility (conditional recommendation based on very

	low certainty in the evidence of effects). **6- Complete versus partial fundoplication in adult and pediatric patients with GERD who are candidates for surgery.** 3a. The panel suggests that adult patients with GERD who are candidates for surgery be treated with either partial or complete fundoplication based on patients' values (conditional recommendations based on low certainty in the evidence of effects). 3b. For pediatric patients without large hiatal hernia, the panel suggests either partial or complete fundoplication approaches guided by shared surgeon-patient decision-making (conditional recommendations based on low certainty in the evidence of effects). 4. Division of short gastric vessels or no division in adult patients with GERD undergoing fundoplication for adults undergoing fundoplication for GERD, the panel suggests either division or no division of short gastric vessels (conditional recommendations based on very low certainty in the evidence of effects). 5. Minimal versus maximal dissection in pediatric patients with GERD undergoing fundoplication in the pediatric GERD population without large hiatal hernias undergoing fundoplication, the panel suggests minimal rather than maximal dissection during fundoplication (conditional recommendations based on moderate certainty in the evidence of effects).
N/A	**2023 AGA Clinical Practice Update on the Diagnosis and Management of Extraesophageal Gastroesophageal Reflux Disease: Expert Review** [9] <u>Missed guidelines:</u> • Initial testing to evaluate reflux should be tailored to patients' clinical presentation and can include upper endoscopy and ambulatory reflux monitoring studies of acid suppressive therapy.

	• Testing can be considered for those with an established objective diagnosis of GERD who do not respond to high doses of acid suppression. Testing can include pH-impedance monitoring while on acid suppression to evaluate the role of ongoing acid or non-acid reflux. • Alternative treatment methods to acid suppressive therapy (e.g., lifestyle modifications, alginate containing antacids, external upper esophageal sphincter compression device, cognitive behavioral therapy, neuromodulators) may serve a role in management of EER symptoms. • Shared decision-making should be performed before referral for anti-reflux surgery for EER when the patient has clear, objectively defined evidence of GERD. However, a lack of response to PPI therapy predicts lack of response to anti-reflux surgery and should be incorporated into the decision process.
N/A	**2022 AGA Clinical Practice Update on New Technology and Innovation for Surveillance and Screening in Barrett's Esophagus: Expert Review** [10] <u>Missed guidelines:</u> All patients with BE should be placed on at least daily proton pump inhibitor therapy. Patients with nondysplastic BE should undergo surveillance endoscopy in 3 to 5 years. In patients undergoing surveillance after endoscopic eradication therapy, random biopsies should be taken of the esophagogastric junction, gastric cardia, and the distal 2 cm of the neo squamous epithelium as well as from all visible lesions, independent of the length of the original BE segment.
N/A	**2022 Romanian Guidelines for the Diagnosis and Treatment of GERD induced Respiratory Manifestations** [11] <u>Missed guidelines:</u> Gastroesophageal reflux disease (GERD) may cause

	bronchial asthma. (Level of evidence: moderate.) Bronchial asthma may cause GERD. (Level of evidence: low.) GERD may cause chronic cough. (Level of evidence: moderate.) Chronic cough may cause GERD. (Level of evidence: low.) GERD may cause other respiratory diseases [idiopathic pulmonary fibrosis (IPF), obstructive sleep apnea hypopnea syndrome (OSAHS), chronic obstructive pulmonary disease (COPD), cystic fibrosis, bronchiectasis, aspiration pneumonia]. (Level of evidence: moderate.) PPIs therapy could be efficient in treating GERD-induced respiratory symptoms. (Level of evidence: moderate.) Baclofen is efficient in treating GERD and GERD induced respiratory symptoms. (Level of evidence: moderate.) Prokinetic agents are efficient in treating GERD-induced respiratory symptoms. (Level of evidence: low.) H2 blockers are inefficient in treating GERD-induced respiratory symptoms. (Level of evidence: low.) GERD-induced respiratory symptoms patients have a low quality of life (level of evidence: high.)
N/A	**2022 AGA Clinical Practice Update on De-Prescribing of Proton Pump Inhibitors: Expert Review** [12] <u>Missed guidelines:</u>

	• Most patients with an indication for chronic PPI use who take twice-daily dosing should be considered for step down to once-daily PPI. • Patients with complicated GERD, such as those with a history of severe erosive esophagitis, esophageal ulcer, or peptic stricture, should generally not be considered for PPI discontinuation. • Patients with known Barrett's esophagus, eosinophilic esophagitis, or idiopathic pulmonary fibrosis should generally not be considered for a trial of de-prescribing. • PPI users should be assessed for upper GI bleeding risk using an evidence-based strategy before de-prescribing. • Patients at high risk for upper GI bleeding should not be considered for PPI deprescribing. • Patients who discontinue long-term PPI therapy should be advised that they may develop transient upper GI symptoms due to rebound acid hypersecretion. • When de-prescribing PPIs, either dose tapering, or abrupt discontinuation can be considered. • The decision to discontinue PPIs should be based solely on the lack of an indication for PPI use, and not because of concern for PPIassociated adverse events (PAAEs). The presence of a PAAE or a history of a PAAE in a current PPI user is not an independent indication for PPI withdrawal. Similarly, the presence of underlying risk factors for the development of an adverse event associated with PPI use should also not be an independent indication for PPI withdrawal.
N/A	**2022 AGA Clinical Practice Update on the Personalized Approach to the Evaluation and Management of GERD: Expert Review** [13] <u>Missed guidelines:</u> • In patients with proven GERD, Roux-en-Y gastric bypass is an effective primary anti-reflux

	intervention in obese patients, and a salvage option in non-obese patients, whereas sleeve gastrectomy has potential to worsen GERD. • In patients with proven GERD, laparoscopic fundoplication and magnetic sphincter augmentation are effective surgical options, and transoral incisionless fundoplication is an effective endoscopic option in carefully selected patients. • Clinicians should personalize adjunctive pharmacotherapy to the GERD phenotype, in contrast to empiric use of these agents. Adjunctive agents include alginate antacids for breakthrough symptoms, nighttime H2 receptor antagonists for nocturnal symptoms, baclofen for regurgitation or belch predominant symptoms, and prokinetics for coexistent gastroparesis. • Clinicians should provide patients presenting with troublesome heartburn, regurgitation, and/ or non-cardiac chest pain without alarm symptoms a 4- to 8-week trial of single-dose PPI therapy. With inadequate response, dosing can be increased to twice a day or switched to a more effective acid suppressive agent once a day. When there is adequate response, PPI should be tapered to the lowest effective dose.

Appendix 3. PubMed Search

Query	Filters	Search Details	Results
((((((((((((((((Gastroesophageal Reflux[MeSH Terms]) OR (Gastric Acid Reflux[Title/Abstract])) OR (Acid Reflux, Gastric[Title/Abstract])) OR (Reflux, Gastric Acid[Title/Abstract])) OR (Gastric Acid Reflux Disease[Title/Abstract])) OR (Gastro-Esophageal Reflux Disease[Title/Abstract])) OR (Gastro Esophageal Reflux Disease[Title/Abstract])) OR	Guideline, in the last 5 years	("gastroesophageal reflux"[MeSH Terms] OR "gastric acid reflux"[Title/Abstract] OR "acid reflux gastric"[Title/Abstract] OR "reflux gastric acid"[Title/Abstract] OR "gastric acid reflux disease"[Title/Abstract] OR "gastro esophageal reflux disease"[Title/Abstract] OR "gastro esophageal reflux disease"[Title/Abstract] OR "gastro esophageal reflux	23

(Gastro-Esophageal Reflux Diseases[Title/Abstract])) OR (Reflux Disease, Gastro-Esophageal[Title/Abstract])) OR (Gastro-oesophageal Reflux[Title/Abstract])) OR (Gastro oesophageal Reflux[Title/Abstract])) OR (Reflux, Gastro-oesophageal[Title/Abstract])) OR (Gastroesophageal Reflux Disease[Title/Abstract])) OR (GERD[Title/Abstract])) OR (Reflux, Gastroesophageal[Title/Abstract])) OR (Esophageal Reflux[Title/Abstract])) OR (Gastro-Esophageal Reflux[Title/Abstract])) OR (Gastro Esophageal Reflux[Title/Abstract])) OR (Reflux, Gastro-Esophageal[Title/Abstract])		diseases"[Title/Abstract] OR (("Reflux"[All Fields] OR "refluxant"[All Fields] OR "refluxate"[All Fields] OR "refluxates"[All Fields] OR "refluxed"[All Fields] OR "refluxers"[All Fields] OR "refluxes"[All Fields] OR "refluxing"[All Fields] OR "refluxive"[All Fields]) AND "disease gastro esophageal"[Title/Abstract]) OR "gastro oesophageal reflux"[Title/Abstract] OR "gastro oesophageal reflux"[Title/Abstract] OR "reflux gastro oesophageal"[Title/Abstract] OR "gastroesophageal reflux disease"[Title/Abstract] OR "GERD"[Title/Abstract] OR "reflux gastroesophageal"[Title/Abstract] OR "esophageal reflux"[Title/Abstract] OR "gastro esophageal reflux"[Title/Abstract] OR "gastro esophageal reflux"[Title/Abstract] OR "reflux gastro esophageal"[Title/Abstract]) AND ((y_5[Filter]) AND (guideline[Filter]))	

Appendix 4. Treatment Algorithm