Quality Care Network

Clinical Practice Guideline

Gastroesophageal Reflux Disease (GERD)

Gastroesophageal reflux disease (GERD) is also referred to as "acid indigestion, acid reflux, acid regurgitation, heartburn and reflux," according to the National Institute of Diabetes & Digestive and Kidney Diseases (NIDDK, ND). The American Society for Gastrointestinal Endoscopy (ASGE), provides that about 20% of adult Americans have heartburn twice a week. GERD can be linked to other "non-digestive tract conditions, may contribute an aggravating compounding effect on other diseases, prolong hospitalizations, and increase subsequent medical costs." (Chen, 2015). The UH Quality Care Network (UHQCN) and the physician-led board of directors developed and reviewed this Clinical Practice Guideline (CPG).

**These Clinical Practice Guidelines are guidelines only. In no way should these Clinical Practice Guidelines be used as a substitute for clinical or medical judgment.*

Contributing Factors

Eating and Lifestyle Risk factors

- Elevated body mass index (BMI) is associated with increased GERD risk
- Elevated dietary fat intake is linked to a higher risk of GERD and erosive esophagitis.
- Carbonated drink consumption is a risk factor for heartburn during sleep in patients with GERD

(WGO, 2015)

Complications

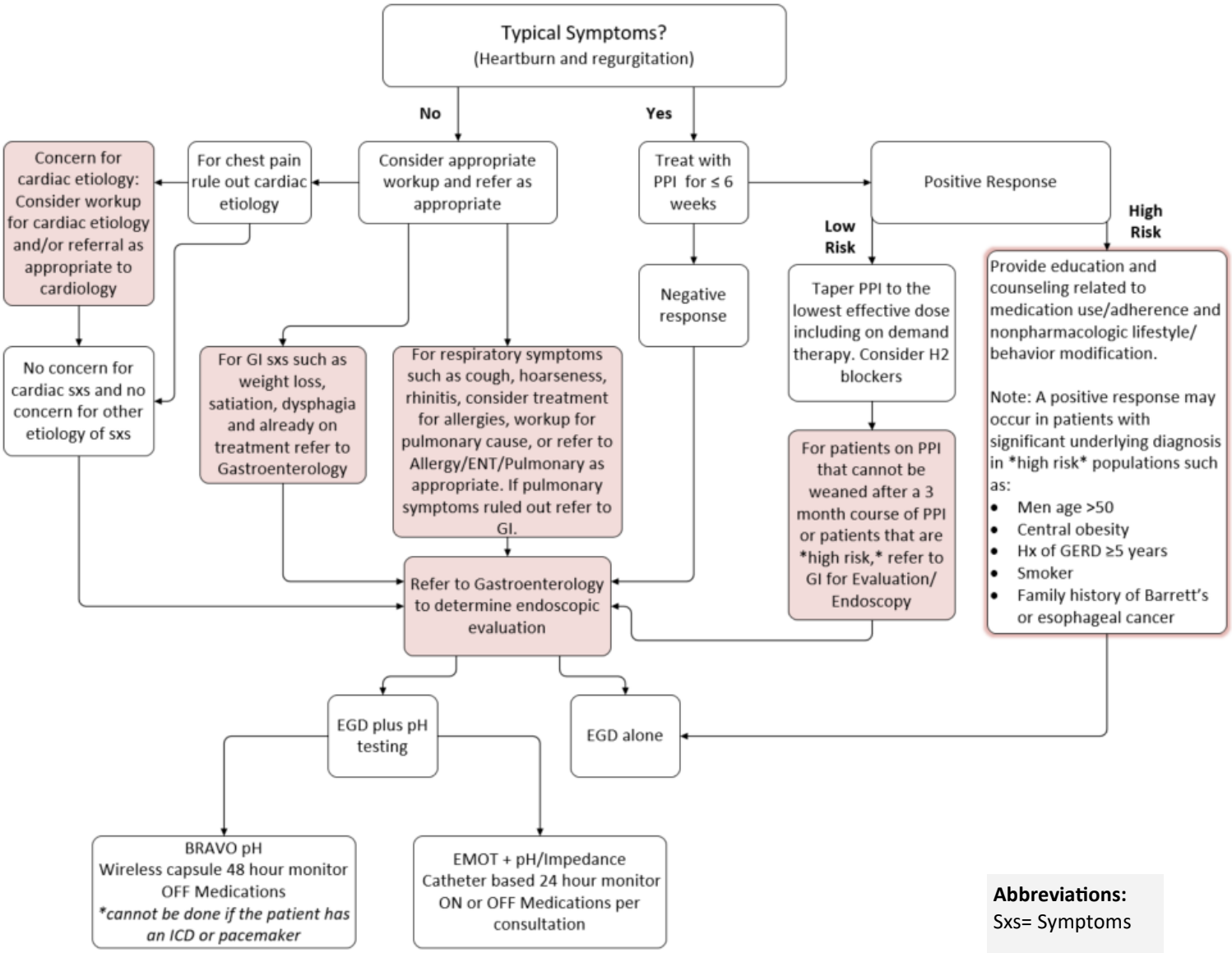
- Erosive esophagitis
- Barrett's esophagus
- Esophageal strictures
- Esophageal adenocarcinoma
- Asthma
- Chronic laryngitis
- Laryngeal and tracheal stenosis
- Chronic cough
- Dental erosions
- Chronic sinusitis
- Recurrent pneumonitis

(Kahrilas, 2018)

Symptoms of GERD

- **<u>Typical symptoms include</u>: Heartburn and regurgitation**
- **<u>Atypical symptoms include:</u> dyspepsia, epigastric pain, nausea, bloating and belching may be indicative of GERD but overlap with other conditions (Katz, Gerson, Vela, 2013), cough, hoarseness, and rhinitis**
    - ****Regurgitation tends to be less responsive to medication and should be considered for other anti-reflux interventions.***

Treatment & Management



Lifestyle Role as a Risk Factor to GERD & Symptom Management

- Coffee – role uncertain, mechanism unknown, and may be related to caffeine consumption
- Alcohol – role unclear, excessive long term use may be associated with esophageal malignancy, but may be independent of effect of alcohol
- Smoking – role is unclear, like alcohol is associated with increased risk of malignancy (WGO, 2015)
- Educate on raising the head of the bed for symptom relief.
- Counsel patients on the importance of weight loss for patients that are overweight and refer to obesity guideline.
    - BMI >30 increased risk of GERD**:** Provide education and counseling related to weight loss such as diet and exercise. Educate and engage the patient to determine the best patient specific treatment plan.
    - For patients with a BMI 30-34.9, consider education related to diet and exercise, medications, and balloons.
    - For patients with a BMI >35 consider referral for additional support such as targeted weight loss education or additional treatment options such as diet and exercise, medications, and balloons. If the patient has comorbidities, they may be considered a surgical candidate, consider referral if indicated.

Tests

Esophageal Test	Mode	Test description
pH with impedance – Off medications	Catheter	Ambulatory 24 hour naso-esophageal catheter to assess for non-acid and acid reflux simultaneously
pH with impedance – On medications	Catheter	Ambulatory 24 hour naso-esophageal catheter to assess volume reflux
Dual pH probe with laryngopharyngeal reflux (LPR) testing	Catheter	Ambulatory 24 hour dual probe catheter to assess oropharyngeal symptoms
pH Bravo – Off medications	Wireless	Ambulatory 48 hour esophageal capsule placed during EGD to monitor pH wirelessly ***Not indicated with patients with ICD or Pacemaker***
EMOT - Esophageal motility study	Catheter	Naso-esophageal pressure testing during swallowing

Why is this work-up necessary?

- These tests can aid in diagnosing GERD or other diseases. Test results may require additional work-up and/or indicate treatment with anti-reflux procedures. Regurgitation for example, may require treatment of hiatal hernia repair, Nissen Fundoplication or Toupet Fundoplication.

Scheduling

The full range of Digestive Health Testing are available at UH Ahuja Medical Center, UH Cleveland Medical Center and UH Parma Medical Center. UH St. John's Medical Center provides BRAVO testing and UH Geauga provides Manometry testing. For assistance in scheduling contact:

- UH Endoscopy 216-844-ENDO (3636)
- UH Gastroenterology 216-844-8500
- UH Surgery 216-844-7874
- UH Physician Referrals 800-552-8338/ 216-844-7553
- If connected to the UH Intranet, please click the blue hyperlink for the: online referral form

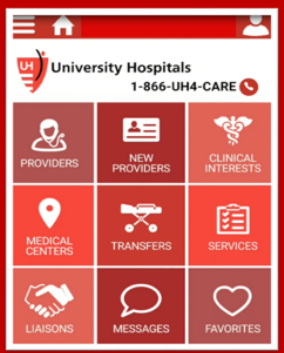
	ICD10 Code
Gastroesophageal Reflux Disease	**K21.9**

UH4CARE

- Call 1-800-UH4-CARE to schedule an appointment with a UH Quality Care Network Provider

UH Provider App

- On your telephone or mobile device, download the UH Provider App
- Use this App to refer to a specialist



Accuracy Matters.

- **Timely and appropriate documentation has long term implications that affect the overall cost and quality of patient care.**
- **It is essential that the most appropriate and specific diagnosis codes are entered at each and every patient encounter.**

Common Initial Oral dosages for adults

Histamine-2 Receptor Antagonist (H2 Blocker's)

Famotidine 10-20 mg twice daily	$
Ranitidine 75-150 mg twice daily	$ - $
Nizatidine 75-150 mg twice daily	$$-$$$$
Cimetidine 200-400 mg twice daily	$-$$

Proton Pump Inhibitors (PPI's)

Omeprazole 20-40 mg capsules once daily	$ - $
Omeprazole/ Sod. Bicarbonate 20-1100 mg capsules	$
Lansoprazole 15-30 mg capsules once daily	$$
Esomeprazole 20-40 mg capsules once daily	$
Pantoprazole 20-40 mg tablets once daily	$
(*) Dexlansoprazole 30-60 mg capsules once daily	$$$$
(*) Rabeprazole 20 mg tablets once daily	$$$$

*** Only available with a prescription**

Common Initial Oral Dose Cost Estimates

**Please note these are estimates without prescription coverage. When determining costs, please keep in mind if the patient has insurance and the patient's insurance.*

$= least expensive under $30/30 day supply
$= under$100/30 day supply
$$= under $150/30 day supply
$$$= under$250/30 day supply
$$$$= $300 and above 30/ day supply

Social Determinants of Health Assessment

In order to engage and empower patients to be active in their care, it is also necessary to assess Social Determinants of Health (SDOH). Patients can be unwillingly impacted by SDOH, which will affect a patient's capacity to adhere to his/her treatment plan. Keep this in mind and assess accordingly, to provide proper referrals to encircle the patient with support to achieve his/her optimal health.

Consider the following:

- Financial restrictions can impact a family's ability to afford nutritious foods and medications.
- Geography can impact accessibility of healthy and affordable food.
- The patient's own understanding and perceptions.
- Capacity to exercise as well as physical and behavioral limitations that may require referrals to physical therapy or exercise support.
- Patient may have behavioral and/or psychological barriers that may be influencing and perpetuating lifestyle habits.
- Health literacy and comprehension.

Resources

- Greater Cleveland Foodbank
- United Way
- UH Smoking Cessation
- ChooseMyPlate
- EatRight

Medications & GERD

Patients should be counseled and provided anticipatory guidance related to treatment efficacy and potential side effects. Please note this is not meant to be an extensive list. Consider patient-specific drug interactions and patient-specific needs.

For a comprehensive list of side effects refer to your drug reference guide. For more detailed information refer to Appendix A-C.

Dose and timing of administration — PPIs should be administered 30 to 60 minutes before breakfast for maximal inhibition of proton pumps. If administering twice daily, first dose should be administered before breakfast and the second dose before dinner. PPI's should not be crushed or altered (Katz 2013, and Hershcovici 2010).

The intact granules should not be chewed or crushed; however, several options are available for those patients unable to swallow capsules. For alternate oral administration, view the administration tab for the specified drug monograph in Lexi-Drugs.

Discontinuing PPIs — PPIs should be prescribed at the lowest dose and for the shortest duration appropriate to the condition being treated. Some experts recommend a step-down approach in order to avoid worsening or rebound symptoms. One strategy is to decrease the dose by 50% over 2 to 4 weeks. If the patient is already on the lowest possible dose, alternate-day therapy may be considered. If symptoms worsen during treatment or after discontinuation, patient should be re-evaluated (Kim 2018).

H2 blockers— H2 blockers are more effective with PRN dosing due to diminished response with long-term consecutive use.

- **Famotidine: 20mg once or twice daily OR 40mg daily (maximum 40mg/day)**
- **Ranitidine: 75mg or 150mg once or twice daily (maximum 300mg/day)**

References

Chen, Y. (2015). Gastroesophageal reflux disease and non-digestive tract diseases. Expert Review of Gastroenterology & Hepatology. 9:5, (685-692). DOI: https://doi.org/10.1586/17474124.2015.1012495.

Fredberg, D. E., Kim, L.S. & Yang, Y. (2017) The Risks and benefits of long-term use of proton pump inhibitors: Expert review and best practice advice from the American Gastronterological Association. Gastrroenterology 152:706-715.

Hershcovici T, Fass R. An algorithm for diagnosis and treatment of refractory GERD. *Best Pract Res Clin Gastroenterol*. 2010;24 (6):923-936.[PubMed 21126704]

Katz, P.O, Gerson, L.B., Vela, M.F. (2013) Guidelines for the diagnosis and management of gastroesophageal reflux disease. American Journal Gastroenterology 108:308-328. DOI: 10.1038/ajg.2012.444.

Kahrilas, P.J., Talley, N.J. , Grover, S. (2018). Clinical manifestations and diagnosis of gastroesophageal reflux in adults. UpToDate. Retrieved from: https://www.uptodate.com/contents/clinical-manifestations-and-diagnosis-of-gastroesophageal-reflux-in-adults?search=Incidence%20GERD&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1.

Kim J, Blackett JW, & Jodorkovsky D. (2018) Strategies for effective discontinuation of proton pump inhibitors. *Curr Gastroenterol Rep*. 2018;20(6):27. doi: 10.1007/s11894-018-0632-y.

National Institute of Diabetes and Digestive and Kidney Diseases. (2014). Definition & facts for GER & GERD. Retrieved from: https://www.niddk.nih.gov/health-information/digestive-diseases/acid-reflux-ger-gerd-adults/definition-facts.

Roman, S. , Gyawali C.P, Savarino, E. Yadlapati, R., Zerbib, F., Wu, J., Vela, M., Tutuian, R., Tatum, R., Sifrim, D., Keller, J., Fox, M., Pandolfino, J.E., Bredenoord, A.J., the GERD consensus Group. (2016). Ambulatory reflux monitoring for diagnosis of gas-troesophageal reflux disease: Update of the porto consensus and recommendations from an international consensus group. Neurogastroenterology & Motility. 2017. 29e13067. DOI: https://doi.org/10.1111/nmo.13067.

UpToDate. (2018). Treatment of erosive or nonerosive gastroesophageal reflux disease. Retrieved from: https://www.uptodate.com/contents/image?imageKey=GAST%2F89545&topicKey=GAST%2F2258&search=treatment%20of%20erosive%20or%20nonrosive%20gastoesophageal&rank=3~150&source=see_link

World Gastroenterology Organization Global Guidelines. (2015). GERD: Global perspective on gastroesophageal reflux disease. Retrieved from: http://www.worldgastroenterology.org/guidelines/global-guidelines/gastroesophageal-reflux-disease/gastroesophageal-reflux-disease-english.

Special thanks to the CPG Development Team: Brad Hillard, DO, MBA, John Dumot, DO, Leena Khaitan, MD, MPH, Dany Raad, MD, Katarina Greer, MD, Jeffrey Marks, MD, Amitabh Chak, MD, Todd Zeiger, MD, George Topalsky, MD, Deanna Cox, MSN, RN, Tammy Brand, PharmD, RPh, Victoria McCrimmon, MSN, RN-BC, CCM, Lisa Haddix, BSN, RN, CCM, Theresa Widenhofer, ADN, RN-BC .

Appendix A: Medications

Comparison of Drug Interactions with Proton Pump Inhibitors

(*As shown in* UpToDate, 2018)

Concomitant drug	Omeprazole	Lansoprazole	Rabeprazole	Pantoprazole	Esomeprazole
Warfarin	PT decreased by 10 percent	-	-	-	-
Diazepam	T1/2 increased by 130 percent	-	-	-	Decreased clearance
Phenytoin	T1/2 increased by 27 percent	-	-	-	-
Theophylline	-	AUC increased by 10 percent	-	-	Unknown
Digoxin	AUC increased by 10 percent	-	AUC, Cmax, T1/2 increased	-	Unknown
Carbamazepine	AUC increased by 75 percent	-	-	-	Unknown

PT: prothrombin time; Cmax: maximum plasma concentration; AUC: area under the curve.

Adapted from: Gugler R, Jensen JC, Gastroenterology 1985; 89:1235; Diaz D, Fabre I, Daujat M, et al, Gastroenterology 1990; 99:737; Meyer UA, Eur J Gastroenterol Hepatol 1996; 8(Suppl 1):S21; Parsons ME, Eur J Gastroenterol Hepatol 1996; 8(Suppl 1):S15; Lew EA, Aliment Pharmacol Ther 1999; 13(Suppl 5):11; Lorf T, et al, Eur J Clin Pharmacol 2000; 55:733.

Graphic 53616 Version 3.0

UpToDate. (2018). Comparison of drug interactions with proton pump inhibitors.
Retrievedfrom:https://www.uptodate.com/contents/image?imageKey=GAST%2F53616&topicKey=GAST%2F5&source=outline_link.

Drug interactions with PPI's

Metabolism via hepatic cytochrome P450 may lead to specific drug interactions in some individuals. The potential of interactions varies considerably. Some important drug interactions with PPI's include: Clopidogrel, HIV protease inhibitors (Rilpivirine and Atazanavir) and methotrexate. (Kim, Jodorkovsky, & Blackett, 2018).

Appendix B: "Best Practice" (As Shown in AGA Clinical Practice Updates)

Best Practice Recommendations

Best Practice Advice 1: Patients with GERD and acid-related complications (i.e., erosive esophagitis or peptic stricture) should take a PPI for short-term healing and for long-term symptom control.

Rationale: PPIs are highly effective in healing esophagitis and for GERD symptom control, and this benefit is likely to outweigh PPI-related risks. There is no evidence for or against PPIs in asymptomatic patients with healed esophagitis or for PPIs beyond 12 months.

Best Practice Advice 2: Patients with uncomplicated GERD who respond to short-term PPIs should subsequently attempt to stop or reduce them. Patients who cannot reduce PPIs should consider ambulatory esophageal pH/impedance monitoring before committing to lifelong PPIs to help distinguish GERD from a functional syndrome. The best candidates for this strategy may be patients with predominantly atypical symptoms or those who lack an obvious predisposition to GERD (eg, central obesity, large hiatal hernia).

Rationale: Short-term PPIs are highly effective for uncomplicated GERD. Most patients with uncomplicated GERD respond to short-term PPIs and are subsequently able to reduce PPIs to less than daily dosing. Because patients who cannot reduce PPIs face lifelong therapy, we would consider testing for an acid-related disorder in this situation. However, there is no high-quality evidence on which to base this recommendation.

Best Practice Advice 3: Patients with Barrett's esophagus and symptomatic GERD should take a long-term PPI.

Rationale: PPIs have a clear symptomatic benefit and a possible benefit in slowing progression of Barrett's. There is likely to be a net benefit for long-term PPIs in these patients.

Best Practice Advice 4: Asymptomatic patients with Barrett's esophagus should consider a long-term PPI.

Rationale: The evidence that PPIs slow progression of Barrett's is low in quality but the evidence of PPI adverse effects is also low in quality. Because there is no high quality evidence on either side of this question, this is a weak recommendation and this decision should be individualized with patients.

Best Practice Advice 5: Patients at high risk for ulcer-related bleeding from NSAIDs should take a PPI if they continue to take NSAIDs.

Rationale: PPIs are highly effective in preventing ulcer-related bleeding in appropriately selected patients who take NSAIDs, and this benefit is likely to outweigh PPI-related risks.

Best Practice Advice 6: The dose of long-term PPIs should be periodically reevaluated so that the lowest effective PPI dose can be prescribed to manage the condition.

Rationale: Long-term PPI users often receive PPIs at doses higher than necessary to manage their condition. Since PPI reduction is often successful, it is logical to periodically reevaluate PPI dosing so that the minimum necessary dose is prescribed.

Best Practice Advice 7: Long-term PPI users should not routinely use probiotics to prevent infection.

Rationale: There is no evidence for or against probiotics to prevent infections in long-term users of PPIs.

Best Practice Advice 8: Long-term PPI users should not routinely raise their intake of calcium, vitamin B12 or magnesium beyond the Recommended Dietary Allowance (RDA).

Rationale: There is no evidence for or against use of vitamins or supplements beyond the RDA in long-term users of PPIs. Many adults fall below the RDA in several vitamins or minerals and, in these adults, it is reasonable to raise intake to meet the RDA regardless of PPI use.

Best Practice Advice 9: Long-term PPI users should not routinely screen or monitor bone mineral density, serum creatinine, magnesium, or vitamin B12.

Rationale: There is no evidence for or against dedicated testing for patients taking long-term PPIs. Such screening (eg, for iron or vitamin B12 deficiency) can be offered but is of no proven benefit.

Best Practice Advice 10: Specific PPI formulations should not be selected based on potential risks.

Rationale: There is no convincing evidence to rank PPI formulations by risk.

(Freedberg, Kim, & Yang, 2017)

Summary Notes

from Appendix B: "Best Practice" (Freedberg, Kim & Yang 2007).* For any *questions or concerns related to PPIs or please follow-up with your pharmacist or contact a GI Specialists

If clinically indicated, consider PPIs for the following patients:

- *Patients with GERD and acid complications*
  - *For uncomplicated GERD that are responsive to short term PPI use– attempt to reduce/stop PPI use. If unable to wean dosing refer to GI for follow-up testing and evaluation.*
- *Patients with Barrett's esophagus (asymptomatic and symptomatic)*
- *Patients with a high risk for ulcer bleeds second to NSAIDs*

Long Term PPI Use

- *Dosages should be re-evaluated to reduce dosing to the lowest effective possible dose*
- *Should NOT routinely use probiotics*
- *Should NOT raise their intake of calcium, vitamin B12 or magnesium beyond the Recommended Daily Allowance*

Appendix C: "Summary of Evidence for Potential PPI– Associated Adverse Effects

(As Shown in: AGA Clinical Practice Updates)

Table 1. Summary of Evidence for Potential PPI-Associated Adverse Effects

Potential adverse effect	Types of studies	Threats to validity	Overall quality of evidence
Kidney disease	• Observational only	• Modest effect size • Residual confounding would bias towards harm • Absence of dose-response effect	Very low
Dementia	• Observational only	• Modest effect size • Residual confounding would bias towards harm	Very low
Bone fracture	• Observational only	• Inconsistent results • Modest effect size • Residual confounding would bias towards harm	Low or very low
Myocardial infarction	• Observational • RCT	• Results differ between RCTs and observational studies • Secondary analysis of RCT data • Modest effect size • Residual confounding would bias towards harm	Very low
Small intestinal bacterial overgrowth	• Observational • Crossover	• Sparse data • Residual confounding would bias towards harm • Protopathic bias	Low
Spontaneous bacterial peritonitis	• Observational only	• Modest effect size • Residual confounding would bias towards harm	Very low
Clostridium difficile infection	• Observational only	• Modest effect size • Residual confounding would bias towards harm	Low
Pneumonia	• Observational • RCT	• Results differ between RCTs and observational studies • Secondary analysis of RCT data • Modest effect size • Absence of dose-response effect • Residual confounding would bias towards harm • Protopathic bias	Very low
Micronutrient deficiencies	• Observational only	• Inconsistent results • Modest effect size • Absence of dose-response effect • Residual confounding would bias towards harm	Low or very low
Gastrointestinal malignancies	• Observational • RCT	• Results differ between RCTs and observational studies • RCTs use surrogate outcomes • Modest effect size • Residual confounding would bias towards harm • Confounding by indication and protopathic bias	Very low

NOTE. Assessments regarding the quality of evidence are based on the methodology of the GRADE Working Group (see inset).[77]

(Freedberg, Kim, & Yang, 2017)