ACG/CAG guideline on Management of Dyspepsia

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By: Reza Gholami

DEFINITION OF DYSPEPSIA AND SCOPE OF THE GUIDELINE

Dyspepsia was originally defined as any symptoms referable to the upper gastrointestinal tract.

The Rome committee has developed iterative definitions of dyspepsia that have become more specific culminating in Rome IV

- These definitions have attempted to minimize the inclusion of gastro-esophageal reflux disease in those with dyspepsia by excluding patients with heartburn and acid regurgitation

- Rome definitions have been helpful in better-standardizing patients that are included in studies of dyspepsia but are less relevant to clinical practice as there is considerable overlap in symptom presentation

- We have used a clinically relevant definition of dyspepsia as predominant epigastric pain lasting at least 1 month.

- This can be associated with any other upper gastrointestinal symptom such as epigastric fullness, nausea, vomiting, or heartburn, provided epigastric pain is the patient’s primary concern.

- Functional dyspepsia refers to patients with dyspepsia where endoscopy (and other tests where relevant) has ruled out organic pathology that explains the patient’s symptoms.

- This guideline will focus on initial investigations for dyspepsia such as Helicobacter pylori (H. pylori) testing and endoscopy as well as pharmacological therapies such as H. pylori treatment, PPIs, and prokinetic therapy.

- The group was chosen to represent a US and Canadian secondary and tertiary care perspective on managing dyspepsia with experience in guideline methodology, motility, endoscopy, and pharmacological therapies.

- STATEMENT 1. WE SUGGEST DYSPEPSIA PATIENTS AGED 60 OR OVER HAVE AN ENDOSCOPY TO EXCLUDE UPPER GASTROINTESTINAL NEOPLASIA

Gastric cancer is the third commonest cause of cancer mortality worldwide with nearly a million cases annually and often presents with dyspepsia.

- The risk of malignancy is predominantly related to age and so previous ACG guidelines have suggested that routine endoscopy to investigate dyspepsia should only be performed in patients' aged 55 and over.

- We have raised this threshold further to >60 years of age as evidence that endoscopy was cost-effective at the 55-year-old threshold at that time was borderline in economic analyses.

- STATEMENT 2. WE DO NOT SUGGEST ENDOSCOPY TO INVESTIGATE ALARM FEATURES FOR DYSPEPSIA PATIENTS UNDER THE AGE OF 60 TO EXCLUDE UPPER GI NEOPLASIA

- Previous guidelines have typically recommended upper GI endoscopy at any age when alarm features (e.g., weight loss, anemia, dysphagia, persistent vomiting) are present

- However, a systematic review of seven studies evaluating over 46,000 dyspepsia patients undergoing upper GI endoscopy found that alarm features had limited value

- Alarm features also had limited utility in detecting any organic pathology (malignancy, peptic ulcer disease, or esophagitis)

- Individual alarm features such as weight loss, anemia, or dysphagia had sensitivities and specificities of ~66% with a positive likelihood ratio of 2.74 (95% CI=1.47-5.24)

- This means that if a dyspepsia patient has an alarm feature they have a 2-3-fold risk of having underlying upper GI malignancy.

- However, the risk of a person<60 years old having malignancy is typically very low so, even with an alarm feature, the risk is still much <1% and it is very unlikely that endoscopy of all young patients with alarm features would be cost-effective.

- Data published since this systematic review have been administrative database studies that have confirmed that alarm features have a low positive predictive value and so are of limited value in stratifying patients for endoscopy

- The recommendation is conditional as the group felt that a minority of patients <60 years of age with alarm features would warrant endoscopy, particularly if the feature was prominent (e.g., weight loss >20 lb or rapidly progressive dysphagia) or if a combination of features were present.

Risk also increases with age so the threshold to refer for upper GI endoscopy would be lower in a 58-year-old compared to a 28-year-old with dyspepsia and alarm features.

- Family history of upper GI malignancy would also factor into any endoscopy decision.

- STATEMENT 3. WE RECOMMEND DYSPEPSIA PATIENTS UNDER THE AGE OF 60 SHOULD HAVE A NON-INVASIVE TEST FOR H. PYLORI, AND THERAPY FOR H. PYLORI INFECTION IF POSITIVE

- A previous guideline suggested that PPI therapy might be the appropriate first line approach when H. pylori prevalence rates are <15% in the population being tested.

- We felt that it is often difficult to know what the H. pylori prevalence is in the local population

- STATEMENT 4. WE RECOMMEND DYSPEPSIA PATIENTS UNDER THE AGE OF 60 SHOULD HAVE EMPIRICAL PPI THERAPY IF THEY ARE H. PYLORI -NEGATIVE OR WHO REMAIN SYMPTOMATIC AFTER H. PYLORI ERADICATION THERAPY

- It should also be noted that the PPI trials used once-daily standard dosing. It is unlikely that higher doses of PPI will increase benefit in dyspepsia.

- STATEMENT 5. WE SUGGEST DYSPEPSIA PATIENTS UNDER THE AGE OF 60 NOT RESPONDING TO PPI OR H. PYLORI ERADICATION THERAPY SHOULD BE OFFERED PROKINETIC THERAPY

- We felt that prokinetic therapy should be offered after H. pylori test and treat and/ or PPI therapy has failed as PPI therapy is more effective in gastroesophageal reflux disease and peptic ulcer disease and has greater efficacy in FD using indirect comparisons of randomized data

- STATEMENT 6. WE SUGGEST DYSPEPSIA PATIENTS UNDER THE AGE OF 60 NOT RESPONDING TO PPI OR H. PYLORI ERADICATION THERAPY SHOULD BE OFFERED TRICYCLIC ANTIDEPRESSANT THERAPY

- The recommendation is conditional based on the low quality of evidence, the adverse events associated with TCAs and considerations that some patients will not like the perceived stigma of taking an antidepressant.

- The decision to use TCAs will therefore be made on a case-by-case basis and the group did not find a preference in the order in which prokinetic or TCA therapy is prescribed.

- STATEMENT 7. WE RECOMMEND FUNCTIONAL DYSPEPSIA PATIENTS THAT ARE H. PYLORI POSITIVE SHOULD BE PRESCRIBED THERAPY TO TREAT THE INFECTION

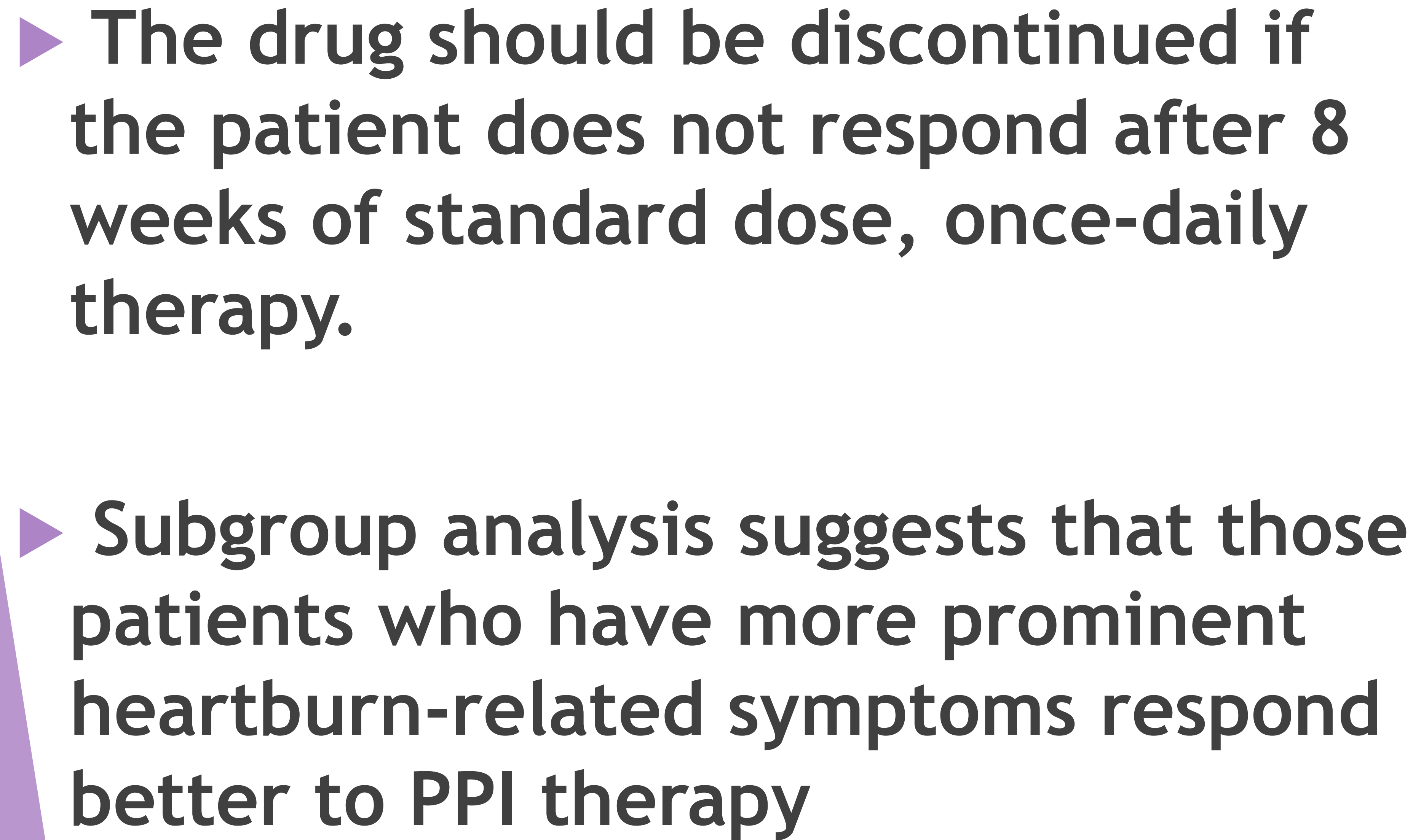
- Patients who have an endoscopy with normal findings and predominant epigastric pain are considered to have FD.

- A positive diagnosis of FD can also be made without endoscopy using clinical symptoms and history

- Patients with a normal endoscopy should have gastric biopsies to assess for the presence of H. pylori infection if prior non-invasive testing has not been performed.

- Although the impact on dyspepsia symptoms is modest, H. pylori eradication may also reduce future risk of gastric cancer and peptic ulcer disease and the benefits of this approach clearly outweigh the harms of antibiotic prescribing.

- STATEMENT 8. WE RECOMMEND FUNCTIONAL DYSPEPSIA PATIENTS WHO ARE H. PYLORI NEGATIVE OR WHO REMAIN SYMPTOMATIC DESPITE ERADICATION OF THE INFECTION SHOULD BE TREATED WITH PPI THERAPY


The drug should be discontinued if the patient does not respond after 8 weeks of standard dose, once-daily therapy.
Subgroup analysis suggests that those patients who have more prominent heartburn-related symptoms respond better to PPI therapy

- Antidepressant therapies have been shown in randomized trials to reduce symptoms in irritable bowel syndrome.

- There is a large overlap between irritable bowel syndrome and FD

- STATEMENT 10. WE SUGGEST FUNCTIONAL DYSPEPSIA PATIENTS NOT RESPONDING TO PPI, H. PYLORI ERADICATION THERAPY OR TRICYCLIC ANTIDEPRESSANT THERAPY SHOULD BE OFFERED PROKINETIC THERAPY

- Patients with FD often have disorders of gastric motility and many pharmacological agents have been developed to improve gastric emptying

- The quality of evidence was graded as very low as all of the domperidone data had unclear or high risk of bias and none met eligibility criteria

- STATEMENT 11. WE SUGGEST FUNCTIONAL DYSPEPSIA PATIENTS NOT RESPONDING TO DRUG THERAPY SHOULD BE OFFERED PSYCHOLOGICAL THERAPIES

- STATEMENT 12. WE DO NOT RECOMMEND THE ROUTINE USE OF COMPLEMENTARY AND ALTERNATIVE MEDICINES FOR FUNCTIONAL DYSPEPSIA

- **Complementary and alternative medicines (CAM) are used by about 20% of the general population for gastrointestinal symptoms**

- STATEMENT 13. WE RECOMMEND AGAINST ROUTINE MOTILITY STUDIES FOR PATIENTS WITH FUNCTIONAL DYSPEPSIA

- Delayed gastric emptying, using either scintigraphic tests or breath tests, has been identified in up to 30% of patients with FD, although the extent of this delay is usually mild

- Unfortunately, however, identifying the abnormal pathophysiologic mechanisms that underlie the development of FD symptoms has not directly altered treatment strategies.

- STATEMENT 14. WE SUGGEST MOTILITY STUDIES FOR SELECTED PATIENTS WITH FUNCTIONAL DYSPEPSIA WHERE GASTROPARESIS IS STRONGLY SUSPECTED

- Gastroparesis can be diagnosed using a combination of symptoms (e.g., nausea, vomiting, abdominal pain, early satiety, bloating), an upper endoscopy not showing evidence of mechanical obstruction

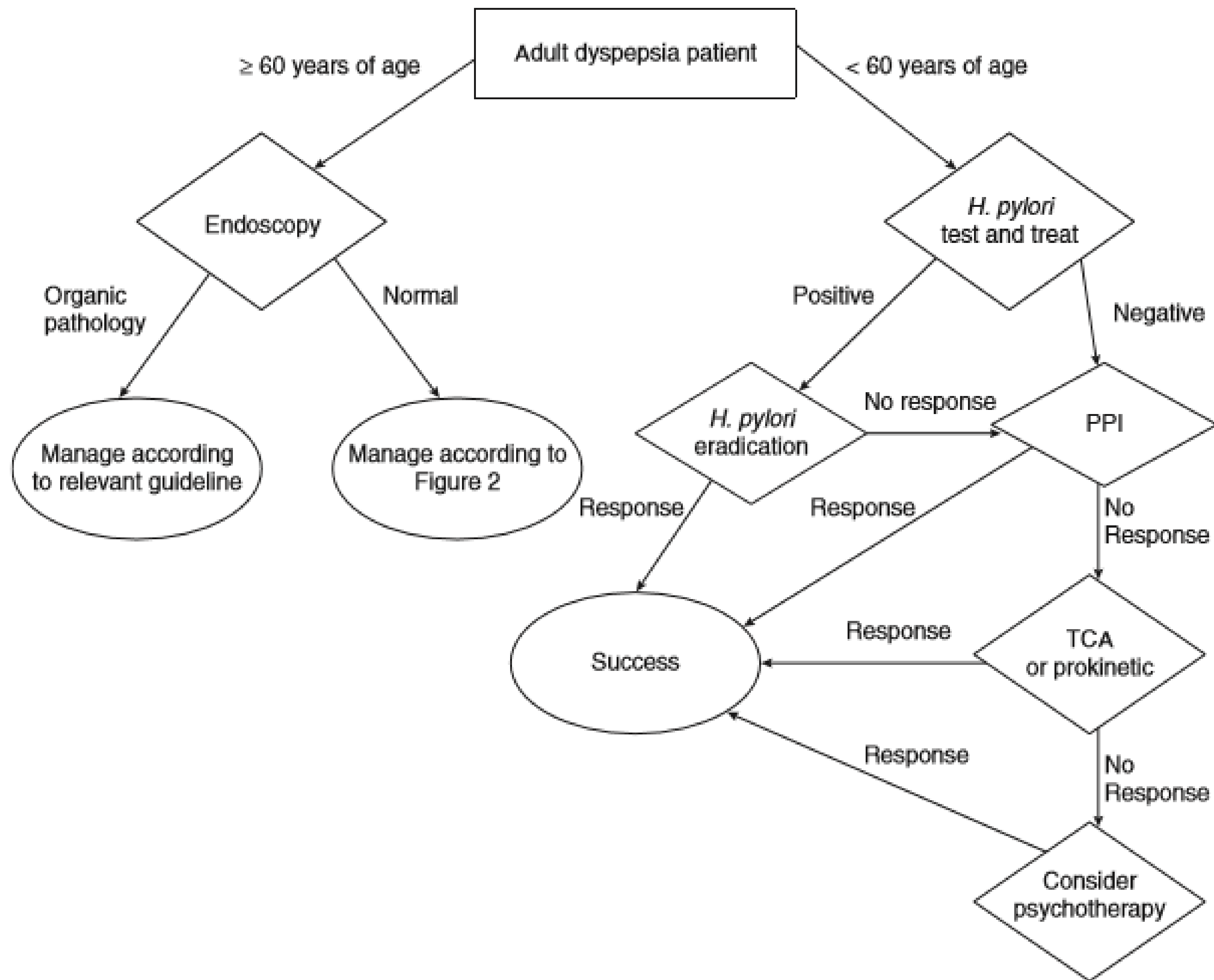


Figure 1. Algorithm for the management of undiagnosed dyspepsia.

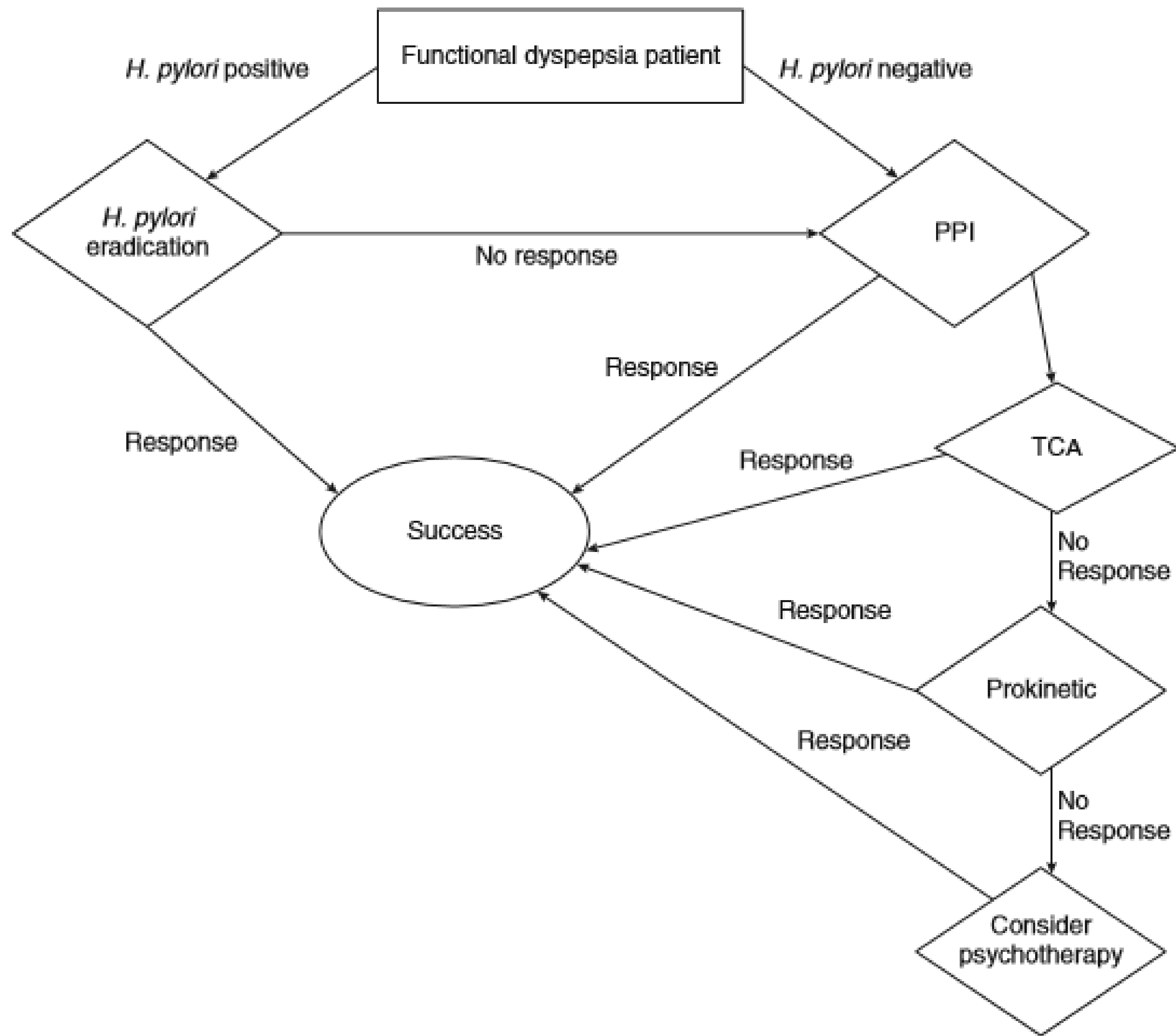


Figure 2. Algorithm for the treatment of functional dyspepsia.

Thank you

Any comment?