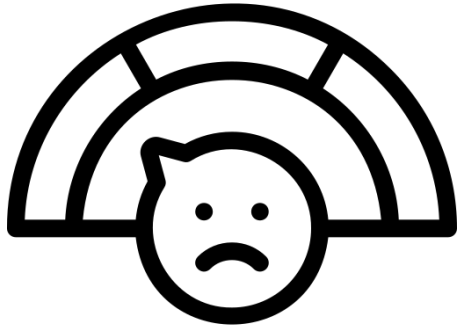
Approach to Dyspepsia, Uninvestigated and Functional Dyspepsia

Dr Gillian Gaskin
Facilitator: Dr N Seabi
11 March 2024

Dyspepsia: Scope of the problem

Globally ~20% of the population have symptoms of dyspepsia



Normal life expectancy but poor quality of life

High cost to patient, health budgets and society US health care service over $18 billion per annum

Need for cost effective management strategies

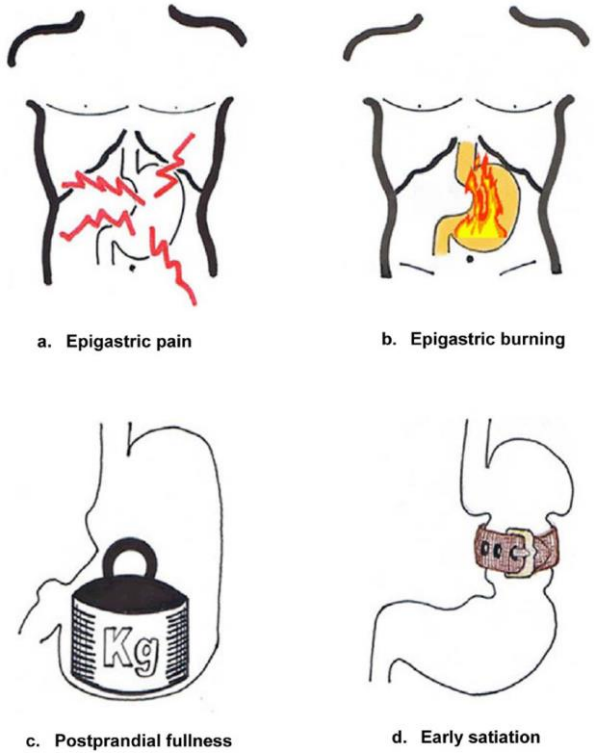
Black CJ, et al. Gut 2022;71:1697–1723

Definition

Dyspepsia:

An umbrella term to describe digestive symptoms that are localized to the epigastrium

- Cardinal symptoms
  - Epigastric pain
  - Epigastric burning
  - Postprandial fullness
  - Early satiety



- Associated symptoms:
  - Belching and nausea
  - Upper abdominal bloating
  - Heartburn

Black CJ et al. Therapeutic Advances in Gastroenterology. 2018;11.

Aetiology

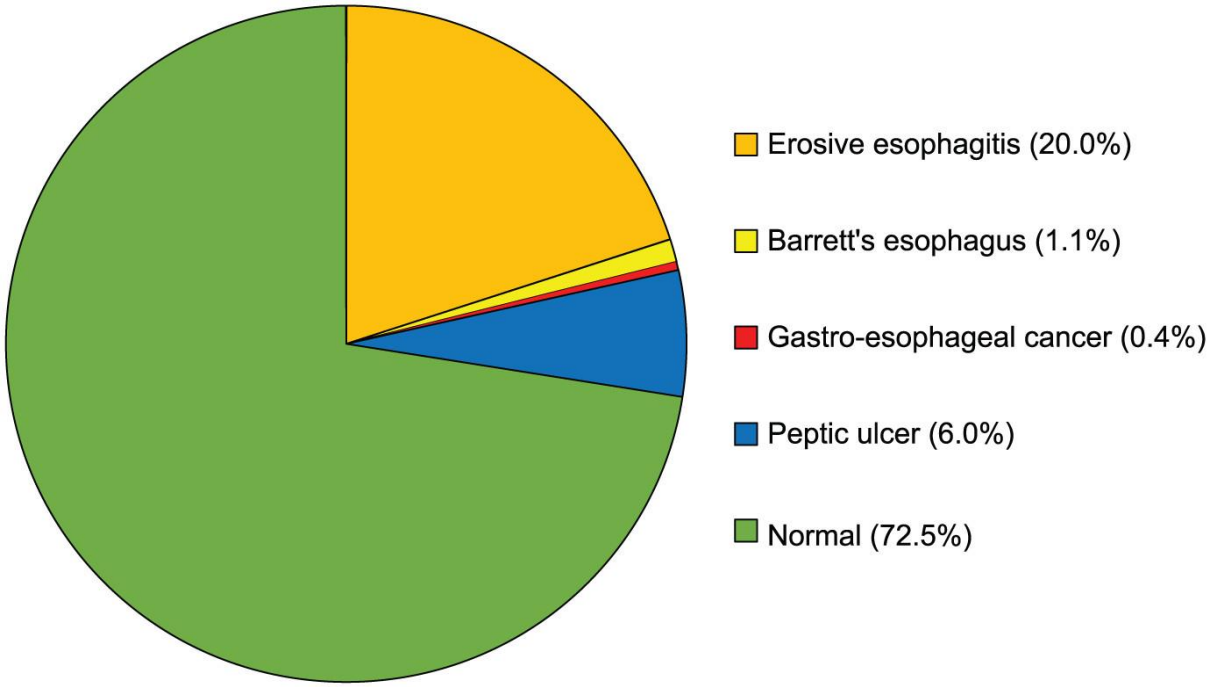
BOX 14.1 Organic Causes of Dyspepsia

LUMINAL GI TRACT
Chronic gastric volvulus
Chronic gastric or intestinal ischemia
Food intolerance
Gastric infections (CMV, fungus, tuberculosis, syphilis)
Gastric or esophageal neoplasms
Gastroesophageal reflux
Gastroparesis (diabetes mellitus, postvagotomy, scleroderma, chronic intestinal pseudo-obstruction, postviral, idiopathic)
IBS
Infiltrative gastric disorders (Ménétrier disease, Crohn disease, eosinophilic gastroenteritis, sarcoidosis, amyloidosis)
Parasites (*Giardia lamblia, Strongyloides stercoralisrom*)
PUD

MEDICATIONS

PANCREATICOBILIARY DISORDERS
Biliary pain: cholelithiasis, choledocholithiasis, SOD
Chronic pancreatitis
Pancreatic neoplasms

SYSTEMIC CONDITIONS
Adrenal insufficiency
Diabetes mellitus
Heart failure
Hyperparathyroidism
Intra-abdominal malignancy
Myocardial ischemia
Pregnancy
Renal insufficiency
Thyroid disease



Functional Dyspepsia (FD):
Typical symptoms without structural or metabolic pathology identified

Ford AC et al. Clin Gastroenterol Hepatol 2010; 8: 830–837
Sleisenger and Fordtran's. Gastrointestinal and Liver Disease. 11th Edition

Uninvestigated Dyspepsia(UD)

- 40% of people with dyspepsia will consult a primary physician
- Physician role to decide how to best to manage the individual patient

- Going into the process:
  - Language and cultural factors often “muddy the waters”
  - Do your best to understand and quantify what the patient is trying to convey
  - Avoid unconscious physician bias to steer the diagnosis

- Coming out of the process:
  - Be prepared to give a label of functional dyspepsia
  - Tendency to mislabel patients as ‘GERD’: greater physician comfort and optimism

Koduru P. et al. Clinical Gastroenterology and Hepatology 2018;16:467–479

Focused History and Examination

- Symptom onset and duration
- Alarm symptoms
- Upper/Lower GI symptoms
- Preceding infections
- Food sensitivities
- Overlapping symptoms (DBGI)
- Family hx of GI cancers, IBD, celiac disease
- Medication- NSAIDs/Opiods

TABLE 2. Alarm features for dyspeptic patients

Age ≥50 years **
Family history of upper GI malignancy in a first-degree relative
Unintended weight loss
GI bleeding or iron deficiency anemia
Dysphagia
Odynophagia
Persistent vomiting
Abnormal imaging suggesting organic disease

** differing age cut offs in various guidelines

Sleisenger and Fordtran's. Gastrointestinal and Liver Disease. 11th Edition
Shaukat A et al, GIE.2015. 82:2

Laboratory Testing

- Cost-effective routine lab testing has not been established

Suggested routine	Selected cases
• Full blood count • Serum electrolytes • Liver biochemical tests • Thyroid function tests	• Serum amylase • Celiac antibodies • Stool testing for ova and parasites/Giardia antigen • Pregnancy test

Sleisenger and Fordtran's. Gastrointestinal and Liver Disease. 11th Edition

Indications for Endoscopy

British Guidelines (2022) Black CJ, et al. Gut 2022;71:1697–1723

Urgent 2-week wait endoscopy	Non-urgent endoscopy
1. ≥55 years old with dyspepsia and weight loss 2. Age >40, from area with high gastric cancer rates or significant family history	1. ≥55 years old with treatment-resistant dyspepsia 2. ≥55 years old with dyspepsia, nausea, vomiting or a raised platelet count 3. Any patient with alarm symptoms

American Guidelines (2017) Moayyedi P et al. Am J Gastroenterol 2017; 112:988–1013

1. Any dyspepsia patient aged ≥60 to exclude upper gastrointestinal neoplasia
2. Lower age threshold if born or spent childhood in South East Asia/ South America or significant family history

South African Context

Age is a predictor of significant endoscopic findings in dyspepsia patients in South Africa

S Cheddie,[1] CG Manneh,[1] BM Owczarek,[1] Y Moodley[2]

[1] *Department of Surgery, Madadeni Hospital, University of KwaZulu-Natal, South Africa*
[2] *Faculty of Health and Environmental Sciences, Central University of Technology, South Africa*

- N- 584
- 432 (74%) <60ys
- 152 (26%) ≥ 60ys
- < 60ys- 6.7% significant findings
  ≥ 60ys – 17.1% significant findings
  (p-value < 0.001)
- ≥ 60ys OR (2.87) p < 0.00

- N-167 (>18 and <60ys)
- 40.7% (68/167) significant pathology
- 20.3% (34/167) normal gastroscopy
- 38.9% (65/167) benign pathology

World Journal of Surgery and Surgical Research

Research Article
Published: 08 Jul, 2023

The Cut-off Age for Gastroscopy in the Management of Dyspepsia Patients in a Tertiary Hospital in Central South Africa

Kayombo ET and Smit SJA*

Department of General Surgery, University of the Free State, South Africa

Dyspepsia: No Indication for Endoscopy What Next?

Prompt Endoscopy and Directed Treatment

"Test and Treat" Strategy for H Pylori

- or Test and scope

Empiric Anti-Secretory Drugs

Black CJ, et al. Gut 2022;71:1697–1723

Prompt Endoscopy and Directed Treatment

- Reassurance to patient and physician- reduce anxiety- reassuring effect is short lived
- May detect early gastric cancer at a curable stage- weak evidence
- **Expensive and invasive** and majority of structural diseases can be addressed empirically
- Approach not recommended in guidelines
- Rome IV diagnostic criteria for functional dyspepsia requires a negative endoscopy

Black CJ, et al. Gut 2022;71:1697–1723
Sleisenger and Fordtran's. Gastrointestinal and Liver Disease. 11th Edition

“Test and Treat” Strategy for H Pylori

- 5% of dyspepsia in the community is due to to H. pylori
- Non invasive testing- **stool antigen** or **urea breath test**
- “Test and treat” relevant and cost-effective when prevalence rates are 20% or higher (SA rates >70%)
- Confirming eradication- controversial
- “Test and scope” approach- Not more effective, not adopted in guidelines

Black CJ, et al. Gut 2022;71:1697–1723
Sleisenger and Fordtran’s. Gastrointestinal and Liver Disease. 11th Edition

Empiric Anti-Secretory Drugs

- Anti secretory drugs will be effective in the 20% of patients with dyspepsia who will have PUD or erosive oesophagitis
- PPI therapy is also efficacious in 1/3 of patients with FD
- Proton pump inhibitors (PPIs) are more effective than antacids and histamine receptor antagonists
- Disadvantage- relapse after discontinuation of therapy and potential rebound gastric hypersecretion

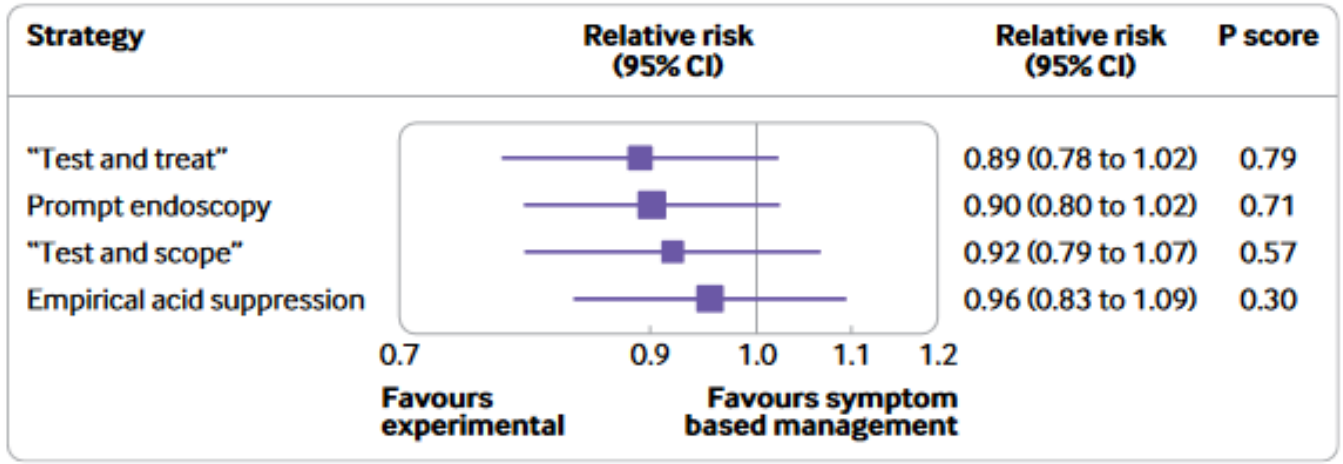
Black CJ, et al. Gut 2022;71:1697–1723
Sleisenger and Fordtran's. Gastrointestinal and Liver Disease. 11th Edition

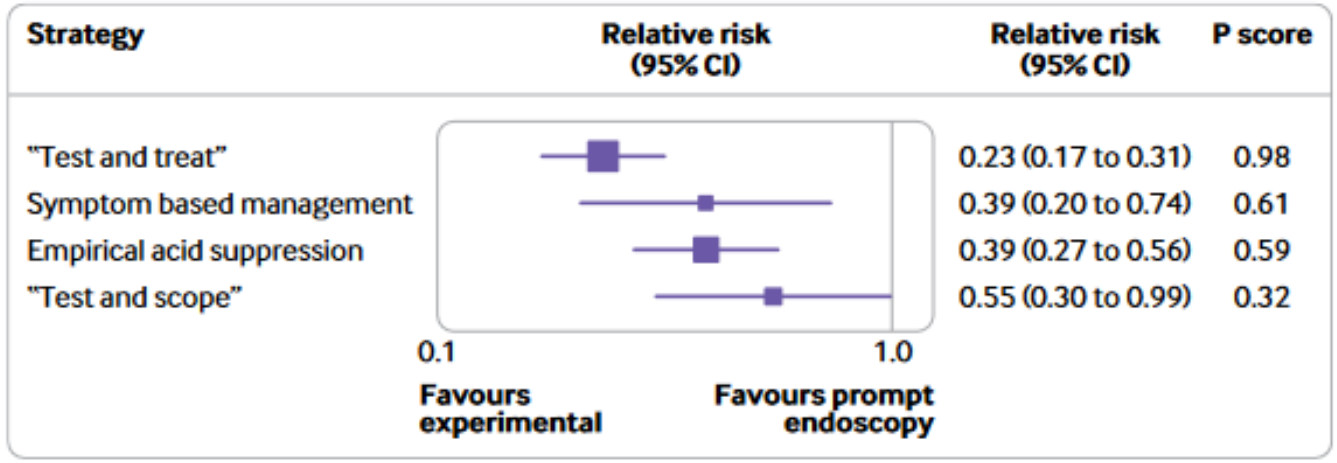
Effectiveness of management strategies for uninvestigated dyspepsia: systematic review and network meta-analysis

Leonardo H Eusebi,[1] Christopher J Black,[2,3] Colin W Howden,[4] Alexander C Ford[2,3]

British medical Journal. 2019;367:l6483

- 15 RCTs
- 6162 patients
- No strategy superior
- “Test and treat” was ranked first in reducing RR of symptoms at 12 months
- “Test and treat” were significantly less likely to require endoscopy



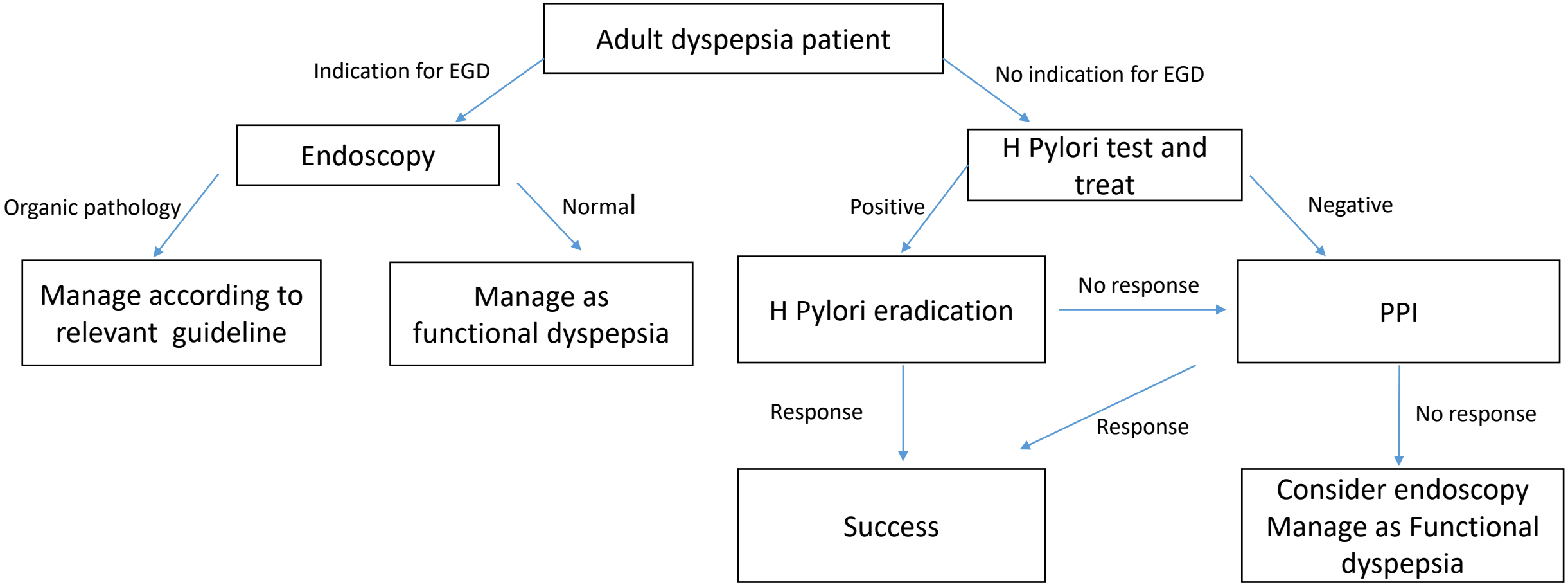


Refractory Symptoms

- Refractory symptoms
  - Upper endoscopy-GI malignancy
- Refractory symptoms and weight loss
  - Test for celiac disease and Giardia infection
- Severe postprandial fullness, refractory N&V
  - gastric emptying study, scintigraphy
  - Small bowel x-ray
- Refractory intermittent epigastric pain or burning
  - Oesophageal pH with impedance monitoring
- Long-standing refractory or debilitating symptoms
  - Psychological or psychiatric assessments
- Severe pain or weight loss
  - US/ CT/ EUS pancreaticobiliary disease

Sleisenger and Fordtran's. Gastrointestinal and Liver Disease. 11th Edition

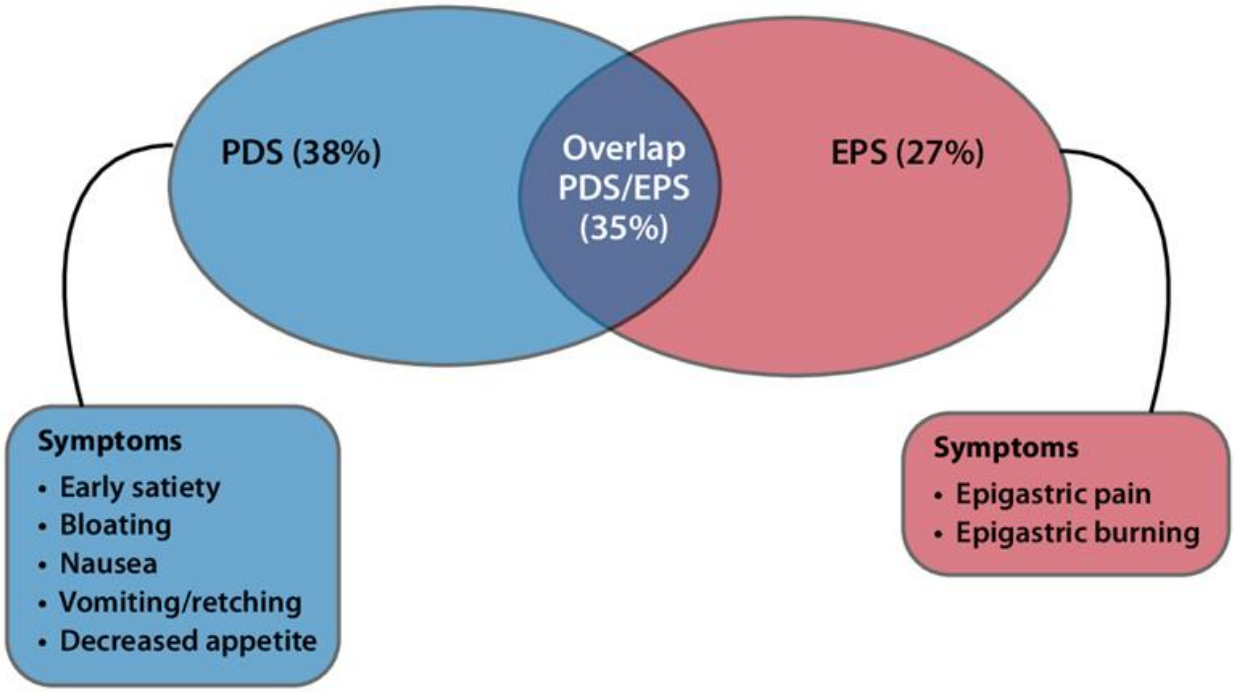
Algorithm Approach to Uninvestigated Dyspepsia



Functional Dyspepsia (FD)

- A disorder of gut-brain interaction (DGBI)

- FD is categorized into two subgroups based on symptoms:
  - Postprandial distress syndrome (PDS)
  - Epigastric pain syndrome (EPS)



Kimberly N et al. Gastroenterol Hepatol. 2020 Feb; 16 (2):66-74

Table 1 The Rome IV criteria for functional dyspepsia[3]

Diagnostic criteria for functional dyspepsia

One or more of the following:

- Bothersome epigastric pain.
- Bothersome epigastric burning.
- Bothersome postprandial fullness.
- Bothersome early satiation.
- Symptom onset at least 6 months prior to diagnosis.
- Symptoms should be active within the past 3 months.
- And, no evidence of structural disease (including at upper endoscopy) likely to explain the symptoms.

Diagnostic criteria for epigastric pain syndrome (EPS)

Must include *one* or *both* of the following symptoms at least 1 day a week.

1. Bothersome epigastric pain (ie, severe enough to impact on usual activities).
2. Bothersome epigastric burning (ie, severe enough to impact on usual activities).

Supportive criteria:

1. Pain may be induced by ingestion of a meal, relieved by ingestion of meal or may occur while fasting.
2. Postprandial epigastric bloating, belching and nausea can also be present.
3. Persistent vomiting likely suggests another disorder;.
4. Heartburn is not a dyspeptic symptom, but may often coexist.
5. The pain does not fulfil biliary pain criteria.
6. Symptoms that are relieved by evacuation of faeces or gas generally should not be considered as part of dyspepsia.
7. Other digestive symptoms (such as gastro-oesophageal reflux disease and irritable bowel syndrome) may coexist with the EPS.

Diagnostic criteria for postprandial distress syndrome (PDS)

Must include one or both of the following symptoms at least 3 days a week:

1. Bothersome postprandial fullness (ie, severe enough to impact on usual activities).
2. Bothersome early satiation (ie, severe enough to prevent finishing a regular sized meal).

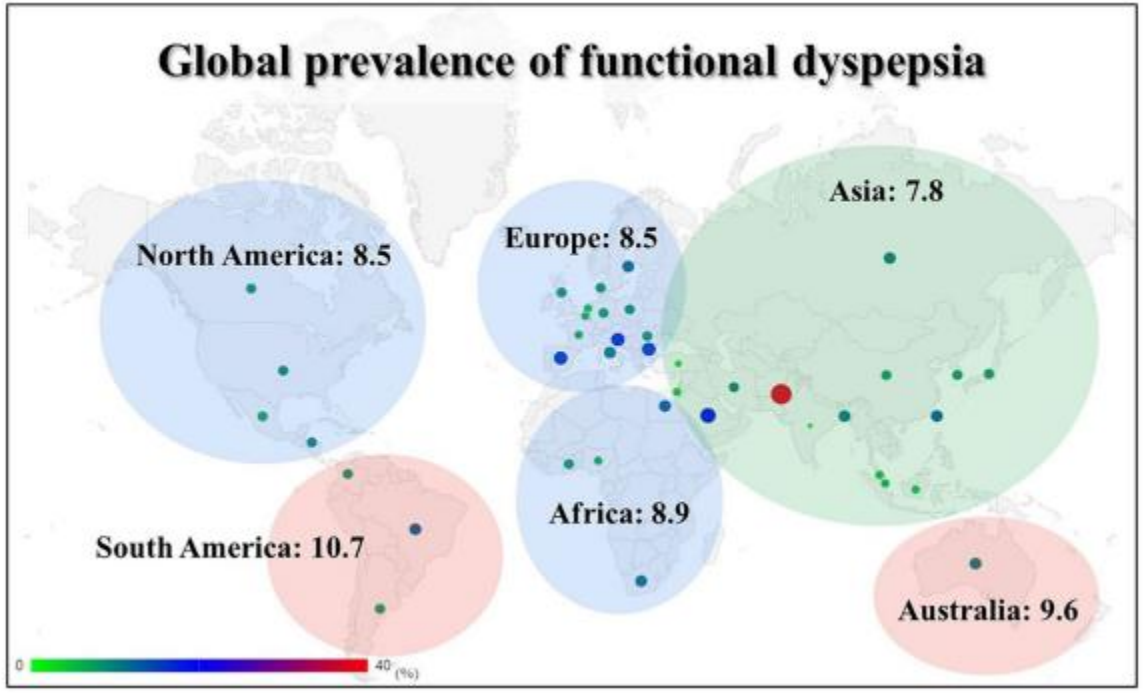
Supportive criteria:

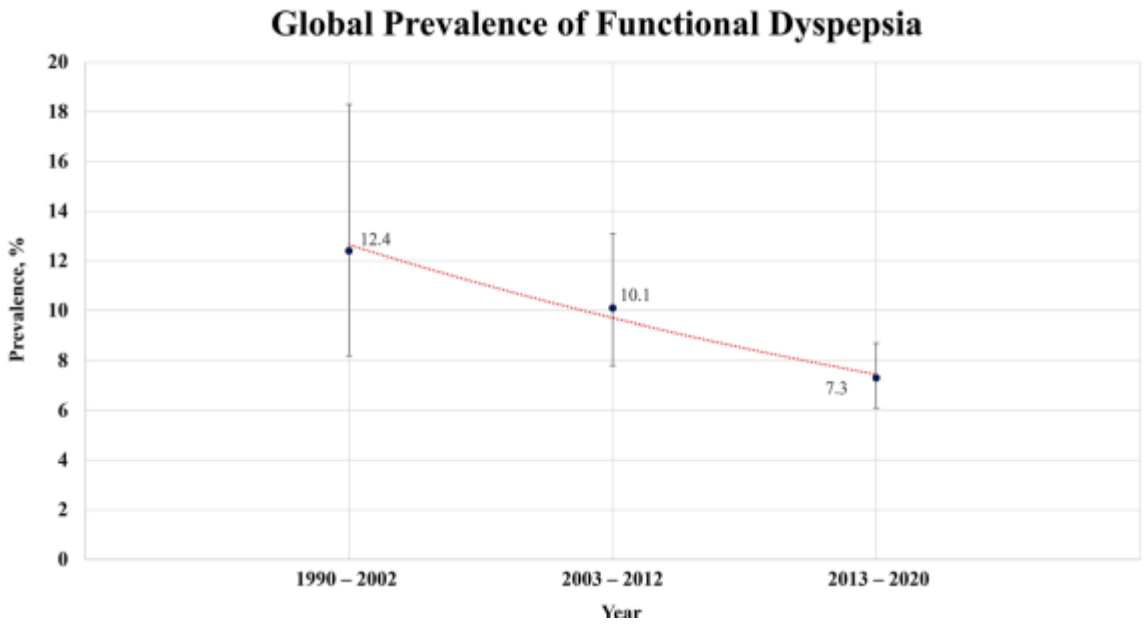
1. Postprandial epigastric pain or burning, epigastric bloating, excessive belching, and nausea can also be present.
2. Vomiting warrants consideration of another disorder.
3. Heartburn is not a dyspeptic symptom, but may often coexist.
4. Symptoms that are relieved by evacuation of faeces or gas should generally not be considered as part of dyspepsia.
5. Other individual digestive symptoms or groups of symptoms (such as gastro-oesophageal reflux disease and irritable bowel syndrome) may coexist with PDS.

Epidemiology of FD

Global prevalence of functional dyspepsia according to Rome criteria, 1990–2020: a systematic review and meta-analysis

Kwanjoo Lee[1], Chang-il Kwon[1], Abdullah Özgür Yeniova[2], Ai Koyanagi[3], Louis Jacob[3,4], Lee Smith[5], Seung Won Lee[6], Masoud Rahmati[7,8], Ju-Young Shin[9], Jae Il Shin[10✉], Wonyoung Cho[11✉] & Dong Keon Yon[11,12✉]

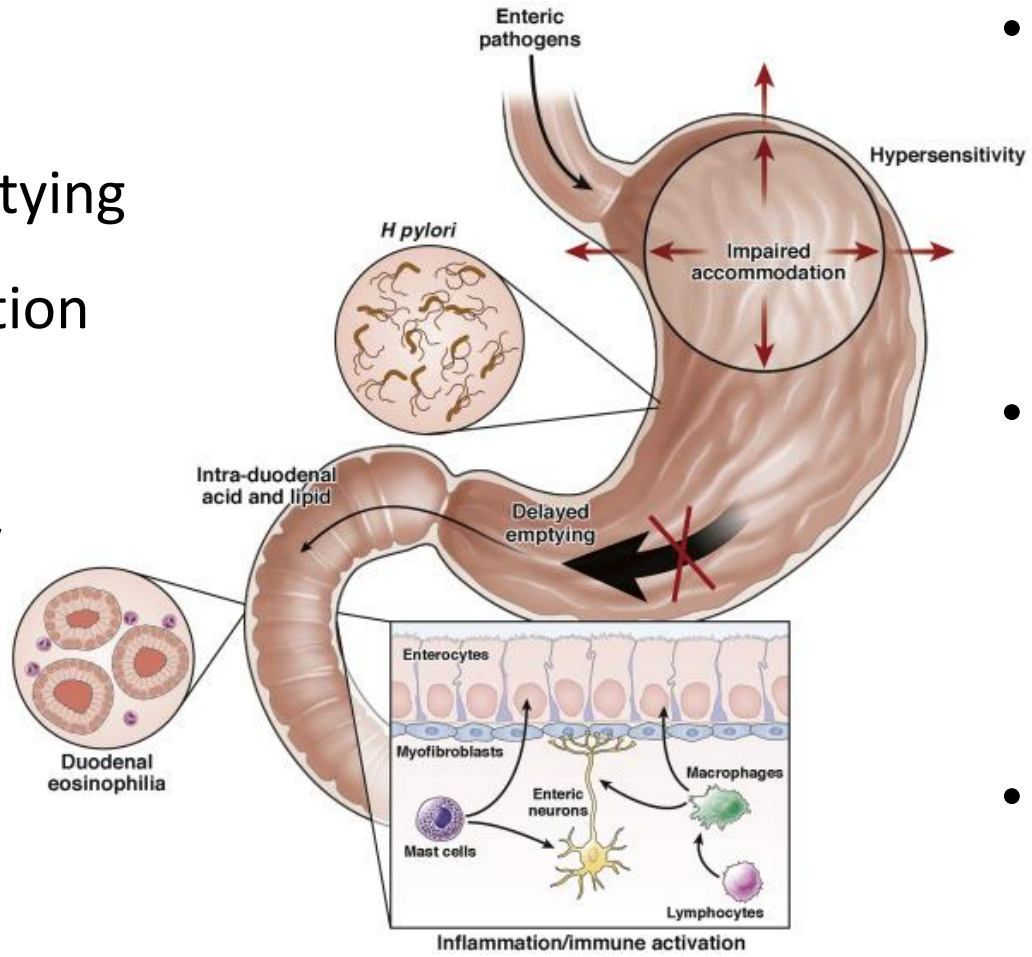




Lee et al. Nature Portfolio. Scientific reports. (2024) 14:4172

Pathophysiology of Functional Dyspepsia

- Motility disturbance
  - Delayed gastric emptying
  - Gastric accommodation
- Visceral hypersensitivity
- Altered gut microbiota



- Altered mucosal function
  - Duodenal sensitivity
  - Duodenal eosinophillia
- Inflammation and immune function
  - Post infectious
  - H pylori
- Altered central nervous system processing

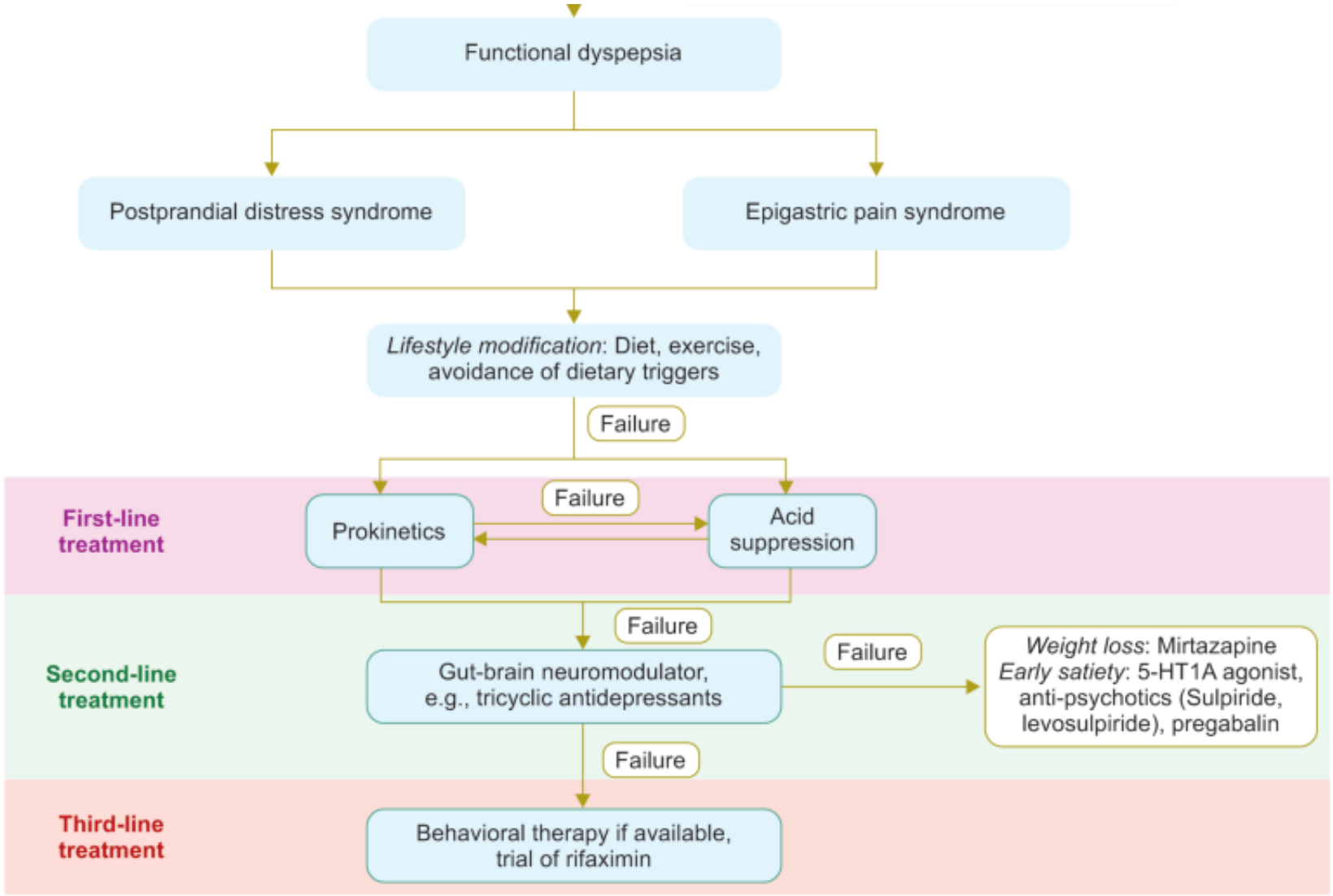
Koduru P. et al. Clinical Gastroenterology and Hepatology 2018;16:467–479

Management of FD

- Confident diagnosis
- Effective and empathic doctor–patient relationship
- Management partnership between primary and secondary care
- Screen for and treat underlying psychological diagnosis
- Be aware of high rates of overlapping DBGI

Black CJ, et al. Gut 2022;71:1697–1723

Management Algorithm



Bhatia S. Functional Dyspepsia—Approach in 2023. Chapter 27. Progress in Gastroenterology and Hepatology 2023

Non-Pharmacological Treatments

- **General**
  - No prospective studies -lifestyle and dietary modification
  - Dietary fat
  - Smoking
  - Aerobic exercise

- **Gut–brain behavioural therapies**
  - Psychodynamic therapy, CBT, stress management, mindfulness, and hypnotherapy
  - Overall evidence in FD is limited
  - largest study of gut–brain behavioural therapy in FD[2]
    - 158 patients meeting Rome III criteria
    - Med Rx + psychotherapy or med Rx alone
    - High rate of non-completion in treatment arm (45%)
    - Symptom improvement favoured the treatment arm

1. Black CJ, et al. Gut 2022;71:1697–1723
2. Orive M et al. J Psychosom Res 2015;78:563–8

Pharmacological Treatments

- **Eradication therapy for H pylori**
  - Treat all H pylori positive FD patients
  - Zhao et al
    - Improvements in symptoms > in the Rx group at 1 year (OR- 1.38)
  - Moayyedi et al
    - 22 RCTs , 4896 H pylori +ve
    - RR= 0.91 (95% CI 0.88 to 0.94)
    - NNT 12.5 (95% CI 10-20)

- **Anti secretory drugs**
  - Histamine-2-receptor antagonists
    - Systematic review in 2006- H2RA's effective
    - Relative risk reduction 23% vs placebo
  - Proton pump inhibitors (PPIs)
    - Systematic review in 2017- PPIs effective
    - Response rate of 31% vs 25.8%
    - NNT 11[3]
    - 4-8 week trial PPI, lowest dose to control symptoms
  - Potassium competitive acid blockers (PCABs) no RCTs yet

1. Black CJ, et al. Gut 2022;71:1697–1723
2. Moayyedi et al. Am J Gastroenterol 2017; 112:988–1013
3. Pinto-Sanchez et al. Cochrane Database Syst Rev. 2017;11(11):CD011194.

Pharmacological Treatments

- **Prokinetics**
  - More readily available prokinetics- metoclopramide- not effective
  - Safety profile concerns
  - Other prokinetics- some efficacy- limited availability
- **Neuromodulators**
  - TCA trials more robust compared to others
    - 8 RCTs -RR reduction 0.76; 95% CI (0.62 to 0.94)
    - Counsel of side effects
    - Start low, slow titration (max 30-50mg dly)
  - Other neuromodulators
    - No significant efficacy data
    - Antipsychotics /Anti depressants
    - Pregabalin

Black CJ, et al. Gut 2022;71:1697–1723

Pharmacological Treatments

- **Herbal preparations**
  - Over 44 herbal preparations
  - STW5- Iberogast
  - Rikkunshito
- **Rifaximin**
  - Treat dysbiosis
  - 2 RCTs- benefit over placebo
  - Promising agent requires further studies

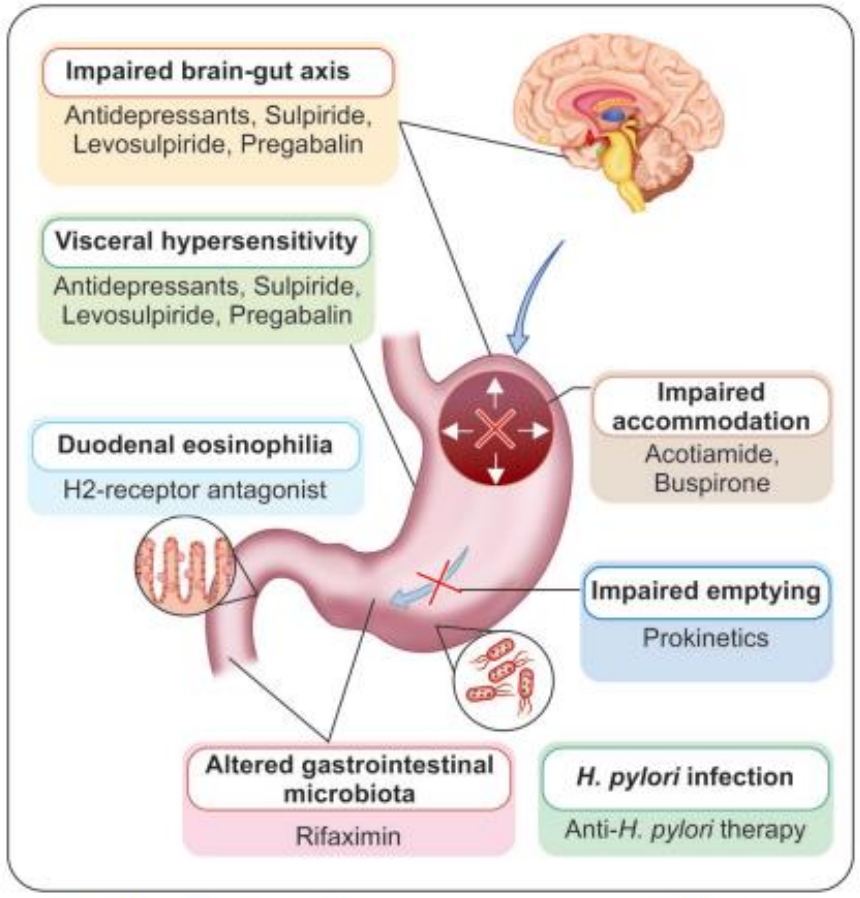


Fig. 1: Pathophysiology of functional dyspepsia with their pharmacotherapeutic targets.
Abbreviation: H. Pylori: Helicobacter pylori

Bhatia S. Functional Dyspepsia—Approach in 2023. Chapter 27. Progress in Gastroenterology and Hepatology 2023

Conclusion

- FD is a complex, multifactorial DGBI- highly prevalent in the community
- An effective approach to the diagnosis and management of FD important to healthcare systems, patients and society
- Effective communication, making a positive diagnosis- reduces unnecessary investigation
- Many areas for potential research