6 ทศวรรษรามาธิบดี
สู่สถาบันการแพทย์ในระดับสากล

Dyspepsia

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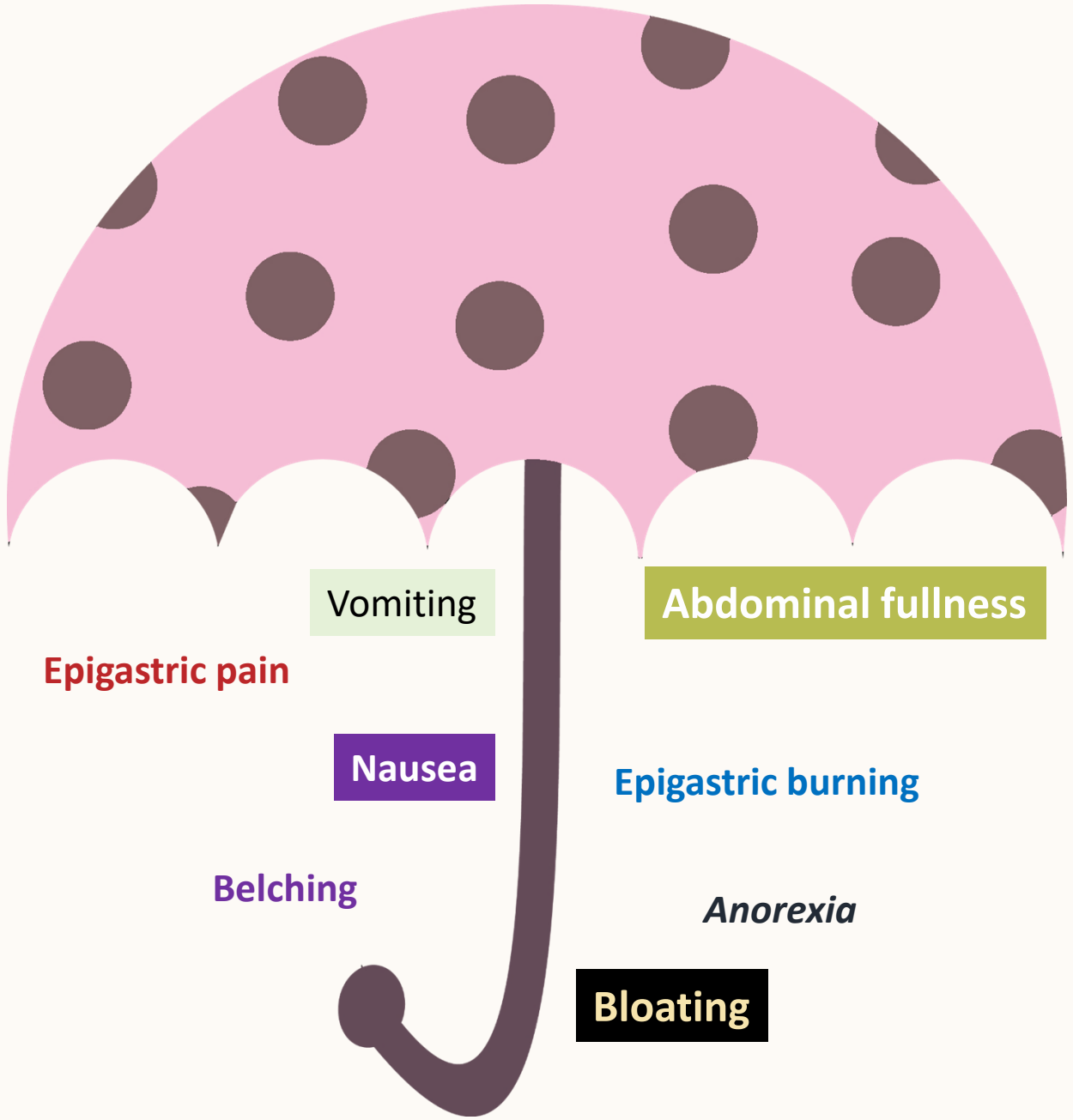
AGENDA

1. Dyspepsia Definition
2. Classification of Dyspepsia
3. Functional Dyspepsia approach and management

DEFINITION

"Episodic recurrent or persistent abdominal **pain or discomfort**, or any other symptoms referable to the upper alimentary tract, excluding bleeding or jaundice, of duration 4 weeks or longer"



Uninvestigated Dyspepsia

70-80%

Functional Dyspepsia

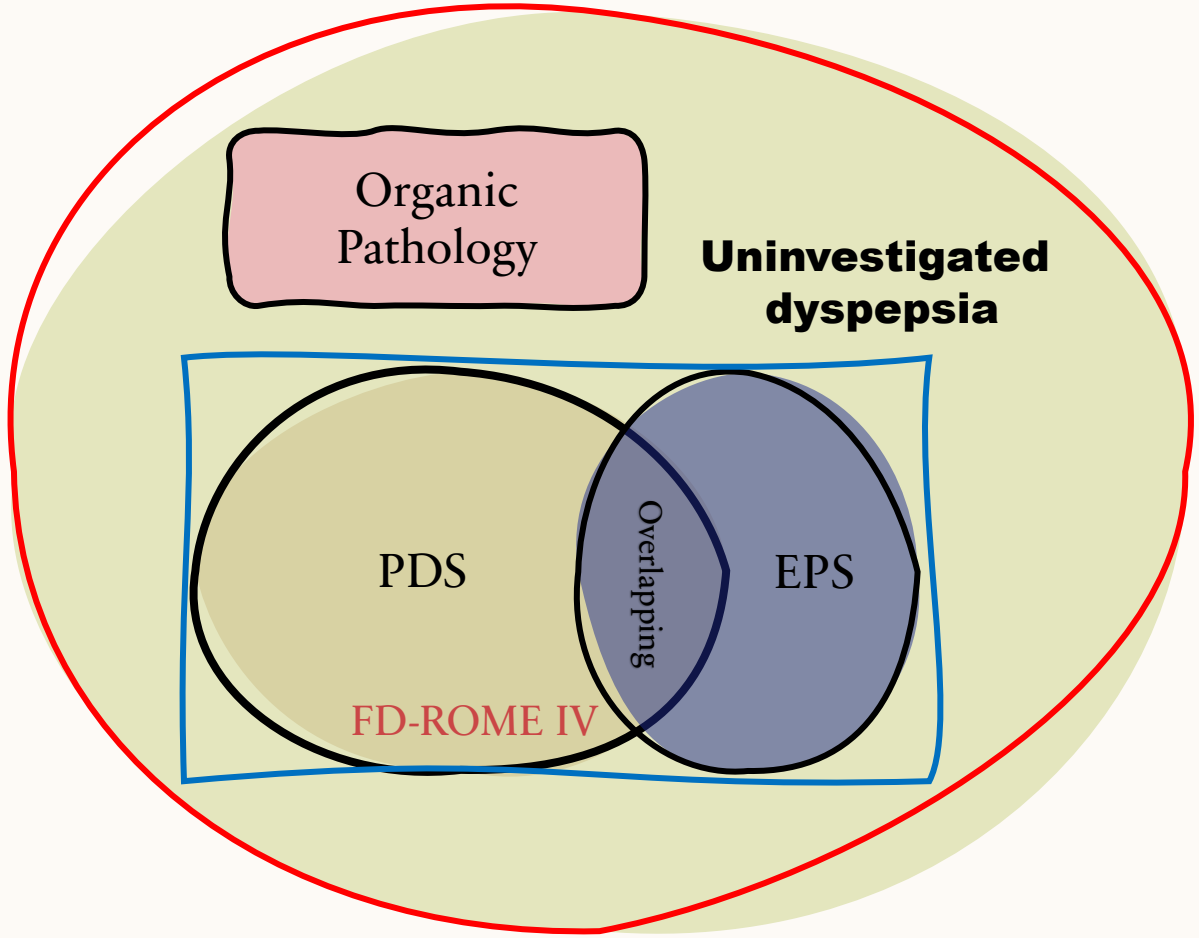
20-30%

Organic Dyspepsia

Classification of Dyspepsia

Organic pathology

1) HP infection
2) Pancreatic disease
3) PUD
4) Hepatobiliary disease
5) UGI cancer
6) Systemic conditions
7) etc. i.e. Medications



Ther Adv Gastroenterol 2018;11: 1–17

Uninvestigated dyspepsia

Medical history & Physical examination

Endoscopy if….

- Have risk factor eg. NSAIDs user
- Age above threshold
- Alarm symptoms: unreliable parameters

Three common strategies

- Prompt diagnostic endoscopy & Directed treatment
- Test and treat *Helicobacter pylori* infection
- Empirical antisecretory

Alarm features

- Evidence of UGIB, such as hematemesis, melena, maroon stool, or iron deficiency without other causes
- Early satiety
- Unexplained weight loss (>10% body weight)
- Persistent vomiting due to an unknown cause (defined as vomiting >10 times in 24 hours or vomiting after each meal)
- Family history of upper GI cancer in a first-degree relative

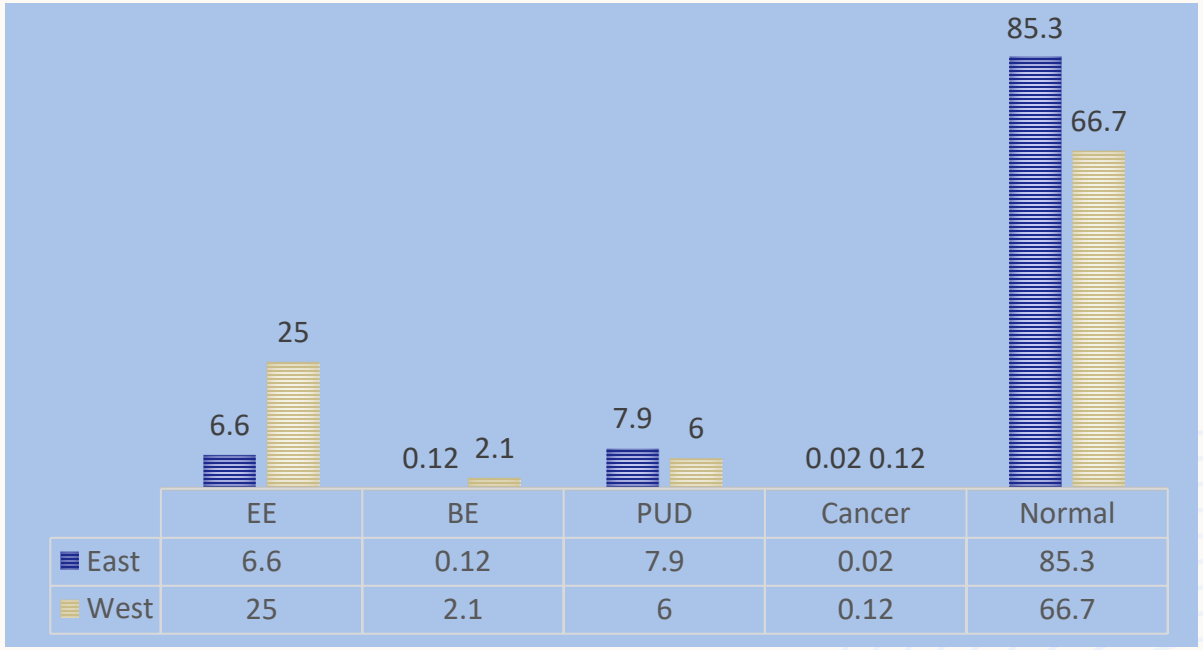
THE PREVALENCE OF CLINICALLY SIGNIFICANT ENDOSCOPIC FINDINGS IN SUBJECTS WITH DYSPEPSIA

Updated Systematic Review and Meta-analysis

- Prevalence of endoscopic findings among **41,763 participants**
- 40.4% with dyspepsia

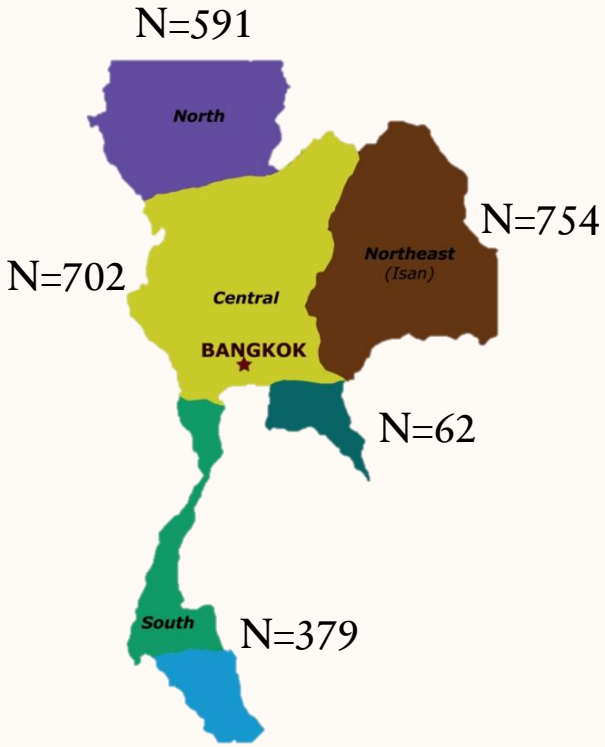
Findings	N	Pool prevalence (95% CI)
Erosive esophagitis	3435	12 (3.6–24.2)
Barrett esophagus	3004	0.6 (0.0–1.9)
Peptic ulcer	3965	7.2 (4.0–11.1)
Gastric cancer	3350	0.006 (0.0–0.02)
Esophageal cancer	3350	0.12 (0.0–0.12)

Pooled prevalence in Asian vs Western studies



Clinical Gastroenterology and Hepatology 2023;21:1739–1749

ENDOSCOPY IN A COMMUNITY-BASED EXAMINATION IN THAILAND



- 2488 participants from 5 different geographic regions in Thailand
- Dyspeptic symptoms 62.8%, Asymptomatic 37.2%, Female 68%, mean age 50 years, ***alarming 13.3%***
- Do upper endoscopy & Questionnaires
- Endoscopic findings:

Findings	**%**
Normal	73.4
DU & GU	0.8
Esophagitis	5.3
Gastric cancer	0.08
Esophageal cancer	0.04

Chula Med J 2013;57(3):293-303

ข้อเสนอแนะที่ 1: ผู้ป่วยที่ควรได้รับการแนะนำให้ทดสอบเชื้อ *เฮลิโคแบคเตอร์ไพโลไร (Helicobacter pylori; H. pylori)* คือ

1. ผู้เป็นโรคแผลเปปติก (peptic ulcer) หรือ ผู้ป่วยที่มีรอยถลอกในกระเพาะอาหาร (gastric erosions)
2. ผู้ที่ใช้ยา NSAIDs/แอสไพริน (ASA) ระยะยาวร่วมกับมีประวัติโรคแผลเปปติก หรือมีปัจจัยเสี่ยงหลายอย่างของการเกิดเลือดออกในทางเดินอาหารส่วนบน
3. ผู้เป็นมะเร็งต่อมน้ำเหลืองชนิด Marginal zone B-cell lymphoma (MALT lymphoma)
4. ผู้ที่มีอาการ dyspeptic และไม่ตอบสนองต่อยาต้านการหลั่งกรด (anti-secretory drug)
5. ผู้ที่มีญาติสายตรง (1st degree relative) เป็นมะเร็งกระเพาะอาหาร
6. ผู้ที่เป็นมะเร็งกระเพาะอาหาร

FUNCTIONAL DYSPEPSIA ROME IV

	Rome IV criteria	Frequency	Remarks and other symptoms
FD	Bothersome postprandial fullness, early satiation, epigastric pain or burning **AND** no evidence of structural disease likely to explain symptoms	≥1 symptom	-Vomiting suggests another disorder. -Symptoms should not be relieved by evacuation of feces or gas. -Symptoms of GERD and IBS may coexist with FD (PDS and EPS).
PDS	Bothersome postprandial fullness and/or early satiation severe enough to interfere with daily activities or to prevent finishing a meal	≥3 days/week	Postprandial epigastric pain or burning, epigastric bloating, excessive belching, nausea and heartburn can be present
EPS	Bothersome epigastric pain and/or burning severe enough to interfere with daily activities	≥1 day/week	Postprandial epigastric bloating, belching and nausea can be present. Pain may be induced/relieved by meal ingestion or occur while fasting and does not fulfil biliary pain criteria.

Note: Symptoms occurs for the past 3 months with onset ≥6 mons before diagnosis

Rome IV, Gastroduodenal Disorders: Gastroenterology 2016;150:1380–1392

Rome IV criteria for FD

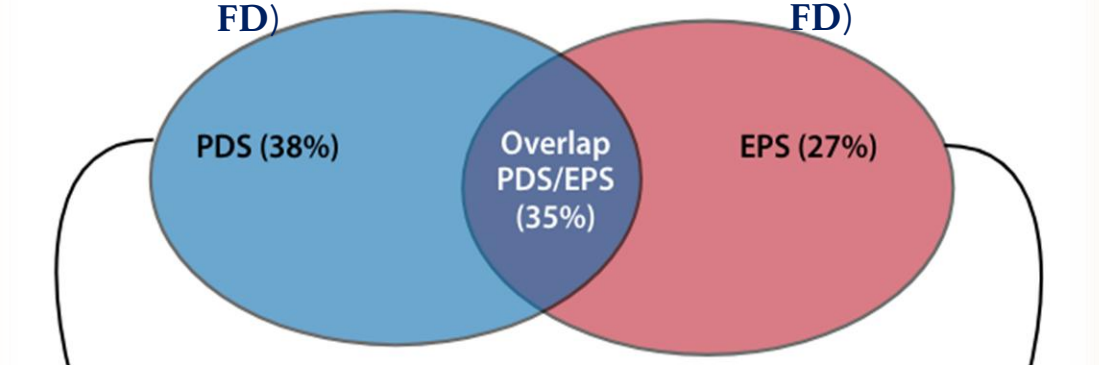
- Presence of ≥1 symptom(s) of postprandial fullness, early satiety, epigastric pain, or epigastric burning
- No evidence of structural disease that could explain the symptoms

PDS
Postprandial fullness or early satiety ≥3 days/week for the past 3 months and onset ≥6 months before diagnosis

EPS
Epigastric pain and/or burning ≥1 day(s)/week for the past 3 months and onset ≥6 months before diagnosis

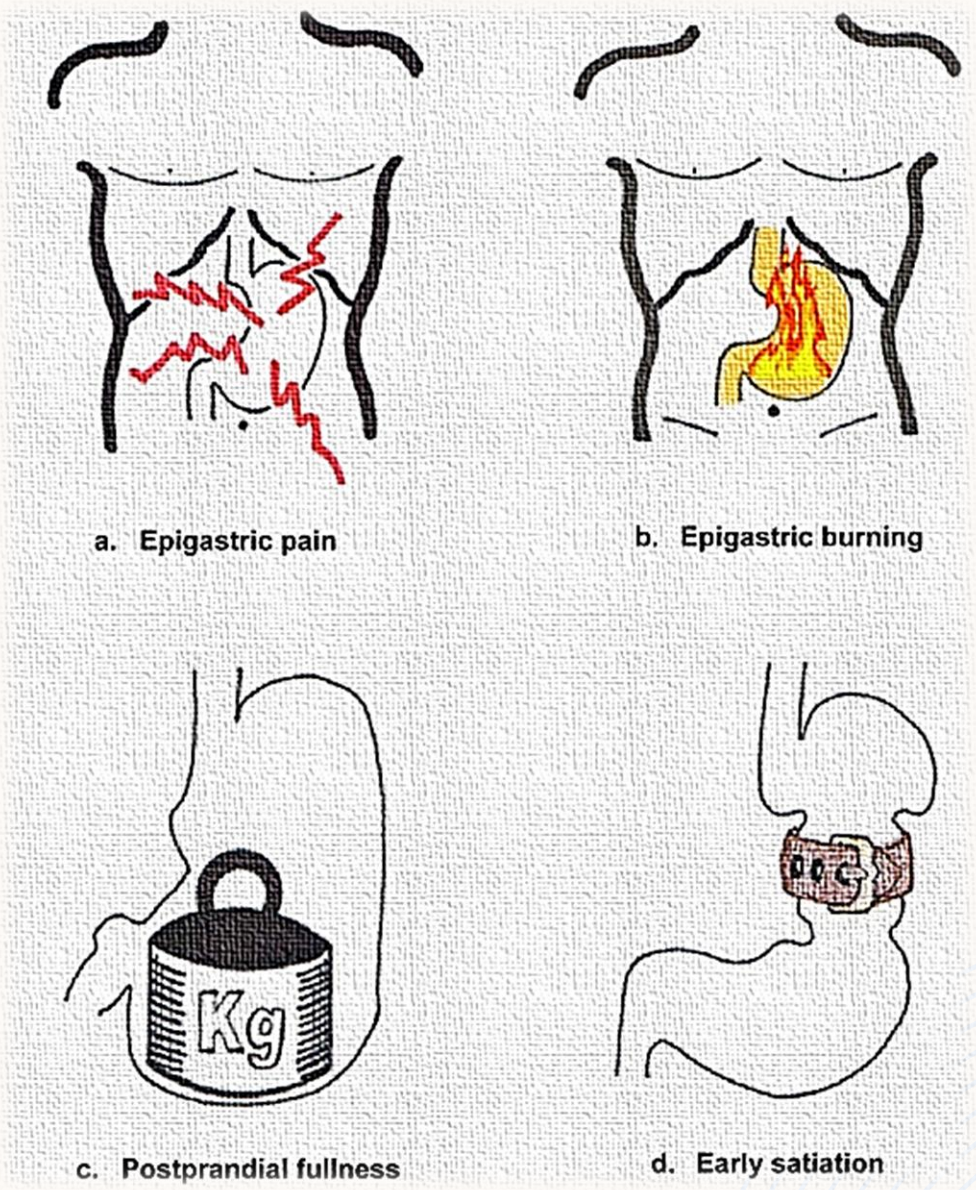
(meal-related FD)

(meal-unrelated FD)



Symptoms
- Early satiety
- Bloating
- Nausea
- Vomiting/retching
- Decreased appetite

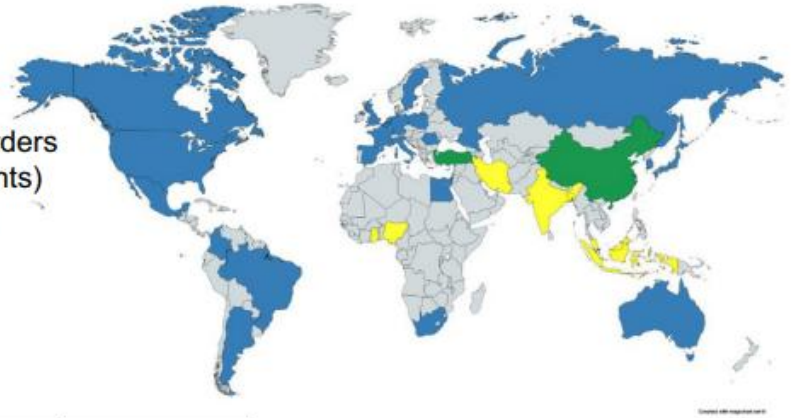
Symptoms
- Epigastric pain
- Epigastric burning



Engl J Med. 2015;373(19):1853-1863
Ther Adv Gastroenterol 2018;11: 1–17
Gastroenterology & Hepatology 2020;16(2):66-74

FUNCTIONAL DYSPEPSIA
ROME IV GLOBAL EPIDEMIOLOGY STUDY

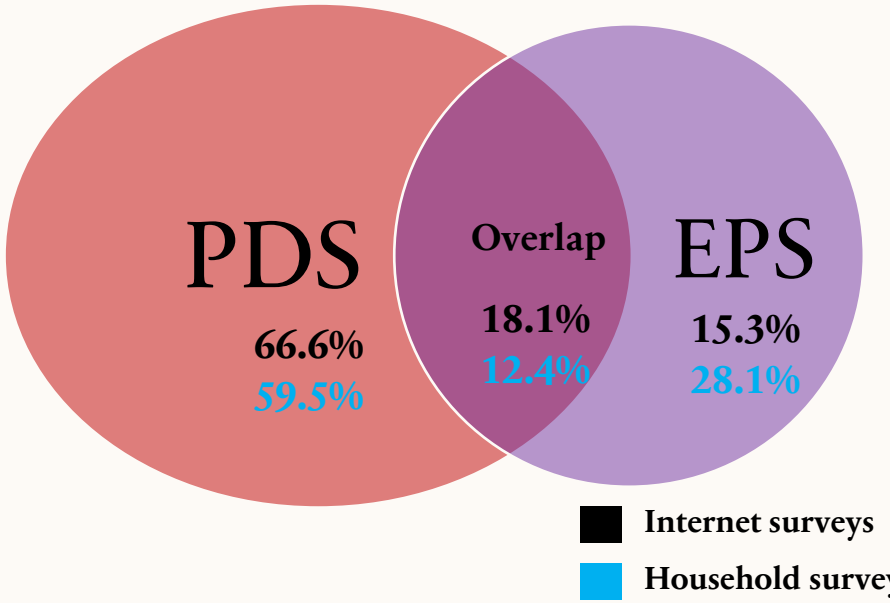
A global epidemiological study of functional GI disorders
- 73,076 adults surveyed (33 countries, 6 continents)
- Data collection: By Internet (24 countries, blue), by household interview (7 countries, yellow), or both methods (China and Turkey, green).



Prevalence of meeting criteria for at least one of 22 functional GI disorders (%):

	All Participants	Females	Males
Internet surveys	40.3	46.5	34.2
Household surveys	20.7	23.1	18.3

Gastroenterology

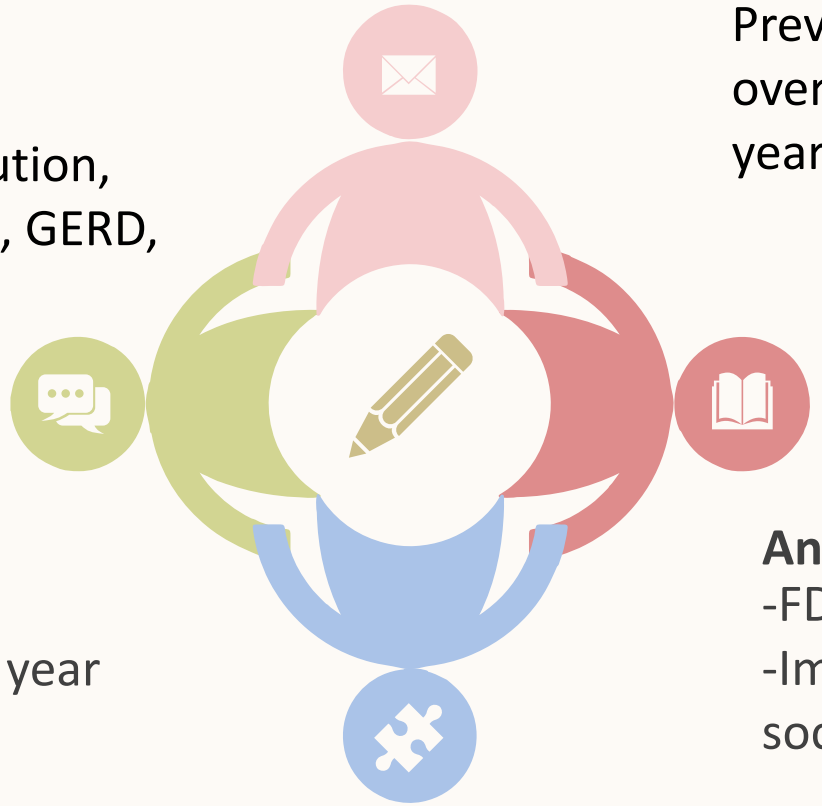


	Overall	Sex		Age group		
		Female	Male	18-39	40-64	>65
DGBIs	N=54127	N=26578	N=27549	N=23003	N=22281	N=8843
FD	7.2 (7.0, 7.4)	8.7 (8.4, 9.1)	5.8 (5.5, 6.0)	9.2 (8.8, 9.5)	6.6 (6.2, 6.9)	3.8 (3.4, 4.2)

Gastroenterology 2021;160:99–114

NATURAL HISTORY AND IMPACT

Long-term natural history is a chronic, fluctuating disorder;
1. ~50% have persistent symptoms,
2. 10-20% experience symptom resolution,
3. 30-40% have a change to either IBS, GERD, or a combination of both



Prevalence remains relatively stable over time, between 13-16% in two 10-year follow-up studies

Incidence of FD is 3-5% per year

Anxiety influenced natural history
-FD does not affect survival
-Impact on patients and from a socioeconomic perspective

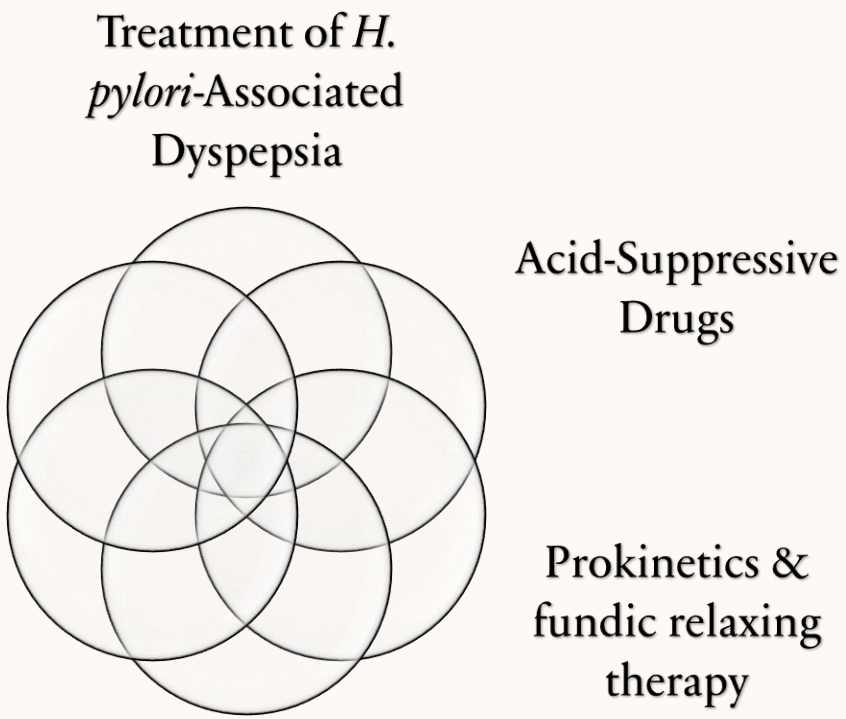
Digestion 2010; 81: 53-61
Am J Gastroenterol 2012; 107: 912-21

LIFESTYLE ADVISE FOR DYSPEPSIA

- Avoid NSAIDs use
- Avoid carbonated drinks
- Avoid irritating food stuffs
- Stop smoking
- Stop/ reduce alcohol
- Stop/ reduce caffeine
- Small frequent meals
- Maintain an ideal weight
- Reduce stress, more relax
- Avoid tight garment

TREATMENT OPTIONS FOR FD

<u>*H. pylori* eradication</u>
NNT 12.5–15



<u>Acid-suppressive therapy</u>

H2RAs	NNT 7
PPI	NNT 10
PCAB	NA

<u>Prokinetics</u>
NNT 12
(without cisapride)

<u>Neuromodulators</u>
NNT 6

GE Port J Gastroenterol 2023;30:86–97

Cochrane Library

Cochrane Database of Systematic Reviews

Proton pump inhibitors for functional dyspepsia (Review)

25 RCTs with 8453 participants

PPI versus placebo for functional dyspepsia

Patient or population: functional dyspepsia
Setting: secondary and tertiary centres
Intervention: PPI
Comparison: placebo

NNT=11

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with placebo	Risk with Proton pump inhibitors (PPI)				
Global symptoms of dyspepsia (> 2 weeks)	Study population		**RR 0.88** (0.82 to 0.94)	6172 (18 RCTs)	⊕⊕⊕⊝ **Moderate**[1]	Measurement of no improvement.
	714 per 1000	**629 per 1000 (586 to 671)**				
Quality of life Psychological General Well-Being Index (Scale from: 22 to 132) and SF-36 (Scale from: 0 to 100) combined	**The mean post-treatment PGWB score was 99.84, the mean post-treatment SF-36 score was 66.2**	**SMD 0.01 higher** (0.09 lower to 0.11 higher)		1630 (3 RCTs)	⊕⊕⊕⊝ **Moderate**[2]	Higher scores means better quality of life.
Adverse events	Study population		**RR 0.99** (0.73 to 1.33)	2693 (6 RCTs)	⊕⊕⊕⊝ **Moderate**[1]	Number of adverse events.
	191 per 1000	**189 per 1000** (140 to 254)				

Cochrane Database Syst Rev. 2017 Nov 21;2017(11):CD011194.

ACID SUPPRESSIVE THERAPY

FD- not usually related to increase in acid output, but increased sensitivity to acid

PPIs

- Standard or half dose is OK, **NO** role of double dosage
- Duration 4-8 weeks
- Discontinued q 6-12 mons to reduce long-term risk of therapy

H2RAs

- Proven efficacy over placebo with a 23% reduction of symptoms, NNT=7

PCAB

- Small retrospective study with a 48.8% rate of symptomatic improvement

GE Port J Gastroenterol 2023;30:86–97

How to detect HP infection?

Test	Sensitivity	Specificity
Invasive Methods		
Rapid urease test	90%	95-100%
Histology	>95%	>95%
Culture	70-90%	100%
Non-invasive Methods		
Stool antigen test (ELISA-monoclonal)	>92%	>92%
Urea breath test	>95%	>95%
Serology (Validated ELISA IgG)	85-92%	79-83%

EFFICACY OF HP ERADICATION FOR FUNCTIONAL DYSPEPSIA: UPDATED META-ANALYSIS

Eradication therapy was superior to control for symptom

– Cure

(RR of symptoms not being cured=0.91; 95% CI 0.88-0.94, NNT=14; 95% CI 11-21)

– Improvement

(RR of symptoms not improving=0.84; 95% CI 0.78-0.91, NNT=9; 95% CI 7-17)

Ford AC, et al. Gut 2022.

Cochrane Library

Cochrane Database of Systematic Reviews

Prokinetics for functional dyspepsia (Review)

29 studies with 10,044 participants compared six prokinetics with placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	Risk with Prokinetic				
Not symptom-free or no symptom improvement Follow-up: 2 to 12 weeks	**Study population** 74 per 100	60 per 100 (55 to 66)	**RR 0.81** (0.74 to 0.89)	10,044 (29 RCTs)	⊕⊝⊝⊝ **VERY LOW** 1 2 3 4	
Post-treatment symptoms scores Follow-up: 2 to 6 weeks	The mean post-treatment symptoms scores was 2.3 to 5.6 (different scales were used)	**SMD 0.36 lower** (0.65 lower to 0.07 lower)	-	2914 (6 RCTs)	⊕⊕⊝⊝ **LOW** 5 6 7	Higher scores means worse symptoms
Mean difference symptoms scores Follow-up: 2 to 12 weeks	The mean difference symptoms scores was -10 to 3.43 (different scales were used)	**SMD 0.65 lower** (1.5 lower to 0.2 higher)	-	1822 (11 RCTs)	⊕⊝⊝⊝ **VERY LOW** 1 3 5 8	Positive scores means worse symptoms
Change of QoL scores Follow-up: 3 to 12 weeks	The mean change of QoL scores was 2.8 to 13.2 (different scales were used)	**SMD 0.11 higher** (0.1 lower to 0.33 higher)	-	1774 (5 RCTs)	⊕⊝⊝⊝ **VERY LOW** 5 6 9	Higher scores means better quality of life
Adverse events Follow-up: 2 to 8 weeks	**Study population** 31 per 100	34 per 100 (29 to 39)	**RR 1.09** (0.95 to 1.25)	3811 (17 RCTs)	⊕⊝⊝⊝ **VERY LOW** 1 2 4 5 8	

Prokinetic is effective in reducing global symptoms of FD

a. NNT for additional beneficial outcome, NNTB =7
b. Considerable heterogeneity; $I^2 = 91\%$ ($P < 0.00001$)

Pittayanon R, *et al*. Cochrane Database of Systematic Reviews 2018, Issue 10. Art. No.: CD009431.

TAKE-HOME MESSAGES

- Dyspepsia is one of the most common GI conditions in daily practice
- After excluding organic causes, the initial management steps involve discontinuing dyspepsia-inducing medications and implementing lifestyle modifications
- *H. pylori*: **test-and-treat** is essential
- The pharmacological options include acid-suppressive therapy, prokinetics, and neuromodulators

THANK YOU

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