Effectiveness of Low FODMAPs Diet Compared With Standard Dietary Advice in Functional Dyspepsia

Date of document: 4 November 2026

Research Proposal

Effectiveness of low FODMAPs dietary advice compared with traditional dietary advice in patients with functional dyspepsia, a randomized controlled trial

Rationale

Functional dyspepsia is a chronic functional disorder with a complex of symptoms which originated from gastroduodenal region. (1, 2) The current standard for diagnosis of the disease is the ROME IV criteria with characteristic symptoms including postprandial fullness, early satiety, epigastric pain and burning. Structural disease must be excluded through routine investigation.

The global prevalence of uninvestigated dyspepsia is 21% (3) In recent systematic review, according to ROME criteria the prevalence ranges from 17.6% to 6.9% in ROME I and IV criteria respectively. (4)

There are multiple proposed pathophysiologies, including gastric sensorimotor abnormalities, duodenal barrier defect and immune activation, microbiome alteration and gut-brain axis dysfunction. (2, 5-8, 10-15)

FODMAPs (Fructo, oligo, Di-, Monosaccharides and Polyols) are poorly absorbable and highly fermentable substances that cause internal fermentation which leads to increased osmotic pressure, resulting in increased gas and water in the small intestine which triggers mechano-chemoreceptors and contributes to the symptoms. (9)

Several studies have clearly demonstrated that low-FODMAPs diet significantly decreases IBS-symptoms. (20, 23)

However, evidence to support the use of dietary intervention in FD is limited. So, this randomized-controlled trial aimed to evaluate the effectiveness of a low FODMAPs diet in improving gastrointestinal symptoms and quality of life in individuals with functional dyspepsia

Review Literature

Literature Review

Functional dyspepsia is a chronic functional disorder with a complex of symptoms which originated from gastroduodenal region. (1, 2)

According to the Rome V criteria, the diagnosis requires one or more of the following symptoms: postprandial fullness, early satiation, epigastric pain, or epigastric burning, with symptoms present for at least 8 weeks and symptom onset at least 6 months before diagnosis. Structural disease must be excluded through routine investigation.

The two subgroups are categorized by predominant symptoms including epigastric pain syndrome and postprandial distress syndrome. However, there is still significant overlap between these two groups.

The global prevalence of uninvestigated dyspepsia is 21%, with significantly higher prevalence in women, smokers, NSAID users and in those with H. pylori-positive.(3) In recent systematic review, according to ROME criteria the prevalence range from 17.6% to 6.9% in ROME I and IV criteria respectively. (4) Postprandial distress syndrome is the most prominent subtype with 66.6% prevalence, follwedby overlapping case 18.1% and less frequently epigastric pain syndromewith 15.3% prevalence. (4)

20%5B1%5D.)

Pathophysiology

Pathophysiology is believed to be multifactorial with heterogeneity of symptoms. (2)

Gastrointestinal sensory and motor dysfunction

Gastric motor dysfunction including impaired gastric accommodations and delayed gastric emptying were thought to be cause of dyspeptic symptoms especially post-prandial distress syndrome(5, 10) Stomach hypersensitivity is considered to be the cause of epigastric pain syndrome and can also be associated with postprandial fullness. (6-8) The increased hypersensitivity can lead to misinterpretation of normal gastric filling as uncomfortable sensation. (7) However, emerging data points towards the duodenum being a key factors of the symptoms, therefore, gastric sensorimotor abnormalities could be secondary cause of the FD.(10)

Duodenal barrier defect and immune activation

In healthy individuals, intact duodenal barrier separates duodenal luminal content from mucosal immune system.(10) Psychological stress increases duodenal permeability by activating innate immune cells through corticotropin-releasing hormones. The recruited eosinophil and mast cells will be activated and degranulated, which leads to mucosal damage.(16) Increased duodenal mucosal eosinophil counts have been found to be associated with postprandial symptoms.(11) Chemical or mechanical triggers activate the duodeno-gastric feedback which affect the gastric sensorimotor function which generate FD symptoms. (10)

Gut microbiota and bile acid

Gut microbiota and bile salts have a bidirectional relationship as bacterial are responsible for bile reabsorption and conjugation, and specific bile acids have selective antimicrobial effects.(12-15) It is found that meal-related symptoms are correlated with increased duodenal bacterial load. (13) Mucosal inflammation could lead to gut microbiome alteration and cause changes in bile acid. In the same way, changes in bile acid amounts can also lead to proinflammatory bacterial overgrowth which induces further mucosal damage and inflammation.(12-15)

Gut-Brain axis dysfunction

Epithelial barrier defect and gut dysbiosis can regulate gut-brain communications via the hypothalamic-pituitary-adrenal axis. (2) Psychological stress can induce eosinophils to release substance P and corticotropin-releasing hormone, which leads to dysfunction of duodenal barrier dysfunction. (16) Gut dysbiosis can cause alteration of neurotransmitters function by synthesis or consumption of the substances leading to abnormal signaling to the brain and emotional state. (17)

PAGI-SYM score

The **Patient Assessment of Upper Gastrointestinal Symptom Severity Index (PAGI-SYM)** is a validated patient-reported instrument used to evaluate the severity of upper gastrointestinal symptoms, such as postprandial fullness, early satiety, epigastric pain, bloating, nausea, and heartburn. It is commonly used in both clinical practice and research to assess symptom burden and monitor treatment outcomes in patients with functional dyspepsia and other upper gastrointestinal disorders. (18)

The **Thai version of the PAGI-SYM** was translated using a standardized forward–backward translation process and culturally adapted. It has been validated in Thai patients, demonstrating good reliability and validity for assessing upper gastrointestinal symptom severity. (19)

FODMAPs And Functional dyspepsia

FODMAPs (Fructo, oligo, Di-, Monosaccharides and Polyols) are poorly absorbable and highly fermentable substances that may induce bloating and gas sensations. Common high-FODMAP foods include wheat, onions, garlic, legumes, milk and yogurt, apples, pears, mangoes, honey, mushrooms, and sugar-free products containing polyols. (20)

The internal fermentation caused by FODMAPs diet leads to increased osmotic pressure, resulting in increased gas and water in the small intestine which triggers mechano-chemoreceptors and contributes to the symptoms.(9) There are studies demonstrated that FODMAPs diet may be linked to mucosal inflammation and colonic barrier dysfunction through microbiome-mediated mast cell activation. (21,22)

Several studies including multiple randomized controlled trials have clearly demonstrated that low-FODMAPs diet significantly decreases irritable bowel syndromes (IBS)symptoms. (23,26)However, evidence to support the use of LFD dietary intervention in FD is limited.

A crossover study, Potter, et al (2020), reported improvement in dyspeptic symptoms in patients with FODMAP restriction. (24) However the study has some limitations, such as small sample size and including participants with overlapping IBS symptoms. Observational studies have similarly demonstrated potential therapeutic roles in patients following low-FODMAP dietary advice compared with baseline or traditional dietary recommendations. (25,27)

Moreover, a double-blind pilot randomized controlled trial evaluated a simplified low-FODMAP diet, which restricts only fructans and galacto-oligosaccharides, compared with the traditional low-FODMAP diet in patients with irritable bowel syndrome with diarrhea. Both diets produced similar improvements in abdominal pain, bloating, and overall symptoms, although the traditional diet showed slightly better effects on stool consistency. The simplified approach was better tolerated and easier to follow, suggesting it may serve as a practical first-line strategy for patients with mild symptoms. (28)

The current studies have several llimitations. Most studies are small, or observational in design, limiting causal inference. There are rarely any randomized head-to-head comparisons with

standardized control dietary advice. Additionally, psychological burdens—common in FD—have not been sufficientky evaluated

Therefore, this randomized controlled trial aims to address these gaps by evaluating the effectiveness of low-FODMAP dietary advice in improving gastrointestinal symptoms and quality of life in patients with functional dyspepsia.

Objectives

Primary objective

- To compare the effectiveness of simplified low FODMAPs dietary advice with traditional dietary advice in improving FD symptoms at 2 weeks by using PAGI-SYM scores

Secondary objective

- To compare change in PAGI-SYM score of low FODMAPs dietary advice with traditional dietary advice in improving FD symptoms over a period of time
- To compare the quality of life of individual with FD who receives low FODMAPs dietary advice with those who received traditional dietary advice as measured by:
    - Health-related quality of life using the EQ-5D-5L score
    - Depressive symptoms using the Thai version of the Patient Health Questionnaire-9 (Thai-PHQ-9)
    - Sleep quality using the Pittsburgh Sleep Quality Index (PSQI)
- **To assess changes in** body weight before and after the restriction phase.
- **To evaluate the adverse event of the intervention**,
- **To assess dietary adherence and dietary modification**, by measuring the percentage reduction in FODMAP intake from baseline to end of restriction phase
- To evaluate the response to the dietary intervention by comparing the proportion of participants who achieve a clinically meaningful improvement (>30%) in PAGI-SYM score after 2 weeks between the low-FODMAP diet group and the traditional dietary advice group.

Hypothesis

- Is low FODMAPs diet more effective in improving symptoms in functional dyspepsia than traditional dietary advice?
- Does low-FODMAP dietary advice result in a greater improvement in PAGI-SYM scores compared with traditional dietary advice in patients with functional dyspepsia over a 2-week period?

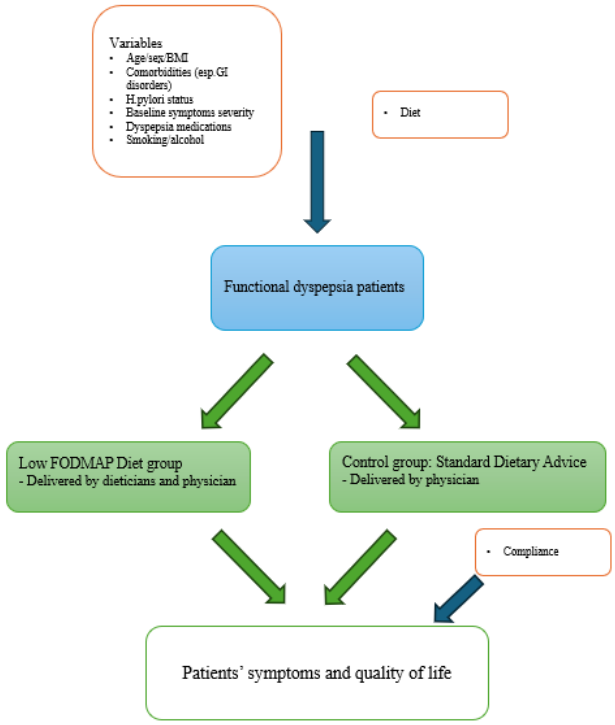
- Does low-FODMAP dietary advice improve health-related quality of life compared with traditional dietary advice after 2 weeks?
- Does low-FODMAP dietary advice reduce depressive symptoms compared with traditional dietary advice?
- Does low-FODMAP dietary advice improve sleep quality compared with traditional dietary advice?
- Is there a significant change in body weight after low-FODMAP dietary advice compared with traditional dietary advice?
- Does low-FODMAP dietary advice result in changes in bowel habits compared with traditional dietary advice?
- Does low-FODMAP dietary advice result in a greater reduction in FODMAP intake compared with traditional dietary advice over 2 weeks?
- Does low-FODMAP dietary advice, compared with traditional dietary advice, result in a higher proportion of participants achieving a >30% improvement in the PAGI-SYM score after 2 weeks?

Keywords

- Functional dyspepsia, low FODMAPs diet

Conceptual Framework

Conceptual Framework



Research Design

Randomized controlled trial

Research Methodology

(Population) Patient diagnosed with functional dyspepsia with postprandial distress syndrome or overlapping subgroup

(Target Population)

Patient with

- Diagnosis or referred to King Chulalongkorn memorial Hospital with the diagnosis of functional dyspepsia in PDS or PDS/EPS overlap subgroup
- Received low FODMAPs dietary advice from dietician

Control Population

- Diagnosis or referred to King Chulalongkorn memorial Hospital with the diagnosis of functional dyspepsia in PDS or PDS/EPS overlap subgroup
- Received standard dietary advice from dietician

Eligibility Criteria

Inclusion Criteria

Participants will be eligible for enrollment if they meet all of the following criteria:

1. Adults aged 18 to 70 years at the time of screening
2. Diagnosis of functional dyspepsia in accordance with the Rome V criteria, confirmed by a normal upper gastrointestinal endoscopy performed within the previous 6 months.
3. Negative testing for *Helicobacter pylori* infection (urea breath test, stool antigen test, or histology, as applicable).
4. Functional dyspepsia subtype classified as:
    - Predominantly Postprandial Distress Syndrome (PDS), or
    - PDS with overlapping Epigastric Pain Syndrome (EPS).
5. Moderate-to-severe symptom burden, defined as a score ≥ 2 on at least one of the following subscales (postprandial fullness, bloating, or upper abdominal pain) of the PAGI-SYM
6. Ability and willingness to comply with study procedures and the prescribed dietary intervention.

Exclusion Criteria

Participants will be excluded if any of the following criteria are met:

1. Diagnosis of Irritable Bowel Syndrome (IBS) according to the Rome IV criteria.
2. Presence of organic gastrointestinal disease, including but not limited to:
    - Inflammatory bowel disease
    - Peptic ulcer disease
    - Celiac disease
    - Active gastrointestinal malignancy
3. Active systemic malignancy or severe systemic illness.
4. Current or prior diagnosis of an eating disorder, or evidence of clinically significant malnutrition.
5. Current adherence (within the past 4 weeks) to a low FODMAP diet or other restrictive dietary pattern that significantly alters fermentable carbohydrate intake (e.g., gluten-free, lactose-free, ketogenic, low-residue, Specific Carbohydrate Diet, or structured elimination diets)

6. Use of antibiotics, probiotics, or medications known to significantly affect gastrointestinal motility or microbiota within 4 weeks prior to enrollment (unless on a stable dose and deemed acceptable by the investigator).
7. Pregnancy or lactation.
8. Previous abdominal surgery except appendectomy, cesarian section and tubal resection

Informed consent process

- All eligible participants will be provided with a written Participant Information Sheet detailing the study background, objectives, procedures, potential risks and benefits, data collection methods, data storage, confidentiality safeguards, and intended use of research data.
- Written informed consent will be obtained from each participant prior to the performance of any study-related procedures.
- Participation in the study will be entirely voluntary. Participants will have the right to decline participation or withdraw their consent at any time during the study without providing a reason and without any consequences to their ongoing medical care or legal rights.

Research flow

- Eligible patients will receive both verbal and written information describing the study objectives, procedures, potential risks, and expected commitments. Written informed consent will be obtained prior to any study-related assessments
- At enrollment, the following baseline data will be collected: Demographic and clinical characteristics, Symptom severity using the PAGI-SYM**,** A 7-day food diary (covering dietary intake prior to randomization) Baseline average FODMAP intake will be calculated by a registered dietitian using standardized nutritional analysis software
- Randomization will be performed using a computer-generated simple randomization sequence. Allocation concealment will be ensured using sequentially numbered, sealed opaque envelopes prepared by an independent researcher not involved in participant recruitment or assessment. Classified patients into two groups: standard dietary advice and Low-FODMAPs dietary advice
- The intervention detail at the first visit
    - All participants will receive traditional verbal dietary advice for functional dyspepsia delivered by a physician (P.Y.) for 5 minutes. The advice includes routine clinical practice and includes recommendations to consume smaller, more frequent meals; avoid large, high-fat, spicy, or fried meals; limit caffeine, carbonated beverages, and alcohol; and identify and avoid individual trigger foods.
    - Participants allocated to the Low-FODMAP group will receive additional structured simplified low-FODMAP dietary advice delivered by a physician (P.Y.) The advice

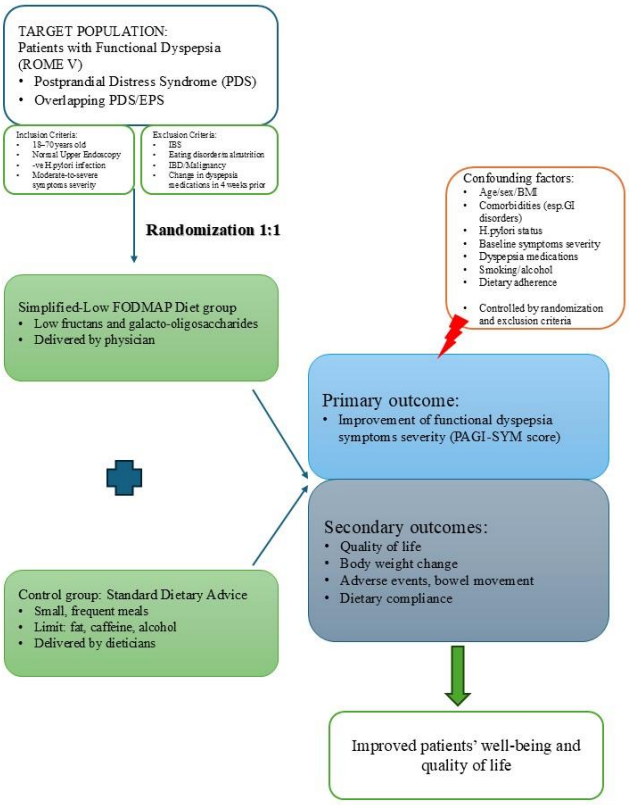
aims to restrict selected high-FODMAP subgroups—specifically fructans and galacto-oligosaccharides—for 2 weeks aligning with the FODMAP dietary advice for patients with IBS.

- Participants will be asked to evaluate the perceived benefit of the dietary intervention and indicate whether they wish to continue the dietary modification. Those who choose to proceed will enter an open-label extension phase for a total of 8 weeks.

- Symptoms score (PAGI-SYM), upper and lower GI symptoms, bowel movements symptoms, nutritional status (body weight and BMI) and anxiety and depression symptoms will be taken at baseline and weekly during study period
- Food diary, quality of life, sleep quality in the past 7 days will be recorded at baseline and at the end of the study

- Safety Monitoring
    - Adverse events and any self-reported side effects including upper and lower GI symptoms, weight changes, anxiety and depression related to dietary modification will be recorded throughout the study period.

Research flow



	Trial period									
	Enrolment		Post randomization		Open-Label extension phase					Close out
Timepoint	D-7 to 0	0	Wk1	Wk2	Wk3	Wk4	Wk5	Wk6	Wk7	Wk8
Enrolment										
Eligibility screen	X									
Informed consent	X									
Randomisation		X								
Intervention (Restriction phase)										
LowFODMAPs dietary advice		X								
Standard dietary advice		X								
Assessment (By phonecalls)										
Food diary		X	X	X	X	X	X	X	X	X
Stool diary		X	X	X	X	X	X	X	X	X
PAGI-SYM		X	X	X	X	X	X	X	X	X
EQ-5D-5L		X		X						X
PHQ-9		X		X						X
Sleep quality index		X		X						X

Sample calculation

- As we are considering a continuous outcome for two independent groups, we use size calculation for an independent t-test:
- For independent samples case (continuous outcomes):
    - **N pergroup = $2 \times (Z_1 - \alpha/2 + Z_1 - \beta)^2 \sigma^2 / MCD^2$**
- **α** (two-sided) = 0.05
- **Power** = 0.80

  ⟶ **β**=0.20
- Minimal clinical difference (MCD) is reference from previous studies (Van den Houte, et al 2024) = 20
- Standard deviation (**σ)** is calculated from
    - **SD (σ) = $\sqrt{N} \times$ (upper limit CI – lower limit CI) / 3.92**
    - reference from previous studies (Van den Houte, et al 2024)
- **σ_1** (SD pre value) = 33.67
- **σ_2** (SD post value) = 28.01
    - **σ_d = sqrt($\sigma_1^2 + \sigma_2^2 - 2\rho\sigma_1\sigma_2$)**
- **σ_d (**SD difference) = 31.22
- Correlation (rho) = 0.5 (moderate variability of outcome)
- N per group 39 (Total N 78)
- After adjusting for 20% Drop out, total N would be 98

Data Collection

Baseline characteristic

1. Age
2. Gender
3. Race
4. BMI
5. Comorbidities
6. Predominant symptoms

7. Food diary (Patient has to record each item in every meal, symptoms, bowel habit daily)

Outcome of interest

Primary outcome

1. Upper gastrointestinal symptoms (Baseline and after run-in phase)
    - PAGI-SYM score (Patient Assessment of Upper Gastrointestinal Disorders Symptoms Questionnaire)

Secondary outcome

1. Quality of life
    - Health-Related Quality of Life: EQ-5D-5L score
    - Patient Health Questionnaire-9, screening for depression: Thai-PHQ score
    - Sleep quality: Pittsburgh Sleep Quality Index (PSQI)
2. Change in body weight: Body weight before-after restriction phase
3. Adverse event
    - Bowel habit change
    - Others
4. FODMAPs intake (% decrease)
5. Response to intervention
6. Compliance to dietary advice

Data Analysis and Statistics

The statistical analysis will be performed using the Statistical Package for the Social Sciences (SPSS) for MAC version 22.0 (SPSS Inc., Chicago IL, USA).

Generalized Estimating Equations (GEE) or linear mixed model will be used for primary and secondary outcome, to compare symptoms and quality of life between two groups over a period of time

It will be considered whether the baseline value of our outcome variable should be adjusted

The proportion of responders will be compared between the low-FODMAP diet group and the traditional dietary advice group using the Chi-square test or Fisher's Exact Test where appropriate.

For descriptive statistics, continuous variables (Age, BMI) will be presented as mean with standard deviation and categorical variables (Gender, race, comorbidities, and etc.) will be presented as frequency and percentages. The Pearson chi-square test or Fisher exact test will be used for

comparison of categorical data. T test or Mann-Whitney U test will be used, where appropriate, to test the significant difference between the two groups. p-values ≤ 0.05 will be considered statistically significant.

Expected or Anticipated Benefit Gain

- To understand the role of low FODMAPs diet in the improvement of functional dyspepsia
- To compare the effectiveness between the traditional dietary advice and low FODMAPs dietary advice in treatment of functional dyspepsia

Challenges

- Participants dropped out or loss of follow-up
- Poor compliance of participants to the diet assigned
- Data collection might be missed

Risk and Investigator's Responsibility

- Risk of adverse events of low FODMAPs diet, such as bowel habit change, nutritional status change
- Investigators will take responsibility to report any adverse events occurred to the participants.

Venue of the Study

- Gastrointestinal unit, Department of internal medicine, Faculty of medicine, chulalongkorn university

References

1. Talley NJ, Ford AC. Functional Dyspepsia. N Engl J Med. 2015;373(19):1853-63.

2.Ford AC, Mahadeva S, Carbone MF, Lacy BE, Talley NJ. Functional dyspepsia. Lancet. 2020;396(10263):1689-702.

3. Ford AC, Marwaha A, Sood R, Moayyedi P. Global prevalence of, and risk factors for, uninvestigated dyspepsia: a meta-analysis. Gut. 2015;64(7):1049-57.

4.Barberio B, Mahadeva S, Black CJ, Savarino EV, Ford AC. Systematic review with meta-analysis: global prevalence of uninvestigated dyspepsia according to the Rome criteria. Aliment Pharmacol Ther. 2020;52(5):762-73.

5.Tack J, Piessevaux H, Coulie B, Caenepeel P, Janssens J. Role of impaired gastric accommodation to a meal in functional dyspepsia. Gastroenterology. 1998;115(6):1346-52.

6. Farré R, Vanheel H, Vanuytsel T, Masaoka T, Törnblom H, Simrén M, et al. In functional dyspepsia, hypersensitivity to postprandial distention correlates with meal-related symptom severity. Gastroenterology. 2013;145(3):566-73.

7. Tack J, Caenepeel P, Fischler B, Piessevaux H, Janssens J. Symptoms associated with hypersensitivity to gastric distention in functional dyspepsia. Gastroenterology. 2001;121(3):526-35.

8. Vandenberghe J, Vos R, Persoons P, Demyttenaere K, Janssens J, Tack J. Dyspeptic patients with visceral hypersensitivity: sensitisation of pain specific or multimodal pathways? Gut. 2005;54(7):914-9.

9.Oshima T. Functional Dyspepsia: Current Understanding and Future Perspective. Digestion. 2024;105(1):26-33.

10. Wauters L, Talley NJ, Walker MM, Tack J, Vanuytsel T. Novel concepts in the pathophysiology and treatment of functional dyspepsia. Gut. 2020;69(3):591-600.

11.Walker MM, Aggarwal KR, Shim LS, Bassan M, Kalantar JS, Weltman MD, et al. Duodenal eosinophilia and early satiety in functional dyspepsia: confirmation of a positive association in an Australian cohort. J Gastroenterol Hepatol. 2014;29(3):474-9.

12.Staley C, Weingarden AR, Khoruts A, Sadowsky MJ. Interaction of gut microbiota with bile acid metabolism and its influence on disease states. Appl Microbiol Biotechnol. 2017;101(1):47-64.

13.Zhong L, Shanahan ER, Raj A, Koloski NA, Fletcher L, Morrison M, et al. Dyspepsia and the microbiome: time to focus on the small intestine. Gut. 2017;66(6):1168-9.

14.Kakiyama G, Pandak WM, Gillevet PM, Hylemon PB, Heuman DM, Daita K, et al. Modulation of the fecal bile acid profile by gut microbiota in cirrhosis. J Hepatol. 2013;58(5):949-55.

15.Pavlidis P, Powell N, Vincent RP, Ehrlich D, Bjarnason I, Hayee B. Systematic review: bile acids and intestinal inflammation-luminal aggressors or regulators of mucosal defence? Aliment Pharmacol Ther. 2015;42(7):802-17.

16.Zheng PY, Feng BS, Oluwole C, Struiksma S, Chen X, Li P, et al. Psychological stress induces eosinophils to produce corticotrophin releasing hormone in the intestine. Gut. 2009;58(11):1473-9.

17. Mertens KL, Kalsbeek A, Soeters MR, Eggink HM. Bile Acid Signaling Pathways from the Enterohepatic Circulation to the Central Nervous System. Front Neurosci. 2017;11:617.

18. Barrett JS. *Extending our knowledge of fermentable, short-chain carbohydrates for managing gastrointestinal symptoms*. J Gastroenterol Hepatol. 2013;28(Suppl 4):8–14.

19. Revicki DA, Rentz AM, Dubois D, et al. *Development and validation of a patient-assessed gastroparesis symptom severity measure: the Gastroparesis Cardinal Symptom Index.* Aliment Pharmacol Ther. 2003;18(1):141–150.

20. Chitapanarux T, Gonlachanvit S, et al. *Validation of the Thai version of the Patient Assessment of Upper Gastrointestinal Symptom Severity Index (PAGI-SYM)*. J Med Assoc Thai. 2011;94(12):1461–1468.

21. Ajamian M, Rosella G, Newnham ED, Biesiekierski JR, Muir JG, Gibson PR. Effect of Gluten Ingestion and FODMAP Restriction on Intestinal Epithelial Integrity in Patients with Irritable Bowel Syndrome and Self-Reported Non-Coeliac Gluten Sensitivity. Mol Nutr Food Res. 2021;65(5):e1901275.

22. Singh P, Grabauskas G, Zhou SY, Gao J, Zhang Y, Owyang C. High FODMAP diet causes barrier loss via lipopolysaccharide-mediated mast cell activation. JCI Insight. 2021;6(22).

23. Dionne J, Ford AC, Yuan Y, Chey WD, Lacy BE, Saito YA, et al. A Systematic Review and Meta-Analysis Evaluating the Efficacy of a Gluten-Free Diet and a Low FODMAPs Diet in Treating Symptoms of Irritable Bowel Syndrome. Am J Gastroenterol. 2018;113(9):1290-300.

24. Potter MDE, Duncanson K, Jones MP, Walker MM, Keely S, Talley NJ. Wheat sensitivity and functional dyspepsia: a pilot, double-blind, randomized, placebo-controlled dietary crossover trial with novel challenge protocol. Nutrients. 2020;12(7):1936.

25. Staudacher HM, Nevin AN, Duff C, Kendall BJ, Holtmann GJ. Epigastric symptom response to low FODMAP dietary advice compared with standard dietetic advice in individuals with functional dyspepsia. Neurogastroenterol Motil. 2021;33(11):e14148.

26. Goyal O, Batta S, Nohria S, Kishore H, Goyal P, Sehgal R, et al. Low fermentable oligosaccharide, disaccharide, monosaccharide, and polyol diet in patients with diarrhea-predominant irritable bowel syndrome: A prospective, randomized trial. J Gastroenterol Hepatol. 2021;36(8):2107-15.

27. Van den Houte K, Broeders B, Tóth J, Routhiaux K, Mariën Z, Van den Bergh J, et al. Outcome of a FODMAP restriction diet with subsequent blinded reintroduction in functional dyspepsia/postprandial distress syndrome. Gut. 2025.

28. Singh P, Chey SW, Nee J, Eswaran S, Lembo A, Chey WD. Is a simplified, less restrictive low FODMAP diet possible? Results from a double-blind, pilot randomized controlled trial. *Clin Gastroenterol Hepatol.* 2025;23(2):362–364. doi:10.1016/j.cgh.2024.04.021.