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Cognitive-Behavioral Therapy Approaches for Functional Dyspepsia: A Systematic Review of Monotherapy and Combination with Drugs

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Objectives: To evaluate the effectiveness and safety of cognitive-behavioral therapy (CBT) for functional dyspepsia (FD), including metacognitive therapy (MCT), dialectical behavior therapy (DBT), and mindfulness-based cognitive therapy (MBCT), applied either as monotherapy or in combination with pharmacological treatments.

Methods: We systematically reviewed randomized controlled trials (RCTs) published since 2010 in English, Chinese, and Korean databases. Eligible studies included adults with FD and compared CBT alone or in combination with drugs against drug monotherapy or usual care. Meta-analysis was conducted when interventions and outcomes were comparable; otherwise, a narrative synthesis was performed. The risk of bias was assessed using the Cochrane tool.

Results: Nine RCTs (n=831) were included. One trial of CBT alone demonstrated improvements in anxiety and dyspeptic symptoms compared to controls. Most trials investigated CBT approaches in conjunction with drugs, yielding greater reductions in anxiety and depression, improved gastrointestinal symptom scores, and enhanced disease-specific quality of life compared to drugs alone; one trial noted benefits lasting for six months. Across the various modalities, MBCT tended to enhance quality of life and mindfulness, MCT was effective in reducing anxiety, and DBT improved emotion regulation and gastrointestinal relief. Adverse events were rare and generally mild. Key limitations included incomplete reporting of allocation concealment and assessor blinding, small sample sizes, single-center designs, and variability in concomitant medications and outcomes.

Conclusions: CBT approaches offer clinically meaningful benefits for FD, both as monotherapy and, more robustly, as adjuncts to pharmacotherapy, with an acceptable safety profile. However, concerns regarding risk of bias and heterogeneity limit certainty. Future research should involve larger, well-designed multicenter RCTs with standardized protocols and long-term follow-up.

Key Words: Functional dyspepsia, Cognitive behavioral therapy, Systematic review.

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I. INTRODUCTION

Functional dyspepsia (FD) is a symptomatic syndrome characterized by chronic, recurrent gastrointestinal symptoms in the absence of organic diseases such as peptic ulcer, gastrointestinal malignancy, gastroesophageal reflux disease, or pancreatobiliary disorders. Its typical features include bothersome postprandial fullness—an uncomfortable sensation as if food remains in the stomach—bothersome early satiation, in which fullness occurs soon after beginning a meal and prevents continued eating, as well as bothersome epigastric pain and bothersome epigastric burning sensation[1].

The pathophysiology of functional dyspepsia is highly complex and cannot be explained by a single mechanism. It is likely that multiple mechanisms act in combination to produce dyspeptic symptoms. Among these, disordered gastric motility and visceral hypersensitivity are the two most important factors for understanding the condition's pathophysiology. In addition, gastric acid, diet, chronic duodenal inflammation, Helicobacter pylori infection, psychosocial factors, and other genetic and environmental influences are understood to affect gastric motor dysfunction and/or visceral hypersensitivity directly or indirectly[2]. Furthermore, psychological factors play an important role in the onset and persistence of functional dyspepsia symptoms. Psychosocial factors, including anxiety, depression, and stress, have been reported to exacerbate visceral hypersensitivity and gastric motility abnormalities in the upper gastrointestinal tract via the brain–gut axis, thereby increasing symptom perception and functional impairment[3].

Among treatments targeting psychological factors, cognitive behavioral therapy (CBT) has emerged as a widely accepted intervention for functional gastrointestinal disorders, contributing to symptom improvement and enhanced quality of life[4].

Recently, clinical trials specifically addressing CBT for FD have been reported, providing accumulating evidence that CBT, in combination with pharmacotherapy (e.g., PPIs, prokinetics), confers significant symptom relief. Structured CBT programs addressing visceral hypersensitivity, anxiety, and dysfunctional cognitions (such as symptom catastrophizing and avoidance behaviors) have been shown to improve core symptoms—including postprandial discomfort and epigastric pain or burning sensation—as well as patient-reported functional impairment[5].

CBT has evolved beyond its traditional form into so-called "third-wave" approaches, such as dialectical behavior therapy (DBT) and mindfulness-based cognitive therapy (MBCT), which incorporate acceptance, mindfulness, and emotion regulation strategies into the CBT[6]. DBT is one type of CBT that synthesizes CBT change strategies with acceptance-based strategies which assist the patient in gaining greater awareness and acceptance of his/her current situation[7,8]. MBCT is a form of CBT that combines CBT strategies with mindfulness- and acceptance-based practices. It integrates cognitive techniques, such as identifying and modifying maladaptive thoughts, with structured training in nonjudgmental present-moment awareness and acceptance[9]. Through these mechanisms, MBCT reduces rumination and cognitive reactivity, strengthens emotion regulation and decentering—the ability to observe thoughts and feelings as transient mental events—and thereby yields clinical benefits, including symptom relief, lower relapse risk, and improved functioning[10]. CBT has evolved in contemporary practice to also encompass Metacognitive Therapy (MCT). MCT is a distinct model that targets metacognitive beliefs and attentional control as core mechanisms, thereby reducing worry and rumination[11].

FD is influenced by psychological factors, and psychotherapeutic interventions are therefore expected to be beneficial. However, studies applying psychotherapy to FD in Korea remain limited. Previous systematic reviews have primarily focused on pharmacological therapies or broad categories of psychotherapeutic interventions in functional gastrointestinal disorders, but a focused synthesis of CBT approaches (MCT, DBT, MBCT) in FD is still lacking. Therefore, this study aims to address this gap by systematically reviewing randomized controlled trials of CBT-based interventions for FD, with particular attention to both monotherapy and combined approaches with pharmacological treatments.

II. METHODS

The review protocol was developed in advance but was not registered in PROSPERO or any other public registry, as registration was not a formal requirement for the target domestic journal at the time of study initiation. The protocol document is available from the authors upon reasonable request.

1. Database selection and literature search

Clinical studies published between January 2010 and July 2025 were searched using the following databases: PubMed (pubmed.ncbi.nlm.nih.gov) and ScienceDirect (www.sciencedirect.com) for English-language sources; CNKI (China National Knowledge Infrastructure, www.cnki.net) for Chinese-language sources; and OASIS (oasis.kiom.re.kr), DBPia (www.dbpia.co.kr), RISS (www.riss.kr), and the Korean Traditional Knowledge Portal (www.koreantk.com) for Korean-language sources. The search was conducted in July 2025.

The keywords used were as follows: for English databases: “Functional Dyspepsia”, “Gastroduodenal disorder”, “Cognitive Behavioral Therapy”, “CBT”, “Mindfulness based cognitive therapy”, “MBCT”, and “psychotherapeutic treatment”; for CNKI: “功能性消化不良”, “功能性胃肠障碍”, “功能性胃肠疾病”, “认知行为治疗”, “认知行为疗法”, and “正念认知疗法”; for Korean databases: “기능성소화불량” and “인지행동치료”.

The detailed search strategies for each database are presented in Table 1.

2. Inclusion and exclusion criteria

In this systematic review, we included RCTs targeting patients diagnosed with FD. Non-RCTs, observational studies, case reports were excluded. There were no restrictions on the participants’ age, sex, or other demographic characteristics. Given the variety of psychological therapies classified under CBT, this study included all relevant CBT modalities such as CBT, MCT, DBT, and MBCT. These interventions could be administered alone or combined with pharmacotherapy. The control group was not restricted to specific conditions.

3. Study selection and data analysis

1) Literature screening and selection

Two reviewers (GTC and BSK) independently screened titles/abstracts and full texts against the eligibility criteria. Discrepancies were resolved through discussion, and if consensus was not reached, a third reviewer (KEL) adjudicated.

All retrieved studies were initially screened based on titles and abstracts. Automation tools were not used. Full-text articles of potentially eligible studies were then thoroughly reviewed to determine final inclusion. In the case of Chinese language studies, full texts were examined when it was difficult to assess eligibility through titles and abstracts alone.

2) Data extraction and analysis

Data extraction was performed independently by

Table 1. Search Strategies

Database	Search strategy
PubMed	#1 Functional dyspepsia [title/abstract] #2 Gastroduodenal disorder [title/abstract] #3 #1 OR #2 #4 Cognitive behavioral therapy [title/abstract] #5 CBt [title/abstract] #6 Mindfulness based cognitive therapy [title/abstract] #7 MBCT [title/abstract] #8 Psychotherapeutic treatment [title/abstract] #9 #4 OR #5 OR #6 OR #7 OR #8 #10 #3 AND #9
ScienceDirect	#1 Functional dyspepsia [title/abstract/keyword] #2 Gastroduodenal disorder [title/abstract/keyword] #3 #1 OR #2 #4 (Cognitive Behavioral Therapy OR CBT) #5 (Mindfulness based cognitive therapy OR MBCT) #6 Psychotherapeutic treatment #7 #4 OR #5 OR #6 #8 #3 AND #7
CNKI	"功能性消化不良" OR "功能性胃肠障碍" OR "功能性胃肠疾病" AND "认知行为治疗" OR "认知行为疗法" OR "正念认知疗法" OR "心理治疗"
Korean databases	"기능성소화불량" [title/abstract] AND "인지행동치료" [title/abstract] *Classified mainly according to interventions targeting cognitive behavioral therapy and psychotherapeutic treatment after retrieval.*

two reviewers using a piloted extraction form. Any disagreements were resolved by consensus or consultation with a third reviewer.

Full texts of the selected studies were reviewed to extract the following information: study design, number of participants in the intervention and control groups, type of intervention and control treatments, outcome measures, and treatment effects. Based on the extracted information, the characteristics and findings of each study were analyzed.

For risk of bias assessment, the Cochrane Risk of Bias (RoB) tool was applied according to the Cochrane Handbook for Systematic Reviews of Interventions. Analyses were conducted on available case data[12].

Publication bias was planned to be assessed visually using funnel plots if at least 10 studies were available for a given outcome. Because fewer than 10 studies were ultimately included per outcome, formal assessment of publication bias was not feasible.

Given the limited number of comparable studies and the substantial heterogeneity observed, we did not perform a formal GRADE assessment. Instead, the certainty of evidence was judged qualitatively.

4. Data extraction and synthesis

Meta-analysis was conducted for studies that shared comparable interventions and primary outcome measures. For studies not suitable for meta-analysis, narrative synthesis was performed. For dichotomous variable, relative risk (RR) with a 95% confidence interval (CI) was calculated. For continuous variable, standardized mean difference (SMD) with 95% CI was used. Calculations were performed using Review Manager (RevMan) version 5.4 software.

To assess heterogeneity among studies, the chi-square test ($p<0.10$) and Higgins I2 statistic ($I2>50\%$) were used. When heterogeneity was detected, a random effects model was applied for data synthesis. Otherwise, a fixed-effects model was used.

III. RESULTS

1. Literature selection

A total of 267 records were identified through database searches. After removal of 9 duplicates and 15 records excluded for other reasons, 243 unique records were screened. Of these, 230 were excluded based on title/abstract. 13 full-text articles were assessed for eligibility, and 4 were excluded. Finally, 9 RCTs met the inclusion criteria and were included in this review. The study selection process is illustrated in the PRISMA 2020 flow diagram (Fig. 1).

2. Literature analysis

1) Overview of literature

A total of 9 RCTs were included in this study, all of which were conducted in Iran, Singapore and China. The intervention groups mostly involved combined intervention including various forms of CBT; MCT, DBT, MBCT and drug therapy (PPIs; Omeprazole, Pantoprazole, Rabeprazole, H2 Blockers, Prokinetic Agents; Domperidone, Mosapride, Antidepressants; Nortriptyline, Mirtazapine, Sertraline, Calming herbs; the specific formulations were not specified). Depending on the study, CBT and drug therapy combined, or each was applied alone. The control groups included drug therapy or no intervention. Some studies did not specify the names of the drugs. The data analysis results are presented in Table 2. The abbreviations of primary outcome measures are presented in Table 3.

2) Risk of bias assessment

The Risk of bias was assessed using the Cochrane RoB tool (Fig. 2, 3). Regarding random sequence generation and allocation concealment, only two studies, Orive (2015)[13] and Teh (2021)[14], described adequate

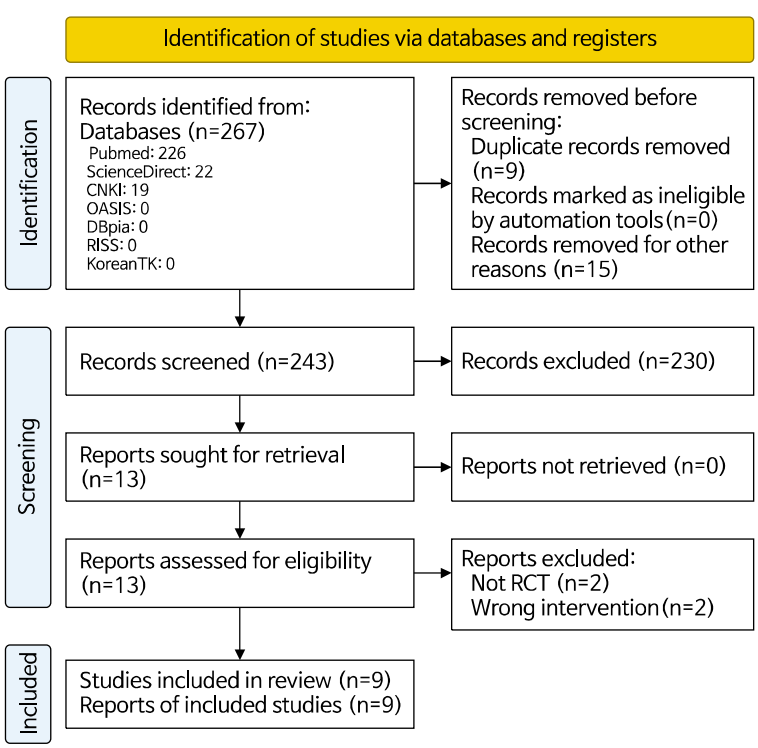


Fig. 1. Flow chart of literature selection.

Table 2. Key Data of Studies

First author (year)	Intervention/control (A/B)	Duration	Evaluation index	Result
Batebi (2020)	A: MCT (n=17) B: Nortriptyline (n=16) C: Omeprazole+Domperidone (n=15)	10 weeks	1. HAMA 2. HAMD 3. DERS	1. A>B ($p<0.001$), B>C ($p<0.01$), A>C ($p<0.001$) 2. A>B ($p>0.05$), B>C ($p<0.001$), A>C ($p<0.001$) 3. A≈B≈C ($p>0.05$)
Orive (2015)	A: CBT+PPIs+H2 blockers+Prokinetic (n=60) B: PPIs+H2 blockers+Prokinetic (n=72)	10 weeks	1. GDSS 2. DRHS 1) Severity of symptom 2) Pain intensity 3) Pain disability 4) Satisfaction with dyspepsia health 3. HADS 1) Depression 2) Anxiety 4. SCI	1. A>B ($p<0.01$) 2. 1) A>B ($p<0.05$) 2) A>B ($p<0.05$) 3) A>B ($p<0.05$) 4) A>B ($p<0.01$) 3. 1) A≈B ($p>0.05$) 2) A>B ($p<0.05$) 4. A>B ($p<0.01$)
Tavakoli (2020)	A: DBT+Pantoprazole (n=20) B: Pantoprazole+Sertraline (n=20) C: Pantoprazole (n=20)	8 weeks	1. BAI 2. PAGI-SYM	1. A≈B ($P>0.05$), A>C ($p<0.001$), B>C ($p<0.01$) 2. A>C>B ($p<0.001$)
Teh (2021)	A: MBCT+Rabeprazole+Mosapride (n=15) B: Rabeprazole+Mosapride (n=13)	8 weeks	1. SCA-FD 2. SCA-GH 3. SF-NDI 4. DASS-21 1) Total 2) Depression 3) Anxiety 4) Stress 5. EuroQoL-VAS	1. A>B (trend, $p=0.063$) 2. A≈B ($p>0.05$) 3. A>B ($p<0.05$) 4. 1)~4) A≈B ($p>0.05$) 5. A≈B ($p>0.05$)
Wu (2024)	A: MBCT+Rabeprazole+Mosapride (n=34) B: Rabeprazole+Mosapride (n=40)	8 weeks	1. GOSS 2. GIS 3. FFMQ 4. SAS 5. SDS 6. PSQI 7. SCL-90 8. Gastric emptying status	1. A>B ($p<0.05$) 2. A>B ($p<0.05$) 3. A>B ($p<0.05$) 4. A>B ($p<0.001$) 5. A>B ($p<0.01$) 6. A>B ($p<0.001$) 7. A>B ($p<0.01$) 8. A≈B ($p>0.05$)
Wang (2020)	A: CBT+Domperidone+Sertraline (n=123) B: Domperidone+Sertraline (n=133)	12 weeks	1. Total Symptom Score (Epigastric pain, Burning sensation, Abdominal distension, Early satiety, Belching) 2. SAS 3. SDS	1. A>B ($p<0.05$) 2. A>B ($p<0.05$) 3. A>B ($p<0.05$)
Zhou (2012)	A: CBT+Prokinetic+PPIs+Calming herbs (n=27) B: Prokinetic+PPIs+Calming herbs (n=26)	10 weeks	1. Total Symptom Score (Epigastric pain, Burning sensation, Abdominal distension, Early satiety, Belching) 2. SAS 3. SDS 4. Recurrence rate	1. A>B ($p<0.01$) 2. A>B ($p<0.01$) 3. A>B ($p<0.01$) 4. A>B ($p<0.01$)
Xin (2024)	A: CBT+Mirtazapine+Domperidone (n=45) B: Domperidone (n=45)	8 weeks	1. Efficacy rate 2. SCL-90 1) Somatization 2) Obsessive-Compulsive 3) Interpersonal Sensitivity 4) Depression 5) Anxiety 6) Hostility 7) Phobic Anxiety 8) Paranoid Ideation	1. A>B ($p<0.05$) 2. 1) A>B ($p<0.05$) 2) A>B ($p<0.01$) 3) A>B ($p<0.05$) 4) A>B ($p<0.01$) 5) A>B ($p<0.01$) 6) A>B ($p<0.05$) 7) A>B ($p<0.01$) 8) A>B ($p<0.001$)

Table 2. Continued 1

First author (year)	Intervention/control (A/B)	Duration	Evaluation index	Result
			3. GIS	3.
			1) Nausea	1) A>B ($p<0.001$)
			2) Vomiting	2) A>B ($p<0.05$)
			3) Abdominal Distension	3) A>B ($p<0.001$)
			4) Epigastric Pain	4) A>B ($p<0.05$)
			5) Early Satiety	5) A>B ($p<0.001$)
			6) Heartburn	6) A>B ($p<0.001$)
			7) Stomach Discomfort	7) A>B ($p<0.001$)
			8) Poor Appetite	8) A>B ($p<0.001$)
Zeng (2024)	A: CBT+Domperidone (n=45) B: Domperidone (n=45)	28 weeks	1. Efficacy rate	1) A≈B ($p>0.05$)
			1. SDS	2. A>B ($p<0.001$)
			2. SAS	3. A>B ($p<0.001$)
			3. GIQLI	4. A>B ($p<0.001$)
			4. GSRS	5. A>B ($p<0.001$)
			5. HAMA	6. A>B ($p<0.001$)
			6. HAMD	7. A>B ($p<0.05$)
			7. Complication Rate	8. A>B ($p<0.01$)
			8. Intervention Satisfaction Rate	

BAI: Beck Anxiety Inventory, DASS-21: Depression Anxiety Stress Scale–21 items, DERS: Difficulties in Emotion Regulation Scale, DRHS: Dyspepsia-Related Health Scale, EuroQol-VAS: EuroQol Visual Analog Scale, FFMQ: Five Facet Mindfulness Questionnaire, GDSS: Glasgow Dyspepsia Severity Score, GIS: Gastrointestinal Symptom Score, GIQLI: Gastrointestinal Quality of Life Index, GOSS: Global Overall Symptom Scale, GSRS: Gastrointestinal Symptom Rating Scale, HADS: Hospital Anxiety and Depression Scale, HAMA: Hamilton Anxiety Rating Scale, HAMD: Hamilton Depression Rating Scale, PAGI-SYM: Patient Assessment of Upper Gastrointestinal Symptom Severity Index, PSQI: Pittsburgh Sleep Quality Index, SAS: Zung Self-Rating Anxiety Scale, SCA-FD: Subjective Clinical Assessment of Functional Dyspepsia Symptoms, SCA-GH: Subjective Clinical Assessment of General Health, SCI: Subjective Clinical Improvement, SCL-90: Symptom Checklist-90, SDS: Zung Self-Rating Depression Scale, SF-NDI: 10-item Short Form of the Nepean Dyspepsia Index.

Table 3. Abbreviations of Outcome Measures

Abbreviation	Full term
HAMA	Hamilton Anxiety Rating Scale
HAMD	Hamilton Depression Rating Scale
DERS	Difficulties in Emotion Regulation Scale
PPIs	Proton Pump Inhibitors
GDSS	Glasgow Dyspepsia Severity Score
DRHS	Dyspepsia Related Health Scale
HADS	Hospital Anxiety and Depression Scale
SCI	Subjective Clinical Improvement
PAGI-SYM	Patient Assessment of Gastrointestinal Symptom Severity Index
SCA-FD	Subjective Clinical Assessment of Functional Dyspepsia Symptoms
SCA-GH	Subjective Clinical Assessment of General Health
DASS-21	Depression, Anxiety and Stress Scale–21 items
EuroQoL-VAS	EuroQoL-Visual Analog Scale
SF-NDI	10-item Short Form of Nepean Dyspepsia Index
GOSS	Global Overall Symptom Scale
GIS	Gastrointestinal Symptom Score
FFMQ	Five Facet Mindfulness Questionnaire
SAS	Zung Anxiety Self Rating Scale
SDS	Zung Depression Self Rating Scale
PSQI	Pittsburgh Sleep Quality Index
SCL-90	Symptom Checklist-90
GSRS	Gastrointestinal Symptom Rating Scale
GIQLI	Gastrointestinal Quality of Life Index

procedures and were rated as low risk.

Blinding of participants and personnel was infeasible due to the nature of psychological interventions, and most trials did not report assessor blinding; thus, performance and detection bias were rated as high risk across the majority of studies.

Incomplete outcome data were adequately addressed in some studies, such as Orive (2015) and Xin (2024)[15], but imbalanced attrition or unclear handling of missing data in others, including Batebi (2020)[16] and Wu (2024)[17], led to high or unclear ratings.

Selective reporting was judged low risk only in Orive (2015), which provided trial registration, whereas all other studies were rated as unclear.

Other potential sources of bias included small sample sizes, single-center designs, and lack of fidelity monitoring, leading to mostly unclear or high risk ratings.

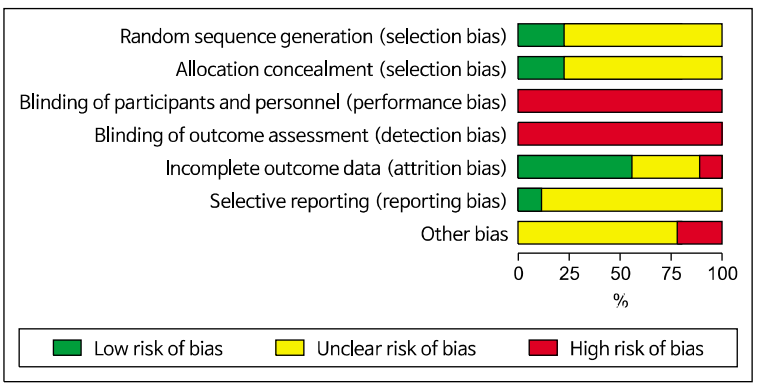


Fig. 2. Risk of bias graph.

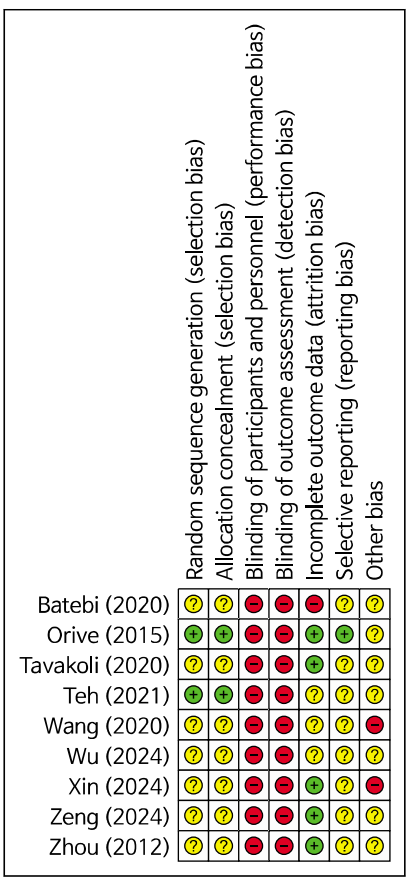


Fig. 3. Risk of bias summary.
(+): Low risk of bias. (-): High risk of bias. (?): Unclear of bias.

3) Evaluation index

Among the 9 included studies, a total of 831 participants were evaluated using a range of outcome measures. Anxiety and depression were the most frequently assessed domains, with HAMA and HAMD reported in three studies each, HADS in two studies, SAS and SDS in two studies each, and BAI, DASS-21, SCL-90, DERS, FFMQ, and PSQI applied in one study each. Gastrointestinal symptoms were evaluated in seven studies using instruments such as GDSS (1 study), DRHS (1 study), SCI (1 study), PAGI-SYM (1 study), SCA-FD (1 study), SCA-GH (1 study), GIS (2 studies), Total Symptom Score (2 studies), GOSS (1 study), GSRS (1 study), and gastric emptying status (1 study). Quality of life measures were reported in three studies, including EuroQoL-VAS, SF-NDI, and GIQLI. Clinical outcomes such as efficacy rate, recurrence rate, complication rate, and intervention satisfaction rate were evaluated in one to two studies each.

4) Interventions and participants

Among the 9 included trials, only one investigated monotherapy (MCT, 10 weeks), while the others examined CBT approaches combined with pharmacotherapy. The combined interventions included DBT plus pantoprazole (8 weeks), MBCT plus rabeprazole and mosapride (8 weeks, 2 trials), and CBT combined PPIs (omeprazole, pantoprazole, rabeprazole), H2 blockers, prokinetic agents (domperidone, mosapride), or antidepressants (nortriptyline, mirtazapine, sertra-

line) for 10~12 weeks. Other studies applied CBT plus prokinetic agents/PPIs with Calming herbs (10 weeks) or CBT plus domperidone (28 weeks).

As summarized in Table 2, all interventions lasted at least 8 weeks (range: 8~28 weeks), and most trials reported clinically meaningful improvements at the end of the treatment period.

Most of the included RCTs enrolled adults with FD diagnosed by Rome III or IV criteria (e.g., Teh 2021; Wu 2024; Tavakoli 2020; Xin 2024; Batebi 2020). Organic disease was generally excluded by upper GI endoscopy or, in some cases, additional imaging (Batebi 2020; Tavakoli 2020; Teh 2021; Wu 2024; Zeng 2024). Several trials required chronic symptoms for ≥3~6 months (Teh 2021; Wu 2024), while others specifically enrolled patients with comorbid anxiety/depression (Wang 2020; Batebi 2020). Additional conditions included stable medication use (Teh 2021) or prior H. pylori eradication (Wu 2024). Where reported, both sexes were included without significant baseline differences (Tavakoli 2020; Wu 2024).

5) Treatment effects

A total of 9 RCTs were analyzed. Meta-analysis was conducted for studies with comparable intervention methods and primary outcome measures; other studies were synthesized descriptively.

In three-arm trials, Group A indicates the intervention, Group B the active comparison, and Group C the control. In two-arm trials, Group A is the intervention and Group B the control.

Raw data for each study, including pre- and post-treatment values, effect sizes, and p-values, are summarized separately in Table 4.

(1) CBT approaches alone

One RCTs evaluated CBT variants as stand-alone interventions.

Batebi (2020): Group A demonstrated significantly greater reductions in anxiety (HAMA) and depression (HAMD) compared with Group B and Group C. Improvements in DERS were observed only within Group A but did not reach between-group significance.

(2) Add-on effects of CBT approaches combined with drugs

Most included trials investigated CBT approaches combined with pharmacotherapy.

① Psychological outcomes

Anxiety (SAS): Three studies (Wang 2020[18]; Wu 2024; Zhou 2012[19]) consistently favored Group A. Meta-analysis showed a significant effect (SMD=0.75, 95% CI: 0.19~1.30, p=0.009) with substantial heterogeneity (I^2=71%) (Fig. 4).

Depression (SDS): The same three studies favored Group A. Pooled analysis confirmed a robust effect (SMD=0.65, 95% CI: 0.35~0.95, p<0.0001) with very low heterogeneity (I^2=5%) (Fig. 5).

② Efficacy rate

Xin (2024) and Zeng (2024)[20] both reported higher response rates in Group A, but statistical significance was reached only in Xin (2024). Pooled analysis indicated a non-significant trend (RR=1.13, 95% CI: 0.99~1.30, p=0.07; I^2=55%) (Fig. 6).

③ Quality of life

MBCT trials (Teh 2021; Wu 2024; Zeng 2024) reported consistent improvements on disease-specific instruments (SF-NDI, GIQLI), whereas results for the generic EuroQoL-VAS were mixed.

④ Gastrointestinal symptoms

Multiple trials demonstrated significant reductions in GDSS, GSRS, PAGI-SYM, GIS, and Total Symptom Scores across treatment durations ranging from 8 to 28 weeks. Orive (2015) additionally reported sustained improvements at 6-month follow-up (SCI).

⑤ Other psychological indices

Broader measures such as HADS, BAI, DASS-21, and SCL-90 also improved in Group A, with additional benefits noted for mindfulness (FFMQ) and

Table 4. Raw Data Summary Table

Study (year)	Outcome	Group A (pre→post)	Group B (pre→post)	Group C (pre→post)	Pairwise p-values	Notes
Batebi (2020)	HAMA	32.1±8.9→ 14.1±6.1	34.7±6.6→ 23.6±7.6	35.6±6.9→ 36.1±6.5	A>B (p<0.001) B>C (p=0.001) A>C (p<0.001)	
	HAMD	26.5±6.5→ 14.3±3.7	24.7±5.2→ 19.1±5.6	31.1±5.3→ 32.2±5.9	A>B (p=0.146) B>C (p<0.001) A>C (p<0.001)	
	DERS	132.1±18.0→ 79.4±25.8	115.6±24.4→ 106.1±24.7	105.7±14.7→ 107.2±17.3	A≈B≈C	
Orive (2015)	GDSS	11.9±3.5→ 5.8±3.8	11.4±2.7→ 7.8±4.0	-	A>B (p<0.0001)	
	DRHS – Severity	61.1±19.2→ 73.7±16.8	60.0±15.8→ 65.3±17.6	-	A>B (p=0.0013)	
	DRHS – Pain intensity	41.9±23.4→ 65.9±20.1	44.0±22.5→ 56.9±27.0	-	A>B (p=0.0022)	
	DRHS – Pain disability	54.7±29.0→ 79.3±22.1	57.4±26.0→ 71.8±26.6	-	A>B (p=0.0129)	
	DRHS – Satisfaction	36.4±20.1→ 61.1±23.8	35.0±21.5→ 47.4±24.6	-	A>B (p=0.0052)	
	HADS-A	10.1±2.7→ 9.5±3.0	9.2±2.2→ 9.6±2.6	-	A>B (p=0.0437)	
	HADS-D	9.8±2.1→ 9.0±1.6	9.6±1.7→ 11.6±6.0	-	A>B (p=0.0668)	
	SCI 6 mo Follow-up	18/29 (62.1%)	13/35 (37.1%)	-	p<0.01	
Tavakoli (2020)	BAI	20.6±6.4→ 14.9±5.2	21.1±6.4→ 13.8±5.1	18.9±5.3→ 16.3±5.3	A≈B (p>0.05) A>C (p<0.001) B>C (p<0.01)	
	PAGI-SYM	46.4±10.9→ 31.0±10.8	47.7±10.1→ 43.8±9.4	42.8±10.5→ 35.0±9.2	A>C>B (p<0.001)	
Teh (2021)	SF-NDI (Δ)	-8.8±7.5	-0.7±7.2	-	A>B (p=0.018)	Only change scores reported
	DASS-21 total (Δ)	-19.8±29.5	-5.5±6.6	-	A>B (p=0.130)	Only change scores reported
Wu (2024)	GOSS	22.2±6.7→ 14.8±3.3	19.8±6.0→ 17.2±5.1	-	A>B (p=0.021)	
	GIS	17.9±6.4→ 11.2±4.4	16.0±6.3→ 14.1±5.4	-	A>B (p=0.015)	
	FFMQ	127.9±16.1→ 141.7±16.8	128.4±12.2→ 130.6±9.1	-	A>B (p=0.001)	
	SAS	47.9±10.7→ 36.4±6.9	47.5±9.7→ 44.2±9.7	-	A>B (p<0.001)	
	SDS	49.2±9.0→ 41.3±4.1	48.7±7.9→ 44.7±5.8	-	A>B (p=0.007)	
	PSQI	15.9±8.5→ 7.9±3.1	15.5±6.0→ 12.7±5.4	-	A>B (p<0.001)	
	SCL-90 total	144.8±36.2→ 117.8±20.5	147.6±39.7→ 134.1±27.8	-	A>B (p=0.005)	
	Gastric emptying	92.9% effective	88.5% effective	-	p=0.657	
Wang (2020)	SAS	52.7±8.7→ 47.0±7.9	53.1±8.5→ 49.8±7.0	-	A>B (p<0.001)	
	SDS	55.4±7.9→ 48.9±7.8	55.7±7.4→ 51.8±7.3	-	A>B (p<0.001)	
	Symptom score	10.1±1.4→ 4.3±1.4	9.9±1.4→ 6.7±1.4	-	A>B (p<0.001)	

Table 4. Continued 1

Study (year)	Outcome	Group A (pre→post)	Group B (pre→post)	Group C (pre→post)	Pairwise p-values	Notes
Zhou (2012)	SAS (⊿)	-10.1±1.7	-8.8±2.1	-	A>B (p=0.010)	Only change scores reported
	SDS (⊿)	-23.1±2.8	-19.9±4.6	-	A>B (p=0.010)	Only change scores reported
	Symptom score (⊿)	-4.9±2.9	-4.2±2.7	-	A>B (p=0.010)	Only change scores reported
	Recurrence 12 mo	3/27 (11.1%)	7/26 (26.9%)	-	p<0.01	
Xin (2024)	GIS—Nausea	2.1±1.0→ 1.1±0.2	2.1±1.0→ 1.2±0.1	-	A>B (p<0.001)	
	GIS—Vomiting	1.3±0.2→ 0.6±0.8	1.2±0.2→ 0.9±0.5	-	A>B (p=0.029)	
	GIS—Abdominal distension	1.9±1.3→ 0.8±0.4	1.9±1.3→ 1.1±0.2	-	A>B (p<0.001)	
	GIS—Epigastric pain	1.4±1.4→ 0.4±0.8	1.4±1.4→ 0.9±1.1	-	A>B (p=0.019)	
	GIS—Early satiety	2.0±0.9→ 0.9±0.1	2.0±0.9→ 1.1±0.2	-	A>B (p<0.001)	
	GIS—Heartburn	0.9±1.3→ 0.4±0.1	1.3±1.0→ 0.6±0.2	-	A>B (p<0.001)	
	GIS—Stomach discomfort	2.4±1.2→ 0.7±0.2	2.5±1.0→ 0.9±0.2	-	A>B (p<0.001)	
	GIS—Poor appetite	2.0±1.1→ 0.9±0.1	2.0±1.1→ 1.1±0.2	-	A>B (p<0.001)	
	SCL-90 Anxiety	1.9±0.8→ 1.4±0.3	1.8±0.8→ 1.6±0.3	-	A>B (p=0.005)	
	Efficacy rate	44/45 (97.8%)	36/45 (80.0%)	-	p<0.05	
Zeng (2024)	HAMA	23.1±4.5→ 12.6±3.3	23.4±4.1→ 15.8±3.7	-	A>B (p<0.001)	
	HAMD	21.7±3.9→ 10.5±3.6	21.5±3.7→ 13.7±3.9	-	A>B (p<0.001)	
	SAS	53.4±3.9→ 24.6±4.0	53.8±3.4→ 35.3±4.3	-	A>B (p<0.001)	
	SDS	60.8±4.7→ 28.3±5.0	60.9±4.6→ 36.8±5.0	-	A>B (p<0.001)	
	GIQLI	81.2±6.5→ 116.5±6.2	81.2±7.0→ 90.7±6.7	-	A>B (p<0.001)	
	GSRS	15.5±1.9→ 4.6±0.4	15.6±2.0→ 9.5±1.3	-	A>B (p<0.001)	
	Efficacy rate	44/45 (97.8%)	41/45 (91.1%)	-	p>0.05	
	Complications	2/45 (4.4%)	8/45 (17.8%)	-	p=0.044	
	Satisfaction	44/45 (97.8%)	38/45 (84.4%)	-	p=0.001	

Values are presented as mean±standard deviation (SD) or number (%).
BAI: Beck Anxiety Inventory, DASS-21: Depression Anxiety Stress Scale–21 items, DERS: Difficulties in Emotion Regulation Scale, DRHS: Dyspepsia-Related Health Scale, EuroQol-VAS: EuroQol Visual Analog Scale, FFMQ: Five Facet Mindfulness Questionnaire, GDSS: Glasgow Dyspepsia Severity Score, GIS: Gastrointestinal Symptom Score, GIQLI: Gastrointestinal Quality of Life Index, GOSS: Global Overall Symptom Scale, GSRS: Gastrointestinal Symptom Rating Scale, HADS: Hospital Anxiety and Depression Scale, HAMA: Hamilton Anxiety Rating Scale, HAMD: Hamilton Depression Rating Scale, PAGI-SYM: Patient Assessment of Upper Gastrointestinal Symptom Severity Index, PSQI: Pittsburgh Sleep Quality Index, SAS: Zung Self-Rating Anxiety Scale, SCA-FD: Subjective Clinical Assessment of Functional Dyspepsia Symptoms, SCA-GH: Subjective Clinical Assessment of General Health, SCI: Subjective Clinical Improvement, SCL-90: Symptom Checklist-90, SDS: Zung Self-Rating Depression Scale, SF-NDI: 10-item Short Form of the Nepean Dyspepsia Index.

sleep quality (PSQI) where assessed.

(3) Safety and tolerability

Safety reporting was limited across trials. Where described, adverse events were generally mild or comparable between groups. Zeng (2024) observed a lower complication rate in Group A compared to Group B (4.4% vs 17.8%). No serious adverse events were reported.

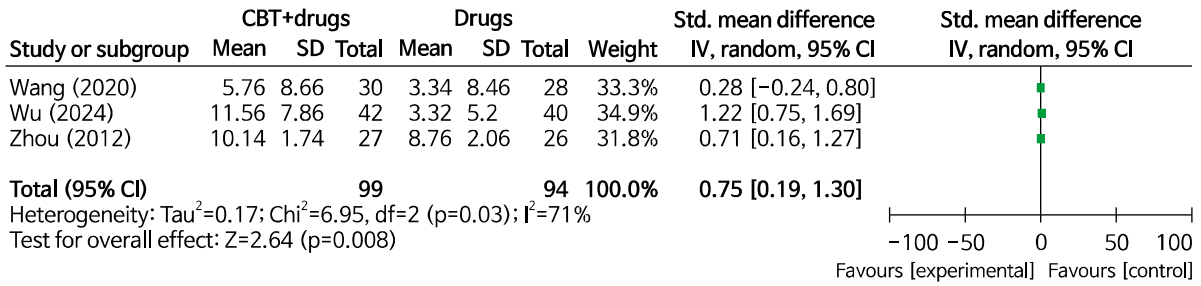


Fig. 4. CBT approaches+Drugs vs. Drugs in SAS scores.
IV, random, 95% CI. Heterogeneity: I^2=12%, p=0.28; overall effect: Z=3.05, p=0.002.

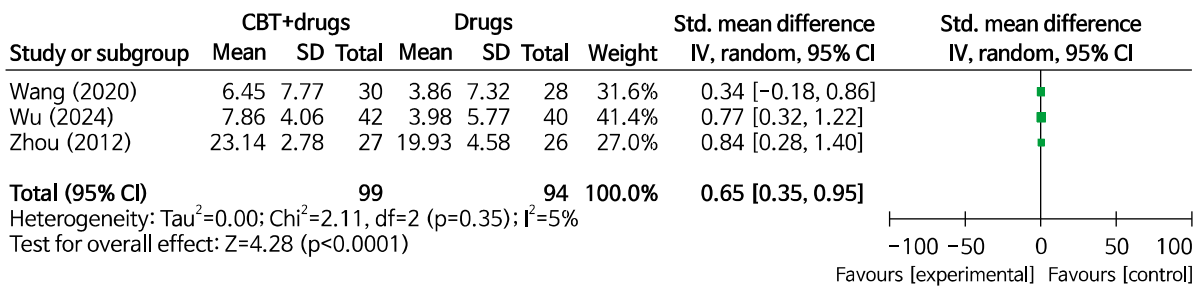


Fig. 5. CBT approaches+Drugs vs. Drugs in SDS scores.
IV, random, 95% CI. Heterogeneity: I^2=9%, p=0.31; overall effect: Z=2.87, p=0.004.

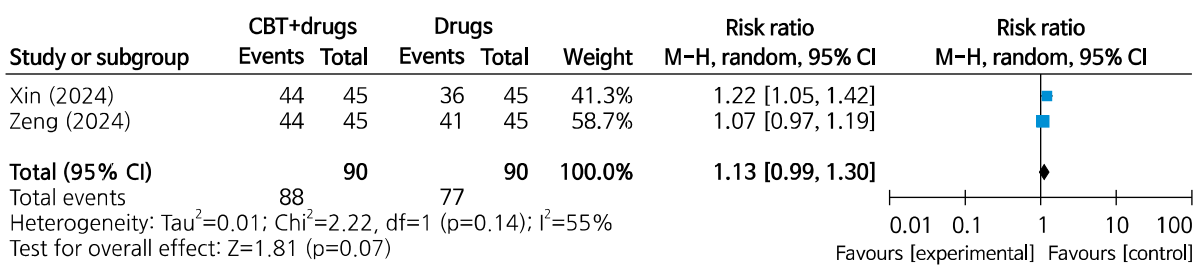


Fig. 6. CBT approaches+Drugs vs. Drugs in efficacy rate.
M-H, random, 95% CI. Heterogeneity: I^2=0%, p=0.77; overall effect: Z=2.22, p=0.026.

IV. DISCUSSION

FD is a common functional gastrointestinal disorder caused by a combination of gastrointestinal motility abnormalities, visceral hypersensitivity, and psychological factors[21]. Despite standard treatment, many patients continue to experience symptoms, highlighting the need for complementary therapeutic strategies beyond pharmacological treatment[22]. Many patients with FD continue to experience symptoms despite conventional pharmacological treatment, highlighting the limitations of drug monotherapy[23]. In particular, FD is closely associated with psychological factors such as anxiety, depression, and stress[24], making it difficult to expect sufficient improvement with medication alone. Given the close association of FD symptoms with anxiety, depression, and stress, these diverse CBT approaches can serve as valuable therapeutic strategies in the integrated management of the disorder.

CBT aims to regulate emotional and physical symptoms by helping the therapist and patient collaboratively identify problematic thoughts and behavioral patterns and modify them. Through various techniques, including cognitive restructuring, behavioral experiments, self-monitoring, relaxation training, and exposure, patients are guided to practice continuous self-regulation in their daily lives[25]. This traditional concept of CBT has subsequently expanded into 'CBT approaches', such as MCT, DBT, and MBCT. These approaches share the basic principles of cognitive and behavioral modification, but at the same time integrate new mechanisms such as mindfulness, acceptance, and emotion regulation, with the goal of alleviating symptoms and improving quality of life[6]. Since FD symptoms are closely related to anxiety, depression, and stress, these diverse CBT approaches can serve as useful therapeutic strategies in the integrated management of the disorder.

In the included RCTs, Group A generally referred to CBT approaches (alone or combined with pharmacotherapy), whereas Group B referred to drug monotherapy or usual care. This framework helps interpret the comparative effects across trials.

This systematic review synthesized 9 RCTs evaluating CBT approaches for FD. Both stand-alone interventions and adjunctive CBT approaches combined with drugs demonstrated significant improvements in anxiety, depression, gastrointestinal symptoms, and disease-specific quality of life compared with controls. In particular, trials MCT alone (Batebi (2020)) reported meaningful benefits in anxiety and dyspeptic symptoms, although small sample sizes and methodological shortcomings temper certainty. Multiple studies demonstrated that CBT approaches combined with pharmacological therapy (e.g., Wang (2020), Zhou (2012), Xin (2024), Zeng (2024)) provided greater improvements than pharmacotherapy alone, supporting the utility of CBT approaches as effective adjunctive interventions. Orive (2015) further suggested durability of benefit at six-month follow-up. Across modalities, MBCT was particularly beneficial for quality of life and mindfulness (Teh (2021), Wu (2024)), MCT showed pronounced effects in anxiety reduction (Batebi (2020)), and DBT contributed to improvements in emotion regulation alongside gastrointestinal relief (Tavakoli (2020)). These findings support the need for tailored strategies according to patients' psychological and symptom profiles.

Risk of bias was variable across included studies. Only two trials, Orive (2015) and Teh (2021), adequately reported random sequence generation and allocation concealment and were rated as low risk. Blinding of participants and personnel was not feasible given the psychological nature of the intervention, and most trials did not report assessor blinding, resulting in high performance and detection bias. Incomplete outcome data were adequately handled in some studies through ITT analyses or negligible dropout (Orive (2015), Xin (2024)), whereas others showed imbalanced attrition or unclear handling (Batebi (2020), Wu (2024)), resulting in unclear or high attrition bias. Selective reporting was low risk only in Orive (2015), while all other studies lacked trial registration or prespecified protocols. Additional concerns included small sample sizes, single-center recruitment, composite interventions without attention controls, and insufficient treatment fidelity monitoring.

Heterogeneity was also observed. Variation in concomitant pharmacotherapies (PPIs, prokinetics, antidepressants, herbal preparations), treatment durations (6~28 weeks), intervention formats (CBT, MCT, DBT, MBCT), and outcome measures contributed to between-study variability. These differences may have influenced the magnitude of observed effects, particularly across symptom subdomains such as ear-

ly satiety, epigastric pain, or bloating. Future studies should consider standardizing pharmacological regimens or quantitatively accounting for such variability in subgroup analyses or meta-regression.

Safety was generally acceptable. Adverse events were rarely reported and, when available, were mild and comparable between groups. For instance, Group A showed a lower complication rate compared with Group B (Zeng (2024)), while adverse event rates in Group A were comparable to Group B (Xin (2024)). Nevertheless, systematic safety reporting was insufficient across most trials, limiting robust conclusions about tolerability.

Taken together, the present evidence indicates that CBT approaches can significantly improve psychological and gastrointestinal outcomes in FD, functioning as an important non-pharmacological treatment option beyond the limits of drug therapy. However, methodological shortcomings and heterogeneity across existing studies reduce the certainty of evidence, and cautious interpretation is warranted. Moreover, because only a few outcomes could be meta-analyzed and substantial heterogeneity remained, a formal GRADE assessment was not conducted; instead, the certainty of evidence was judged qualitatively.

Future research should prioritize robust trial design with adequate randomization and allocation concealment, pre-registration with prespecified outcomes, attention-control comparators, standardized CBT protocols, fidelity monitoring, multicenter recruitment, and long-term follow-up. Comparative studies among CBT, MCT, DBT, and MBCT are also necessary to delineate modality-specific benefits and optimize individualized treatment models for patients with FD.

V. CONCLUSION

This systematic review found that CBT approaches significantly improved anxiety, depression, gastrointestinal symptoms, and quality of life in patients with FD. Across the included trials, significant improvements were consistently reported on standardized scales such as HADS and SAS/SDS for anxiety and depression, GIS for gastrointestinal symptoms, Quality-of-life for SF-NDI, EuroQol-VAS, and GIQLI.

Benefits were observed both as stand-alone interventions and, more prominently, when combined with pharmacotherapy, with generally favorable safety profiles.

However, heterogeneity across studies and methodological limitations reduced the overall certainty of evidence. Future large-scale, standardized RCTs and direct comparisons among CBT approaches are needed.

REFERENCES

1. Oh JH, Kwon JG, Jung HK, Tae CH, Song KH, Kang SJ, et al. Clinical practice guidelines for the treatment of functional dyspepsia in Korea. Korean J Med. 2021;96(2):116-138. doi:10.3904/kjm.2021.96.2.116
2. Lee KJ. Diagnosis and treatment of functional dyspepsia. J Korean Med Assoc. 2016;59(4):311-318. doi:10.5124/jkma.2016.59.4.311
3. Miwa H, Watari J, Fukui H, Oshima T, Tomita T, Sakurai J, Kondo T, Matsumoto T. Current understanding of pathogenesis of functional dyspepsia. J Gastroenterol Hepatol. 2011;26 Suppl 3:53-60. doi:10.1111/j.1440-1746.2011.06633.x
4. Ford AC, Mahadeva S, Carbone MF, Lacy BE, Talley NJ. Functional dyspepsia. Lancet. 2020;396(10263):1689-1702. doi:10.1016/S0140-6736(20)30469-4
5. Kim YS, Kim NY. Functional dyspepsia: a narrative review with a focus on sex-gender differences. J Neurogastroenterol Motil. 2020;26(3):322-334. doi:10.5056/jnm20026
6. Hayes SC, Hofmann SG. The third wave of cognitive behavioral therapy and the rise of process-based care. World Psychiatry. 2017;16(3):245-246. doi:10.1002/wps.20442
7. Linehan MM, Korslund KE, Harned MS, Gallop RJ, Lungu A, Neacsiu AD, et al. Dialectical behavior therapy for high

suicide risk in individuals with borderline personality disorder: a randomized clinical trial and component analysis. JAMA Psychiatry. 2015;72:475-82. doi:10.1001/jamapsychiatry.2014.3039
8. Ben-Porath DD, Wisniewski L, Warren M. Differential Treatment Response for Eating Disordered Patients With and Without a Comorbid Borderline Personality Diagnosis Using a Dialectical Behavior Therapy (DBT)-Informed Approach. Eat Disord. 2009;17:225-41. doi: 10.1080/10640260902848576
9. Williams JMG, Crane C, Barnhofer T, Brennan K, Duggan DS, Fennell MJV, et al. Mindfulness-Based Cognitive Therapy for Preventing Relapse in Recurrent Depression: A Systematic Review. J Consult Clin Psychol. 2014;82(2):275-286. doi:10.1037/a0035036
10. McManus F, Surawy C, Muse K, Vazquez-Montes M, Williams JMG. A Randomized Clinical Trial of Mindfulness-Based Cognitive Therapy Versus Unrestricted Services for Health Anxiety (Hypochondriasis). J Consult Clin Psychol. 2012;80(5):817-828. doi:10.1037/a0028782
11. Wells A. Metacognitive therapy for anxiety and depression. New York: Guilford Press; 2009.
12. Higgins JPT, Green S, editors. Cochrane handbook for systematic reviews of interventions Version 5.1.0. Chichester (UK). John Wiley & Sons, Ltd. 2011.
13. Orive M, Barrio I, Orive VM, Matellanes B, Padierna JA, Cabriada J, et al. A randomized controlled trial of a 10-week group psychotherapeutic treatment added to standard medical treatment in patients with functional dyspepsia. J Psychosom Res. 2015;78(6):563-568. doi:10.1016/j.jpsychores.2015.03.003
14. Teh KKJ, Ng YK, Doshi K, Tay SW, Hao Y, Ang LY, et al. Mindfulness-based cognitive therapy in functional dyspepsia: a pilot randomized trial. J Gastroenterol Hepatol. 2021;36(7):1863-1871. doi:10.1111/jgh.15389
15. Xin Y, Zhao Z, Zhao Q. Clinical effect of cognitive-behavioral therapy combined with mirtazapine in the treatment of functional dyspepsia on anxiety and depression. Psychol Mon. 2024;19(03):139-145. doi:10.19738/j.cnki.psy.2024.03.039
16. Batebi S, Masjedi Arani A, Jafari M, Sadeghi A, Saberi Isfeedvajani M, Davazdah Emami MH. A randomized clinical trial of metacognitive therapy and nortriptyline for anxiety, depression, and difficulties in emotion regulation of patients with functional dyspepsia. Res Psychother Psychopathol Process Outcome. 2020;23(2):157-166. doi:10.4081/ripppo.2020.448
17. Xing L, Wu L, Li Z, Hu Y, Wang J, Zhang X, et al. The effect of mindfulness-based cognitive therapy on the clinical efficacy and psychological state in patients with functional dyspepsia: a randomized controlled trial. Scand J Gastroenterol. 2024;59(8):900-905. doi:10.1080/00365521.2024.2368250
18. Wang Z, Gao Z, Zhang H. Study on drug therapy combined with cognitive behavioral therapy for functional dyspepsia. Jiangsu Sci Technol Inf. 2020;(25):74-77.
19. Zhou Q, Teng Q. A controlled study of group cognitive-behavioral therapy on functional dyspepsia. Med Philos. 2012;33(6B):36-39.
20. Zeng D, Wang X, Wang W, Lian L, Zhao P, Wang L, et al. Clinical efficacy of cognitive behavioral therapy combined with domperidone in the treatment of functional dyspepsia. Chin J Clin. 2024;52(5):529-533. doi:10.3969/j.issn.2095-8552.2024.05.008
21. Drossman DA. Functional gastrointestinal disorders: history, pathophysiology, clinical features and Rome IV. Gastroenterology. 2016;150(6):1262-1279. doi:10.1053/j.gastro.2016.02.032
22. Lacy BE, Weiser K, Kennedy A, Crowell MD, Talley NJ. Functional dyspepsia: the economic impact to patients. Aliment Pharmacol Ther. 2013;38(2):170-177. doi: 10.1111/apt.12355
23. Moayyedi PM, Lacy BE, Andrews CN, Enns RA, Howden CW, Vakil N. ACG and CAG Clinical Guideline: Management of Dyspepsia. Am J Gastroenterol. 2017;112(7):988-1013. doi:10.1038/ajg.2017.154
24. Van Oudenhove L, Vandenberghe J, Demyttenaere K, Tack J. Psychosocial factors, psychiatric illness, and functional gastrointestinal disorders: a historical perspective. Dig Dis Sci. 2010;55(2):277-85. doi:10.1007/s10620-009-0952-1
25. Hofmann SG, Asnaani A, Vonk IJJ, Sawyer AT, Fang A. The efficacy of cognitive behavioral therapy: a review of meta-analyses. Cognit Ther Res. 2012;36(5):427-440. doi:10.1007/s10608-012-9476-1