

Cochrane Database of Systematic Reviews

Acupuncture for functional dyspepsia (Review)

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[Intervention Review]

Acupuncture for functional dyspepsia

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ABSTRACT

Background

Functional dyspepsia (FD) has been a worldwide complaint. More effective therapies are needed with fewer adverse effects than are seen with conventional medications. Acupuncture, as a traditional therapeutic method, has been widely used for functional gastrointestinal disorders in the East. Manual acupuncture and electroacupuncture have been recognized treatments for FD, but to date, no robust evidence has been found for the effectiveness and safety of these interventions in the treatment of this condition.

Objectives

This review was conducted to assess the efficacy and safety of manual acupuncture and electroacupuncture in the treatment of FD.

Search methods

Trials meeting the inclusion criteria were identified through electronic searches of the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, the Allied and Complementary Medicine Database (AMED), Chinese Biology Medicine Disc (CBMdisc), China National Knowledge Infrastructure (CNKI), the Wanfang Database, the VIP Database, and six trial registries. Handsearching was done to screen the reference sections of potential trials and reviews.

Selection criteria

Randomized controlled trials (RCTs) were included if investigators reported efficacy and safety of manual acupuncture or electroacupuncture for patients with FD diagnosed by Rome II or Rome III criteria, compared with medications, blank control, or sham acupuncture.

Data collection and analysis

Data were extracted by independent review authors. Study limitations were assessed by using the tool of The Cochrane Collabration for assessing risk of bias. For dichotomous data, risk ratios (RRs) and 95% confidence intervals (95% CIs) would be applied, and for continuous data, mean differences (MDs) and 95% CIs. A fixed-effect model was applied in the meta-analysis, or a descriptive analysis was performed. The quality of evidence for the outcome measure was assessed by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methods.

Main results

Seven studies were included in the review, involving 542 participants with FD (212 males and 330 females). These studies generally had an unclear risk of bias based on inadequate descriptions of allocation concealment and a high risk of bias based on lack of blinding. None of the studies reported on outcomes of the Functional Digestive Disorder Quality of Life questionnaire (FDDQL), the Satisfaction With



Dyspepsia Related Health scale (SODA), the Digestive Health Status Instrument (DHSI), or effective/inefficient rate and symptom recurrence six months from completion of acupuncture treatment.

Four RCTs of acupuncture versus medications (cisapride, domperidone, and itopride) were included in the review. No statistically significant difference was noted in the reduction in FD symptom scores and the frequency of FD attack by manual acupuncture, manual-electroacupuncture, or electroacupuncture compared with medications. In three trials of acupuncture versus sham acupuncture, all descriptive or quantitative analysis results implied that acupuncture could improve FD symptom scores and scores on the Neck Disability Index (NDI), the 36-Item Short Form Health Survey (SF-36), the Self-Rating Anxiety Scale (SAS), and the Self-Rating Depression Scale (SDS) more or as significantly as sham acupuncture. With regard to adverse effects, acupuncture was superior to cisapride treatment (one study; all minor events), but no statistically significant difference was reported between acupuncture and sham acupuncture. No adverse effects data were reported in studies examining manual acupuncture versus domperidone, manual-electroacupuncture versus domperidone, or electroacupuncture versus itopride.

Nevertheless, all evidence was of low or very low quality. The body of evidence identified cannot yet permit a robust conclusion regarding the efficacy and safety of acupuncture for FD.

Authors' conclusions

It remains unknown whether manual acupuncture or electroacupuncture is more effective or safer than other treatments for patients with FD.

PLAIN LANGUAGE SUMMARY

Acupuncture for treating functional dyspepsia

Functional dyspepsia (FD) has been a worldwide gastric disorder. More effective therapies are needed with fewer adverse effects than are seen with conventional medications. In the East, acupuncture has been recognized for a long time as a positive therapy for the treatment of functional gastric disorders. To date, no robust evidence on its efficacy and safety has been found. The evidence obtained has overwhelmingly supported no significance of acupuncture compared with medications and superiority of acupuncture compared with sham acupuncture in FD treatment; however, the low quality of evidence obtained has not permitted a robust conclusion concerning the efficacy and safety of acupuncture in the treatment of FD.

SUMMARY OF FINDINGS

Summary of findings for the main comparison. Manual acupuncture compared with cisapride for functional dyspepsia

Manual acupuncture compared with cisapride for functional dyspepsia

Patient or population: patients with functional dyspepsia **Settings:** outpatients of Yangqing TCM Hospital in Beijing, China

Intervention: manual acupuncture

Comparison: cisapride

Outcomes	Illustrative comparative risks* (95% CI) Assumed risk Corresponding risk		Relative effect (95% CI)	No. of partici-	Quality of the evi- Comments dence
			(33 % Ci)	(studies)	(GRADE)
	CISAPRIDE	MANUAL ACUPUNCTURE			
Symptom scores of FD Graded by 4 levels ¹	911 per 1000 ²	929 per 1000 (829 to 1000) ²	RR 1.02 (0.91 to 1.16)	90 (1 study)	⊕⊝⊝⊝ very low ^{3,4,5}
Adverse effects Discomfort after treatment	311 per 1000	65 per 1000 (22 to 215)	RR 0.21 (0.07 to 0.69)	90 (1 study)	⊕⊝⊝⊝ very low ^{3,4}
Frequency of FD symptoms Number of FD attacks per week	600 per 1000 ⁶	624 per 1000 (450 to 840) ⁶	RR 1.04 (0.75 to 1.4)	90 (1 study)	⊕⊙⊙⊝ very low ^{3,4}

^{*}The basis for the assumed risk (eg, median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio.

GRADE Working Group grades of evidence.

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

¹0 points meant no symptoms, 1 point stood for slight symptoms, 2 points indicated moderate symptoms but not sufficient to affect daily life, and 3 points represented symptoms severe enough to affect daily life. Effective rate = (symptom scores after treatment-symptom scores before treatment)*100%. When equal to or greater than 25%, this meant "effective," equal to or greater than 50% meant "marked effective,; and equal to or greater than 75% meant "healing" effect. "Effective," "marked effective," and "healing" are categorized as "positive effect," and "invalid" as "negative effect."

²Event of FD symptom scores means positive effect.

³Blinding was not easy to conduct because of the heterogeneity of acupuncture and drug control. Also, FD symptom scores at baseline were not reported. Thus, we consider this evidence would be downgraded by 2 levels because of its risk of bias.

⁴The number of participants was lower than the optimal information sample size, so the quality of evidence was downgraded by 1 level for imprecision.

⁵FD symptom scores at baseline were not reported

⁶Event of FD symptom frequency means no FD attacks per week.

Summary of findings 2. Manual acupuncture compared with domperidone for functional dyspepsia

Manual acupuncture compared with domperidone for functional dyspepsia

Patient or population: patients with functional dyspepsia

Settings: outpatients from People's Hospital of Guangxi Zhuang Autonomous Region, Guangxi Province, China

Intervention: manual acupuncture

Comparison: domperidone

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No. of partici- pants	Quality of the evidence	Comments
	Assumed risk	Corresponding risk	(30 % 0.1)	(studies)	(GRADE)	
	DOMPERIDONE	MANUAL ACUPUNCTURE				
Symptom scores of FD Graded by 4 levels ¹	733 per 1000 ²	909 per 1000 (711 to 1000) ²	RR 1.24 (0.97 to 1.58)	62 (1 study)	⊕⊕⊙⊝ low ^{3,4}	

^{*}The basis for the **assumed risk** (eg, median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; RR: Risk ratio.

GRADE Working Group grades of evidence.

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

¹0 points meant no symptoms, 1 point stood for slight symptoms, 2 points indicated moderate symptoms but not sufficient to affect daily life, and 3 points represented symptoms severe enough to affect daily life. Effective rate = (symptom scores after treatment-symptom scores before treatment)*100%. When equal to or greater than 25%, this meant "effective," equal to or greater than 50% meant "marked effective," and equal to or greater than 75% meant "healing" effect. "Effective," "marked effective," and "healing" are categorized as "positive effect," and "invalid" as "negative effect."

²Event of FD symptom scores means positive effect.

³Blinding was probably not done, thus the evidence was downgraded by 1 level.

⁴The number of participants was lower than the optimal information sample size, so the quality of evidence was downgraded by 1 level for imprecision.

Summary of findings 3. Manual-electroacupuncture compared with domperidone for functional dyspepsia

Manual-electroacupuncture compared with domperidone for functional dyspepsia

Patient or population: patients with functional dyspepsia

Settings: outpatients from Shanghai No. 5 People's Hospital Affiliated to Fudan University, Shanghai, China

Intervention: manual-electroacupuncture

Comparison: domperidone

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No. of partici- pants (studies)	Quality of the evi- dence (GRADE)	Comments
	Assumed risk	Corresponding risk		(Sea alles)	(0.0.02)	
	DOMPERIDONE	MANUAL-ELEC- TROACUPUNCTURE				
Symptom scores of FD Graded by 4 levels ¹	823 per 1000 ²	938 per 1000 (823 to 1000) ²	RR 1.14 (1 to 1.3)	126 (1 study)	⊕⊝⊝⊝ very low ^{3,4}	
Symptom scores of ulceration subtype Graded by 4 levels ¹	97 per 1000 ⁵	78 per 1000 (25 to 243) ⁵	RR 0.81 (0.26 to 2.51)	126 (1 study)	⊕⊝⊝⊝ very low ^{3,6}	
Symptom scores of regurgitation subtype Graded by 4 levels ¹	32 per 1000 ⁵	29 per 1000 (14 to 60) ⁵	RR 0.89 (0.42 to 1.86)	126 (1 study)	⊕⊝⊝⊝ very low ^{3,6}	
Symptom scores of dyskinesia subtype Graded by 4 levels ¹	5	5	RR 1.2 (0.76 to 1.89)	126 (1 study)	⊕⊝⊝⊝ very low ^{3,6}	
Symptom scores of nonspecific subtype Graded by 4 levels ¹	5	5	RR 1.45 (0.77 to 2.76)	126 (1 study)	⊕⊝⊝⊝ very low ^{3,6}	

^{*}The basis for the assumed risk (eg, median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI). **CI:** Confidence interval; **RR:** Risk ratio.

GRADE Working Group grades of evidence.

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

¹0 points meant no symptoms, 1 point stood for slight symptoms, 2 points indicated moderate symptoms but not sufficient to affect daily life, and 3 points represented symptoms severe enough to affect daily life. Effective rate = (symptom scores after treatment-symptom scores before treatment)*100%. When equal to or greater than 25%, this meant "effective," equal to or greater than 50% meant "marked effective," and equal to or greater than 75% meant "healing" effect. "Effective," "marked effective," and "healing" are categorized as "positive effect," and "invalid" as "negative effect."

²Event of FD symptom scores means positive effect.

³Blinding was probably not done. Also, FD symptom scores at baseline were lacking. Thus, the evidence was downgraded by 2 levels.

⁴FD symptom scores at baseline were omitted.

⁵Event of FD subtype symptom scores means positive effect.

⁶The number of participants was lower than the optimal information sample size, so the quality of evidence was downgraded by 1 level for imprecision.

Summary of findings 4. Electroacupuncture compared with itopride for functional dyspepsia

Electroacupuncture compared with itopride for functional dyspepsia

Patient or population: patients with functional dyspepsia

Settings: outpatients from Wuhan Hospital of Traditional Medicine and Western Medicine, Hubei Province, China

Intervention: electroacupuncture

Comparison: itopride

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect - (95% CI)	No. of partici- pants	Quality of the evi- dence	Comments	
	Assumed risk	Corresponding risk	(studies) (GRADE)				
	ITOPRIDE	ELECTROACUPUNCTURE					
Symptom scores of FD Graded by 4 levels ¹	875 per 1000 ²	971 per 1000 (858 to 1000) ²	RR 1.11 (0.98 to 1.27)	80 (1 study)	⊕⊕⊝⊝ low ^{3,4}		

^{*}The basis for the assumed risk (eg, median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; RR: Risk ratio.

GRADE Working Group grades of evidence.

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

¹0 points meant no symptoms, 1 point stood for slight symptoms, 2 points indicated moderate symptoms but not sufficient to affect daily life, and 3 points represented symptoms severe enough to affect daily life. Effective rate = (symptom scores after treatment-symptom scores before treatment)*100%. When equal to or greater than 25%, this meant "effective," equal to or greater than 50% meant "marked effective," and equal to or greater than 75% meant "healing" effect. "Effective," "marked effective," and "healing" are categorized as "positive effect," and "invalid" as "negative effect."

²Event of FD symptom scores means positive effect.

³Blinding was probably not done, thus the evidence was downgraded by 1 level.

⁴The number of participants did not reach the optimal information sample size, thus we consider the evidence to be downgraded by 1 level.

Summary of findings 5. Acupuncture compared with sham acupuncture for functional dyspepsia

Acupuncture compared with sham acupuncture for functional dyspepsia

Patient or population: patients with functional dyspepsia

Settings: outpatients from No, 1 Affiliated Hospital of Hunan University of TCM, the Guan'anmen Hospital of China Academy of Chinese Medicine Science, the Korean Ori-

ental Medicine Clinics **Intervention:** acupuncture **Comparison:** sham acupuncture

Outcomes	Illustrative comparative	Relative effect (95% CI)	No. of partici- pants	Quality of the evidence	Comments	
	Assumed risk	Corresponding risk	(3370 CI)	(studies)	(GRADE)	
	SHAM ACUPUNCTURE	ACUPUNCTURE				
FD symptom scores Graded by 4 levels ¹ Follow-up: 1~3 months	See comment	See comment	Not estimable	116 (2 studies)	⊕⊕⊙⊝ low ^{2,3}	
FD symptom scores at follow-up Graded by 4 levels ¹ Follow-up: 1~3 months	See comment	See comment	Not estimable	116 (2 studies)	⊕⊕⊙⊝ low ^{2,3}	
Nepean Dyspepsia Symptom Index Follow-up: 0~1 months	See comment	See comment	Not estimable	128 (2 studies)	⊕⊕⊝⊝ low ^{2,3}	
Nepean Dyspepsia Life Quality Index Follow-up: 0~1 months	See comment	See comment	Not estimable	128 (2 studies)	⊕⊕⊙⊝ low ²	
Nepean Dyspepsia Symptom Index at follow-up 1 month Follow-up: 1 month	Mean Nepean Dyspepsia Symptom Index at fol- low-up 1 month in the control groups was 27.69 points	Mean Nepean Dyspepsia Symptom Index at follow-up 1 month in the intervention groups was 16.63 lower (24.513 to 8.75 lower)		60 (1 study)	⊕⊕⊙⊝ low ^{2,3}	

Nepean Dyspepsia Life Quality Index at follow-up of 1 month Follow-up: 1 month	Mean Nepean Dyspepsia Life Quality Index at fol- low-up of 1 month in the control groups was 82.10 points	Mean Nepean Dyspepsia Life Quality Index at follow-up 1 month in the intervention groups was 13.64 higher (8.22 to 19.06 higher)	60 (1 study)	⊕⊕⊙⊝ low ²
SF-36 SF-36 scale Follow-up: 1~3 months	Mean SF-36 ranged across control groups from 56~75.53 points	Mean SF-36 in the intervention groups was 12.18 higher (8.45 to 15.91 higher)	116 (2 studies)	⊕⊕⊙⊝ low ^{2,3}

^{*}The basis for the **assumed risk** (eg, median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval.

GRADE Working Group grades of evidence.

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

¹0 points meant no symptoms, 1 point stood for slight symptoms, 2 points indicated moderate symptoms but not sufficient to affect daily life, and 3 points represented symptoms severe enough to affect daily life.

²Blinding cannot be confirmed because of the difficulty of the acupuncture operation. Thus, we consider evidence to be downgraded by 1 level.

³The number of participants did not reach the optimal information sample size; thus we consider the evidence to be downgraded by 1 level.



BACKGROUND

Description of the condition

Functional dyspepsia (FD) is a common complaint regardless of geographic location (Mahadeva 2006). The prevalence of FD diagnosed by Rome I or Rome II criteria has been noted to vary between 11% and 29.2% (Mahadeva 2006). Patients who report one or more of a set of symptoms (bothersome postprandial fullness, early satiation, epigastric pain, and epigastric burning) for three months, with symptom onset at least six months before diagnosis, and who lack indicators of structural disease likely to explain the symptoms (including evidence from upper endoscopy) will be given a diagnosis of FD (Rome III 2006).

The main therapeutic methods used in patients with FD include prokinetic agents, *Helicobacter pylori* eradication, proton pump inhibitors (PPIs), tricyclic antidepressants (TCAs), histamine type 2 receptor antagonists, and serotonin reuptake inhibitors. However, the efficacy of these approaches remains unsatisfactory because of associated adverse effects. Take prokinetic drugs, for example. Despite early promising results, itopride and mosapride were reported to be no better than placebo in a study in Japan (Holtmann 2006). Less than 60% of patients with FD report improved symptoms with medication, and the efficacy of drug therapy usually varies (Mönkemüller 2006). Also, the adverse effects associated with drugs and the recurrence of symptoms reported by patients have presented challenges for researchers and clinicians.

Scientifoth ervation that hope hope is a sanormal function and bacterial flora, visceral hypersensitivity, braingut interactions, genetic predisposition, early family environment, and psychosocial factors (Drossman 2006). This suggests the complicated pathologic mechanisms and the heterogeneity of the disease.

Description of the intervention

Acupuncture is onethenosimportantherapeutimodalities adition thinesemedicin (ECM). Acupuncture uses fine needles that may pierce through specific anatomic points (named 'acupoints') so that certain healing effects are produced (Deng 1997). Acupuncture has been applied for a long time in the treatment of dyspepsia. LI 4 (Hegu) on the Large Intestine Meridian, ST36 (Zu Sanli) on the Stomach Meridian, and CV12 (Zhongwan) are the best known acupoints in the treatment of dyspepsia. Traditional acupuncture commonly includes manual acupuncture; however, in recent decades, electrical acupuncture, in which an electrical stimulator is connected to the acupuncture needle, has been used frequently (Lao 1996). Now, manual acupuncture and electroacupuncture are the most frequently used acupuncture techniques for treatment of this condition.

How the intervention might work

Discomfort or pain or both are requisite symptoms of FD. Research has demonstrated that acupuncture could improve gastric emptying and accommodation to improve the symptoms of FD (Xu 2004). Investigators have further observed that acupuncture to the abdomen can excite sympathetic nerves via spinal reflexes, causing inhibition of gastric motilities; acupuncture of the limbs excites vagus nerves via supraspinal reflexes,

causing an increase in gastric motility (Noguchi 2008). Functional neuroimaging studies have revealed that in patients with FD, resting cerebral glycometabolism differs significantly from that in healthy individuals, and the anterior cingulate cortex, insula, thalamus, middle cingulate cortex, and cerebellum might be key regions that determine the severity of symptoms (Zeng 2011); symptom improvement was found to be relevant with deactivation of the primary somatosensory area and the cerebellum as a response to acupuncture stimulation (Zeng 2009).

Why it is important to do this review

Manual acupuncture and electroacupuncture have been recognized treatments for FD in the East, but to date, no robust evidence has shown their effectiveness and safety in the treatment of patients with FD.

OBJECTIVES

This review was conducted to assess the efficacy and safety of manual acupuncture and electroacupuncture in the treatment of FD.

METHODS

Criteria for considering studies for this review

Types of studies

Only randomized controlled trials (RCTs) reporting clinical assessment were included. Quasi-RCTs, cross-over trials, cluster-randomized trials, and other study designs were excluded. Language restriction was not applied during study selection.

Types of participants

Studies involving participants older than 17 years of age who met Rome II or Rome III diagnostic criteria for FD were included without limitations related to gender or race. Studies involving participants with structural, systemic, or metabolic disease, severe psychiatric sickness, or a history of abdominal operations were excluded.

Types of interventions

Trials involving manual acupuncture or electroacupuncture were included. Also included were studies in which acupuncture techniques and other treatments were provided to the intervention group, as long as all methods except acupuncture therapy were applied to both treatment and control groups. Studies in which any acupuncture techniques were compared with one other or with Chinese herbs were excluded.

Comparisons

- Manual acupuncture or electroacupuncture or their combination versus no treatment.
- Manual acupuncture or electroacupuncture or their combination versus placebo acupuncture (sham acupuncture, minimal acupuncture, etc.).
- 3. Manual acupuncture or electroacupuncture or their combination versus medication.

Types of outcome measures

Primary outcomes

1. Symptomatic improvement in any of the following.



- a. Symptom scores.
- b. Nepean Dyspepsia Index (NDI).
- Functional Digestive Disorder Quality of Life questionnaire (FDDOL).
- d. Satisfaction With Dyspepsia Related Health scale (SODA).
- e. Digestive Health Status Instrument (DHSI).
- f. Effective rate, inefficient rate, etc.
- No symptom recurrence six months from completion of acupuncture treatment.

Secondary outcomes

- 1. Medical Outcome Study Short Form Health Survey (SF-36).
- Self-Rating Depression Scale (SDS), Self-Rating Anxiety Scale (SAS).
- 3. Adverse events.

Search methods for identification of studies

Trials meeting the inclusion criteria were identified through electronic searches and by handsearching.

Electronic searches

The following bibliographic databases were searched.

- The Cochrane Central Register of Controlled Trials (CENTRAL) 2012, Issue 1 (part of *The Cochrane Library*) (Appendix 1).
- MEDLINE (1950 to February 2012) (Appendix 2).
- EMBASE (1980 to February 2012) (Appendix 3).
- AMED (Allied and Complementary Medicine Database) (1985 to February 2012) (Appendix 4).
- CNKI (China National Knowledge Infrastructure) (1999 to February 2012) (Appendix 5).
- VIP Database (1999 to February 2012) (Appendix 6).
- CBMdisc (Chinese Biology Medicine Disc) (1999 to February 2012) (Appendix 7).
- Wanfang Database (1999 to February 2012) (Appendix 8).

Chinese databases were searched back to 1999, the date when the ROME II diagnostic criteria were first used, and when functional dyspepsia was first known by Chinese researchers.

Trial registries were searched using the keywords "functional dyspepsia" and "acupuncture."

- ACTR (http://www.actr.org.au/).
- BNRR (http://www.nrr.nhs.uk).
- CCT (http://www.controlled-trials.com).
- Chinese Clinical Trial Register (www.chictr.org).
- Clinical Trials (http://www.clinicaltrials.gov),
- Trial Central (http://www.trialscentral.org/).

Searching other resources

Handsearching was done to screen reference sections of identified studies for potential trials or reviews.

Data collection and analysis

Selection of studies

Review author Lan L inspected English titles and abstracts identified by the literature search of MEDLINE, EMBASE, AMED, CENTRAL, and several trial registries. Review author Liu ML scanned the Chinese search lists of CBM, CNKI, VIP, and Wanfang databases. When it was not known from titles and abstracts whether a study should be included, copies of trials were requested for further identification. All identified trials were downloaded in full-text form, and references were inspected to search for potential RCTs of acupuncture for FD. Studies excluded or awaiting classification were recorded in detail, and a third review author (Wu X) checked them randomly.

Data extraction and management

Review authors Liu ML, Zeng F, and Ying L drafted data extraction items and performed a pretest. Disagreement led to consultation with Lan L. Then Zeng F and Ying L independently extracted data into Review Manager software (RevMan 2011). If needed, authors of trials were contacted and were asked to provide incomplete data.

Assessment of risk of bias in included studies

Two review authors independently assessed the risk of bias in each included trial, involving sequence generation; allocation concealment; blinding of participants, personnel, and outcome assessors; incomplete outcome data; and selective reporting. Consensus was used to resolve disagreements, and a third review author was consulted when disagreement persisted.

The Grading of Recommendations Assessment, Development and Evaluation (GRADE system) was applied to confirm the level of evidence and the strength of the recommendation.

Measures of treatment effect

Meta-analysis was conducted on the basis of homogeneity of included trials. For dichotomous data, risk ratios (RRs) and 95% confidence intervals (95% CIs) were applied. For continuous data, mean differences (MDs) and 95% CIs were used for analyses.

Dealing with missing data

The problem of missing data was resolved by contacting the original investigators to request the missing information. If data were not obtained, trials with incomplete data involving inclusion criteria would be listed in the Characteristics of studies awaiting classification section, along with a description of the reason, and will be included in updates of this review (Higgins 2011).

Assessment of heterogeneity

The I² statistic was used to assess heterogeneity (Higgins 2003). Values lower than 50% suggested homogeneity; values of 50% or higher were indicative of heterogeneity. However, when values were very close to but lower than 50%, review authors determined whether meta-analysis would be conducted.

Data synthesis

A fixed-effect model was applied in the meta-analysis if heterogeneity did not exist. When inconsistency was noted, causes of heterogeneity were detected first by subgroup analysis. If this did



not occur, a random-effects model was applied. Results obtained by the random-effects model were interpreted with caution.

Subgroup analysis and investigation of heterogeneity

Subgroup analysis was not performed because of the small number of trials.

Sensitivity analysis

Sensitivity analysis was not conducted because of lack of available

RESULTS

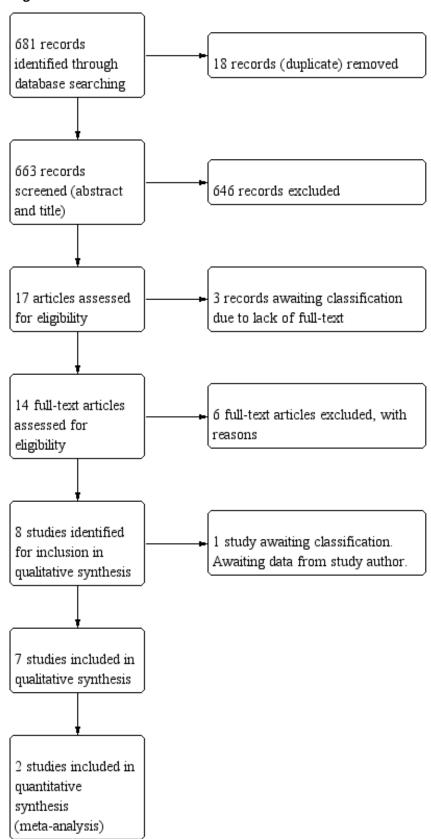
Description of studies

Results of the search

A total of 681 citations were retrieved through the literature search. Upon screening of titles, abstracts, and full text, 17 potential studies were found to meet the inclusion criteria, three of which were awaiting classification for lack of full text to confirm study details. One study was awaiting classification because of difficulty associated with getting in touch with the study author and having unclear data explained, and six studies were excluded with reasons. Eventually, seven studies were included. Details can be seen in Figure 1.



Figure 1. Study flow diagram.





Included studies

External characteristics

Seven RCTs were verified to be included, five of which were fully published papers (Chang 2010; Park 2009; Shi 2009; Tang 2006; Zhou 2005); two studies were unpublished (Jin 2011; Yang 2009). Among the seven trials, five were written in Chinese (Chang 2010; Jin 2011; Shi 2009; Tang 2006; Yang 2009) and two in English (Park 2009; Zhou 2005).

Participants

Seven trials included 542 participants with FD—212 males and 330 females. All participants were Chinese and were enrolled as hospital outpatients, except those from the Korean population studied in Park 2009. Participant age was reported to range from 18 years (Shi 2009) to 70 years (Jin 2011). Duration of FD symptoms before recruitment ranged from three months (Tang 2006) to 480 months (Jin 2011). Rome II criteria were used to diagnose FD in three trials (Park 2009; Tang 2006; Zhou 2005), and Rome III criteria were used for the other four trials (Chang 2010; Jin 2011; Shi 2009; Yang 2009).

For the inclusion criteria, the highlight character of included participants in seven studies was absent from organic diseases. Also, two studies described clearly that medication intake was avoided before enrollment or treatment. Yang 2009 instructed participants to refrain from taking any gastrointestinal drugs for at least 15 days before recruitment, and Zhou 2005 demanded that participants withdraw from anticholinergic, anticonvulsant, emetic, or H-receptor antagonist treatment one week before the start of acupuncture treatment. Additionally, participants in Tang 2006 were required to have symptoms lasting at least one month before enrollment.

Among exclusion criteria, pregnancy was mentioned in four studies (Chang 2010; Jin 2011; Shi 2009; Yang 2009). One study described in the exclusion criteria people with a tendency toward bleeding and those with unconsciousness (Yang 2009).

Interventions

All included trials provided details of baseline comparability, except Zhou 2005 and Shi 2009. Interventions applied included manual acupuncture or electroacupuncture versus oral drugs in four studies (Shi 2009; Tang 2006; Yang 2009; Zhou 2005), and manual acupuncture versus sham acupuncture (puncturing sham acupoints) in three studies (Chang 2010; Jin 2011; Park 2009). Zhou 2005 compared manual acupuncture treatment on CV12, PC6, and LI4 acupoints combined with electroacupuncture on ST36 and SP6 acupoints with domperidone usage of three weeks' duration. Tang 2006 compared four-week manual acupuncture treatment on ST36, CV12, PC6, LR3, BL15, BL19, BL20, BL21, and ST44 acupoints with four-week domperidone administration. Yang 2009 compared four-week electroacupuncture treatment on ST34, ST36, ST40, and ST42 acupoints with four-week itopride administration. Shi 2009 compared manual acupuncture using mainly ST36, CV12, and PC6 acupoints with cisapride of three weeks' treatment duration. Park 2009 applied two-week manual acupuncture on LI4, LR3, PC6, SP4, ST36, and CV12 acupoints compared with puncturing on sham acupoints lateral to the aforementioned acupoints. Chang 2010 and Jin 2011 separately compared manual acupuncture on acupoints of the formulae composed of ST32, ST36, ST40, ST42 or ST36, and KI 3, with sham acupuncture on points lateral to the aforesaid acupoints of four weeks' duration. Only Chang 2010 and Jin 2011 reported separately follow-up assessment one month and three months after interventions were provided.

For acupuncture interventions, therapists in included trials were licensed doctors and were required to perform lifting, thrusting, and rotating manipulations. Needle brands and sizes were clearly described in Park 2009, Chang 2010, and Jin 2011. Although acupoints used were heterogeneous, acupuncture style was traditional Chinese acupuncture, except that of Park 2009, in which acupoints were selected on the basis of traditional Chinese acupuncture theory. "De-qi" sensations were considered vital for efficacy in traditional Chinese acupuncture. All studies except Park 2009 were required to perform manipulations to a specific depth until "de-qi" occurred at least three times per week.

For the control interventions, medication was administered orally before three meals per day for a similar treatment duration as acupuncture, and sham acupuncture consisted of puncturing points lateral to acupoints. Co-interventions of manual acupuncture combined with electroacupuncture were found in Zhou 2005.

No trials reported data on acupuncture versus waiting list for treatment of FD.

Outcome measures

For the primary outcome measures, symptom scores of FD were applied in all included studies, except Park 2009, in which zero points meant no symptoms, one point stood for slight symptoms, two points indicated moderate symptoms but not sufficient to affect daily life, and three points represented symptoms severe enough to affect daily life. Investigators also described how to assess efficacy through symptom scores of FD. Shi 2009 calculated the effective rate (difference/(pretreatment score) *100%), limited effective rate to mean positive effect when it was equal to or greater than 25%, and reported efficacy as effective or invalid. Tang 2006 described that efficacy consisted of four levels: healing (no symptoms and no recurrence one month after treatment), marked effective (symptom scores after treatment decreased by more than two-thirds), effective (symptom scores after treatment decreased by more than one-third), and invalid (symptom scores after treatment decreased by less than one-third). Yang 2009 described four similar levels of efficacy, healing (no symptoms or symptom scores decreased by three points), marked effective (symptom scores after treatment decreased by two points), effective (symptom scores after treatment decreased by one point), and invalid (symptom scores after treatment hardly decreased). Zhou 2005 reported the same efficacy assessment as Yang 2009, except without a "healing" description. Chang 2010 and Jin 2011 reported FD scores for pretreatment, post-treatment, and follow-

Another primary outcome (NDI) was used to assess efficacy in Park 2009 and Chang 2010. Both trials separately showed two types of NDI scores between groups: Nepean Dyspepsia Symptom Index (NDSI) and Nepean Dyspepsia Life Quality Index (NDLQI).

None of these studies reported on outcomes of the Functional Digestive Disorder Quality of Life questionnaire (FDDQL), the Satisfaction With Dyspepsia Related Health scale (SODA), the



Digestive Health Status Instrument (DHSI), effective/inefficient rates, and symptom recurrence six months from completion of acupuncture treatment.

For secondary outcome measures, SF-36 was used to assess life quality between groups in Chang 2010 and Jin 2011. SAS, SDS, and adverse events were reported in Jin 2011. Additionally, Shi 2009 assessed frequency of FD symptoms between groups; zero points meant no attack, one point indicated one to three attacks per week, two points showed four to six attacks per week, and three points represented attacks every day as well as adverse effects of interventions. Jin 2011 described scores for each FD symptom before and after treatment. Zhou 2005 also reported symptom scores for each subtype diagnosed by Rome II FD criteria and assessed efficacy as totally effective or invalid.

Excluded studies

Six trials were excluded for the following reasons: One study did not clearly state the dyspepsia diagnostic criterion (Paterson 2003); one study was a cross-over trial (Liu S 2008); one study was a letter to

the editors (Beyazit 2010); three studies were quasi-RCTs in which participants were allocated in terms of visiting time (Chen 2005; Peng 2008; Yang 2009a); three studies were awaiting classification for failure to identify full texts (Cao 2007; Cash 2001; Sun 2006); and one study was excluded because the review authors were unable to get in touch with the study author to have unclear data explained (Zhang 2009b).

Risk of bias in included studies

Results of risk of bias can be seen in Figure 2 and Figure 3. The most frequent bias was noted in blinding. For characteristics of acupuncture manipulations, it is too difficult to conduct blinding for therapists and participants, especially those familiar with acupuncture. Another bias involved lack of comprehensive descriptions of randomization concealment. For the quality of evidence assessment performed using the GRADE system, almost all evidence from outcomes was found to be of low quality (Summary of findings 2; Summary of findings 4; Summary of findings 5) or very low quality (Summary of findings for the main comparison; Summary of findings 3; Summary of findings 5).

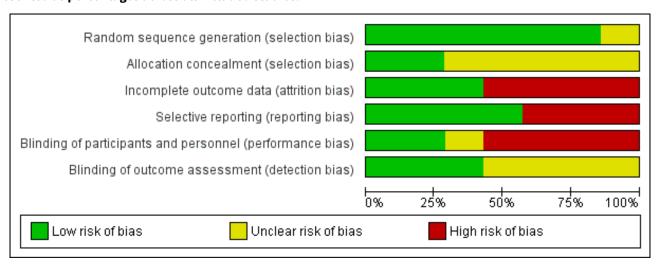


Figure 2. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)
Chang 2010	•	•	•	•	?	•
Jin 2011	•	•	•		•	•
Park 2009	•	?		•	•	•
Shi 2009	•	?	•			?
Tang 2006	•	?	•	•		?
Yang 2009	•	?	•	•		?
Zhou 2005	?	?	•			?



Figure 3. Methodological quality graph: review authors' judgements about each methodological quality item presented as percentages across all included studies.



Allocation

Random sequence generation

Zhou 2005 just briefly mentioned random allocation but neglected to state the random method used and assessed unclear risk of bias. Other included trials described the method of random generation and were determined to have low bias risk.

Random concealment

Central randomization could ensure sequence concealment in Chang 2010; sealed, opaque, and sequentially numbered envelopes were helpful for validating the random unknown in Jin 2011. Other included trials did not describe random concealment and were assessed as having unclear risk of bias.

Blinding

Blinding of participants and personnel

Both Park 2009 and Jin 2011 reported that the same therapist would conduct the manipulations in acupuncture and control groups, and that participants were blinded to the formula. Thus, these trials were assessed as having low risk of bias. Chang 2010 did not offer any explanation of blinding and was assessed to have an unclear risk of bias. As acupuncture was so different from medication, and no details were obtained from the other four included trials, all were assessed as having high risk of bias.

Blinding of outcome assessment

Park 2009, Chang 2010, and Jin 2011 described that assessors were blinded to allocation; therefore these studies were assessed as having low risk of bias. Because they provided no descriptions of blinding, all four of the other trials were assessed as having an unclear risk of bias.

Incomplete outcome data

All included trials were free of incomplete outcome data, except Jin 2011, Shi 2009, and Zhou 2005. Jin 2011 did not provide scores for each FD symptom during the follow-up period. FD symptom scores at baseline were omitted in Shi 2009 and Zhou 2005.

Selective reporting

Scores for each FD symptom during the follow-up period were not reported in Jin 2011. Shi 2009 and Zhou 2005 omitted FD symptom scores at baseline and offered just the scores after treatment for interventions. Therefore, selective omission outcomes reporting may have occurred, leading to bias in both studies.

Effects of interventions

See: Summary of findings for the main comparison Manual acupuncture compared with cisapride for functional dyspepsia; Summary of findings 2 Manual acupuncture compared with domperidone for functional dyspepsia; Summary of findings 3 Manual-electroacupuncture compared with domperidone for functional dyspepsia; Summary of findings 4 Electroacupuncture compared with itopride for functional dyspepsia; Summary of findings 5 Acupuncture compared with sham acupuncture for functional dyspepsia

1 Acupuncture versus medications

Four studies (358 participants) were included (Shi 2009; Tang 2006; Yang 2009; Zhou 2005). Because of the explicit clinical heterogeneity (inhomogeneous interventions and controls) among included studies, descriptive analysis was conducted. No significance was found for manual acupuncture, electroacupuncture, or manual-electroacupuncture compared with medications. Additionally, we detected that manual acupuncture would bring about fewer adverse effects than were seen with cisapride. However, evidence of outcomes was of very low quality.

1.1 Manual acupuncture compared with cisapride

Descriptive analysis was performed on the following outcome measures in Shi 2009 (90 participants).

1.1.1 Symptom scores of FD

Effective rate was calculated as the (symptom scores after treatment - symptom scores before treatment) / symptom scores before treatment*100%. When effective rate was greater than



or equal to 25%, this meant "effective," greater than or equal to 50% meant "marked effective," and greater than or equal to 75% meant "healing" effect. "Effective," "marked effective," and "healing" were categorized as "positive effect," and "invalid" as "negative effect". Then, the outcome data were transformed as dichotomous data. No significance was detected for manual acupuncture compared with cisapride in improving FD symptom scores (RR 1.02, 95% CI 0.91 to 1.16, very low-quality evidence).

1.1.2 Frequency of FD symptoms

Frequency of FD symptoms meant the number of attacks per week. On the basis of extracted data, we separated FD symptoms into two groups: positive effect (no attacks per week) and negative effect (RR 1.04, 95% CI 0.75 to 1.44, very low quality evidence). No significance was detected for manual acupuncture compared with cisapride in reducing the frequency of FD attacks.

1.1.3 Adverse effects

The significant finding for adverse effects showed that manual acupuncture may have fewer adverse effects than are seen with cisapride in the treatment of patients with FD (RR 0.21, 95% CI 0.07 to 0.69, very low-quality evidence).

1.2 Manual acupuncture compared with domperidone

Descriptive analysis was performed for the following outcome measures in Tang 2006 (62 participants).

1.2.1 Symptom scores of FD

FD symptom scores were transformed to dichotomous data, as was described in the aforementioned Section 1.1.1. No significance in FD symptom scores was investigated between manual acupuncture and domperidone (RR 1.24, 95% CI 0.97 to 1.58, low-quality evidence).

1.2.2 Adverse effects

No adverse effects data were reported in this study, which examined manual acupuncture versus domperidone.

1.3 Manual-electroacupuncture compared with domperidone

Zhou 2005 (126 participants) compared manual acupuncture combined with electroacupuncture with domperidone medication.

1.3.1 Symptom scores of FD

FD symptom scores were analyzed as described in the aforementioned method in Section 1.1.1 (RR 1.14, 95% CI 1.00 to 1.30, very low-quality evidence). No significance was detected in FD symptom scores between the manual-electroacupuncture group and the group treated with domperidone.

1.3.2 Symptom scores of FD subtypes

Symptom scores of FD subtypes were as follows: ulceration subtype: RR 0.81, 95% CI 0.26 to 2.51, very low-quality evidence; regurgitation subtype: RR 0.89, 95% CI 0.42 to 1.86, very low-quality evidence; dyskinesia subtype: RR 1.20, 95% CI 0.76 to 1.89, very low-quality evidence; and nonspecific subtype: RR 1.45, 95% CI 0.77 to 2.76, very low-quality evidence. No significance was

detected in symptom scores of FD subtypes between the manualelectroacupuncture group and the group given domperidone.

1.3.3 Adverse effects

No adverse effects data were reported in the study examining manual-electroacupuncture versus domperidone.

1.4 Electroacupuncture compared with itopride

Descriptive analysis was performed for the following outcome measures in Yang 2009 (80 participants).

1.4.1 Symptom scores of FD

FD symptom scores were transformed as dichotomous data as described in the aforementioned method in Section 1.1.1. No significance was investigated in improving FD symptom scores of electroacupuncture compared with itopride (RR 1.11, 95% CI 0.98, 1.27, low-quality evidence).

1.4.2 Adverse effects

No adverse effects data were reported in the study examining electroacupuncture versus itopride.

2. Acupuncture versus sham acupuncture

Three studies (184 participants) were included (Chang 2010; Jin 2011; Park 2009).

2.1 Symptom scores of FD

Chang 2010 (60 participants) and Jin 2011 (56 participants) reported continuous data, and we applied MDs and 95% CIs to describe them as follows: Chang 2010: MD -2.24, 95% CI -2.94 to -1.54, low-quality evidence; and Jin 2011: MD -16.43, 95% CI -20.39 to -12.47, low-quality evidence. Substantial heterogeneity was detected: I² = 98%. Because of the data on FD symptom scores provided, different symptom severity may be the most likely cause of heterogeneity. Therefore, descriptive analysis was performed. Both studies showed that acupuncture can decrease symptom scores of FD more than sham acupuncture can; however, the outcomes were based on low-quality evidence.

2.2 Symptom scores of FD during the follow-up period

Heterogeneity was detected ($I^2 = 88\%$) and may be a result of the length of follow-up. Descriptive analysis was separately conducted in Chang 2010 (MD -2.11, 95% CI -2.94 to -1.28, low-quality evidence) and Jin 2011 (MD -14.28, 95% CI -22.52 to -6.04, low-quality evidence). Both studies suggested that acupuncture would lessen symptom scores of FD during the follow-up period more significantly, but the evidence was of low quality.

2.3 NDI

2.3.1 NDSI

Substantial heterogeneity of NDSI was investigated by a fixed-efffect or a random-effects model: $I^2 = 83\%$ in Chang 2010 and Park 2009 (68 participants); descriptive analysis was conducted. The heterogeneous factors might be due to different symptom severity. Chang 2010 supported that acupuncture could lessen NDSI scores more significantly than sham acupuncture (MD -15.67, 95% CI



-23.77 to -7.57, low-quality evidence). No significance was detected in Park 2009 for acupuncture compared with sham acupuncture in decreasing NDSI (MD 0.95, 95% CI -9.85 to 11.7, low-quality evidence).

2.3.2 NDLQI

Potential inconsistency of NDLQI was detected under a fixed-effect or a random-effects model: I² = 49%. Therefore, we conducted a descriptive analysis. Different symptom severity might be the cause of the heterogeneity. Chang 2010 stood on the side that acupuncture can improve life quality of patients with FD more than sham acupuncture can (MD 11.63, 95% CI 6.12 to 17.14, low-quality evidence). No significance was found in Park 2009 for acupuncture compared with sham acupuncture in improving quality of life (MD 5.14, 95% CI -2.07 to 12.35, low-quality evidence).

2.3.3 NDI at follow-up of one month

Chang 2010 provided NDSI during the follow-up period (MD -16.63, 95% CI -24.51 to -8.75, low-quality evidence) and NDLQI during the follow-up period (MD 13.64, 95% CI 8.22 to 19.06, low-quality evidence). This implied that acupuncture would improve NDI scores at follow-up of one month more than sham acupuncture would; however, the evidence was of low quality.

2.4 SF-36

The I² statistical value of 1% under a fixed-effect model suggested homogeneity in SF-36 between Chang 2010 and Jin 2011. Total effect meant that acupuncture can improve life quality of patients with FD more than sham acupuncture can (MD 12.18, 95% CI 8.45 to 15.91, low-quality evidence).

2.5 SF-36 at follow-up of one month

Results of Chang 2010 (MD 15.44, 95% CI 9.68 to 21.20, low-quality evidence) imply that acupuncture could improve life quality more significantly than sham acupuncture at follow-up of one month.

2.6 SAS

Jin 2011 supported that acupuncture could ameliorate the anxiety of patients with FD more than sham acupuncture could (MD -9.84, 95% CI -14.58 to -5.10, low-quality evidence).

2.7 SDS

Jin 2011 supported the result that acupuncture could also ameliorate depression among patients with FD more than sham acupuncture could (MD -8.76, 95% CI -14.09 to -3.43, low-quality evidence).

2.8 Adverse effects

In Jin 2011, no significance was found for acupuncture compared with sham acupuncture in reducing adverse effects (RR 7.00, 95% CI 0.38 to 129.55, very low-quality evidence). Because of the large effect size with very wide confidence intervals, results indicated serious imprecision; attention should be paid to this interpretation.

DISCUSSION

Summary of main results

Seven RCTs were eventually included. The interventions and controls can be roughly divided into two groups: manual acupuncture, electroacupuncture, or manual-electroacupuncture versus medications (cisapride, domperidone, or itopride); and acupuncture versus sham acupuncture. No comparison between acupuncture and waiting list was included.

Descriptive analysis was applied in all trials of acupuncture versus medications because of the small number of trials and their clinical heterogeneity. No significance was found for acupuncture versus medications in reducing FD symptom scores and frequency of FD attack. In trials of acupuncture versus sham acupuncture, all descriptive or quantitative analysis results implied that acupuncture can improve FD symptom scores, NDI scores, and SF-36, SAS, and SDS more significantly than sham acupuncture, except that no significance was found in Park 2009 for NDI scores. Results for the follow-up period of Jin 2011 and Chang 2010 show that acupuncture might improve symptom scores of FD more than sham acupuncture. Additionally, the descriptive analysis of safety in treating FD showed no significance for acupuncture compared with sham acupuncture in reducing adverse effects (Jin 2011), but indicated that it may bring about fewer side effects than the drug cisapride (Shi 2009). It is worth noting that evidence on the above outcomes was of low or even very low quality.

Overall completeness and applicability of evidence

This review involved RCTs on two major acupuncture methods (manual acupuncture and electroacupuncture) for patients meeting Rome II or Rome III diagnostic criteria for FD. Outcome measures included efficacy and safety assessment, involving the most frequently used tools at present, such as FD symptom scores, NDI, SF-36, SAS, SDS, and so forth. Therefore, results of this review reflect the current situation for acupuncture in FD.

Quality of the evidence

All evidence was assessed to be of low or even very low quality when the GRADE system was used, and the most serious reasons for downgrading included study limitations (blinding) and imprecision (small sample size). The quality of the evidence meant that further research would be very likely to change the estimate of effect, or that we were very uncertain about the estimate. Thus, the body of evidence identified cannot yet allow a robust conclusion regarding the efficacy and safety of acupuncture for FD.

Potential biases in the review process

Some potential biases might be noted during interpretation of the estimate of effect. First, acupuncture manipulation is quite different from the quantitative use of medication. It varies among different therapists or acupuncture techniques, even when the same guidelines are followed. As a result, the heterogeneity of acupuncture manipulations reported in different trials might have an impact on the effect estimate. Second, all seven included trials focused on the Asian style of acupuncture (six Chinese acupuncture trials and one Korean acupuncture trial); Western acupuncture was absent. Regarding differences in acupoint selection, manipulations, and treatment duration and frequency, further review combined with information on different



types of acupuncture would be necessary for an update. Third, potentially high risk of bias might be present in the included trials in the following patterns. Neither trial reported details on randomization concealment and calculation of proper sample size. Also, dropout observation was lacking in each study, so it might be impossible to ensure that all participants did not withdraw during the experiment. Follow-up observation was not brought to the forefront during performance of the experiment.

Agreements and disagreements with other studies or reviews

Two systematic reviews on acupuncture for the treatment of FD were retrieved. In Schneider 2007, clinical trials of acupuncture for functional gastrointestinal disease were included, and only one controlled study (Chen 1998) was available. No significance was detected in Chen 1998 for acupuncture compared with cisapride medication in improving FD symptoms. Another review (Zhu 2008) was different from our review in that RCTs and quasi-RCTs on acupuncture for FD were included; participants were diagnosed by different international criteria; interventions consisted of acupuncture techniques without limitations; and controls included blank control, modern medications, herbs, and sham acupuncture. Results in Zhu 2008 imply that acupuncture may be superior to medication in improving total scores for FD symptoms. On consideration of the complexity of FD diagnostic criteria and heterogeneity of different acupuncture methods as described in the above reviews, we have set the present criteria in considering studies for inclusion in this review. However, low quality of evidence in three systematic reviews was the same and has resulted in lack of robust evidence on the use of acupuncture for FD. The main reasons for downgrading were risk of bias (unclear description of randomization and its concealment, difficulty of conducting blinding in acupuncture studies), absence of sample size calculations and follow-up observations, and so forth. Therefore, upgrading the evidence level of acupuncture studies will require continued effort.

AUTHORS' CONCLUSIONS

Implications for practice

Given the low or very low quality of evidence obtained, it cannot be concluded whether acupuncture is more effective or safer than other treatments in the treatment of FD.

Implications for research

Acupuncture, especially the Chinese style of acupuncture, has special characteristics compared with other treatments. Therefore, some consensus must be reached globally to improve the quality of evidence for acupuncture studies. On one hand, for assessment of risk of bias, blinding of therapists is impossible, and even blinding of participants would require great care. Thus, whether current assessment methods for blinding are suitable for acupuncture studies remains controversial. On the other hand, language limitations have impeded comprehensive understanding of CONSORT (Altman 2001) and STRICTA recommendations (MacPherson 2010). Thus, efforts are needed to improve acupuncture publications, especially those on Chinese acupuncture, in accordance with these guidelines.

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REFERENCES

References to studies included in this review

Chang 2010 (published and unpublished data)

Chang XR, Lan L, Yan J, Wang XJ, Chen HM. Efficacy of acupuncture at Foot-Yangming Meridian in the treatment of patients with functional dyspepsia: an analysis of 30 cases. World Chinese Journal of Digestology 2010;**18**(8):839-44. [DOI: 10.3969/j.issn.1009-3079.2010.08.017]

Jin 2011 {published and unpublished data}

Jin Y. Efficacy of acupuncture in the treatment of patients with functional dyspepsia. Unpublished medicine master dissertation. Beijing University of Chinese Medicine. 2011.

Park 2009 (published and unpublished data)

Park YC, Kang W, Choi SM, Son CG. Evaluation of manual acupuncture at classical and nondefined points for treatment of functional dyspepsia: a randomized-controlled trial. Journal of Alternative and Complementary Medicine 2009;15(8):879-84. [DOI: 10.1089/acm.2008.0369]

Shi 2009 (published and unpublished data)

Shi H, Zhang J, Guo H.

Clinical observation of acupuncture for 90 cases of patients with fur Beijing Journal of Traditional Chinese Medicine 2009;28(9):732-3.

Tang 2006 (published and unpublished data)

Tang S, Xu Z, Tang P, Liang L.

Acupuncture for functional dyspepsia: a randomised controlled trial. Journal of Sichuan Traditional Chinese Medicine 2006;24(4):101-2.

Yang 2009 (published and unpublished data)

Yang M.

Electroacupuncture treatment of functional dyspepsia from a clinical research of Internal Medicine, 2001:159-75. Unpublished medicine master dissertation, Hubei University of TCM. 2009.

Zhou 2005 {published and unpublished data}

Zhou Y, Zheng JG.

Clinical observation on acupuncture treatment of functional dyspepsia. Journal of Acupuncture and Tuina Science 2005;**3**(2):20-2. [DOI: 10.1007/BF02845366]

References to studies excluded from this review

Beyazit 2010 (published and unpublished data)

Beyazit Y, Kekilli M, Purnak T. Effects of transcutaneous electrical acu-stimulation in patients with functional dyspepsia. Alimentary Pharmacology and Therapeutics 2010;31(9):961-8.

Chen 2005 {published and unpublished data}

Chen JY, Pan F, Xu JJ, Zhan CE.

Effects of acupuncture on the gastric motility in patients with function 2000 15 p34 (%):663-94. Chinese Journal of Integrated Traditional and Western Medicine 2005;25(10):880-2.

Liu S 2008 (published and unpublished data)

Liu S, Peng S, Hou X, Ke M, Chen JD. Transcutaneous electroacupuncture improves dyspeptic symptoms and increases high frequency heart rate variability in patients with functional dyspepsia. Neurogastroenterology and Motility 2008;**20**(11):1204-11.

Paterson 2003 {published and unpublished data}

Paterson C, Ewings P, Brazier JE, Britten N.

Treating dyspepsia with acupuncture and homeopathy: reflections on a pilo Complementary Therapies in Medicine 2003;11(2):78-84.

Peng 2008 (published and unpublished data)

Peng SF, Yang JY, Shi ZH.

Electroacupuncture improves gastric motility, autonomic nerve activity and World Chinese Journal of Digestology 2008;16(36):4105-9.

Yang 2009a (published and unpublished data)

Yang M, Zhang H, Zou R.

Effects of acupuncture on the gastric motility in patients with functional dys Chinese Journal of Rehabilitation 2009;24(2):100-2.

References to studies awaiting assessment

nctional dyspepsia.

Cao 2007 {published and unpublished data}

Cao J, Qu F, Zhou J.

Improvement of gastric movement in patients with functional dyspepsia, tre International Journal of Clinical Acupuncture 2007;16(1):23-6.

Cash 2001 (published and unpublished data)

Cash BD, Schoenfeld P.

Alternative medical therapies for dyspepsia: a systematic review of randomi In: Johnson DA, Katz PO, Castell DO editor(s). Dyspepsia.

Philadelphia, PA: American College of Physicians - American

Sun 2006 {published and unpublished data}

Sun D, Cao J.

Observation of the therapeutic effect of acupuncture on 58 cases of function International Journal of Clinical Acupuncture 2006;15(3):169-72.

Zhang 2009b {published and unpublished data}

The clinical observation of Shu Mu with electroacupuncture treatment on fu Unpublished medicine master dissertation, Hubei University of TCM. 2009.

Additional references

Altman 2001

Altman DG, Schulz KF, Moher D, Egger M, Davidoff F, Elbourne D, et al. The revised CONSORT statement for reporting randomized trials: explanation and elaboration. Annals of Internal Medicine

Chen 1998

Chen R, Kang M. Observation on frequency spectrum of electrogastrogram (EGG) in acupuncture treatment of



functional dyspepsia. *Journal of Traditional Chinese Medicine* 1998;**18**:184-7.

Deng 1997

Deng L, Gan Y, He S, Ji X, Li Y, Wang R, et al. Chinese Acupuncture and Moxibustion. Vol. **54**, Beijing: Foreign Languages Press, 1997:71-4.

Drossman 2006

Drossman DA. The functional gastrointestinal disorders and the Rome III process. *Gastroenterology* 2006;**130**:1377–90.

Higgins 2003

Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003;**327**:557-60.

Higgins 2011

Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions, Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. www.cochranehandbook.org.

Holtmann 2006

Holtmann G, Talley NJ, Liebregts T, Adam B, Parow C. A placebo controlled trial of itopride in functional dyspepsia. *New England Journal of Medicine* 2006;**354**:832-40.

Lao 1996

Lao L. Acupuncture techniques and devices. *Journal of Alternative and Complementary Medicine* 1996;**2**:23–5.

MacPherson 2010

MacPherson H, Altman DG, Hammerschlag R, Youping L, Taixiang W, White A, et al. Revised standards for reporting interventions in clinical trials of acupuncture (STRICTA): extending the CONSORT statement. *Journal of Evidence-Based Medicine* 2010;**3**(3):140-55. [PUBMED: 21349059]

Mahadeva 2006

Mahadeva S, Goh KL. Epidemiology of functional dyspepsia: a global perspective. *World Journal of Gastroenterology* 2006;**12**(17):2661-6.

Mönkemüller 2006

Mönkemüller K, Malfertheiner P. Drug treatment of functional dyspepsia. *World Journal of Gastroenterology* 2006;**12**(17):2694-700.

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Noguchi 2008

Noguchi E. Mechanism of reflex regulation of the gastroduodenal function by acupuncture. *Evidence-based Complementary and Alternative Medicine* 2008;**5**(3):251-6.

RevMan 2011 [Computer program]

The Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager (RevMan). Version 5.1. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2011.

Rome III 2006

Rome III Diagnostic Criteria for Functional Gastrointestinal Disorders. http://www.romecriteria.org/assets/pdf/19_RomeIII_apA_885-898.pdf (accessed 7 July 2014).

Schneider 2007

Schneider A, Streitberger K, Joos S. Acupuncture treatment in gastrointestinal diseases: a systematic review. *World Journal of Gastroenterology* 2007;**13**(25):3417-24.

Xu 2004

Xu S, Zha H, Hou X, Gao Z, Zhang Y, Chen JD, et al. Electroacupuncture accelerates solid gastric emptying in patients with functional dyspepsia. *Gastroenterology* 2004;**126**:A-437.

Zeng 2009

Zeng F, Song WZ, Liu XG, Xie HJ, Tang Y, Shan BC, et al. Brain areas involved in acupuncture treatment on functional dyspepsia patients: a PET-CT study. *Neuroscience Letters* 2009;**456**(1):6-10.

Zeng 2011

Zeng F, Qin W, Liang F, Liu J, Tang Y, Liu X, et al. Abnormal resting brain activity in patients with functional dyspepsia is related to symptom severity. *Gastroenterology* 2011;**141**(2):499-506.

Zhu 2008

Zhu H. Acupuncture for functional dyspepsia: a systematic review. Unpublished medicine master dissertation. Chengdu University of TCM. 2008.

Chang 2010

Methods Eligibility criteria: Rome III diagnostic criteria for functional dyspepsia

Study duration: 4 weeks

Sequence generation: randomization allocation mentioned without details

Randomization concealment: not described



Chang 2010 (Continued)

Blind participants: not described

Blind assessors: not described Blind therapists: not described

Baseline comparability: Mean and standard deviation (SD) in age, disease course, and FD symptom

scores were shown; no significance was found

Follow-up: NDI, SF-36, and FD symptom scores assessed 1 month after interventions

Participants

Setting: outpatients from the First Affiliated Hospital of Hunan University of TCM, Changsha City, Hunan

Province, China

Total number: 60

Male/Female (n/n): 19/41

Mean age (± SD) or age range, years: between 21 and 51

Duration of functional dyspepsia before recruitment: 1.7 to 6.5 years

Important inclusion criteria (clearly describe): without organic disease

Important exclusion criteria (clearly describe): with pregnancy, lactation, or gestation-in-plan

Interventions

ACUPUNCTURE GROUP

Number allocated to acupuncture: 30

Style of acupuncture: manual acupuncture

Needles: sterile needles, gauge 32, length of 25 mm and 40 mm, single-use, made by Suzhou Medical

Appliance Co., Ltd (Jiangsu, China)

Numbers and names of points stimulated: a formula of 4 acupoints stimulated involving ST32, ST36,

ST40, and ST42

Insertion depth: 0.3 to 0.5 cm

Manipulation after insertion: lifting and thrusting while rotating

"De-qi" required or not: yes

Duration of treatment (minutes): 30

Frequency of treatment per week: 5 times

Total length of treatment period (weeks): 4

Description of therapists' qualifications: no, but participants were treated by TCM doctors

CONTROL GROUP

Number allocated to control: 30

Style of control: sham acupuncture (puncturing sham acupoints)

Needles: sterile needles, gauge 32, length of 25 mm and 40 mm, single-use, made by Suzhou Medical Appliance Co., Ltd (Jiangsu, China)

Numbers and names of points stimulated: a formula of 4 sham acupoints stimulated involving points lateral to ST32, ST36, ST40, and ST42 between Stomach Meridian and Gallbaldder Meridian

Insertion depth: 0.3 to 0.5 cm



Chang 2010 (Continued)

Manipulation after insertion: lifting and thrusting while rotating

"De-qi" required or not: yes

Duration of treatment (minutes): 30

Frequency of treatment per week: 5 times

Total length of treatment period (weeks): 4

Description of therapists' qualifications: no, but participants were treated by TCM doctors

CO-INTERVENTIONS IN GROUPS: no

Outcomes

1. NDI

<u>Conclusion from original data</u>: Significance in both groups was reported in scores after treatment versus before treatment, at follow-up versus before treatment. Significance was found in acupuncture group compared with sham acupuncture group

1.1 Nepean Dyspepsia Symptom Index (NDSI)

ACUPUNCTURE GROUP: pretreatment 42.53 ± 16.642 ; post-treatment 17.86 ± 12.660 ; **follow-up** 14.14 ± 13.120

CONTROL GROUP: pretreatment 39.45 \pm 16.917; post-treatment 30.45 \pm 16.917; **follow-up** 27.69 \pm 14.707

1.2 Nepean Dyspepsia Life Quality Index (NDLQI)

ACUPUNCTURE GROUP: pretreatment 76.43 \pm 13.337; post-treatment 91.60 \pm 6.237; **follow-up** 94.20 \pm 6.706

 $\textbf{CONTROL GROUP:} \ pretreatment\ 77.97 \pm 9.813; \ post-treatment\ 81.51 \pm 10.522; \ \textbf{follow-up}\ 82.10 \pm 9.813; \ post-treatment\ 81.51 \pm 10.522; \ \textbf{follow-up}\ 82.10 \pm 9.813; \ post-treatment\ 81.51 \pm 10.522; \ \textbf{follow-up}\ 82.10 \pm 9.813; \ post-treatment\ 81.51 \pm 10.522; \ \textbf{follow-up}\ 82.10 \pm 9.813; \ post-treatment\ 81.51 \pm 10.522; \ \textbf{follow-up}\ 82.10 \pm 9.813; \ post-treatment\ 81.51 \pm 10.522; \ \textbf{follow-up}\ 82.10 \pm 9.813; \ post-treatment\ 81.51 \pm 10.522; \ \textbf{follow-up}\ 82.10 \pm 9.813; \ post-treatment\ 81.51 \pm 10.522; \ \textbf{follow-up}\ 82.10 \pm 9.813; \ post-treatment\ 81.51 \pm 10.522; \ \textbf{follow-up}\ 82.10 \pm 9.813; \ post-treatment\ 81.51 \pm 10.522; \ \textbf{follow-up}\ 82.10 \pm 9.813; \ post-treatment\ 81.51 \pm 10.522; \ \textbf{follow-up}\ 82.10 \pm 9.813; \ post-treatment\ 81.51 \pm 10.522; \ \textbf{follow-up}\ 82.10 \pm 9.813; \ post-treatment\ 81.51 \pm 10.522; \ \textbf{follow-up}\ 82.10 \pm 9.813; \ post-treatment\ 81.51 \pm 10.522; \ \textbf{follow-up}\ 82.10 \pm 9.813; \ post-treatment\ 81.51 \pm 10.522; \ \textbf{follow-up}\ 82.10 \pm 9.813; \ post-treatment\ 81.51 \pm 10.522; \ \textbf{follow-up}\ 82.10 \pm 9.813; \ post-treatment\ 81.51 \pm 10.522; \ \textbf{follow-up}\ 82.10 \pm 9.813; \ post-treatment\ 81.51 \pm 10.522; \ \textbf{follow-up}\ 82.10 \pm 9.813; \ post-treatment\ 81.51 \pm 10.522; \ \textbf{follow-up}\ 82.10 \pm 9.813; \ post-treatment\ 81.51 \pm 10.522; \ \textbf{follow-up}\ 82.10 \pm 9.813; \ post-treatment\ 81.51 \pm 10.522; \ \textbf{follow-up}\ 82.10 \pm 9.813; \ post-treatment\ 81.51 \pm 9.813; \ p$

2. Symptom scores of FD

<u>How to assess</u>: 0 points: no symptoms; 1 point: slight symptoms; 2 points: moderate symptoms but not sufficient to affect daily life; 3 points: symptoms severe enough to affect daily life

<u>Conclusion from original data</u>: Significance in both groups was reported in scores after treatment versus before treatment, at follow-up versus before treatment. Significance was found in acupuncture group compared with sham acupuncture group

ACUPUNCTURE GROUP: pretreatment 4.33 ± 1.446 ; post-treatment 1.50 ± 1.036 ; **follow-up** 1.25 ± 1.236

CONTROL GROUP: pretreatment 3.97 ± 1.377 ; post-treatment 3.38 ± 1.568 ; **follow-up** 3.00 ± 1.336

3. SF-36 scale

<u>Conclusion from original data</u>: Significance in both groups was reported in scores after treatment versus before treatment, at follow-up versus before treatment. Significance was found in acupuncture group compared with sham acupuncture group

ACUPUNCTURE GROUP: pretreatment 64.19 ± 14.349 ; post-treatment 82.04 ± 9.084 ; **follow-up** 88.57 ± 5.691

CONTROL GROUP: pretreatment 68.76 ± 11.264; post-treatment 75.53 ± 9.082; **follow-up** 77.70 ± 8.432

Notes

Risk of bias



Chang 2010 (Continued)

Bias	Authors' judgement	Support for judgement
Random sequence genera-	Low risk	Quote: "Sixty patients were divided randomly into two groups"
tion (selection bias)		Comment: Central randomization was confirmed upon telephone visit
Allocation concealment	Low risk	Quote: no description
(selection bias)		Comment: It has been confirmed that allocation concealment was performed by another professional team named Chengdu GCP Centre, using specific software, after visiting the main study staff by phone
Incomplete outcome data	High risk	Quote: not found
(attrition bias) All outcomes		Comment: probably no
Selective reporting (re-	Low risk	Quote: not found
porting bias)		Comment: probably yes
Blinding of participants	Unclear risk	Quote: no description
and personnel (perfor- mance bias) All outcomes		Comment: It could not be validated
Blinding of outcome as-	Low risk	Quote: not mentioned
sessment (detection bias) All outcomes		Comment: It was replied in a phone visit that outcome assessment was done by people unknown to allocation

Jin 2011

Methods	Eligibility criteria: Rome III diagnostic criteria for functional dyspepsia
	Study duration: 4 weeks
	Sequence generation: randomization number table
	Randomization concealment: sealed, opaque, and numbered envelopes
	Blind participants: yes, but not with details
	Blind assessors: yes, other participants unknown to allocation performed the assessment
	Blind therapists: no
	Baseline comparability: Mean and standard deviation (SD) in age, gender, disease course, and FD symptom score were shown; no significance was found
	Follow-up: FD symptom score assessed 3 months after interventions
Participants	Setting: outpatients from the Guan'anmen Hospital of China Academy of Chinese Medical Sciences, Beijing City, China
	Total number: 56
	Male/Female (n/n): 21/35
	Mean age (± SD) or age range, years: between 18 and 70



Jin 2011 (Continued)

Duration of functional dyspepsia before recruitment: 1.0 to 40.0 years

Important inclusion criteria (clearly describe): without organic disease

Important exclusion criteria (clearly describe): with pregnancy, lactation, or gestation-in-plan

Interventions

ACUPUNCTURE GROUP

Number allocated to acupuncture: 28

Style of acupuncture: manual acupuncture

Needles: sterile needles, gauge 32, length of 25 mm, single-use, made by Suzhou Medical Appliance Co., Ltd (Jiangsu, China)

Numbers and names of points stimulated: a formula of 2 main acupoints stimulated involving ST36 and кі з

Insertion depth: 1 cun

Manipulation after insertion: lifting and thrusting while rotating

"De-qi" required or not: yes

Frequency of treatment per week: 3 to 4 times

Total length of treatment period (weeks): 4

Description of therapists' qualifications: yes, therapist was the one with 6 years of acupuncture practice

CONTROL GROUP

Number allocated to control: 28

Style of control: sham acupuncture (puncturing sham acupoints superficially)

Needles: sterile needles, gauge 32, length of 25 mm, single-use, made by Suzhou Medical Appliance Co., Ltd (Jiangsu, China)

Numbers and names of points stimulated: a formula of 2 main sham acupoints stimulated involving points lateral to ST36 and KI 3, which were in charge of the same spinal level as ST36 and KI 3

Insertion depth: 2 to 3 mm

Manipulation after insertion: lifting and thrusting while rotating

"De-qi" required or not: yes

Frequency of treatment per week: 3 to 4 times

Total length of treatment period (weeks): 4

Description of therapists' qualifications: yes, therapist was the same one with 6-year acupuncture practice

CO-INTERVENTIONS IN GROUPS: no

Outcomes

1. Symptom scores of FD

<u>How to assess</u>: 0 points: no symptoms; 1 point: slight symptoms; 2 points: moderate symptoms but not sufficient to affect daily life; 3 points: symptoms severe enough to affect daily life

<u>Conclusion from original data</u>: total scores in each group after treatment versus before treatment decreased significantly, but only total scores in the acupuncture group before treatment versus fol-



Jin 2011 (Continued)

low-up decreased significantly. Significance of total scores in acupuncture group compared with sham acupuncture group was found

ACUPUNCTURE GROUP: pretreatment 24.32 ± 8.28 , post-treatment 2.50 ± 3.28 , **follow-up** 1.68 ± 2.36

CONTROL GROUP: pretreatment 24.79 ± 7.48 , post-treatment 19.4 ± 8.23 , **follow-up** 16.43 ± 7.41 (pretreatment vs follow-up: **P value > 0.05)**

Scores for each FD symptom

ACUPUNCTURE GROUP

Postprandial discomfort: pretreatment 9.00 ± 2.09, post-treatment 1.57 ± 2.28

Early satiety: pretreatment 9.74 \pm 1.91, post-treatment 0.42 \pm 1.43

Epigastric pain: pretreatment 6.81 ± 2.23, post-treatment 0.48 ± 1.03

Epigastric burning sensation: pretreatment 6.31 ± 2.39, post-treatment 0.50 ± 1.50

CONTROL GROUP

Postprandial discomfort: pretreatment 8.89 ± 2.39, post-treatment 6.22 ± 2.59

Early satiety: pretreatment 8.43 ± 2.87, post-treatment 6.05 ± 2.52

Epigastric pain: pretreatment 7.41 \pm 3.02, post-treatment 6.32 \pm 3.41 (pretreatment vs post-treatment: **P value > 0.05)**

Epigastric burning sensation: pretreatment 6.71 ± 2.78 , post-treatment 6.47 ± 3.00 (pretreatment vs post-treatment: **P value > 0.05**)

2. SF-36 scale

<u>Conclusion from original data</u>: Scores in acupuncture group after treatment versus before treatment were increased significantly, as were scores of acupuncture group compared with sham acupuncture group

ACUPUNCTURE GROUP: pretreatment 52.50 ± 13.94, post-treatment 70.00 ± 12.549

CONTROL GROUP: pretreatment 54.00 ± 16.41 , post-treatment 56 ± 13.42 (pretreatment vs post-treatment: **P value > 0.05**)

3. SDS

<u>Conclusion from original data</u>: Scores in acupuncture group after treatment versus before treatment were decreased significantly, as were scores of acupuncture group compared with sham acupuncture group

ACUPUNCTURE GROUP: pretreatment 57.96 \pm 9.55, post-treatment 45.60 \pm 8.75

CONTROL GROUP: pretreatment 57.60 ± 11.84 , post-treatment 54 ± 10.08 (pretreatment vs post-treatment: **P value > 0.01**)

4. SAS

<u>Conclusion from original data</u>: Scores in acupuncture group after treatment versus before treatment were decreased significantly, as were scores of acupuncture group compared with sham acupuncture group

ACUPUNCTURE GROUP: pretreatment 52.30 ± 10.48 , post-treatment 42.3 ± 6.22

CONTROL GROUP: pretreatment 52.36 ± 9.67 , post-treatment 52.2 ± 7.98 (pretreatment vs post-treatment: **P value > 0.05**)

5. Adverse effects



Jin 2011 (Continued)

ACUPUNCTURE GROUP: 3 cases of numb feeling for 3 to 7 days

CONTROL GROUP: 0 cases

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were divided randomly into two groups in the way of randomization number table"
		Comment: probably done for allocation concealment description
Allocation concealment (selection bias)	Low risk	Quote: "allocation concealment was done by sealed, opaque and sequentially numbered envelopes"
		Comment: probably done
Incomplete outcome data	Low risk	Quote: Scores of all FD symptoms during the follow-up period are not shown
(attrition bias) All outcomes		Comment: probably yes
Selective reporting (reporting bias)	High risk	Quote: Scores of all FD symptoms during the follow-up period were not reported
		Comment: probably no
Blinding of participants and personnel (perfor- mance bias)	Low risk	Quote: "therapist was the same one conducting the acupuncture in treatment and control groups, patients were blinded to the formula, and statisticians were not involved into the study"
All outcomes		Comment: The therapist was not blinded; acupoints and sham acupoints are adjacent to each other, so probably blinding or participants was performed; this was probably done to blind statisticians
Blinding of outcome assessment (detection bias)	Low risk	Quote: "other participants but therapist who were unknown the allocation did the assessment"
All outcomes		Comment: probably done

Park 2009

Methods	Eligibility critoria, Domo II diagnostic critoria for functional dyspensia
Methous	Eligibility criteria: Rome II diagnostic criteria for functional dyspepsia

Study duration: 2 weeks

Sequence generation: block randomization mentioned without details

Randomization concealment: not described

Blind participants: participants except the doctor conducting acupuncture blinded, including investi-

gators, participants, and study monitors

Blind assessors: yes, but without details

Blind therapists: not blinded



Park 2009 (Continued)

Baseline comparability: No significance in mean age, gender, weight, height, severity of dyspepsia

symptoms, scores for quality of life, and treatment surmise was found

Participants Setting: patients from the Korean Oriental Medicine Clinics, South Korea

Total number: 68

Male/Female (n/n): 14/54

Mean age (± SD) or age range, years: between 20 and 60

Duration of functional dyspepsia before recruitment: not described

Important inclusion criteria (clearly describe): without organic disease

Important exclusion criteria (clearly describe): with organic disease

Interventions **ACUPUNCTURE GROUP**

Number allocated to acupuncture: 34

Style of acupuncture: manual acupuncture

Needles: sterile needles (diameter 0.25 mm, length 30 mm; made by Dongbang Acupuncture Inc., Seoul, South Korea)

Numbers and names of points stimulated: a formula of 6 acupoints stimulated involving LI4, LR3, PC6, SP4, ST36, and CV12

Insertion depth: 1.0 at LI4, LR3, PC6, and SP4; 2.5 cm at ST36 and CV12

Manipulation after insertion: rotate 90 degrees clockwise 3 times

"De-qi" required or not: not described

Duration of treatment (minutes): 15

Frequency of treatment per week: 3 times

Total length of treatment period (weeks): 2

Description of therapists' qualification: yes, the therapist was a licensed doctor

CONTROL GROUP

Number allocated to control: 34

Style of control: sham acupuncture (puncturing sham acupoints)

Needles: sterile needles (diameter 0.25 mm, length 30 mm; made by Dongbang Acupuncture Inc., Seoul, South Korea)

Numbers and names of points stimulated: 6 sham acupoints stimulated involving points of 10 mm to 20 mm away from LI4, LR3, PC6, SP4, ST36, and CV12

Manipulation: performance done by the same doctor for the acupuncture group

Duration of treatment (minutes): 15

Frequency of treatment per week: 3 times

Total length of treatment period (weeks): 2

Description of therapists' qualifications: yes, the therapist was a licensed doctor

CO-INTERVENTIONS IN GROUPS: no



Park 2009 (Continued)

Outcomes

1. NDI

<u>Conclusion from original data</u>: Dyspepsia symptoms and life quality of participants with FD were significantly improved in both groups, but no significance was found between the 2 groups

1.1 Nepean Dyspepsia Symptom Index (NDSI)

ACUPUNCTURE GROUP: pretreatment 59.59 ± 22.03; post-treatment 34.15 ± 24.74

CONTROL GROUP: pretreatment 55.71 ± 22.94 ; post-treatment 29.32 ± 20.76

1.2 Nepean Dyspepsia Life Quality Index (NDLQI)

ACUPUNCTURE GROUP: pretreatment 67.10 ± 15.06; post-treatment 88.27 ± 7.65

CONTROL GROUP: pretreatment 70.47 ± 19.66; post-treatment 86.50 ± 9.78

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Subjects were allocated into either the classical acupoints (CA) group or the non defined points (NP) group by block randomization"
		Comment: probably done
Allocation concealment	Unclear risk	Quote: no description
(selection bias)		Comment: cannot be identified for the moment
Incomplete outcome data	High risk	Quote: not found
(attrition bias) All outcomes		Comment: probably no
Selective reporting (reporting bias)	Low risk	Quote: not found
		Comment: probably yes
Blinding of participants and personnel (perfor- mance bias) All outcomes	Low risk	Quote: "A licensed doctor performed the acupuncture; other study participants, including investigators, patients, and study monitors, were blinded. The protocol forbade the doctor performing the acupuncture to give information of the treatment regimens to patients or other participants" Comment: probably done
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "A licensed doctor performed the acupuncture; other study participants, including investigators, patients, and study monitors, were blinded. The protocol forbade the doctor performing the acupuncture to give information of the treatment regimens to patients or other participants"
		Comment: probably done

Shi 2009

Methods Eligibility criteria: Rome III diagnostic criteria for functional dyspepsia

Study duration: 3 weeks



Shi 2009 (Continued)

Sequence generation: random number table

Randomization concealment: not described

Blind participants: not described

Blind assessors: not described Blind therapists: not described

Baseline comparability: It was described that no significance in gender, age, disease course, and FD

symptoms was found, but details of FD symptoms at baseline were not offered

Follow-up: no

Participants

Setting: outpatients of Yanqing TCM Hospital in Beijing, China

Total number: 90

Male/Female (n/n): 45/45

Mean age (± SD) or age range, years: between 18 and 66

Duration of functional dyspepsia before recruitment: 3 to 5 years

Important inclusion criteria (clearly describe): without hypertension and organic disease

Important exclusion criteria (clearly describe): with ulcer or organic disorders under gastroscopy; preg-

nancy, lactation or gestation-in-plan

Interventions

ACUPUNCTURE GROUP

Number allocated to acupuncture: 45

Style of acupuncture: manual acupuncture

Numbers and names of points stimulated: a formula of 3 acupoints stimulated involving ST36 (bilateral), CV12, and PC6 (bilateral), adding LR3, LR13, LR14, and SP6 on consideration of TCM syndrome differentiations

Insertion depth: 1 to 1.5 cun

Manipulation after insertion: lifting and thrusting while rotating

"De-gi" required or not: yes

Duration of treatment (minutes): 30

Frequency of treatment per week: 5 times

Total length of treatment period (weeks): 3

Description of therapists' qualifications: no, but participants were treated by TCM doctors

CONTROL GROUP

Number allocated to control: 45

Style of control: orally

Names of medications (if drugs, describe drug names): cisapride

Dose of medication per intake: 5 mg before meals

Frequency of medication per day: 3 times

Total length of treatment period (weeks): 3



Shi 2009 (Continued)

Description of co-medications: no

CO-INTERVENTIONS IN GROUPS: no

Outcomes

1. Symptom scores of FD after treatment

<u>How to assess</u>: 0 points: no symptoms (acupuncture 27 cases, control 26 cases); 1 point: slight symptoms (acupuncture 9 cases, control 10 cases); 2 points: moderate symptoms but not sufficient to affect daily life (acupuncture 5 cases, control 4 cases); 3 points: symptoms severe enough to affect daily life (acupuncture 4 cases, control 5 cases)

Effective rate = (symptom scores after treatment-symptom scores before treatment)*100%. When equal to or greater than 25%, this meant "effective," equal to or greater than 50% meant "marked effective," and equal to or greater than 75% meant "healing" effect. "Effective," "marked effective," and "healing" are categorized as "positive effect," and "invalid" as "negative effect"

Positive effect (acupuncture 42 cases, control 41 cases); negative effect (acupuncture 3 cases, control 4 cases)

Conclusion from original data: No significance was found between acupuncture and control groups

2. Frequency of symptoms

<u>How to assess</u>: 0 points: no attack (acupuncture 28 cases, control 27 cases); 1 point: 1 to 3 attacks per week (acupuncture 10 cases, control 9 cases); 2 points: 4 to 6 attacks per week (acupuncture 5 cases, control 6 cases); 3 points: attacks every day (acupuncture 2 cases, control 3 cases)

Conclusion from original data: No significance was found between acupuncture and control groups

3. Adverse effects

Acupuncture: 2 cases of subcutaneous hematoma and 1 case of vesicle (adverse effect rate 6.7%)

Control: 11 cases of slight dizziness and 3 cases of diarrhea or borborygmus (adverse effect rate 31.1%)

Notes

Details of FD symptoms at baseline were not described clearly in this trial, only the results after treatment was obtained. Also details of randomization and blinding were not described clearly

Weak points: too simply descriptive about baseline and study design

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "random number table"
		Comment: probably done
Allocation concealment (selection bias)	Unclear risk	Quote: not described
		Comment: cannot be confirmed
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: FD symptoms at baseline not described
		Comment: probably yes
Selective reporting (reporting bias)	High risk	Quote: FD symptoms at baseline not reported
		Comment: probably no
Blinding of participants and personnel (perfor- mance bias)	High risk	Quote: not described



Shi 2009 (Continued) All outcomes		Comment: Heterogeneity between acupuncture and drugs could result in performance bias
Blinding of outcome assessment (detection bias)	Unclear risk	Quote: not mentioned whether outcome assessment was done in blinding way
All outcomes		Comment: cannot be confirmed

Tang 2006

Methods	Eligibility criteria: Rome II diagnostic criteria for functional dyspepsia
	Study duration: 4 weeks
	Sequence generation: random number table
	Randomization concealment: not described
	Blind participants: not described
	Blind assessors: not described
	Blind therapists: not described
	Baseline comparability: yes, no significance in gender, age, FD course, and FD symptoms was found between groups
	Follow-up: no
Participants	Setting: outpatients from People's Hospital of Guangxi Zhuang Autonomous Region, Guangxi Province, China
	Total number: 62
	Male/Female (n/n): 29/33
	Mean age (\pm SD) or age range, years: 38.2 \pm 11.3 in acupuncture group and 36.7 \pm 12.8 in control group
	Duration of functional dyspepsia before recruitment: 3 to 108 months
	Important inclusion criteria (clearly describe): symptoms lasting for at least 1 month before enrollment
	Important exclusion criteria (clearly describe): organic disease under gastroscopy
Interventions	ACUPUNCTURE GROUP
	Number allocated to acupuncture: 32
	Style of acupuncture: manual acupuncture
	Numbers and names of points stimulated: a formula of 9 acupoints bilaterally stimulated involving ST36, CV12, PC6, LR3, BL15, BL19, BL20, BL21, and ST44
	Insertion depth: 1 cun
	Manipulation after insertion: lifting and thrusting while rotating
	"De-qi" required or not: yes
	Duration of treatment (minutes): 30
	Frequency of treatment per week: 7 times

Total length of treatment period (weeks): 4 (actually 30 days)



Tang 2006 (Continued)

Description of therapists' qualifications: no, but participants were treated by TCM doctors in the outpatient department

CONTROL GROUP

Number allocated to control: 30

Style of control: orally

Names of medications (if drugs, describe drug names): domperidone

Dose of medication per intake: 10 mg before meals

Frequency of medication per day: 3 times

Total length of treatment period (weeks): 4

Description of co-medications: yes, required that participants not take drugs for gastro discomfort

CO-INTERVENTIONS IN GROUPS: no

Outcomes

Symptom scores of FD

<u>How to assess</u>: 0 points: no symptoms; 1 point: slight symptoms; 2 points: moderate symptoms but not sufficient to affect daily life; 3 points: symptoms severe enough to affect daily life

<u>Conclusion from original data</u>: Significance was found in each group pretreatment and post-treatment and between 2 groups

Healing: no symptoms and no recurrence 1 month after treatment (acupuncture 12 cases, control 4 cases); marked effective: symptom scores after treatment decreased by more than two-thirds (acupuncture 10 cases, control 6 cases); effective: symptom scores after treatment decreased by more than one-third (acupuncture 7 cases, control 12 cases); invalid: symptom scores after treatment decreased by less than one-third (acupuncture 3 cases, control 8 cases)

ACUPUNCUTURE GROUP:

pretreatment 12.5 \pm 3.8, post-treatment 7.3 \pm 3.2 (pretreatment vs post-treatment: P value < 0.01)

CONTROL GROUP:

pretreatment 11.7 ± 3.4, post-treatment 7.8 ± 2.2 (pretreatment vs post-treatment: P value < 0.01)

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "random number table"
		Comment: probably done
Allocation concealment (selection bias)	Unclear risk	Quote: not described
		Comment: cannot be confirmed at present
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: not found
		Comment: probably no
Selective reporting (reporting bias)	Low risk	Quote: not found



Tang 2006 (Continued)		Comment: probably yes
Blinding of participants	High risk	Quote: not described
and personnel (perfor- mance bias) All outcomes		Comment: Heterogeneity between acupuncture and drugs could result in performance bias
6	Unclear risk	Quote: not mentioned whether outcome assessment was done in blinding way
sessment (detection bias) All outcomes		Comment: cannot be confirmed

ang 2009	
Methods	Eligibility criteria: Rome III diagnostic criteria for functional dyspepsia
	Study duration: 4 weeks
	Sequence generation: random number table
	Randomization concealment: not described
	Blind participants: not described
	Blind assessors: not described
	Blind therapists: not described
	Baseline comparability: yes, no significance in gender, age, FD course, and FD symptoms between groups was found
	Follow-up: no
Participants	Setting: outpatients from Wuhan Hospital of Traditional Medicine and Western Medicine, Hubei Province, China
	Total number: 80
	Male/Female (n/n): 39/41
	Mean age (\pm SD) or age range, years: 46.2 \pm 11.7 in acupuncture group and 45.9 \pm 12.1 in control group
	Duration of functional dyspepsia before recruitment: 14.5 \pm 7.8 months in acupuncture group and 14. \pm 7.6 months in control group
	Important inclusion criteria (clearly describe): absent from any gastrointestinal drugs at least 15 days before recruitment
	Important exclusion criteria (clearly describe): any contraindication listed in the catalogue of control drug itopride; pregnancy; tendency toward bleeding; unconsciousness
Interventions	ACUPUNCTURE GROUP
	Number allocated to acupuncture: 40
	Style of acupuncture: electroacupuncture with 2 Hz/100 Hz
	Numbers and names of points stimulated: a formula of 4 acupoints bilaterally stimulated involving ST34, ST36, ST40, and ST42
	Insertion depth: not described
	Manipulation after insertion: manipulations performed until "de-qi" occurred



Yang 2009 (Continued)

"De-qi" required or not: yes

Duration of treatment (minutes): 30

Frequency of treatment per week: 5 times

Total length of treatment period (weeks): 4

Description of therapists' qualifications: no

CONTROL GROUP

Number allocated to control: 40

Style of control: orally

Names of medications (if drugs, describe drug names): itopride tablet

Dose of medication per intake: 50 mg before meals

Frequency of medication per day: 3 times

Total length of treatment period (weeks): 4 (actually 20 treatment days)

Description of co-medications: no

CO-INTERVENTIONS IN GROUPS: no

Outcomes

Symptom scores of FD (P value < 0.05 when acupuncture was compared with control after treatment)

<u>How to assess</u>: 0 points: no symptoms; 1 point: slight symptoms; 2 points: moderate symptoms but not sufficient to affect daily life; 3 points: symptoms severe enough to affect daily life

<u>Conclusion from original data</u>: Significance was found in each group pretreatment and post-treatment and between 2 groups

Healing: no symptoms or symptom scores decreased by 3 points (acupuncture 22 cases, control 12 cases); marked effective: symptom scores after treatment decreased by 2 points (acupuncture 11 cases, control 15 cases); effective: symptom scores after treatment decreased by 1 point (acupuncture 6 cases, control 8 cases); invalid: symptom scores after treatment hardly decreased (acupuncture 1 case, control 5 cases)

ACUPUNCTURE GROUP:

pretreatment 10.21 ± 2.81, post-treatment 5.78 ± 2.01 (pretreatment vs post-treatment: P value < 0.01)

CONTROL GROUP:

pretreatment 10.09 ± 2.95, post-treatment 6.69 ± 1.99 (pretreatment vs post-treatment: P value < 0.01)

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement				
Random sequence genera-	Low risk	Quote: "random number table"				
tion (selection bias)		Comment: probably done				
Allocation concealment	Unclear risk	Quote: not described				
(selection bias)		Comment: cannot be confirmed				



Yang 2009 (Continued)								
Incomplete outcome data (attrition bias)	High risk	Quote: not found						
All outcomes		Comment: probably no						
Selective reporting (reporting bias)	Low risk	Quote: not found						
porting bias)		Comment: probably yes						
Blinding of participants and personnel (perfor-	High risk	Quote: not described						
mance bias) All outcomes		Comment: Heterogeneity between acupuncture and drugs could result in performance bias						
Blinding of outcome as- sessment (detection bias)	Unclear risk	Quote: not mentioned whether outcome assessment was done in blinding way						
All outcomes		Comment: cannot be confirmed						

Zhou 2005

Methods	Eligibility criteria: Rome II diagnostic criteria for functional dyspepsia							
	Study duration: 3 weeks							
	Sequence generation: unclear, mentioned just "randomly" in the trial							
	Randomization concealment: not described							
	Blind participants: not described							
	Blind assessors: not described							
	Blind therapists: not described							
	Baseline comparability: It was described that comparability between groups can be seen in baseline values for gender, age, and FD course, but no descriptions of baseline comparability of FD symptoms were reported							
	Follow-up: no							
Participants	Setting: Shanghai No. 5 People's Hospital Affiliated to Fudan University, Shanghai, China							
	Total number: 126							
	Male/Female (n/n): 45/81							
	Mean age (± SD) or age range, years: cannot be extracted directly							
	Duration of functional dyspepsia before recruitment: not mentioned							
	Important inclusion criteria (clearly describe): medication affecting the observation such as anticholinergic, anticonvulsant, emetic, $\rm H_2$ -receptor antagonist had to be withdrawn 1 week before acupuncture treatment							
	Important exclusion criteria (clearly describe): participants with gastrointestinal cancer, peptic ulceration, cholecystitis gallstones, pancreatic disease, diabetes, and hyperthyroidism. All participants had to receive gastroscopy and X-ray 4 weeks before treatment to exclude organic disorders							
Interventions	ACUPUNCTURE GROUP							
	Number allocated to acupuncture: 64							



Zhou 2005 (Continued)

Style of acupuncture: manual acupuncture combined with electroacupuncture

Numbers and names of points stimulated: a formula of 5 acupoints stimulated involving CV12, ST36 (bilateral), PC6 (bilateral), and LI4 (bilateral)

Insertion depth: not mentioned

Manipulation after insertion: Reinforcement and reduction of manipulations were performed until "deqi." Then needles on ST36 and SP6 were connected with G6805 electro apparatus for 20 minutes

"De-qi" required or not: yes

Duration of treatment (minutes): at least 20

Frequency of treatment per week: 7 times

Total length of treatment period (weeks): 3

Description of therapists' qualifications: no, but acupuncture treatments were conducted in the hospital

CONTROL GROUP

Number allocated to control: 62

Style of control: orally

Names of medications (if drugs, describe drug names): domperidone

Dose of medication per intake: 10 mg before meals

Frequency of medication per day: 3 times

Total length of treatment period (weeks): 3

Description of co-medications: not mentioned

CO-INTERVENTIONS IN GROUPS: manual acupuncture combined electroacupuncture

Outcomes

1. Symptom scores of FD

<u>How to assess</u>: 0 points: no symptoms; 1 point: mild but not obvious sensations; 2 points: slightly severe symptoms but not sufficient to affect daily life; 3 points: symptoms severe enough to affect daily life

<u>Conclusion from original data</u>: Total effective rate in acupuncture group showed significant difference from that of control group ($Chi^2 = 3.97, P < 0.05$)

Marked effective: Symptom scores after treatment decreased by 2 points (acupuncture 38 cases, control 22 cases); effective: Symptom scores after treatment decreased by 1 point (acupuncture 22 cases, control 29 cases); invalid: Symptom scores after treatment hardly decreased (acupuncture 4 cases, control 11 cases)

2. Efficacy assessment about subtypes of FD by symptom scores

<u>Conclusion from original data</u>: Compared with medication group, no significance of the number of total effective cases showed in ulceration, regurgitation and dyskinesia subtypes, except nonspecific subtype

ACUPUNCTURE GROUP

Total effective: 5 cases of ulceration subtype, 11 cases of regurgitation subtype, 26 cases of dyskinesia subtype, 18 cases of nonspecific subtype

Invalid: 2 cases of ulceration subtype, 2 cases of regurgitation subtype, 0 cases of dyskinesia subtype, 0 cases of nonspecific subtype



Zhou 2005	(Continued)
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MEDICATION GROUP

Total effective: 6 cases of ulceration subtype, 12 cases of regurgitation subtype, 21 cases of dyskinesia subtype, 12 cases of nonspecific subtype

Invalid: 3 cases of ulceration subtype, 0 cases of regurgitation subtype, 3 cases of dyskinesia subtype, 5 cases of nonspecific subtype

Notes

FD symptom description before treatment was lacking. Therefore, baseline FD symptoms in 2 groups cannot be known, whether comparable or not

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: mentioned just "randomly" in the description
tion (selection bias)		Comment: cannot be confirmed so far
Allocation concealment	Unclear risk	Quote: not described
(selection bias)		Comment: cannot be identified
Incomplete outcome data	Low risk	Quote: Lack of FD symptom description before treatment
(attrition bias) All outcomes		Comment: probably yes
Selective reporting (re-	High risk	Quote: Lack of FD symptom description before treatment
porting bias)		Comment: probably no
Blinding of participants	High risk	Quote: not described
and personnel (perfor- mance bias) All outcomes		Comment: Heterogeneity between acupuncture and drugs could result in performance bias
Blinding of outcome as-	Unclear risk	Quote: not mentioned whether outcome assessment was done in blinding way
sessment (detection bias) All outcomes		Comment: cannot be confirmed for the moment

Abbreviations:

FD: functional dyspepsia. NDI: Nepean Dyspepsia Index.

NDLQI: Nepean Dyspepsia Life Quality Index. NDSI: Nepean Dyspepsia Symptom Index.

SD: standard deviation.

SF-36: 36-Item Short-Form Health Survey. TCM: traditional Chinese medicine.

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Beyazit 2010	Was a letter to the editors
Chen 2005	The trial was a quasi-RCT in which participants were allocated as the visiting time



Study	Reason for exclusion
Liu S 2008	The trial was excluded because of its cross-over trial design
Paterson 2003	FD diagnostic criteria were not known from the description
Peng 2008	The trial was a quasi-RCT in which participants were allocated as the visiting time
Yang 2009a	The trial was a quasi-RCT in which participants were allocated as the visiting time

Peng 2008	The trial was a quasi-RCT in which participants were allocated as the visiting time
Yang 2009a	The trial was a quasi-RCT in which participants were allocated as the visiting time
Characteristics of stud	dies awaiting assessment [ordered by study ID]
Cao 2007	
Methods	
Participants	
Interventions	
Outcomes	
Notes	Full text cannot be obtained, so details of the trial cannot be had
Cook 2004	
Methods	
Participants	
Interventions	
Outcomes	
Notes	Full text cannot be obtained, so details of the trial cannot be had
Sun 2006 Methods	
Participants	
Interventions	
Outcomes	
Notes	Full text cannot be obtained, so details of the trial cannot be had



Zhang 2009b

Methods Eligibility criteria: Rome III diagnostic criteria for functional dyspepsia

Study duration: 4 weeks

Sequence generation: random number table

Randomization concealment: not described

Blind participants: not described

Blind assessors: not described
Blind therapists: not described

 $Baseline\ comparability: yes, baseline\ comparability\ between\ groups\ can\ be\ seen\ in\ gender, age, FD$

course, and FD symptoms

Follow-up: no

Participants Setting: Traditional Chinese Medicine Hospital of Wuhan, Hubei Province, China

Total number: 48

Male/Female (n/n): 27/21

Mean age (\pm SD) or age range, years: 35.70 \pm 11.43 in acupuncture group and 35.23 \pm 11.25 in control

group

Duration of functional dyspepsia before recruitment: 18.40 ± 12.72 months in acupuncture group

and 18.17 \pm 13.54 months in control group

Important inclusion criteria (clearly describe): no entry to other clinical trials when recruitment; ab-

sent from any gastrointestinal drugs at least 15 days before recruitment

Important exclusion criteria (clearly describe): any contraindication listed in the catalogue of con-

trol drug itopride; pregnancy; tendency toward bleeding; unconsciousness

Interventions ACUPUNCTURE GROUP

Number allocated to acupuncture: 24

Style of acupuncture: electroacupuncture with 2 Hz/100 Hz

Numbers and names of points stimulated: a formula of 3 acupoints stimulated involving CV12,

ST36 (lateral), and BL21 (bilateral)

Insertion depth: not described clearly

Manipulation after insertion: rotating, lifting, and thrusting until "de-qi"

"De-qi" required or not: yes

Duration of treatment (minutes): 30

Frequency of treatment per week: 5 times

Total length of treatment period (weeks): 4

 $Description\ of\ the rapists'\ qualifications:\ No,\ but\ the\ acupuncture\ treatment\ was\ performed\ in\ the$

outpatent department

CONTROL GROUP

Number allocated to control: 24

Style of control: orally



Zhang 2009b (Continued)

Names of medications (if drugs, describe drug names): itopride tablet

Dose of medication per intake: 50 mg before meals

Frequency of medication per day: 3 times

Total length of treatment period (weeks): 4 (actually 20 treatment days).

Description of co-medications: no

CO-INTERVENTIONS IN GROUPS: no

Outcomes

1. Symptom scores of FD

<u>How to assess</u>: 0 points: no symptoms; 1 point: slight symptoms; 2 points: moderate symptoms but not sufficient to affect daily life; 3 points: symptoms severe enough to affect daily life

<u>Conclusion from original data</u>: Significance was found in acupuncture group compared with control group

Healing: no symptoms or symptom scores decreased by 3 points (acupuncture 14 cases, control 10 cases); marked effective: symptom scores after treatment decreased by 2 points (acupuncture 5 cases, control 7 cases); effective: symptom scores after treatment decreased by 1 point (acupuncture 3 cases, control 2 cases); invalid: symptom scores after treatment hardly decreased (acupuncture 2 cases, control 5 cases)

Scores for each FD symptom

ACUPUNCTURE GROUP

Postprandial discomfort: pretreatment 2.00 \pm 0.63, post-treatment 0.85 \pm 0.47(pretreatment vs post-treatment: P value < 0.01)

Early satiety: pretreatment 1.98 \pm 0.50, post-treatment 0.75 \pm 0.36 (P value < 0.05)

Epigastric pain: pretreatment 1.92 ± 0.44 , post-treatment 0.72 ± 0.35 (P value < 0.05)

Epigastric burning sensation: pretreatment 1.47 \pm 0.49, post-treatment 1.42 \pm 0.48 (**P value > 0.05**)

CONTROL GROUP

Postprandial discomfort: pretreatment 2.02 ± 0.68 , post-treatment 0.87 ± 0.37 (pretreatment vs post-treatment: P value < 0.05)

Early satiety: pretreatment 1.96 \pm 0.52, post-treatment 1.07 \pm 0.49 (**P value > 0.05**)

Epigastric pain: pretreatment 1.95 \pm 0.51, post-treatment 1.02 \pm 0.47 (P value > **0.05**)

Epigastric burning sensation: pretreatment 1.51 \pm 0.52, post-treatment 1.39 \pm 0.44 (P value > **0.05**)

2. SF-36 scale

<u>Conclusion from original data</u>: No significance was found between acupuncture and control groups. Life quality in acupuncture group was improved for each item. However, items except for physiologic performance in the control group showed no significance

ACUPUNCTURE GROUP

Physiologic function: pretreatment 90.39 \pm 9.17, post-treatment 94.32 \pm 7.09 (pretreatment vs post-treatment: P value < 0.05)

Physiologic performance: pretreatment 55.37 \pm 12.26, post-treatment 75.89 \pm 20.98 (P value < 0.05)

Body pain: pretreatment 60.27 ± 23.80 , post-treatment 81.32 ± 20.74 (P value < 0.01)

General health: pretreatment 64.38 \pm 15.31, post-treatment 82.31 \pm 15.78 (P value < 0.05)



Zhang 2009b (Continued)

Vitality: pretreatment 69.33 \pm 13.01, post-treatment 82.72 \pm 15.03 (P value < 0.05)

Social function: pretreatment 64.33 ± 15.08 , post-treatment 85.74 ± 15.10 (P value < 0.05)

Role-emotion: pretreatment 49.88 ± 23.20 , post-treatment 79.99 ± 23.94 (P value < 0.01)

Mental health: pretreatment 73.32 ± 15.03 , post-treatment 80.77 ± 18.02 (P value < 0.05)

CONTROL GROUP

Physiologic function: pretreatment 91.17 \pm 7.02, post-treatment 92.08 \pm 7.04 (pretreatment vs post-treatment: **P value > 0.05**)

Physiologic performance: pretreatment 58.67 ± 19.99 , post-treatment 59.76 ± 20.00 (P value < 0.05)

Body pain: pretreatment 56.72 \pm 13.43, post-treatment 57.23 \pm 13.55 (**P value > 0.05**)

General health: pretreatment 68.10 ± 14.76 , post-treatment 70.20 ± 15.01 (**P value > 0.05**)

Vitality: pretreatment 68.03 \pm 12.21, post-treatment 71.23 \pm 12.84 (**P value > 0.05**)

Social function: pretreatment 66.00 ± 14.17 , post-treatment 68.01 ± 14.99 (**P value > 0.05**)

Role-emotion: pretreatment 51.00 \pm 19.12, post-treatment 53.27 \pm 19.78 (**P value > 0.05**)

Mental health: pretreatment 75.13 \pm 13.60, post-treatment 76.32 \pm 14.00 (**P value > 0.05**)

Notes

With MD data transformation, SF-36 results were unclear and required explanation; however, we could not get in touch with the study author

DATA AND ANALYSES

Comparison 1. Manual acupuncture compared with cisapride

Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
1 Symptom scores of FD	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
2 Frequency of FD symptoms	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3 Adverse effects	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only

Analysis 1.1. Comparison 1 Manual acupuncture compared with cisapride, Outcome 1 Symptom scores of FD.

Study or subgroup	Manual acupuncture	Control	Risk Ratio				Weight	Risk Ratio	
	n/N	n/N		M-H, Fixed, 95% CI					M-H, Fixed, 95% CI
Shi 2009	42/45	41/45	+				0%	1.02[0.91,1.16]	
	Favo	Favours acupuncture		0.7	1	1.5	2	Favours control	



Analysis 1.2. Comparison 1 Manual acupuncture compared with cisapride, Outcome 2 Frequency of FD symptoms.

Study or subgroup	Manual acupuncture	Control	Risk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H, Fixed, 95% CI		M-H, Fixed, 95% CI
Shi 2009	28/45	27/45		0%	1.04[0.75,1.44]
	Favo	urs acupuncture	0.5 0.7 1 1.5 2	Favours control	

Analysis 1.3. Comparison 1 Manual acupuncture compared with cisapride, Outcome 3 Adverse effects.

Study or subgroup	Manual acupuncture	Control	Risk Ratio			Weight	Risk Ratio		
	n/N	n/N		М-Н,	Fixed, 95	% CI			M-H, Fixed, 95% CI
Shi 2009	3/45	14/45		-	-			0%	0.21[0.07,0.69]
	Favo	Favours acupuncture		0.2	1	5	20	Favours control	

Comparison 2. Manual acupuncture compared with domperidone

Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
1 Symptom scores of FD	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only

Analysis 2.1. Comparison 2 Manual acupuncture compared with domperidone, Outcome 1 Symptom scores of FD.

Study or subgroup	Manual acupuncture	Control	Risk Ratio				Weight	Risk Ratio	
	n/N	n/N		М-Н,	Fixed, 9	5% CI			M-H, Fixed, 95% CI
Tang 2006	29/32	22/30			-	-		0%	1.24[0.97,1.58]
	Favo	urs acupuncture	0.5	0.7	1	1.5	2	Favours control	

Comparison 3. Manual-electroacupuncture compared with domperidone

Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
1 Symptom scores of FD	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
2 Symptom scores of FD in ulceration subtype	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3 Symptom scores of FD in regurgitation subtype	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4 Symptom scores of FD in dyskinesia subtype	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only



Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
5 Symptom scores of FD in nonspecific subtype	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only

Analysis 3.1. Comparison 3 Manual-electroacupuncture compared with domperidone, Outcome 1 Symptom scores of FD.

Study or subgroup	Manual-electro acupunct.	Control	Risk Ratio				Weight	Risk Ratio	
	n/N	n/N		M-l	H, Fixed, 95%	CI			M-H, Fixed, 95% CI
Zhou 2005	60/64	51/62			-	- ,		0%	1.14[1,1.3]
	Favoi	ırs acupuncture	0.5	0.7	1	1.5	2	Favours control	

Analysis 3.2. Comparison 3 Manual-electroacupuncture compared with domperidone, Outcome 2 Symptom scores of FD in ulceration subtype.

Study or subgroup	manual-electro acupunct.	Control	Risk Ratio			Weight	Risk Ratio		
	n/N	n/N		M-H	Fixed, 95	% CI			M-H, Fixed, 95% CI
Zhou 2005	5/64	6/62			+			0%	0.81[0.26,2.51]
	Favou	rs experimental	0.01	0.1	1	10	100	Favours control	

Analysis 3.3. Comparison 3 Manual-electroacupuncture compared with domperidone, Outcome 3 Symptom scores of FD in regurgitation subtype.

Study or subgroup	manual-electro acupunct.	Control	Risk Ratio			Weight	Risk Ratio				
	n/N	n/N			M-H, F	ixed,	95% CI				M-H, Fixed, 95% CI
Zhou 2005	11/64	12/62			_	+				0%	0.89[0.42,1.86]
	Favor	ire acupunctura	0.1	0.2	0.5	1	2	5	10	Envours control	

Analysis 3.4. Comparison 3 Manual-electroacupuncture compared with domperidone, Outcome 4 Symptom scores of FD in dyskinesia subtype.

Study or subgroup	manual-electro acupunct.	Control	Risk Ratio					Weight	Risk Ratio		
	n/N	n/N			M-H, F	ixed,	95% CI				M-H, Fixed, 95% CI
Zhou 2005	26/64	21/62		,		+	_			0%	1.2[0.76,1.89]
	Favou	ırs acupuncture	0.1	0.2	0.5	1	2	5	10	Favours control	_



Analysis 3.5. Comparison 3 Manual-electroacupuncture compared with domperidone, Outcome 5 Symptom scores of FD in nonspecific subtype.

Study or subgroup	manual-electro acupunct.	Control			Ri	sk Rat	tio			Weight	Risk Ratio
	n/N	n/N			M-H, F	ixed,	95% CI				M-H, Fixed, 95% CI
Zhou 2005	18/64	12/62				+				0%	1.45[0.77,2.76]
	Favou	rs acupuncture	0.1	0.2	0.5	1	2	5	10	Favours control	

Comparison 4. Electroacupuncture compared with itopride

Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
1 Symptom scores of FD	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only

Analysis 4.1. Comparison 4 Electroacupuncture compared with itopride, Outcome 1 Symptom scores of FD.

Study or subgroup	Elec- troacupuncture	Control	Risk Ratio					Weight	Risk Ratio
	n/N	n/N		M-H,	Fixed, 95	% CI			M-H, Fixed, 95% CI
Yang 2009	39/40	35/40			+	-		0%	1.11[0.98,1.27]
	Favours ele	ectroacununctur	0.5	0.7	1	1.5	2	Favours control	

Comparison 5. Acupuncture compared with sham acupuncture

Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
1 Symptom scores of FD	2		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2 Symptom scores of FD during follow-up period	2		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3 Nepean Dyspepsia Symptom Index	2		Mean Difference (IV, Random, 95% CI)	Totals not selected
4 Nepean Dyspepsia Life Quality Index	2	128	Mean Difference (IV, Fixed, 95% CI)	9.23 [4.85, 13.61]
5 Nepean Dyspepsia Symptom Index (at 1 month follow-up)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
6 Nepean Dyspepsia Life Quality Index (at 1 month follow-up)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
7 SF-36	2	116	Mean Difference (IV, Fixed, 95% CI)	12.18 [8.45, 15.91]
8 SF-36 (at 1 month follow-up)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only



Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
9 SAS	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
10 SDS	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
11 Adverse effects	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only

Analysis 5.1. Comparison 5 Acupuncture compared with sham acupuncture, Outcome 1 Symptom scores of FD.

Study or subgroup	Acı	upuncture	Sham	Mean Difference					Mean Difference		
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI		Fixed, 95% CI			Fixed, 95% CI	
Chang 2010	30	-2.8 (1.3)	30	-0.6 (1.5)			+			-2.24[-2.94,-1.54]	
Jin 2011	28	-21.8 (7.2)	28	-5.4 (7.9)						-16.43[-20.39,-12.47]	
			Fav	ours acupuncture	-20	-10	0	10	20	Favours sham acupunc- ture	

Analysis 5.2. Comparison 5 Acupuncture compared with sham acupuncture, Outcome 2 Symptom scores of FD during follow-up period.

Study or subgroup	Ac	upuncture	Sham	acupuncture	Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI	Fixed, 95% CI
Chang 2010	30	-3.1 (1.7)	30	-1 (1.6)	+	-2.11[-2.94,-1.28]
Jin 2011	28	-22.6 (9.9)	28	-8.4 (19.9)		-14.28[-22.52,-6.04]
			Fav	ours acupuncture	-20 -10 0 10 20	Favours control

Analysis 5.3. Comparison 5 Acupuncture compared with sham acupuncture, Outcome 3 Nepean Dyspepsia Symptom Index.

Study or subgroup	Favour	s acupuncture	Sham	n acupuncture		Mea	n Differe		Mean Difference	
	N	Mean(SD)	N	Mean(SD)		Ran	dom, 95	% CI		Random, 95% CI
Chang 2010	30	-24.7 (15.1)	30	-9 (16.9)			-			-15.67[-23.77,-7.57]
Park 2009	34	-25.4 (23.5)	34	-26.4 (21.9)			+			0.95[-9.85,11.75]
			Fav	ours acupuncture	-50	-25	0	25	50	Favours sham acupunc- ture

Analysis 5.4. Comparison 5 Acupuncture compared with sham acupuncture, Outcome 4 Nepean Dyspepsia Life Quality Index.

Study or subgroup	Acu	Acupuncture		Sham acupuncture		Mean Difference				Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI						Fixed, 95% CI
Chang 2010	30	15.2 (11.6)	30	3.5 (10.2)				-	_	63.09%	11.63[6.12,17.14]
Park 2009	34	21.2 (13)	34	16 (17)			+	•		36.91%	5.14[-2.07,12.35]
Total ***	64		64					•		100%	9.23[4.85,13.61]
		Fave	ours sham	acupuncture	-20	-10	0	10	20	Favours acu	ıpuncture



Study or subgroup	Acı	Acupuncture Sham acupuncture			Mean Difference					Weight Mean Differenc		
	N	Mean(SD)	N	Mean(SD)		Fix	ed, 95%	6 CI			Fixed, 95% CI	
Heterogeneity: Tau ² =0; Chi ² =	1.96, df=1(P=0.	16); I ² =49.08%										
Test for overall effect: Z=4.13	(P<0.0001)											
		Fav	ours shar	m acupuncture	-20	-10	0	10	20	Favours acur	nuncture	

Analysis 5.5. Comparison 5 Acupuncture compared with sham acupuncture, Outcome 5 Nepean Dyspepsia Symptom Index (at 1 month follow-up).

Study or subgroup	Acu	ouncture	Sham a	Sham acupuncture Mean Difference			Mean Difference Weight			Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)		ı	ixed, 95%	CI			Fixed, 95% CI
Chang 2010	30	-28.4 (15.2)	30	-11.8 (15.9)	_					0%	-16.63[-24.51,-8.75]
			Favours	acupuncture	-100	-50	0	50	100	Favours shar	m acupuncture

Analysis 5.6. Comparison 5 Acupuncture compared with sham acupuncture, Outcome 6 Nepean Dyspepsia Life Quality Index (at 1 month follow-up).

Study or subgroup	Acuj	puncture	Sham a	Sham acupuncture Mean Difference			Mean Difference Weight			Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI					Fixed, 95% CI	
Chang 2010	30	17.8 (11.6)	30	4.1 (9.8)			+			0%	13.64[8.22,19.06]
		Fave	ours sham	acupuncture	-100	-50	0	50	100	Favours acui	puncture

Analysis 5.7. Comparison 5 Acupuncture compared with sham acupuncture, Outcome 7 SF-36.

Study or subgroup	Acu	puncture	Sham a	acupuncture	Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI		Fixed, 95% CI
Chang 2010	30	17.9 (6.1)	30	6.8 (10.4)	-	75.04%	11.08[6.78,15.38]
Jin 2011	28	17.5 (13.3)	28	2 (15.1)	-	24.96%	15.5[8.04,22.96]
Total ***	58		58		•	100%	12.18[8.45,15.91]
Heterogeneity: Tau ² =0; Chi ² =	1.01, df=1(P=0.3	1); I ² =1.07%					
Test for overall effect: Z=6.4(F	o<0.0001)						
		Fav	ours sham	acupuncture	-20 -10 0 10 20	Favours acu	upuncture

Analysis 5.8. Comparison 5 Acupuncture compared with sham acupuncture, Outcome 8 SF-36 (at 1 month follow-up).

Study or subgroup	Acup	ouncture	Sham a	cupuncture	re Mean Difference			Weight	Mean Difference	
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI					Fixed, 95% CI
Chang 2010	30	24.4 (12.5)	30	8.9 (10.2)		+			0%	15.44[9.68,21.2]
		Fave	ours sham	acupuncture	-50 -25 0 25 50			Favours acu	puncture	



Analysis 5.9. Comparison 5 Acupuncture compared with sham acupuncture, Outcome 9 SAS.

Study or subgroup	Acu	puncture	Sham a	Sham acupuncture		Mean Difference					Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI					Fixed, 95% CI	
Jin 2011	28	-10 (9.1)	28	-0.2 (9)	1					0%	-9.84[-14.58,-5.1]
			Favours	acupuncture	-20	-10	0	10	20	Favours shan	n acupuncture

Analysis 5.10. Comparison 5 Acupuncture compared with sham acupuncture, Outcome 10 SDS.

Study or subgroup	Acu	puncture	Sham acupuncture		Mean Difference					Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI					Fixed, 95% CI	
Jin 2011	28	-12.4 (9.2)	28	-3.6 (11.1)			-			0%	-8.76[-14.09,-3.43]
			Favours	acupuncture	-20	-10	0	10	20	Favours shar	m acupuncture

Analysis 5.11. Comparison 5 Acupuncture compared with sham acupuncture, Outcome 11 Adverse effects.

Study or subgroup	Acupuncture	Acupuncture Sham acupuncture		Risk Ratio				Weight	Risk Ratio
	n/N	n/N		M-H, Fixed, 95% CI					M-H, Fixed, 95% CI
Jin 2011	3/28	0/28	_			-		0%	7[0.38,129.55]
	Favou	0.001	0.1	1	10	1000	Favours sham acupunct	ture	

APPENDICES

Appendix 1. CENTRAL search strategy

- 1. ((disturbance\$ or disorder\$ or difficult\$ or dysfunction\$ or disease\$ or impair\$ or condition\$ or abnormal\$ or illness\$ or patholog\$ or discomfort\$ or hazard\$ or damage\$ or injur\$ or irritab\$ or pain\$ or distress\$ or burning) adj2 postprandial).mp.
- 2. indigestion.mp.
- 3. (Intestin\$ or Digest\$ or Gastr\$ or gut or epigastr\$ or stomach\$).mp.
- 4. 3 and 2
- 5. dyspepsia.mp. or exp Dyspepsia/
- 6. (epigastric adj2 pain).ti,ab.
- 7. (epigastric adj2 burn\$).mp.
- 8. (Rome adj2 criteria).mp.
- 9. or/1,4-8
- 10.exp Acupuncture Therapy/ or exp Acupuncture/ or exp Acupuncture Points/
- 11.exp acupressure/ or exp electroacupuncture/ or exp meridians/ or exp moxibustion/
- 12.acupuncture.mp.
- 13.electroacupuncture.mp.
- 14.acupoint\$.mp.
- 15.meridian\$.mp.
- 16.deqi.mp. [mp=title, original title, abstract, mesh headings, heading words, keyword]
- 17.moxibustion\$.mp.
- 18.or/10-17
- 19.9 and 18
- 20.limit 19 to yr="2009 2012"



Appendix 2. MEDLINE search strategy

- 1. ((disturbance\$ or disorder\$ or difficult\$ or dysfunction\$ or disease\$ or impair\$ or condition\$ or abnormal\$ or illness\$ or patholog\$ or discomfort\$ or hazard\$ or damage\$ or injur\$ or irritab\$ or pain\$ or distress\$ or burning) adj2 postprandial).mp.
- 2. indigestion.mp.
- 3. (Intestin\$ or Digest\$ or Gastr\$ or gut or epigastr\$ or stomach\$).mp.
- 4. 3 and 2
- 5. dyspepsia.mp. or exp Dyspepsia/
- 6. (epigastric adj2 pain).ti,ab.
- 7. (epigastric adj2 burn\$).mp.
- 8. (Rome adj2 criteria).mp.
- 9. or/1,4-8
- 10.exp Acupuncture Therapy/ or exp Acupuncture/ or exp Acupuncture Points/
- 11.exp acupressure/ or exp electroacupuncture/ or exp meridians/ or exp moxibustion/
- 12.acupuncture.mp.
- 13.electroacupuncture.mp.
- 14.acupoint\$.mp.
- 15.meridian\$.mp.
- 16.deqi.mp. [mp=title, abstract, original title, name of substance word, subject heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]
- 17.moxibustion\$.mp.
- 18.or/10-17
- 19.9 and 18
- 20.limit 19 to ed=20090801-20120107

Appendix 3. EMBASE search strategy

- 1. ((disturbance\$ or disorder\$ or difficult\$ or dysfunction\$ or disease\$ or impair\$ or condition\$ or abnormal\$ or illness\$ or patholog\$ or discomfort\$ or hazard\$ or damage\$ or injur\$ or irritab\$ or pain\$ or distress\$ or burning) adj2 postprandial).mp.
- 2. indigestion.mp.
- 3. (Intestin\$ or Digest\$ or Gastr\$ or gut or epigastr\$ or stomach\$).mp.
- 4. 3 and 2
- 5. dyspepsia.mp. or exp Dyspepsia/
- 6. (epigastric adj2 pain).ti,ab.
- 7. (epigastric adj2 burn\$).mp.
- 8. (Rome adj2 criteria).mp.
- 9. or/1,4-8
- 10.exp Acupuncture Therapy/ or exp Acupuncture/ or exp Acupuncture Points/
- 11.exp acupressure/ or exp electroacupuncture/ or exp meridians/ or exp moxibustion/
- 12.acupuncture.mp.
- 13.electroacupuncture.mp.
- 14.acupoint\$.mp.
- 15.meridian\$.mp.
- 16.deqi.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
- 17.moxibustion\$.mp.
- 18.or/10-17
- 19.9 and 18
- 20.limit 19 to em=200933-201202

Appendix 4. AMED search strategy

- 1. ((disturbance\$ or disorder\$ or difficult\$ or dysfunction\$ or disease\$ or impair\$ or condition\$ or abnormal\$ or illness\$ or patholog\$ or discomfort\$ or hazard\$ or damage\$ or injur\$ or irritab\$ or pain\$ or distress\$ or burning) adj2 postprandial).mp.
- 2. indigestion.mp.
- 3. (Intestin\$ or Digest\$ or Gastr\$ or gut or epigastr\$ or stomach\$).mp.



- 4. 3 and 2
- 5. dyspepsia.mp. or exp Dyspepsia/
- 6. (epigastric adj2 pain).ti,ab.
- 7. (epigastric adj2 burn\$).mp.
- 8. (Rome adj2 criteria).mp.
- 9. or/1,4-8
- 10.exp Acupuncture Therapy/ or exp Acupuncture/ or exp Acupuncture Points/
- 11.exp acupressure/ or exp electroacupuncture/ or exp meridians/ or exp moxibustion/
- 12.acupuncture.mp.
- 13.electroacupuncture.mp.
- 14.acupoint\$.mp.
- 15.meridian\$.mp.
- 16.deqi.mp. [mp=title, original title, abstract, mesh headings, heading words, keyword]
- 17.moxibustion\$.mp.
- 18.or/10-17
- 19.9 and 18
- 20.limit 19 to yr="2009 2012"

Appendix 5. CNKI search strategy

((关键词=针灸) or (关键词=针刺) or (关键词=电针)) and ((关键词=消化不良) or (关键词=功能性消化不良) or (关键词=烧灼) or (关键词=食欲不振) or (关键词=上腹不适) or (关键词=上腹痛) or (关键词=腹胀) or (关键词=早饱) or (关键词=嗳气))

Appendix 6. VIP Database search strategy

(K=针灸+K=针刺+K=电针)*(K=消化不良+K=功能性消化不良+K=烧灼+K=食欲不振+K=上腹不适+K=上腹痛+K=腹胀+K=早饱+K=嗳气)

Appendix 7. CBMdisc search strategy

- #1 缺省 =消化不良
- #2 缺省 =功能性消化不良
- #3 缺省 =烧灼
- #4 缺省 =食欲不振
- #5 缺省 =上腹不适
- #6 缺省 =上腹痛
- #7 缺省 =腹胀
- #8 缺省 =早饱
- #9 缺省 =嗳气
- #10 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9
- #11 缺省=针灸
- #12 缺省=针刺
- #13 缺省=电针
- #14 #11 or #12 or #13
- #15 #10 and #14

Appendix 8. Wanfang search strategy

针刺and功能性消化不良



CONTRIBUTIONS OF AUTHORS

Lan Lei, Liu Mailan, and Wu Xi obtained copies of trials and selected the identified trials.

Lan Lei, Zeng Fang, Ying Li, and Liu Mailan extracted data and assessed the risk of bias of included trials.

Lan Lei and Liu Guanjian performed analyses of data.

Lan Lei and Zeng Fang were responsible for the draft of the review.

Lan Lei and Liang Fan-rong were responsible for submitting the systematic review and updating it.

DECLARATIONS OF INTEREST

Ling Ying, one author of this review, once participated in an included trial of acupuncture for FD. Therefore, Ling Ying did not take part in the data selection and analysis process.

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External sources

· No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

No significant differences have been noted between the protocol and the review.

INDEX TERMS

Medical Subject Headings (MeSH)

Acupuncture Therapy [adverse effects] [*methods]; Benzamides [adverse effects] [therapeutic use]; Benzyl Compounds [adverse effects] [therapeutic use]; Cisapride [adverse effects] [therapeutic use]; Domperidone [adverse effects] [therapeutic use]; Dyspepsia [*therapy]; Electroacupuncture [methods]; Gastrointestinal Agents [adverse effects] [therapeutic use]; Randomized Controlled Trials as Topic

MeSH check words

Female; Humans; Male