**Purpose of review**
Dyspepsia affects up to 40% of the general population and significantly reduces quality of life. A small proportion of patients have peptic ulcer disease as cause and this can be treated empirically with *Helicobacter pylori* eradication therapy in those that are infected. Approximately 20% have gastro-oesophageal reflux disease and this can be effectively treated with proton pump inhibitor therapy. Patients who remain symptomatic may warrant an endoscopy, but most will have functional dyspepsia. Treatment of functional dyspepsia remains a challenge.

**Recent findings**
Recent large randomized trials suggest tricyclic antidepressant therapy may be effective in functional dyspepsia. A phase III randomized controlled trial reports that a new prokinetic, acotiamide, reduces dyspepsia symptoms in functional dyspepsia patients. There are also preliminary data that suggest buspirone, a drug that promotes gastric accommodation, is also effective in functional dyspepsia. There are also data to suggest that functional dyspepsia is caused by subtle manifestations of inflammation in the upper gastrointestinal tract, possibly caused by food sensitivity or a change in gut flora.

**Summary**
The initial management of dyspepsia is well established, but managing those with continued symptoms is a challenge. Antidepressants and newer gastric motility agents show promise. Targeting the diet and gut microbiome is another area for future research in functional dyspepsia.

**Keywords**
antidepressant therapy, diet, dyspepsia, gut–brain interactions, microbiome

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**INTRODUCTION**
Dyspepsia is a common complaint in the general population. The prevalence varies, both according to geographical region and criteria used to define the condition, but is reported to be as high as 40% [1]. The definition of dyspepsia has evolved over the past 25 years, moving away from one that includes any symptom referable to the upper gastrointestinal tract [2], to the more focused Rome III criteria [3], which exclude heartburn or reflux-type symptoms. When the Rome III criteria are used, the prevalence of dyspepsia in the general population is generally lower, between 3 and 10% [4,5], although at the time of writing, few studies have applied these in the community. The Rome III criteria further subdivide individuals with dyspepsia into two subgroups, epigastric pain syndrome and postprandial distress syndrome, with the main complaint in the latter being early satiety and postprandial fullness. However, recent evidence shows that these overlap in about two-thirds of individuals [6*], suggesting this distinction is somewhat arbitrary.

The underlying cause of dyspepsia may include erosive oesophagitis, peptic ulcer disease, or gastro-oesophageal malignancy, although over three-quarters of individuals will have no structural cause for their symptoms and are labelled as having functional dyspepsia [7]. Whereas patients with dyspepsia symptoms have a normal life expectancy [8], the impact on quality of life is substantial [9], and due to the cost of investigations, medications, and sickness-related absence from work, the financial implications of dyspepsia for society are huge, estimated at $18.4 billion per year in the United States [10**].

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KEY POINTS

- Dyspepsia is common and costly. The SmartPill, a wireless pH sensor, is a novel approach to measuring gastric acidity.
- Tricyclic antidepressant therapy is effective in treating functional dyspepsia.
- Acotiamide is a novel prokinetic that has been shown to be effective in functional dyspepsia in a phase III randomized trial.
- Modulating the diet and the upper gastrointestinal tract microbiome may represent new approaches to managing functional dyspepsia.

In an attempt to conserve scarce resources, the management of patients who present to a primary care physician with dyspepsia, so-called uninvestigated dyspepsia, has moved away from prompt endoscopy for all individuals towards non-invasive approaches such as empirical acid suppression therapy or testing for Helicobacter pylori (H. pylori) and eradicating, if positive [11,12]. A primary care-based study demonstrated that the cost of detecting each case of upper gastrointestinal cancer in patients with dyspepsia was in excess of $80,000 [13], lending credence to this approach. On the contrary, recent evidence suggests that in areas where endoscopy rates are lower, the outcomes for patients diagnosed with gastro-oesophageal malignancy are significantly worse [14*].

ADVANCES IN INVESTIGATION OF DYSPEPSIA

A recent pilot study compared the accuracy of, and patient satisfaction with, wireless capsule endoscopy versus upper gastrointestinal endoscopy in the detection of neoplastic gastric lesions less than 4 cm in size [15]. Eight patients with gastric neoplasia detected at upper gastrointestinal endoscopy underwent capsule endoscopy within 48 h, with positional change every 30 s, according to a prespecified protocol. Despite a higher satisfaction rate with capsule endoscopy compared with upper gastrointestinal endoscopy, only four out of eight gastric cancers were detected, suggesting that this approach will be of limited value in investigating patients with dyspepsia in order to exclude upper gastrointestinal malignancy.

A technique to measure gastric acid output non-invasively, and hence identification of patients who may benefit from acid suppression therapy, has proved relatively elusive. A wireless pH sensor, the SmartPill, has been compared with conventional gastric acid output measurement, via nasogastric tube, in 20 healthy volunteers [16]. The SmartPill was ingested after an overnight fast, and analysis of gastric acid output proved to be accurate and reproducible, with strong correlations with basal, maximal, and peak acid outputs. The authors concluded that this technique could allow the management of both gastro-oesophageal reflux disease (GERD) and other disorders of gastric acid secretion to be directed more precisely.

UPDATE ON CURRENT THERAPIES FOR DYSPEPSIA

Therapies for dyspepsia can be subdivided depending on the underlying disease that is being treated.

Gastro-oesophageal reflux disease

The efficacy of acid suppression therapy, in the form of proton pump inhibitors (PPIs), in the therapy of GERD is undisputed. A meta-analysis of randomized controlled trials (RCTs) demonstrated that PPIs at full dose were superior to both placebo and H2-receptor antagonists (H2RAs) for the healing of erosive oesophagitis [17]. In addition, once healing of oesophagitis was achieved, PPIs at maintenance dose were again superior to both placebo and H2RAs in terms of prevention of relapse of oesophagitis.

Arbaclofen, a gamma-aminobutyric acid agonist with potentially beneficial effects on transient lower oesophageal relaxations, has been tested recently in a phase III trial in patients with GERD [18]. The investigators randomized 156 GERD patients to receive one of four arbaclofen regimens or placebo for 4 weeks. Unfortunately, in the primary analysis, the drug had no significant effect on weekly frequency of heartburn during the study period. Following prespecified secondary analyses according to previous PPI exposure, arbaclofen appeared to be more effective than placebo among patients who had previously responded to PPIs. Further development of this drug for the treatment of GERD has been terminated.

Whether surgery is more effective than medical therapy for patients with GERD remains a contentious issue. The REFLUX trial comparing minimally invasive laparoscopic fundoplication with medical therapy for GERD has now reported data out to 5 years of follow-up [19**]. Symptom questionnaire scores were significantly lower among those allocated to surgery, and there was a trend towards improved quality of life. However, over 40% of those randomized to surgery were taking acid suppression therapy at 5 years. An economic analysis was not performed, so whether surgery is more cost-effective remains unclear.
Peptic ulcer disease
The majority of peptic ulcer disease is caused by either *H. pylori* or NSAIDs. There is clear evidence that for *H. pylori*-positive duodenal and gastric ulcer, eradication therapy is highly effective in preventing future relapse once the initial ulcer has healed, with a number needed to treat (NNT) of 2 and 3, respectively [20]. This approach is also cost-effective [21]. In addition, a recent meta-analysis has demonstrated that eradication therapy prevents future ulcer development among *H. pylori*-positive NSAID users [22]. Among patients with NSAID-induced peptic ulcer, evidence from RCTs suggests that PPIs are superior to H₂RAs [23,24].

Functional dyspepsia
In a Cochrane meta-analysis, H₂RAs and PPIs were more effective than placebo for the treatment of functional dyspepsia [25], with NNTs of 7 and 10, respectively. Subgroup analyses conducted according to predominant symptom revealed that PPIs were effective in those reporting reflux-type symptoms or epigastric pain, but not among patients with dysmotility-like symptoms [26].

In another Cochrane meta-analysis of 24 RCTs of prokinetics [25], the majority of which used cisapride, these drugs were highly effective for functional dyspepsia with a NNT of 6. However, in a subgroup analysis when only high-quality trials were included, the beneficial effect of prokinetics was no longer apparent [27]. Newer prokinetics have also been tested. Iloperidone, which is a dopamine antagonist, was beneficial in one large RCT [28], but subsequent phase III trials did not replicate these findings [29].

*Helicobacter pylori* eradication therapy has a modest, but statistically significant, effect in functional dyspepsia. A meta-analysis of RCTs demonstrated that the NNT was 15, and that this could be a cost-effective strategy, provided the willingness to pay per month symptom-free of dyspepsia was £75 [30]. Evidence continues to accumulate that this approach is of benefit, with a recent Brazilian trial reporting a NNT of 8 [31]. When this RCT was pooled along with all other trials conducted since the publication of the aforementioned meta-analysis, the NNT was similar at 13 [32].

EMERGING CONCEPTS FOR THE CAUSE OF DYSPESIA
We have a reasonable understanding of the pathophysiology of peptic ulcer disease, with the majority of peptic ulcers caused by *H. pylori* or NSAIDs and GERD caused by acid reflux into the oesophagus [33]. This is reflected in the very effective therapies we have for these disorders described above. The cause of functional dyspepsia, however, is unclear, and the efficacy of therapies in functional dyspepsia remains modest [34]. The majority of functional dyspepsia patients continue to have symptoms after 5 years follow-up [35]. Impaired accommodation, delayed gastric emptying, gastric hypersensitivity to distension, and gastroduodenal sensitivity to acid have all been proposed as mechanisms of upper gastrointestinal symptom generation. Anxiety and depression are more common in functional dyspepsia than healthy controls [36*,37], emphasizing the importance of the gut–brain axis in functional dyspepsia. In addition, it has been suggested that alterations in central dopaminergic neurons [38] and white matter microstructure [39**], possibly caused by psychological disturbances, may play a role in functional dyspepsia.

Dyspeptic symptoms are more likely to occur after an acute gastrointestinal infection [40]. This association may be even stronger than it is for irritable bowel syndrome (IBS) [41] and symptoms can persist for at least 8 years [42]. It has been postulated that gastrointestinal infection may alter the microbiome of the upper gastrointestinal tract and induce subtle chronic inflammation [43**,44]). This is supported by the observation that functional dyspepsia patients have an up-regulation of homing T cells in the small bowel associated with delayed gastric emptying [44]. Furthermore, increases in circulating active lymphocytes were correlated with severity of dyspepsia symptoms in functional dyspepsia patients [44]. Inflammation of the upper gastrointestinal tract has also been shown to cause neural remodelling of the upper gastrointestinal tract in animal models and this could explain the disorders of sensitivity and motility seen in functional dyspepsia [45]. Alterations in the gut microbiome have also been shown to impact on behaviour in animal models [46], so it is also possible that the psychological disturbances seen in functional dyspepsia may be related to altered gut flora.

Patients with dyspepsia often describe symptoms in relation to food ingestion. This may be a non-specific effect of food acting on mechanoreceptors in the upper gastrointestinal tract, as well as stimulating acid secretion [47]. Certain food types, such as lipids, can also induce the release of peptides such as cholecystokinin that can have effects on gastrointestinal physiology [48]. There is also the possibility that some functional dyspepsia patients may have an allergy or sensitivity to certain food substances. The classic example of this is gluten sensitivity. This has been described in IBS patients [49,50], but is less well characterized in functional...
dyspepsia [51]. This is surprising as there is a large overlap between IBS and functional dyspepsia [52], and the duodenum is the first point at which gluten sensitivity is manifested [53]. There is some evidence that gluten sensitivity applies to functional gastrointestinal disorders other than IBS [54], but this needs further study. It is also important to evaluate whether other dietary components, such as fermentable polysaccharides, are implicated in the generation of functional dyspepsia symptoms [55,56].

These competing theories on the causation of functional dyspepsia need not be mutually exclusive. The common pathway is subtle changes in the mucosal immune response of the upper gastrointestinal tract [57,58]. This could be caused by sensitivity to food substances or by changes in the microbiome [59]. Indeed, changes in diet can lead to changes in the gut flora [60]. The resultant mucosal inflammation could then drive other pathophysiological changes that are associated with symptoms in functional dyspepsia patients (Fig. 1).

Emerging therapies for functional dyspepsia

Therapy for peptic ulcer disease and GERD is well established and very effective. In contrast, the efficacy of current therapies for functional dyspepsia described above remains modest, largely because we do not understand the pathophysiology of this condition. There are, however, promising approaches that have recently been described.

Antidepressant therapy

Functional dyspepsia is associated with anxiety and depression [36,37], so it is surprising that until recently there had only been a few small trials evaluating antidepressant therapy in functional dyspepsia [61]. This is in contrast to IBS where there is more evidence for the efficacy of both tricyclic antidepressant (TCA) therapy and selective serotonin reuptake inhibitors (SSRIs) [62]. There are now two [63,64] large RCTs that suggest antidepressant therapy is effective at reducing symptoms in functional dyspepsia patients, although the effect was modest in a large multicentre North
American trial [64,65] and only seen for TCAs rather than SSRIs.

**Novel prokinetic and fundus-relaxing drugs**

Motility abnormalities are seen in the majority of functional dyspepsia patients and therefore prokinetic therapy is a logical choice, at least for a subset of functional dyspepsia patients. Initial enthusiasm for this approach has been tempered by the withdrawal of prokinetics such as cisapride from the market because of toxicity concerns. Drugs that alter gastric motility are still being developed, however, and the latest therapies that show promise are acotiamide and buspirone.

Acotiamide promotes acetylcholine release and inhibits acetylcholinesterase to increase the rate of gastric emptying, also enhancing gastric accommodation. A single-centre placebo-controlled RCT [66] reported that acotiamide significantly increased gastric emptying, improved gastric accommodation and reduced upper gastrointestinal symptoms in 34 functional dyspepsia patients. A large Japanese multicentre double-blind RCT [67**] of acotiamide 100 mg three times daily for 4 weeks versus placebo in 897 functional dyspepsia patients found that the active drug significantly reduced dyspepsia symptoms (52 vs. 35%). They reported a NNT of 6 for a reduction of dyspepsia and an NNT of 16 for resolution of all symptoms. Quality of life was also improved and there were no significant adverse events.

Buspirone, a 5-hydroxytryptamine 1A receptor agonist, enhances gastric accommodation in healthy volunteers [68]. A small cross-over RCT [69] has now shown that this drug is effective in relaxing the gastric fundus in 17 functional dyspepsia patients and was also able to significantly reduce symptoms of bloating and postprandial fullness. More studies are required to determine if this approach will be effective in functional dyspepsia.

**Acupuncture in functional dyspepsia**

Functional dyspepsia patients often ask if there are any complementary alternative medical therapies that they can try for their symptoms. These approaches are less well studied in RCTs, but acupuncture has been assessed in two [70,71*] RCTs. Both RCTs were from the same research group and found that acupuncture was superior to sham therapy. Furthermore, acupuncture caused functional brain changes, detected by PET-computed tomography (PET-CT) in the brainstem, anterior cingulated cortex of patients, that correlated with a reduction in dyspepsia symptoms and an improvement in dyspepsia-related quality of life [71*].

**Diet and probiotic therapy for functional dyspepsia**

There are numerous RCTs evaluating probiotic therapy in IBS [72] and yet we were unable to identify any RCT that specifically evaluated this treatment for dyspepsia or functional dyspepsia. This was also the case for dietary interventions in functional dyspepsia. Although we did not conduct a rigorous systematic review on these topics, it is concerning that this has not been thoroughly evaluated given that changes in diet and the microbiome are two plausible mechanisms by which functional dyspepsia symptoms can be generated (Fig. 1).

**CONCLUSION**

Dyspepsia remains a common reason for gastroenterology consultation [73], yet the majority of patients with epigastric pain/discomfort experience inadequate relief with current therapies. New approaches to investigation and treatment of this important problem are being developed such as the SmartPill and newer gastric motility modulating agents. Research into the microbiome of the upper gastrointestinal tract and dietary therapies may also help functional dyspepsia patients in the future.

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**Conflicts of interest**

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**REFERENCES AND RECOMMENDED READING**

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

1. Marwaha A, Ford AC, Lim A, Moayyedi P. The worldwide prevalence of dyspepsia: systematic review and meta-analysis. Gastroenterology 2009; 136 (Suppl 1):A149.
2. Colins-Jones DG, Bloom B, Bodemar G, et al. Management of dyspepsia: report of a working party. Lancet 1988; 331:576–579.
3. Tack J, Talley NJ, Camilleri M, et al. Functional gastroduodenal disorders. Gastroenterology 2006; 130:1466–1479.
4. Mak AD, Wu JC, Chan Y, et al. Dyspepsia is strongly associated with major depression and generalised anxiety disorder: a community study. Aliment Pharmocol Ther 2012; 36:800–810.
5. Zhao Y, Zou D, Wang R, et al. Dyspepsia and irritable bowel syndrome in China: a population-based endoscopy study of prevalence and impact. Aliment Pharmocol Ther 2010; 32:562–572.
Ethnic variation, epidemiological
Small bowel homing T cells are
Helicobacter pylori
Medical treatments for the main-
Zanini B, Ricci C, Bandera F, et al.
Eradication therapy for peptic ulcer
disease
Ford AC, Delaney BC, Forman D, et al.
Prevalence of uninvestigated dys-
Vakil N, Talley NJ, Veldhuyzen van Zanten S, et al.
Abraham NS, Moayyedi P, Daniels B, et al.
eradication treatment for nonulcer dyspep-
Ford AC, Delaney BC, Forman D, et al.
Nonceliac wheat sensitivity
White-matter microstructural changes in
Feinle-Bisset C, Azpiroz F. Dietary lipids and functional gastrointestinal
Holtmann G, Talley NJ, Liebregts T, et al.
Systematic review and economic
cost of detecting malignant
evaluation of Helicobacter pylori eradication treatment for nonulcer dyspep-
Ferril-Bissett C, Apiroz F. Dietary lipids and functional gastrointestinal
Simsen M, Barbosa G, Flint HJ, et al. Intestinal microbiota in functional bowel
disorders: a Rome foundation report. Gut 2013; 62:159–176.
A superb review of how the gut microbiome may relate to functional gastrointestinal-
disease
Bercik P, De Giorgio R, Blennerhassett P, et al.
Dyspepsia by endoscopy in 2741 primary care dyspeptic patients without alarm
lesions. Clin Gastroenterol Hepatol 2009; 7:756–761.
Dyspepsia is strongly associated with major
depression and generalised anxiety disorder: a community study. Aliment
Pharmacol Ther 2012; 36:800–810.
This well designed study of 2011 patients relating to a telephone survey. Dyspepsia was associated with a two-fold increase in the odds of having generalized anxiety disorder.
Filippovic BF, Randjelovic T, Ille T, et al. Anxiety, personality traits and quality of
life in functional dyspepsia-suffering patients. Eur J Intern Med 2013; 24:83– 90.
White matter structure changes have been demonstrated in IBS, but this is the first study to demonstrate that there are changes in 36 functional dyspepsia patients compared to 36 healthy controls. The types of changes seen are those associated with psychological distress.
Zanini B, Ricci C, Bandera F, et al.
Zanini B, Ricci C, Bandera F, et al.
Dyspepsia. Curr Opin Gastroenterol 2012; 28:183–1844.
This is a contemporaneous report of the financial impact of dyspepsia on patients. It is the first study to have examined direct and indirect costs of dyspepsia to society for some time.
Ford AC, Quine M, Moayyedi P, et al. Helicobacter pylori ‘test and treat’ or
endoscopy for managing dyspepsia? An individual patient data meta-analysis. Gastroenterology 2005; 128:1838–1844.
This randomized controlled trial of minimally invasive laparoscopic antireflux surgery compared to medical management for gastro-oesophageal reflux disease in 2741 primary care dyspeptic patients without alarm symptoms. Clin Gastroenterol Hepatol 2009; 7:756–761.
The incidence and gastrointestinal
Aliment Pharmacol Ther 2004; 19:631–641.
Bercik P, Denou E, Collins J, et al.
The intestinal microbiota affect central
Helicobacter pylori infection
Vakil N, Talley NJ, Veldhuyzen van Zanten S, et al.
Abraham NS, Moayyedi P, Daniels B, et al.
norib评分系统
This is a large well designed study that examined the utility of the two functional dyspepsia syndrome subgroups in clinical practice.
Ford AC, Marwaha A, Lim A, et al. What is the prevalence of clinically
dyspepsia-suffering patients. Eur J Intern Med 2013; 24:83– 90.
Ford AC, Delaney BC, Forman D, et al.
Nonceliac wheat sensitivity
White-matter microstructural changes have been demonstrated in IBS, but this is the first study to demonstrate that there are changes in 36 functional dyspepsia patients compared to 36 healthy controls. The types of changes seen are those associated with psychological distress.
Zanini B, Ricci C, Bandera F, et al.
Zanini B, Ricci C, Bandera F, et al.
Dyspepsia. Curr Opin Gastroenterol 2012; 28:183–1844.
This is a contemporaneous report of the financial impact of dyspepsia on patients. It is the first study to have examined direct and indirect costs of dyspepsia to society for some time.
Ford AC, Quine M, Moayyedi P, et al. Helicobacter pylori ‘test and treat’ or
endoscopy for managing dyspepsia? An individual patient data meta-analysis. Gastroenterology 2005; 128:1838–1844.
This randomized controlled trial of minimally invasive laparoscopic antireflux surgery compared to medical management for gastro-oesophageal reflux disease in 2741 primary care dyspeptic patients without alarm symptoms. Clin Gastroenterol Hepatol 2009; 7:756–761.
Dyspepsia is strongly associated with major
depression and generalised anxiety disorder: a community study. Aliment
Pharmacol Ther 2012; 36:800–810.
This well designed study of 2011 patients relating to a telephone survey. Dyspepsia was associated with a two-fold increase in the odds of having generalized anxiety disorder.
Filippovic BF, Randjelovic T, Ille T, et al. Anxiety, personality traits and quality of
life in functional dyspepsia-suffering patients. Eur J Intern Med 2013; 24:83– 90.
White matter structure changes have been demonstrated in IBS, but this is the first study to demonstrate that there are changes in 36 functional dyspepsia patients compared to 36 healthy controls. The types of changes seen are those associated with psychological distress.
Zanini B, Ricci C, Bandera F, et al.
Zanini B, Ricci C, Bandera F, et al.
Dyspepsia. Curr Opin Gastroenterol 2012; 28:183–1844.
This is a contemporaneous report of the financial impact of dyspepsia on patients. It is the first study to have examined direct and indirect costs of dyspepsia to society for some time.
Ford AC, Quine M, Moayyedi P, et al. Helicobacter pylori ‘test and treat’ or
endoscopy for managing dyspepsia? An individual patient data meta-analysis. Gastroenterology 2005; 128:1838–1844.
This randomized controlled trial of minimally invasive laparoscopic antireflux surgery compared to medical management for gastro-oesophageal reflux disease in 2741 primary care dyspeptic patients without alarm symptoms. Clin Gastroenterol Hepatol 2009; 7:756–761.
Dyspepsia is strongly associated with major
depression and generalised anxiety disorder: a community study. Aliment
Pharmacol Ther 2012; 36:800–810.
This well designed study of 2011 patients relating to a telephone survey. Dyspepsia was associated with a two-fold increase in the odds of having generalized anxiety disorder.
Filippovic BF, Randjelovic T, Ille T, et al. Anxiety, personality traits and quality of
life in functional dyspepsia-suffering patients. Eur J Intern Med 2013; 24:83– 90.
White matter structure changes have been demonstrated in IBS, but this is the first study to demonstrate that there are changes in 36 functional dyspepsia patients compared to 36 healthy controls. The types of changes seen are those associated with psychological distress.
Zanini B, Ricci C, Bandera F, et al.
Zanini B, Ricci C, Bandera F, et al.
Dyspepsia. Curr Opin Gastroenterol 2012; 28:183–1844.
This is a contemporaneous report of the financial impact of dyspepsia on patients. It is the first study to have examined direct and indirect costs of dyspepsia to society for some time.
Ford AC, Quine M, Moayyedi P, et al. Helicobacter pylori ‘test and treat’ or
endoscopy for managing dyspepsia? An individual patient data meta-analysis. Gastroenterology 2005; 128:1838–1844.
This randomized controlled trial of minimally invasive laparoscopic antireflux surgery compared to medical management for gastro-oesophageal reflux disease in 2741 primary care dyspeptic patients without alarm symptoms. Clin Gastroenterol Hepatol 2009; 7:756–761.
Dyspepsia is strongly associated with major
depression and generalised anxiety disorder: a community study. Aliment
Pharmacol Ther 2012; 36:800–810.
This well designed study of 2011 patients relating to a telephone survey. Dyspepsia was associated with a two-fold increase in the odds of having generalized anxiety disorder.
Filippovic BF, Randjelovic T, Ille T, et al. Anxiety, personality traits and quality of
life in functional dyspepsia-suffering patients. Eur J Intern Med 2013; 24:83– 90.
White matter structure changes have been demonstrated in IBS, but this is the first study to demonstrate that there are changes in 36 functional dyspepsia patients compared to 36 healthy controls. The types of changes seen are those associated with psychological distress.
Zanini B, Ricci C, Bandera F, et al.
Zanini B, Ricci C, Bandera F, et al.
Dyspepsia. Curr Opin Gastroenterol 2012; 28:183–1844.
This is a contemporaneous report of the financial impact of dyspepsia on patients. It is the first study to have examined direct and indirect costs of dyspepsia to society for some time.
Ford AC, Quine M, Moayyedi P, et al. Helicobacter pylori ‘test and treat’ or
endoscopy for managing dyspepsia? An individual patient data meta-analysis. Gastroenterology 2005; 128:1838–1844.
This randomized controlled trial of minimally invasive laparoscopic antireflux surgery compared to medical management for gastro-oesophageal reflux disease in 2741 primary care dyspeptic patients without alarm symptoms. Clin Gastroenterol Hepatol 2009; 7:756–761.
Dyspepsia is strongly associated with major
depression and generalised anxiety disorder: a community study. Aliment
Pharmacol Ther 2012; 36:800–810.
56. Shepherd SJ, Lomer MC, Gibson PR. Short-chain carbohydrates and functional gastrointestinal disorders. Am J Gastroenterol 2013; 108:707–717.

57. Chang L, Adeyemo M, Karagiannidis I, et al. Serum and colonic mucosal immune markers in irritable bowel syndrome. Am J Gastroenterol 2012; 107:262–272.

58. Schmulson M, Chey WD. Abnormal immune regulation and low grade inflammation in IBS: does one size fit all? Am J Gastroenterol 2012; 107:273–275.

59. Chey WD. The role of food in the functional gastrointestinal disorders: introduction to a manuscript series. Am J Gastroenterol 2013; 108:694–697.

This study and also references 47 and 48 are part of a Rome committee ‘food issue’ that is a useful reference for the state of the art of food intake as it relates to functional gastrointestinal disorders.

60. Jeffery IB, O’Toole PW. Diet-microbiota interactions and their implications for healthy living. Nutrients 2013; 5:234–252.

61. Lacy BE, Talley NJ, Locke GR 3rd, et al. Review article: current treatment options and management of functional dyspepsia. Aliment Pharmacol Ther 2012; 36:3–15.

A great overview of the evidence for current therapies for functional dyspepsia.

62. Ford AC, Talley NJ, Schoenfeld PS, et al. Efficacy of antidepressants and psychological therapies in irritable bowel syndrome: systematic review and meta-analysis. Gut 2009; 58:367–378.

63. Wu JC, Cheong PK, Chan Y, et al. A randomized, double-blind, placebo-controlled trial of low dose imipramine for treatment of refractory functional dyspepsia. Gastroenterology 2011; 140 (Suppl 1):S55.

64. Talley NJ, Locke GR 3rd, Herrick LM, et al. Functional Dyspepsia Treatment Trial (FDTT): a double-blind, randomized, placebo-controlled trial of antidepressants in functional dyspepsia, evaluating symptoms, psychopathology, pathophysiology and pharmacogenetics. Contemp Clin Trials 2012; 33: 529–539.

65. Locke GR, Boursas EP, Howden CW, et al. The functional dyspepsia treatment trial (FDTT) key results. Gastroenterology 2013; 144 (Suppl 1):S140.

66. Kusunoki H, Haruma K, Manabe N, et al. Therapeutic efficacy of acotiamide in patients with functional dyspepsia based on enhanced postprandial gastric accommodation and emptying: randomized controlled study evaluation by real-time ultrasonography. Neurogastroenterol Motil 2012; 24:840–845.

67. Matsueda K, Honge M, Tack J, et al. A placebo-controlled trial of acotiamide for meal-related symptoms of functional dyspepsia. Gut 2012; 61:821–828.

A well designed RCT of a promising therapy for functional dyspepsia.

68. Van Oudenhove L, Kindt S, Vos R, et al. Influence of buspirone on gastric sensorimotor function in man. Aliment Pharmacol Ther 2008; 28:1326–1333.

69. Tack J, Janssen P, Masaoka T, et al. Efficacy of buspirone, a fundus-relaxing drug, in patients with functional dyspepsia. Clin Gastroenterol Hepatol 2012; 10:1239–1245.

70. Ma TT, Yu SY, Li Y, et al. Randomised clinical trial: an assessment of acupuncture on specific meridian or specific acupoint vs. sham acupuncture for treating functional dyspepsia. Aliment Pharmacol Ther 2012; 35:552–561.

71. Zeng F, Qin W, Ma T, et al. Influence of acupuncture treatment on cerebral activity in functional dyspepsia patients and its relationship with efficacy. Am J Gastroenterol 2012; 107:1236–1247.

Interesting study suggesting the effects of acupuncture on improving functional dyspepsia symptoms may be mediated centrally.

72. Moayyedi P, Ford AC, Talley NJ, et al. The efficacy of probiotics in the therapy of irritable bowel syndrome: a systematic review. Gut 2010; 59:325–332.

73. Ford AC, Forman D, Bailey AG, et al. Who consults with dyspepsia? Results from a longitudinal 10-yr follow-up study. Am J Gastroenterol 2007; 102:957–965.