Journal of Psychosomatic Research 77 (2014) 1–12

Contents lists available at ScienceDirect

Journal of Psychosomatic Research

Cognitive–behavioral therapy for irritable bowel syndrome: A meta-analysis

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ARTICLE INFO

Article history:
Received 22 January 2014
received in revised form 16 March 2014
accepted 18 March 2014

Keywords:
Irritable bowel syndrome
Cognitive behavioral therapy
Meta-analysis

ABSTRACT

Objective: To establish whether cognitive behavioral therapy (CBT) improves the bowel symptoms, quality of life (QOL) and psychological states of irritable bowel syndrome (IBS) patients.
Methods: Randomized controlled trials (RCTs) of CBT for adult patients with IBS were searched by using PubMed, Scopus and Web of Science. The standardized mean difference (SMD) with 95% confidence intervals (CIs) of the evidence-based outcome measures of the IBS bowel symptoms, QOL and psychological states at post-treatment and follow-up was calculated. Prespecified subgroup analysis was performed.
Results: Eighteen RCTs satisfied our inclusion criteria. In the subgroup analyses, CBT was more effective in reducing IBS bowel symptoms, QOL and psychological states than waiting list controls at the end of the intervention and short-term follow-up. When compared with controls of basic support and medical treatment, the effect sizes were found to favor CBT for the improvement of IBS bowel symptoms at post-treatment and short-term follow-up, but CBT was not superior to controls in improving QOL and psychological states. When comparing CBT with other psychological controls, the effect sizes were almost non-significant.
Conclusions: For IBS patients, CBT was superior to waiting list, basic support or medical treatment at the end of treatment but not superior to other psychological treatments. The meta-analysis might be limited by the heterogeneities and small sample sizes of the included studies.

Introduction

Irritable bowel syndrome (IBS) is a chronic, relapsing gastrointestinal symptom complex characterized by altered bowel habits and abdominal pain and discomfort, and it affects as many as 5%–20% of individuals in the population [1,2]. The prevalence of IBS is modestly higher in women, and women are more likely to exhibit the constipation-predominant subtype and less likely to meet the criteria for the diarrhea-predominant subtype than men [3]. IBS represents an economic burden on society and decreases IBS patients' health-related quality of life [4,5].

The current treatments for IBS are challenging and unsatisfactory [6]. The medical management tends to provide inadequate relief of IBS bowel symptoms [7], whereas the clinical trials of psychological therapies have demonstrated some improvements, especially cognitive behavior therapy (CBT). Notably, CBT has proven to be an effective therapy for both depression and anxiety disorders [8,9]. In regard to the treatment for patients with somatization and symptom syndromes, CBT appears to be a promising treatment [10]. Although the etiology and pathogenesis of IBS remain elusive, it is recognized that patients with IBS are more likely to suffer from coexistent mood disorder, depression and anxiety than healthy controls [11,12]. Thus, CBT might also be an effective and promising treatment strategy for IBS.

The cognitive behavioral model defines how events, thoughts, emotions, actions and physiological responses interact with each other. CBT as applied to IBS includes several main steps. The first step is to educate, which consists of the explanation of IBS symptoms and the CBT model. At the same time, the patients are encouraged to find the psychological factors that are interacting with their physical symptoms. Then, the patients and the therapist work together to identify the potential associations among their thoughts, emotions and actions with IBS symptoms. Lastly, behavioral therapy, such as stress management is applied [13].

There has been some CBT for IBS studies published, including several separate systematic reviews or meta-analyses, that address whether CBT improved the outcome in IBS [13–17]. These systematic reviews all held the view that CBT was superior to the waiting list controls. However, the evidence of CBT for IBS is controversial when compared with different types of active controls. Shen and Nahas [14] found that CBT was possibly not superior to education or psychoeducational support. In contrast, Kearney and Brown-Chang [15] concluded that CBT was

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http://dx.doi.org/10.1016/j.jpsychores.2014.03.006
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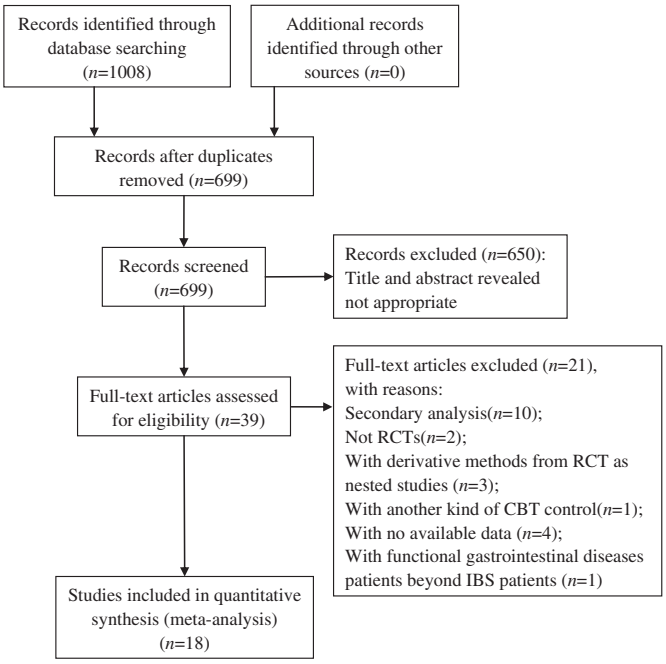

Fig. 1. Flow diagram for the assessment of studies identified in the meta-analysis.

possibly better than education and support. Hutton [13] stated that the effect of CBT was at least as great as the medical treatment for IBS. In recent meta-analyses, Ford et al. [16] concluded that CBT was superior to waiting list controls or physicians' "usual management" in IBS, and Zijdenbos et al. [17] also found that CBT was better than usual care or waiting list in improving symptoms and quality of life but was not superior to placebo. The evidence for the efficacy of CBT might be positive in treating IBS in these reviews [13–17]. However, these recent systematic reviews arrived at disparate conclusions, especially regarding the evidence of CBT for IBS being controversial when compared with active controls other than waiting list controls, and the validity of CBT follow-up has not been established. Finally, several important RCTs published after 2009 were not included in these previous meta-analyses. In this meta-analysis, we attempt to address these discrepancies and provide an up-to-date conclusion to establish the efficacy of CBT for IBS.

Methods

Study selection

To identify the relevant studies, we conducted a search of PubMed, Scopus, the Cochrane Library and Web of Science up to December 31, 2013. The keywords used for IBS and CBT are presented in Appendix A. Randomized controlled trials (RCTs) examining the effects of CBT in adult patients with IBS were eligible for inclusion (see inclusion criteria below).

For the full-text reading and final evaluation, we only included studies published in English. Conference abstracts were not included in our analysis because of the limited data available. Two reviewers (Li & Zhang) independently selected studies that met the predetermined inclusion criteria, and all potentially relevant papers were obtained and evaluated in detail. Any disagreement between investigators was resolved by discussion until consensus.

Manuscripts were included if they met the following criteria: (a) adult participants (over the age of 16 years old) with underlying IBS; (b) studies with randomized controlled research design and the cross-over study with available data of post-treatment outcomes; (c) treatment arm with CBT (self-management CBT, CBT delivered through face-to-face, telephone or web-based, CBT organized by group or individual format, etc.; these types of CBT have been identified as having the same effect as conventional CBT [18,19]); (d) adequate controls (waiting list, physician's usual management, medical treatment or psychological treatment, etc.); and (e) measurable outcomes reported.

The exclusion criteria for the meta-analysis were as follows: (a) not RCT, (b) duplicated trials that included articles that used subsamples from larger studies, (c) studies that used other form of CBT as controls and (d) studies with insufficient data, unless in the studies the authors were able to provide adequate data. After inclusion and excluded, 18 studies remained for analysis (see Fig. 1).

Data collection and methodological quality

Two of our authors subsequently collected the data from the articles meeting the inclusion criteria separately including the following items: author and year, country of origin, mean age, female (%), diagnostic criteria, intervention (method, operator, duration and length of follow-up),control categories, primary outcome measures, secondary outcome measures, intent-to-treat (ITT) data and the Cochrane Collaboration Depression and Anxiety Neurosis Review Group's (CCDAN) scale score [20] (see Table 1). We calculated data such as mean age and female percentage of patients from the manuscripts as far as possible. The outcome measures that were related to our meta-analysis were extracted. The methodological qualities and the risk of bias in individual studies were independently evaluated by the two researchers using the CCDAN scale, which consists of 23 items [21]. The description of the CCDAN scale and the quality scores of each item of the included studies are presented in Appendix B.

Outcome assessment

The primary objective of this study was to evaluate the effect of CBT compared to controls on IBS bowel symptom severity. The effect measurements included almost all the available scales at present, such as The Composite Primary Symptom Reduction (CPSR) Score [22], Irritable Bowel Syndrome Severity Scoring System (IBS-SSS) [23], Bowel Symptom Severity Scale (BSSS) [24], Gastrointestinal Symptom Rating Scale—IBS version (GSRS-IBS) [25], IBS symptom score [26,27], abdominal pain and Rome II scores [28,29]. The secondary outcomes of this study included improvement of IBS QOL scores and psychological states as evaluated by the Hospital Anxiety and Depression (HAD) Scale [30,31], Montgomery Åsberg Depression Rating Scale—Self report (MADRS-S) [32], Beck Depression Inventory (BDI) [33] or health depression score [34]. All evaluations were finished after cessation of treatment, at short-term follow-up and at long-term follow-up with the available data.

Data synthesis and statistical analysis

We included all studies about CBT for IBS compared to controls. The variations of the controls might be a source of the heterogeneity of the meta-analyses. To sort out the sources of the potential heterogeneity, all analyses of the outcomes were classified into subgroups according to the specific types of the controls. The first subgroup included the studies with the symptom-monitoring and waiting list control groups, which included nine trials [19,34–41]. We combined the studies with the control groups of "treatment as usual", "routine clinical care", "standard care" and "self-help support group" as the second subgroup, which included four studies [28,36,42,43], as all of these controls allowed the patients to receive basic support from the gastroenterologist or a "fact sheet" for IBS. The third subgroup included three studies

Table 1
Characteristics of the eighteen studies included in the meta-analysis

Studies	Country	Mean age	Female (%)	Diagnostic criteria	Intervention				Controls	Primary outcome	Secondary outcomes	ITT data	CCDAN score
					Method	Operator	Duration (weeks)	Length of follow-up (months)					
Payne and Blanchard (1995)	USA	40.1	88.2	Rome criteria	CBT	Therapist	8	3	SG or SMWL	CPSR	BDI	NA	24
Blanchard et al. (2007)	USA	49.2	73.3	Rome II	GCBT	Psychologists and advanced doctoral students	10	3	PE or SM	CPSR	NA	yes	29
Boyce et al. (2003)	Australia	42.3	81	Rome I	CBT	Clinical psychologists	8	4.5, 12	SC or relaxation	BSSS	HAD	yes	33
Ljotsson et al. (2011)	Sweden	34.9	74	Rome III	ICBT	Clinical psychologists	10	12	WL	GSRS-IBS	IBS-QOL	NA	30
Hunt et al. (2009)	USA	38.5	81.5	Self-report had been diagnosed with IBS	ICBT	Therapist	5	3	WL	GSRS-IBS	IBS-QOL	yes	21
Kennedy et al. (2005)	England	NA	NA	Rome I	CBT plus mebeverine	Trained primary care nurses	6	3, 6, 12	Mebeverine alone	IBS-SSS	HAD	NA	32
Greene and Blanchard (1994)	USA	38.2	75	Clinical criteria	CBT	Therapist	8	3	SMWL	CPSR	BDI	NA	23
Ljotsson et al. (2010)	Sweden	34.6	84.7	Rome III	ICBT	Graduate psychology student	10	3	WL	GSRS	IBS-QOL; MADRS-S	NA	29
Ljotsson et al. (2011)	Sweden	38.9	79	Rome II	ICBT	Psychology students and psychologists	10	6	ISM	GSRS-IBS	IBS-QOL; HAD	NA	33
Oerlemans et al. (2011)	Netherlands	38.3	84.2	Rome III	CBT	Psychologist	4	3	SC	Abdominal pain	IBS-QOL	yes	26
Mahvi-Shirazi et al. (2012)	Iran	NA	NA	Rome II	CBT plus medical treatment	Psychologist	8	3	Medical treatment	ROME-II score	NA	NA	17
Sanders et al. (2007)	USA	51	78.3	Rome II	S-CBT	Treatment book	8	3	WL	CPSR	IBS-QOL; BSI	NA	23
Heymann-Monnikes et al. (2000)	Germany	37.8	91.7	Rome criteria	CBT plus medical treatment	Clinical psychologists	14	6	Medical treatment	IBS-SS	BDI	NA	20
Haghayegh et al. (2011)	Iran	NA	45.8	Rome II	GCBT	Clinical psychologists	8	2	WL	NA	IBS-QOL; BDI	NA	21
Vollmer and Blanchard (1998)	USA	43.5	56.3	Rome criteria	CBT	Therapist	10	3	GCBT; SMWL	CPSR	NA	NA	25
Tkachuk et al. (2003)	Canada and USA	39.5	96	Rome criteria	GCBT	Therapists	9	3	SM	Abdominal pain	BDI	NA	21
Moss-Morris et al. (2010)	England	39.5	73	Rome I/Rome II	S-CBT	Psychologist	8	6	Treatment as usual	IBS-SSS	HADS	yes	33
Jarrett et al. (2009)	USA	44.3	86.4	Rome II	CSM-IP	Two research nurses	9	3, 6, 12	CSM-T/IP; UC	IBS-SS	IBS-QOL; BSI	NA	23

Abbreviations: ICBT = CBT delivered via internet; GCBT = group-based CBT; S-CBT = self-administered CBT; PE = psychoeducational support group; SM = stress monitoring group; ISM = Internet-delivered Stress Management; SG = self-help support group; SC = standard care; WL = waiting list control; SMWL = symptom monitoring waiting list control; CPSR = The Composite Primary Symptom Reduction Score; GSRS-IBS = the Gastrointestinal Symptom Rating Scale—IBS version; IBS-SS = The IBS symptom score; IBS-SSS = The Irritable Bowel Syndrome Severity Scoring System; BSSS = the Bowel Symptom Severity Scale; IBS-QOL = Irritable Bowel Syndrome Quality of Life score; HAD = The Hospital Anxiety and Depression; BDI = Beck Depression Inventory; MADRS-S = The Montgomery Åsberg Depression Rating Scale—Self report; BSI = Brief Symptom Inventory; CSM-T/IP = Comprehensive Self-Management-Telephone; CSM-IP = Comprehensive Self-Management-In-Person; UC = usual care; NA = not available.

in which the control groups received medical treatments, whereas the treatment groups received CBT in addition to medical treatments [26,29,44]. In one study [43], the medication used was 270 mg of mebeverine taken thrice daily. In the other two studies [26,28], drugs were prescribed according to the patient's symptoms. The fourth subgroup included three trials that involved all relative psychological treatments, such as "stress monitoring", "relaxation" and "psychoeducation" [43,45,46]. The majority of CBT types contain elements or procedures of cognitive therapy. On the other hand, the CBT procedures in the studies included in our study were variable and multicomponent, some of which also included the steps of relaxation [26,28,34,37,42,43], stress monitoring [35,42], psychoeducation [39], etc., which were applied to be the control treatments in other studies [43,45,46]. In the trials that had three treatment arms, we divided one study into two circumstances [36,43,45]. The data of the CBT arm were applied twice by being controlled with the other two control groups separately. In one study [19], subjects were randomly assigned to three groups: group cognitive treatment (GCT), individual cognitive treatment (ICT) and symptom monitoring waiting list, and it was verified that cognitive therapy delivered in group format was as effective as cognitive therapy delivered in an individualized manner. We only extracted the data of the intervention group delivered individually.

Stata 12.0 software was used for the statistical analyses. The SMD values with 95% CIs were calculated for the continuous data, and a random effects model was used. Studies with multiple outcomes were categorized as above (see Table 1) and then grouped together within each domain. These controlled effect sizes could then be interpreted conservatively with Cohen's convention of small (0.2), medium (0.5) and large (0.8) effects [47].

We developed three methods, including IBS bowel symptoms improvement, QOL and psychological states, to evaluate the application of CBT for IBS. Analyses were performed for post-treatment, short-term follow-up (two to six months from post-treatment) and long-term follow-up (nine to 12 months from post-treatment). When the studies presented two or more data analyses at short-term or long-term follow-up simultaneously that had been defined beforehand, we extracted the data of the longer time point. There were different rating scales in each section. If one study reported its result with an opposite scale direction, the result of the study was multiplied by −1. When evaluating IBS bowel symptoms and QOL, a positive effect size always indicated improvement, whereas a negative effect size of psychological state indicated improvement. We contacted the authors of the trials in which data were not fully reported or could not be calculated manually from the information presented in the article. Overall, we successfully contacted the authors of one study. When the necessary data were available, the SMD and its 95% CI were calculated. Cochrane's Q-test and I-squared test were adopted for assessing heterogeneity. Studies are considered heterogeneous when the Cochran's Q-test probability is lower than 0.05. Heterogeneity was classified into low (≤25%), medium (≈50%) and high (≥75%) levels based on I-squared test. Publication bias was examined using Egger's test as well as the funnel plots.

Our review followed PRISMA guidelines.

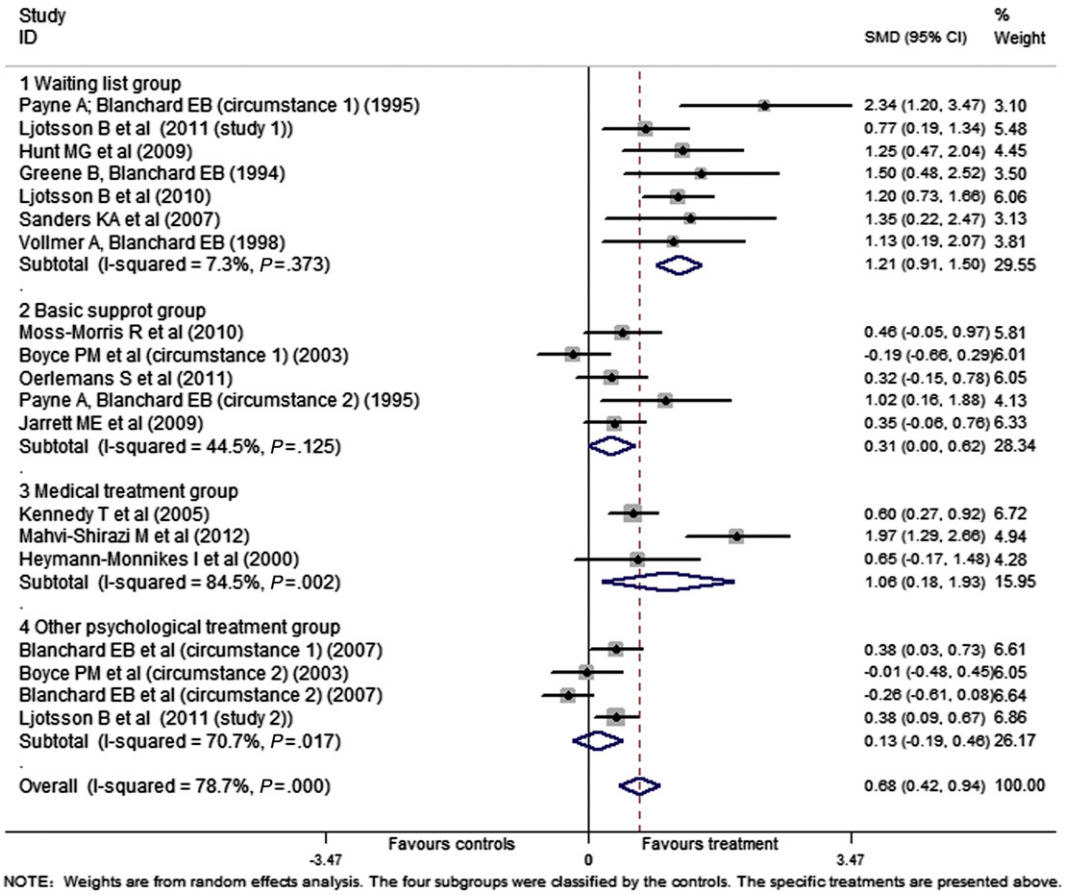

Fig. 2. Effect size estimates for the efficacy of CBT compared to controls in IBS symptom improvement at post-treatment.

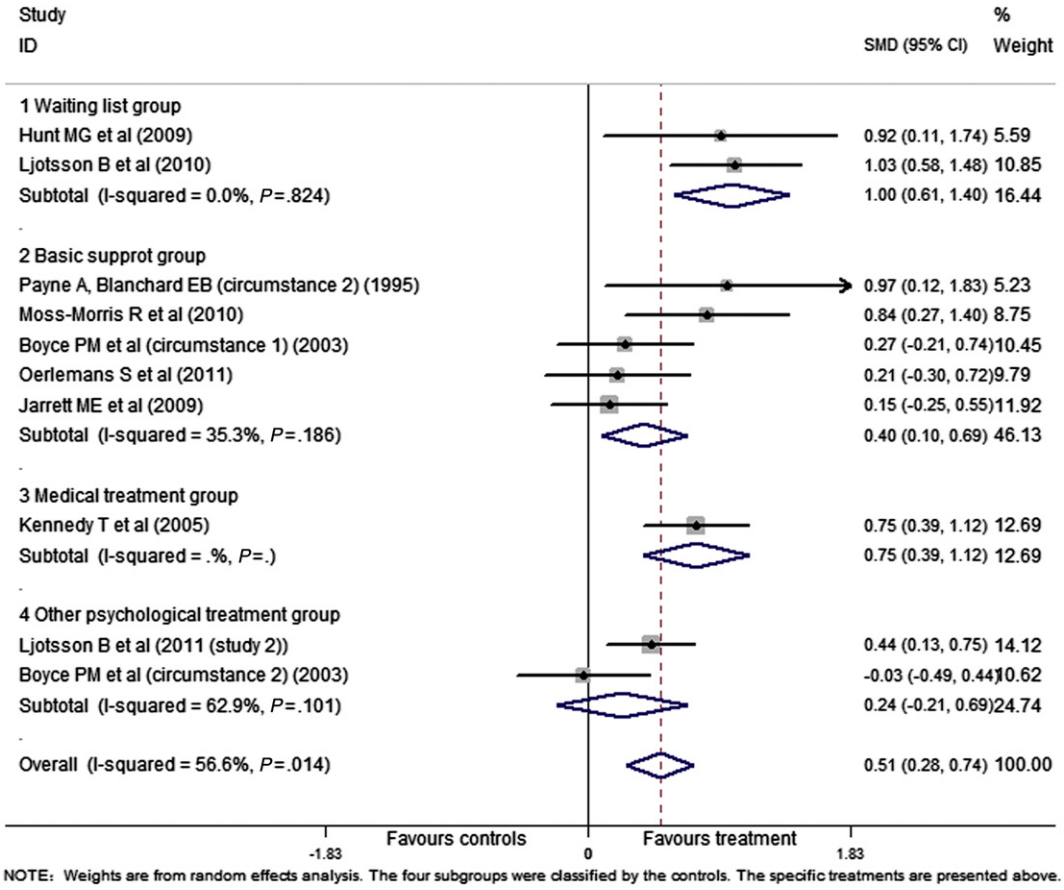

Fig. 3. Effect size estimates for the efficacy of CBT compared to controls in IBS symptom improvement at short-term follow-up.

Results

Study characteristics

A total of 1008 citations were identified, of which 18 were finally selected for analysis (see Fig. 1). We handsearched the references of the previous reviews and found no additional studies. As methods for assessing three-arm trials were introduced in our study, the total number of analyzed circumstances was greater than 18. Treatment durations varied from five to 14 weeks, and the follow-up periods varied from two months to one year. The proportion of female patients recruited by all trials ranged from 45.8% [34] to 96% [41], and the mean age of the patients ranged from 34.5 [39] to 51 [40] years old. The CBT operators included therapists, psychologists, doctoral or graduate clinical psychological students, trained nurses or treatment books for self-administered CBT. Almost all selected studies recruited all types of sub-types of IBS patients except for one trial that recruited only patients with diarrhea-predominant IBS [34]. Five studies reported ITT data at post-treatment [37,39,42,43,45]. The detailed characteristics of the individual studies are presented in Table 1.

Risk of bias in included studies

The quality scores of these 18 studies are shown in Table 1, and the details for each item score of selected studies are presented in Appendix B.

Selection bias

Only two of the eighteen RCTs were performed using allocation concealments [42,43]. The other 16 studies were neither conducted using allocation concealments nor clearly reported the randomization methods.

Performance bias

Complete double-blinding could not be achieved in any of the studies. The blinding of patients was used in two studies, one of which used blinded ID number to send patients to the treatment group [28], and the other study avoided telling the patients about the experimental design [26]. Three studies used the blinding of outcome evaluation [27,43,45]. The blinding of the operator cannot be conducted in a study about CBT because the specific clinical technique requires the operator to face the patient directly. Thus, the therapists were not blinded in these studies.

We also estimated several items, including adequate sample size, record of inclusion/exclusion criteria, number and reasons for withdrawal and so on (Appendix B).

Excluded studies

A total of 49 articles meeting the inclusion criteria were identified, but 31 studies were excluded. Five articles were not published in English [48–52]. Five citations only presented an abstract [53–57]. Ten studies [58–67] reported the second analysis of five other studies [39,42–45] that had already been included in our meta-analysis. Three studies developed derivative methods from RCT as nested studies [68–70]. Two studies were not RCTs [71,72]. One study used another type of CBT as a control [73]. Four studies did not provide extractable data for our meta-analysis [74–77]. One study was performed with patients with functional bowel disorders including IBS [78].

Efficacy of CBT in the treatment of IBS

Symptom score

Continuous post-intervention data were available for 16 studies with 19 circumstances comprising 1380 patients with IBS bowel symptoms. The remaining two trials of the included studies were ineligible, as one [41] did not provide extractable data, and one [34] had not included the IBS bowel symptom outcomes. As shown in Fig. 2, there was a medium to large significant pooled effect size of 0.678 (95% CI: 0.417, 0.939) in favor of CBT over all types of controls at the post-treatment evaluation. In the subgroup analyses, CBT outperformed waiting list and medical controls with large effects and outperformed basic support group with small effects. When CBT was compared with other psychological controls, the SMD indicated minimal and nonsignificant effects. Unfortunately, most of the follow-up studies had a cross-over design and could not be included in the meta-analysis, especially for the long-term follow-up. This resulted in eight trials with the data of nine circumstances at short-term follow-up and two studies with data of three circumstances at long-term follow-up remaining. The overall short-term SMD indicated medium effects 0.508 (see Fig. 3). In the subgroup analyses, the effect sizes were found in favor of CBT over waiting list and medical controls with large effects. When

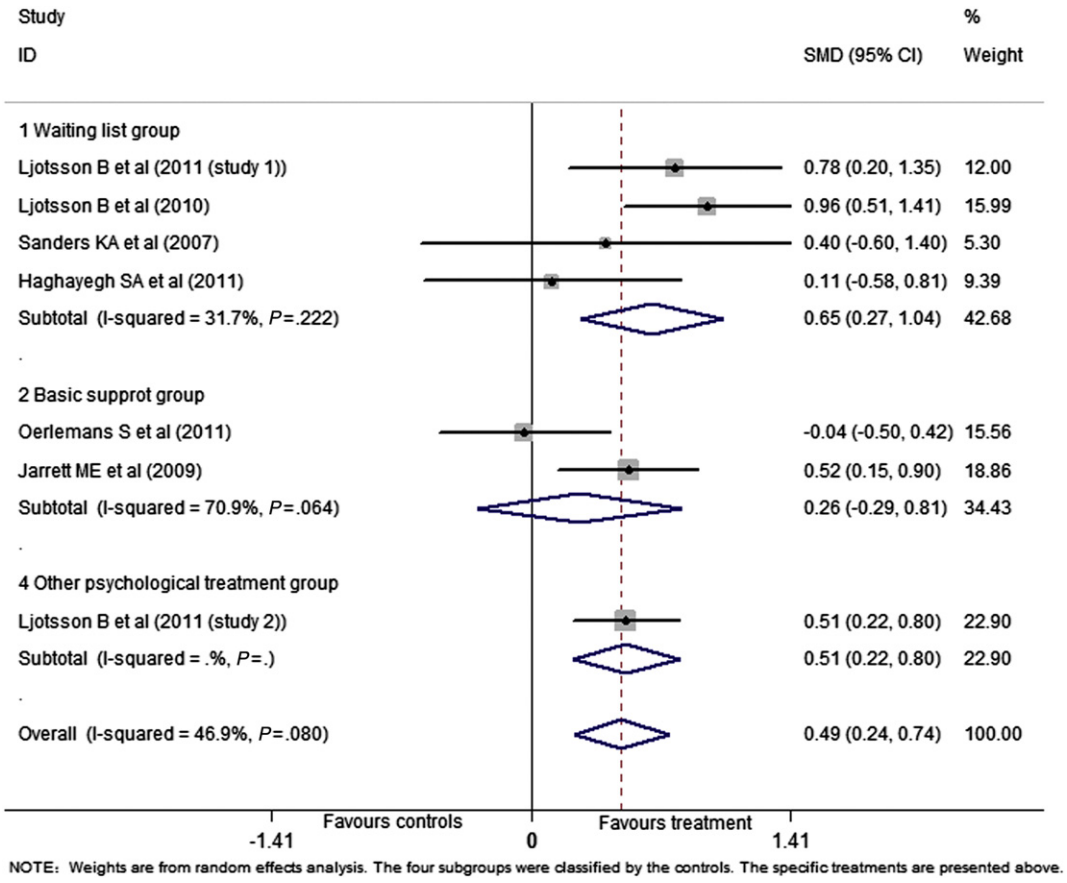

Fig. 4. Effect size estimates for the efficacy of CBT compared to controls in improvement of IBS QOL.

CBT was compared with other psychological controls, the SMD indicated minimal and non-significant effects. We merged all the trials with available long-term follow-up data. The SMD indicated non-significant effects. When we calculated the pooled effect size for the difference of means between pre-treatment and post-treatment of the studies that had long-term follow-up data [27,35,43,44], the SMD was 1.179 (95% CI: 0.963, 1.396). The SMD between pre-treatment and long-term follow-up was 1.030 (95% CI: 0.812, 1.249). The SMD between post-treatment and long-term follow-up was −0.078 (95% CI: −0.291, 0.135), which was not significantly different. The data suggested that the efficacy of CBT for IBS may have been sustained after the treatment phase.

Quality of life

There were a total of seven studies comprising 558 patients that reported IBS QOL scores. One study fulfilling the inclusion criteria had to be excluded at this stage because it reported unusually high negative effect sizes for QOL, and the description of the outcomes in the article was quite different from other studies of approximately the same scale [37]. This study was regarded as an outlier because of its distinctive outcomes. As shown in Fig. 4, there was a medium significant pooled effect size of 0.488 (95% CI: 0.237, 0.740) in favor of CBT over all types of controls at the post-treatment. In the subgroup analyses, CBT outperformed waiting list controls with medium to large effects, and the SMD of CBT compared with basic support groups indicated nonsignificant effects. Only four studies comprising 425 patients provided short-term follow-up data. The pooled short-term SMD indicated small to medium effects (see Fig. 5). The long-term follow-up QOL data were available in two studies [27,35]. The pooled SMD of CBT compared with all types of controls indicated nonsignificant effects. The pooled SMD between pre-treatment and post-treatment was 0.789 (95% CI: 0.471, 1.108), and the SMD between pre-treatment and long-term follow-up was 0.842 (95% CI: 0.486, 1.198). The SMD between post-treatment and long-term follow-up was 0.137 (95% CI: −0.199, 0.472), which was not significantly different. These results suggest that the efficacy of CBT for IBS QOL improvement may also have been sustained.

Psychological states

The data about psychological states (mainly depression and anxiety) were available for 12 studies with 14 circumstances. These studies comprised 910 patients. As shown in Fig. 6, there was a small to medium significant pooled effect size of −0.213 (95% CI: −0.423, −0.003) in favor of CBT over all types of controls at post-treatment. In the subgroup analyses, CBT outperformed waiting list with large effects. When CBT was compared with all types of controls, the SMD indicated non-significant effects. At follow-up, there were a total remaining number of seven trials with eight circumstance data at short-term follow-up and three studies with four circumstance data at long-term follow-up. The overall short-term SMD for these 669 patients indicated non-significant effects (see Fig. 7), as did the subgroup analyses, and the pooled long-term SMD also indicated non-significant effects. The long-term follow-up data concerning psychological states were available in three studies [27,43,44]. The pooled SMD between pre-treatment and post-treatment of the three studies was −0.303 (95% CI: −0.576, −0.031), and the SMD between pre-treatment and long-term follow-up was −0.171 (95% CI: −0.462, 0.120). The SMD between post-treatment and long-term follow-up was 0.125 (95% CI: −0.095, 0.346), which was not significantly different. These results suggest that the efficacy of CBT for IBS may not have been sustained at long-term follow-up.

Subgroup analyses were also conducted according to the controls, whether they included the psychological treatment or not (see Table 2). The CBT effect appeared to be more significant for IBS when compared with non-psychological treatments, and the other psychological treatments appeared to be as effective as CBT.

No adverse events were reported in these studies.

Discussion

This study conducted a meta-analysis to establish the efficacy of CBT for IBS and highlighted some important findings. First, the pooled effect sizes of CBT for IBS appeared to favor the use of CBT for the improvement of IBS bowel symptoms, QOL and psychological states at post-treatment evaluations. At follow-up, our study found that CBT prevailed over controls in improvement of IBS bowel symptoms and QOL at short-term follow-ups, whereas the effect size displayed no significant difference in psychological states at the same time point. However, the test for heterogeneity of the overall included studies was significant. Thus,

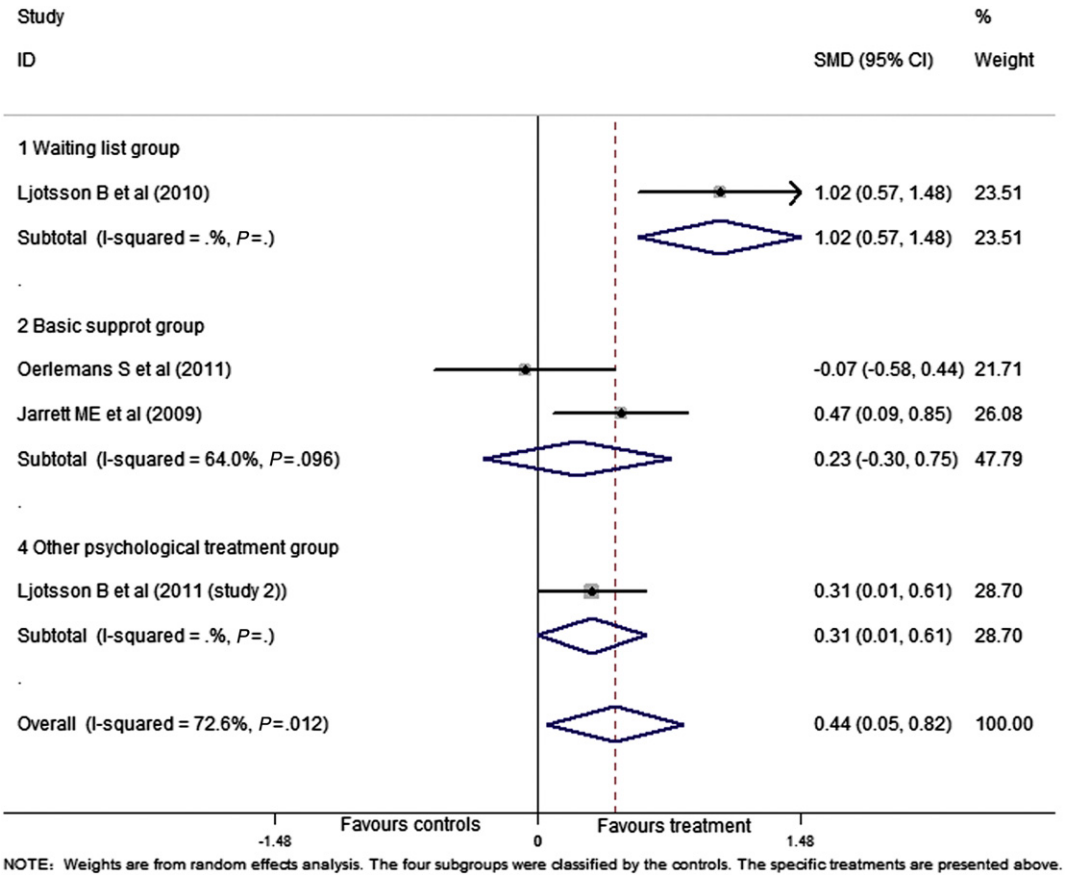

Fig. 5. Effect size estimates for the efficacy of CBT compared to controls in improvement of IBS QOL at short-term follow-up.

it is difficult to make definitive conclusions about all of the pooled average effect sizes because of high degrees of heterogeneity. Second, in the subgroup analyses, CBT was significantly more effective in improving IBS bowel symptoms, QOL and psychological states than waiting list controls at the end of the intervention and short-term follow-up. When compared with basic support controls and medical treatment, the effect sizes were in favor of CBT for the improvement of IBS bowel symptoms at post-treatment and short-term follow-up, but the effect sizes were not superior to the control groups in the improvement of QOL and psychological states. The effect sizes were almost non-significant between CBT and other psychological controls, but the effects of both CBT and other psychological controls appeared to be positive in each study. In the other subgroup analyses, the CBT appeared to be more superior to non-psychological treatment for IBS in the improvement of IBS bowel symptoms, QOL and psychological states at post-treatment and short-term follow-up. Third, when we calculated the pooled effect size of the studies that provided long-term follow-up data, the overall controlled effect sizes for CBT indicated effectiveness at post-treatment and long-term follow-up with large effects for improvements of IBS symptoms and QOL, which suggested that the efficacy of CBT for IBS may persist after the treatment phase.

To our knowledge, there are several systematic reviews that have examined the efficacy of CBT for IBS [13–17]. Our findings are consistent with the previous reviews, demonstrating that CBT may be highly effective in improving IBS bowel symptoms when compared with waiting lists and standard basic support groups [13–15,17]. However, the conclusions of the narrative reviews may be less convincing than meta-analyses as their conclusions were not based on the calculation of overall treatment effects but on the opinions of the authors. Importantly, our study focused on the CBT for IBS and included mostly recent studies. On the other hand, our meta-analysis developed subgroup analyses that included almost all of the possible controls for IBS. Thus, we detected the efficacy of CBT for IBS compared with waiting lists, basic support controls, only standard medical treatment and other psychological therapies. Our study also found that the efficacy of CBT for IBS might be sustained at long-term follow-up.

There are some limitations in our study. One problem is the diversity of CBT formats, which resulted in considerable heterogeneity in our meta-analysis. The operators of the CBT and the duration of the CBT were also different in the studies. As there exists no standardized treatment procedure for CBT, our meta-analysis of CBT for IBS had obvious heterogeneity. We included almost all available control arms and detected that almost none of the controls were the same except for the waiting list controls. Thus, performing subgroup analyses according to the control treatments and categorizing control treatments would be difficult. On the basis of the details reported in the articles, the controls were classified into waiting list controls, basic support controls, medicine alone and other psychological treatments. However, this classification has not been confirmed, and heterogeneity could still be detected in the subgroup analyses. Inevitably, all of the available studies were performed without double-blinding, which may have led to potential placebo effects and observation bias. We also noted that the present study was limited to materials published in English-language journals, which may have led to publication bias.

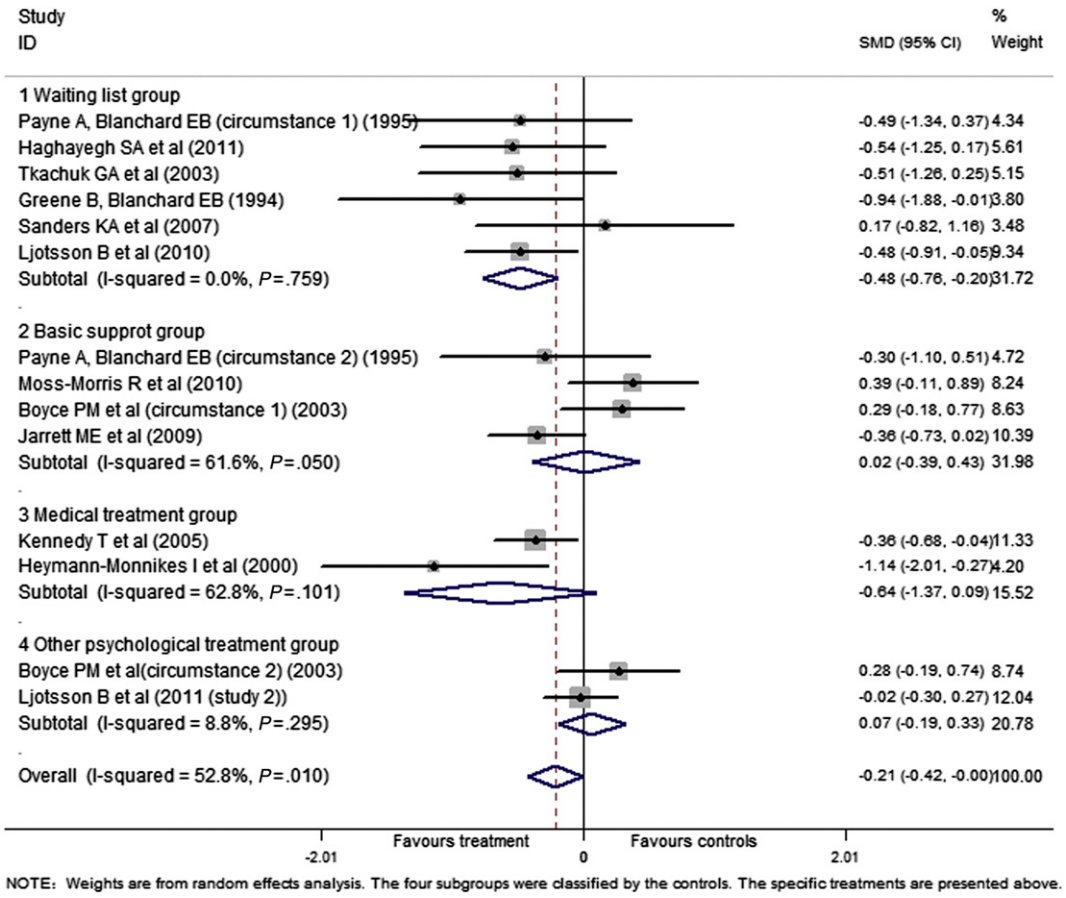

Fig. 6. Effect size estimates for the efficacy of CBT compared to controls in improvement of psychological anxiety and depression at post-treatment.

It has been proven that CBT is superior to waiting list and basic support controls in the treatment of IBS in previous reviews, and our work provides further confirmation for this conclusion. In this meta-analysis, we included almost all types of the control groups and developed the subgroup analyses according to the controls. We found that CBT had a significant advantage in all aspects when compared with a control group of non-psychotherapy, and CBT appeared to maintain the same superiority when compared to other types of psychotherapy. These results imply that the psychological treatment was, at the minimum, a good choice to treat IBS. In other subgroup analyses, we found that the combination of CBT with standard medical treatment would increase the efficacy of using drug therapy alone. We also determined that the efficacy of CBT for IBS might continue at long-term follow-up. However, the evidence is somewhat limited by the variations of CBT procedure, the relatively low quality of the included studies and the small quantity of the valid studies. More high-quality studies are needed, and the CBT should also be standardized.

In conclusion, CBT was superior to waiting lists, basic support controls or medical treatment at post-treatment and short-term follow-up in the treatment of IBS bowel symptoms but was not superior to other psychological treatments. In terms of QOL and psychological states, CBT for IBS was proven to be more effective than waiting list at the end of treatment. The efficiency of CBT may persist after the treatment phase. Our meta-analysis might be limited by the heterogeneities and small sample sizes of the included studies. Nevertheless, the superiority of CBT for the treatment of IBS should not be ignored.

Authorship

Guarantor of the article: Lishou Xiong

Author contributions: LSX contributed to the study concept, design, supervision and takes responsibility for the integrity of the data and the accuracy of the data analysis. All authors approved the final version of the manuscript. LL and SHZ both contributed to the trial selection and data extraction. LL, SHZ and QY performed the analysis and interpretation of data, and LL wrote the article. MHC contributed to the supervision of the manuscript.

Funding

This study was funded by the Planned Science and Technology Project of Guangdong Province (2009B030801138).

Conflict of interest

The authors have no conflict of interests to report.

Acknowledgments

Declaration of personal interests: We are grateful to Professor Roger Jones and Tom Kennedy for answering our data queries and, where applicable, providing us with their original datasets for analysis.

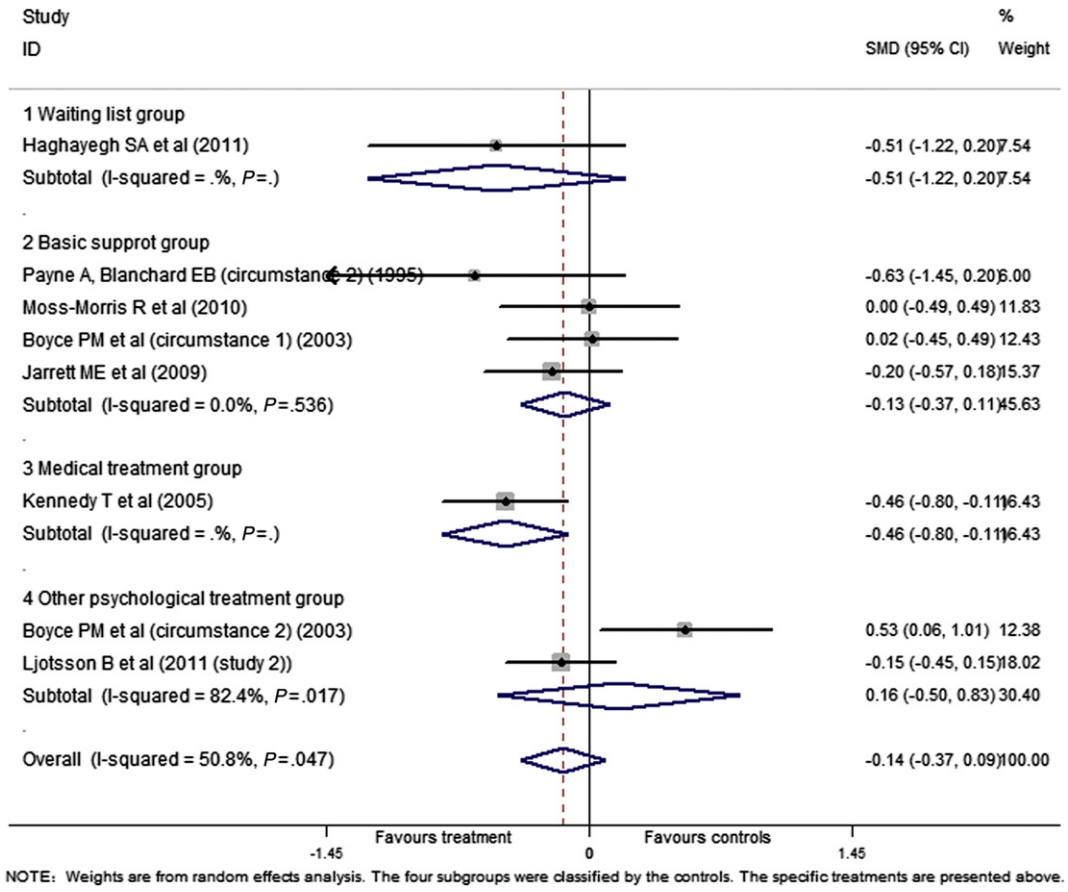

Fig. 7. Effect size estimates for the efficacy of CBT compared to controls in improvement of psychological anxiety and depression at short-term follow-up.

Table 2
Effect sizes and the heterogeneity for the outcomes of CBT for IBS in subgroup analyses of psychological treatments

Outcomes	Subgroup	Post-treatment				Short-term follow-up				Long-term follow-up			
		Effect size		Heterogeneity		Effect size				Heterogeneity		Effect size	
		Heterogeneity											
Hedges' g	95% CI	I^2 (%)	*P*			Hedges' g	95% CI	I^2 (%)	*P*	Hedges' g	95% CI	I^2 (%)	*P*
IBS symptom	NP	0.875	0.568, 1.183*	73.5	<.001	0.597	0.330, 0.864*	53.4	.036	0.058	−0.272, 0.388	48.5	.144
	P	0.133	−0.194, 0.461	70.7	.017	0.241	−0.211, 0.693	62.9	.101	−0.255	−0.723, 0.212	/	/
IBS-QOL	NP	0.477	0.143, 0.810*	55.7	.046	0.483	−0.091, 1.056	80.0	.007	0.643	−0.036, 1.322	72	.059
	P	0.512	0.224, 0.801*	/	/	0.309	0.006, 0.613*	/	/	/	/	/	/
Psychological states	NP	−0.297	−0.533, −0.060*	48.1	.031	−0.258	−0.45, −0.067*	0.6	.412	−0.114	−0.518, 0.29	68.2	.043
	P	0.068	−0.192, 0.327	8.8	.295	0.164	−0.504, 0.833	82.4	.017	0.395	−0.075, 0.865	/	/

Note: * indicates that the effect sizes have significant meaning.
NP: the controls were not psychological treatments.
P: the controls were other psychological treatments.

Appendix A. The text keywords about irritable bowel syndrome and cognitive behavioral therapy

Pubmed: ((((((((((("Irritable Bowel Syndrome"[Mesh])) OR (Irritable Bowel Syndromes)) OR (Syndrome, Irritable Bowel)) OR (Syndromes, Irritable Bowel)) OR (Colon, Irritable)) OR (Irritable Colon)) OR (Colitis, Mucous)) OR (Colitides, Mucous)) OR (Mucous Colitides)) OR (Mucous Colitis))) AND ((((((((((((((((((((((("Cognitive Therapy"[Mesh])) OR (Cognitive Therapies)) OR (Therapies, Cognitive)) OR (Cognition Therapy)) OR (Cognition Therapies)) OR (Therapies, Cognition)) OR (Cognitive Behavior Therapy)) OR (Therapy, Cognitive Behavior)) OR (Cognitive Psychotherapy)) OR (Cognitive Psychotherapies)) OR (Psychotherapies, Cognitive)) OR (Psychotherapy, Cognitive)) OR (Therapy, Cognitive)) OR (Behavior Therapy, Cognitive)) OR (Behavior Therapies, Cognitive)) OR (Cognitive Behavior Therapies)) OR (Therapies, Cognitive Behavior)) OR (Cognitive Behavioral Therapy)) OR (Behavioral Therapies, Cognitive)) OR (Behavioral Therapy, Cognitive)) OR (Therapies, Cognitive Behavioral)) OR (Therapy, Cognitive Behavioral)). 192 articles were detected.

Web of science: (Irritable Bowel Syndrome* OR Irritable Colon OR Mucous Coliti*) AND (Cogniti* Therap* OR Cognitive Behavior* Therap* OR Cognitive Psychotherap*). 278 articles were detected.

Scopus: ((TITLE-ABS-KEY (irritable bowel syndrome)) OR (TITLE-ABS-KEY (irritable colon)) OR (TITLE-ABS-KEY (mucous colitides)) OR (TITLE-ABS-KEY (mucous colitis))) AND ((TITLE-ABS-KEY (cognitive therapy)) OR (TITLE-ABS-KEY (cognition therapy)) OR (TITLE-ABS-KEY (cognitive behavior therapy)) OR (TITLE-ABS-KEY (cognitive

psychotherapy)) OR (TITLE-ABS-KEY (cognitive behavioral therapy))) in article title, abstract, keywords. 538 articles were detected.

Appendix B

Note. 1. Objectives; 2. sample size; 3. follow-up; 4. power calculation; 5. allocation; 6. concealment; 7. treatment description; 8. blinding subjects; 9. sample source; 10. diagnostic criteria; 11. exclusions; 12. demographics; 13. blinding assessor; 14. compliance; 15. side effects; 16. withdrawals; 17. outcome; 18. comparability; 19. analysis of withdrawals; 20. results; 21. analysis; 22. conclusions; 23. interests. SUM1 = total quality score of every study; SUM2 = total score of every single item.

[1] = For the purpose of this exercise, sample size was scored as 2 if power calculations justified it, or if n per group was >100. It was scored as 1 if n per group was 50–100, and as 0 if n per group was <50.

[2] = For the purpose of this exercise, follow-up was scored as 2 if it was six months or longer, 1 if it was between three and six months and 0 if it was less than three months.

[3] = Details on how the allocation code was protected from those involved in patient recruitment. May be achieved by having allocation done by a central independent body, a computer-generated random code, or protection of code by, for example, sealed opaque envelopes.

[4] = Test of integrity of blind is normally done by asking participants to guess their allocated group.

[5] = Source of subjects refers to the setting in which subjects were found, for example inpatients, outpatients, general practice, and community.

[6] = Assessors were assumed to be blind in all trials described as double blind.

[7] = Quality of the conclusions was judged according to the following factors: whether they gave an accurate representation of the results, whether there was a critique of the limitations of the methods used, whether possible sources of bias were considered and whether other relevant literature was discussed. Trials of treatments for depression and neurosis

Appendix B1

The Cochrane Collaboration Depression and Anxiety Neurosis Review Group's (CCDAN) scale score of the included studies in each item

Study	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	SUM1
Payne and Blanchard (1995)	2	0	1	2	2	0	2	0	0	1	0	2	0	0	0	2	2	2	2	2	0	2	0	24
Blanchard et al. (2007)	2	1	1	0	2	0	2	0	2	2	1	2	0	0	0	1	2	2	2	2	1	2	2	29
Moss-Morris et al. (2010)	2	2	2	2	2	2	2	0	2	1	2	2	0	0	0	2	2	2	2	2	0	2	0	33
Boyce et al. (2003)	2	1	2	0	2	2	2	0	2	1	2	2	0	0	0	1	2	2	2	2	2	2	2	33
Ljotsson et al. (2011) (1)	2	2	2	2	2	0	2	0	1	2	2	2	0	0	0	0	2	2	0	2	1	2	2	30
Hunt et al. (2009)	2	0	1	0	1	0	2	0	1	1	0	2	0	0	0	1	2	2	2	2	0	2	0	21
Kennedy et al. (2005)	2	2	2	2	2	0	2	0	2	1	1	2	0	0	0	2	2	2	2	2	0	2	2	32
Greene and Blanchard (1994)	2	0	1	0	1	0	2	0	0	1	2	2	0	0	0	2	2	2	2	2	0	2	0	23
Ljotsson et al. (2010)	2	2	1	2	1	0	2	0	1	1	2	2	0	0	0	1	2	2	2	2	0	2	2	29
Ljotsson et al. (2011) (2)	2	2	2	2	2	0	2	0	1	1	2	2	0	0	0	1	2	2	2	2	2	2	2	33
Oerlemans et al. (2011)	2	2	1	2	1	0	2	0	0	1	2	2	0	0	0	1	2	2	2	2	0	2	0	26
Mahvi-Shirazi et al. (2012)	2	0	1	0	1	0	2	0	2	1	0	1	0	0	0	0	2	2	0	2	0	1	0	17
Sanders et al. (2007)	2	0	1	0	2	0	2	0	2	1	2	2	0	0	0	1	2	2	0	2	0	2	0	23
Heymann-Monnikes et al. (2000)	2	0	2	0	1	0	2	0	0	1	0	2	0	0	0	0	2	2	0	2	2	2	0	20
Haghayegh et al. (2011)	2	0	1	0	1	0	2	0	1	1	0	2	0	0	0	1	2	2	0	2	2	2	0	21
Tkachuk et al. (2003)	2	0	1	0	1	0	2	0	0	1	2	2	0	0	0	0	2	2	0	2	2	2	0	21
Vollmer and Blanchard (1998)	2	0	1	0	1	0	2	0	1	1	2	2	0	0	0	2	2	2	2	2	2	1	0	25
Jarrett et al. (2009)	2	0	2	0	0	0	2	0	2	1	0	0	0	0	0	1	2	2	2	2	1	2	2	23
SUM2	36	14	25	14	25	4	36	0	20	20	22	33	0	0	0	19	36	36	24	36	15	34	14	26

Appendix B2

The Cochrane Collaboration Depression and Anxiety Neurosis Review Group's (CCDAN) scale

Criteria	Score and rating criteria
(1) Objectives and specification main outcomes a priori	0 = objectives unclear 1 = objectives clear but main outcomes not specified a priori 2 = objectives clear with a priori specification of main method for assessment of outcome
(2) Adequate sample size (n per group)[1]	0 = inadequate 1 = moderate 2 = large or specified by power calculations
(3) Appropriate duration of trial including follow-up[2]	0 = too short 1 = reasonable length 2 = long enough for assessment of long-term outcomes
(4) Power calculation	0 = not reported 1 = mentioned without details 2 = details of calculations provided
(5) Method of allocation	0 = unrandomized and likely to be biased 1 = partially or quasi randomized with some bias possible 2 = randomized allocation
(6) Concealment of allocation[3]	0 = not done or not reported 2 = concealment of allocation code detailed
(7) Clear description of treatments (including doses of drugs used) and adjunctive treatment	0 = main treatments not clearly described 1 = inadequate details of main or adjunctive treatments 2 = full details of main and adjunctive treatments

(*Appendix B2 continued*)

Criteria	Score and rating criteria
(8) Blinding of subjects	0 = not done 1 = done but no test of blind[4] 2 = done and integrity of blind tested
(9) Source[5] of subjects described and representative sample recruitment	0 = source of subjects not described 1 = source of subjects given but no information on sampling or use of unrepresentative sample (for example, volunteers) 2 = source of subjects described plus representative sample taken (for example, all consecutive admissions or referrals, or random sample taken)
(10) Use of diagnostic criteria (or clear specification of inclusion criteria)	0 = none 1 = diagnostic criteria or clear inclusion criteria 2 = diagnostic criteria plus specification of severity
(11) Record of exclusion criteria and number of exclusions and refusals reported	0 = criteria and number not reported 1 = criteria or number of exclusions and refusals not reported 2 = criteria and number of exclusions and refusals reported
(12) Description of sample demographics	0 = little/no information (only age/sex) 1 = basic details (for example, marital status/ethnicity) 2 = full description (for example, socioeconomic status, clinical history)
(13) Blinding of assessor[6]	0 = not done 1 = done but no test of blind 2 = done and integrity of blind tested
(14) Assessment of compliance with experimental treatments (including attendance for therapy)	0 = not assessed 1 = assessed for some experimental treatments 2 = assessed for all experimental treatments
(15) Details on side-effects	0 = inadequate details 1 = recorded by group but details inadequate 2 = full side effect profiles by group
(16) Record of number and reasons for withdrawal by group	0 = no info on withdrawals by group 1 = withdrawals by group reported without reason 2 = withdrawals and reason by group
(17) Outcome measures described clearly (and therefore replicable) or use of validated (or referenced) instruments	0 = main outcomes not described clearly 1 = some of main outcomes not clearly described 2 = main outcomes clearly described or valid and reliable instruments used
(18) Information on comparability and adjustment for differences in analysis	0 = no information on comparability 1 = some information on comparability with appropriate adjustment 2 = sufficient information on comparability with appropriate adjustment
(19) Inclusion of all subjects in analyses ('intention to treat' analysis)	0 = less than 95% of subjects included 2 = 95% or more included
(20) Presentation of results with inclusion of data for re-analysis of main outcomes (for example, SDs)	0 = little information presented 1 = adequate information 2 = comprehensive
(21) Appropriate statistical analysis (including correction for multiple tests where applicable)	0 = inadequate 1 = adequate 2 = comprehensive and appropriate
(22) Conclusions justified[7]	0 = no 1 = partially 2 = yes
(23) Declaration of interests (for example, source of funding)	0 = no 2 = yes

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