PART 4

9 BEHAVIOURAL THERAPIES

Clinical Questions

1. Does CBT have a role in managing symptoms?
2. Do psychological interventions have a role in managing symptoms?
3. Does hypnotherapy have a role in managing IBS symptoms?
4. Does bio-feedback have a role in managing symptoms?
5. Does relaxation therapy have a role in managing symptoms?

BACKGROUND

Psychosocial factors are integral to the way in which people experience and interpret symptoms and they influence both illness behaviour and response to treatment. The effects on gastrointestinal function caused by emotional and psychological response include fluctuation in acid secretion; changes in motor activity and gut transit and have been well documented (Wolf 1981). Although it has been shown that there are no greater psychological disturbances in people with IBS than in the general population (Wilhelmsen 2000), anxiety and depression can be major contributing factors in the symptom profiles of IBS. Psychotherapy has been suggested as a possible treatment to reduce pain and symptoms and also to improve quality of life.

There are a range of psychological treatments which can be used in the management of IBS. Psychological therapies may be defined as the treatment of mental and emotional disorders through the use of psychological techniques designed to encourage communication of conflicts and insight into problems, with the goal being relief of symptoms, changes in behaviour leading to improved social and vocational functioning and personality growth.

Relaxation therapy is the simplest form of psychotherapy. The premise is that if response to stress contributes to IBS, reducing autonomic stress responses by relaxation will reduce symptoms, induce a feeling of well- being and increased confidence which will allow people with IBS to feel more able to control the condition. Relaxation can be taught using audio tapes and there are many readily available which people with IBS can access (Jones 2000).

More complex psychological interventions include biofeedback, cognitive behavioural therapy, dynamic psychotherapy and hypnotherapy are usually initiated for people with moderate or severe symptoms who have not responded to other management programmes. These therapies are effective, but time consuming to provide, require specialist input and currently availability varies widely across the UK.

Biofeedback

Biofeedback includes a number of techniques in which a physiological process is monitored and information regarding unconscious bodily functions are shown by audiovisual display to the patient. The patient is taught to bring about changes in the physiological process by using a number of strategies e.g. thoughts, sensations, feelings. The rationale is that the physiological process being monitored is causally related to a clinical condition, in this case IBS, and that alteration of the process can lead to a reduction or resolution of symptoms.

Cognitive Therapy

Cognitive therapy is a therapy that assumes that faulty thought patterns (called cognitive patterns) cause maladaptive behaviour and emotional responses. The treatment focuses on changing thoughts in order to solve psychological and personality problems. Behaviour therapy is also a goal-oriented, therapeutic approach, and it treats emotional and behavioural disorders as maladaptive learned responses that can be replaced by healthier ones with appropriate training. Cognitive-behavioural therapy (CBT) integrates features of behaviour modification into the traditional cognitive restructuring approach. Cognitive-behavioural therapy attempts to change clients' unhealthy behaviour through cognitive restructuring (examining assumptions behind the thought patterns) and through the use of behaviour therapy techniques. CBT can be used as a long-term treatment for irritable bowel syndrome. Different programmes comprise different elements in a variety of combinations, including: helping patients recognise the causes of disease; cognitive restructuring techniques to address unhelpful beliefs; changing underlying depressive or threatening ‘life scripts’; psychotherapy to cope with emotional problems and find new solutions; stress management or relaxation training, using progressive muscle relaxation techniques; breaking habits of learned illness behaviours; practising more adaptive behaviours; assertion and coping skills training. CBT can be administered to patients individually or as a group.

Hypnotherapy

Hypnosis describes a range of naturally occurring states of altered awareness which may vary from momentary distractions and 'absences' through much enhanced states of relaxation to very deep states of inward focus and awareness. The mental processes which can occur in any of these states, appropriately utilised are generally far more flexible and potentially far more powerful in effecting change than those we can achieve in most everyday states of active

conscious awareness. These states may be induced quite formally or quite naturalistically, in an almost unnoticeable way, depending on the requirement of the problem, the capability of the practitioner and the needs of the client (UK Council for Psychotherapy (UKCP) 1992).

Gut-directed hypnotherapy is a specific form of hypnotherapy developed for the management of gastrointestinal disorders. It uses the therapeutic qualities of hypnotherapy, such as deep relaxation, and adds gut-specific treatments and suggestions. 'Gut-directed hypnotherapy' can be used as a treatment for irritable bowel syndrome. IBS is ideal for treatment with hypnosis, as there is no structural damage to the body. During hypnotherapy people learn how to influence and gain control of their gut function and then seem to be able to change the way the brain modulates their gut activity (Whorwell 2005). Firstly, patients are given a brief outline of the anatomy and physiology of the gut and a schematic representation of their symptoms, using a diagram of the colon showing how smooth muscle spasm can give pain, bloating and a disordered bowel habit. Patients are told that the reduction of this spasm and normalisation of smooth muscle activity will reduce pain and bloating and encourage a more normal flow through the bowel. Hypnosis is induced by a standard technique, then over successive sessions, patients are asked to place a hand on their abdomen and feel warmth; then this warmth is related to reduction of spasm and the ability to alleviate pain and distension; patients are told that bowel habit will normalise as their control gradually improves; they visualise the gut as a meandering river and they can adjust the flow along it to a comfortable setting as one would open and close lock gates on a river. Patients may be given a self-hypnosis tape to use at home. Ego-strengthening and confidence-building comments can be made at the end of the sessions. Hypnotherapy can be administered to patients individually or as a group.

Dynamic Psychotherapy

In the NHS psychodynamic psychotherapy is practised by psychiatrists, psychologists, social workers and other professionals who have received additional specialised training in these techniques. Long-term dynamic psychotherapy aims to bring about extensive change in several aspects of a person's functioning. It is a prolonged treatment typically comprising of hourly meetings every week for periods of time up to three years. Short-term or focal dynamic psychotherapy is a modification of the approach in which attention is focused on only one area of the person's experience. This shortens the amount of time required and usually this form of treatment requires between 10 and 20 sessions (University of Newcastle 2005).

The selection of the appropriate psychological approach will depend on the individual person. They may express a preference for a particular intervention but in order to be able to make informed choices people with irritable bowel syndrome need to be made aware of the existence of these psychological treatments and the rationale for their use. It is important that they be made aware that using a psychological treatment does not mean that the syndrome is "all in the

mind." Addressing psychosocial factors is increasingly recognised as an important part of the management of irritable bowel syndrome.

9.1 Relaxation

SELECTION CRITERIA

The selection criteria described in the general methodology section were used, except that crossover studies were excluded as inappropriate due to the carry-over effect of the relaxation interventions.

The following comparisons were included:

- Relaxation versus waiting list control, or symptom monitoring only
- Relaxation versus usual medical care
- Relaxation versus another intervention.

SEARCH STRATEGY FOR IDENTIFICATION OF STUDIES

Searches were performed on the following core databases: MEDLINE, EMBASE, CINAHL, and *The Cochrane Library (*1966 to current day with guidance from the GDG). Additionally, the PSYCINFO database was searched for this review. The search strategies are listed in Appendix B.

Study Design

Three parallel group design randomised trials were included (Blanchard 1993; Forbes 2000; Keefer 2001). Further details are given in the included studies table. Forbes (2000) was conducted in the UK, the other two studies were carried out in the USA. Trials lasted between 6 and 12 weeks. One study was conducted among patients recruited from their personal physician or media publicity (Blanchard 1993); one recruited from gastroenterologists and local media (Keefer 2001), and one recruited from secondary care (Forbes 2000). The total number of patients in the studies was 16 in Blanchard (1993) and Keefer (2001). Forbes (2000) included 25 and 27 patients in the two treatment arms respectively.

Population

All the studies included only people with IBS. Blanchard (1993) and Forbes (2000) did not report the number of participants with bloating; Keefer (2001) reported that seven (of 16) had bloating. None of the studies reported whether the symptoms were post-infective. The mean age of participants was 51.5 years in Keefer (2001), with participants aged between 34 and 76 years; the people with IBS were aged 22 to 64 years in Blanchard (1993), and the median age in Forbes (2000) was 37 years, with a range from 19 to 71 years. All the studies included more women than men. The patients in the Blanchard (1993) study had had IBS for more a mean of

around 13 years, and in Keefer (2001) 15.8 years. The patients in Forbes (2000) had had IBS for more than six months.

In the Blanchard (1993) study, 56% of participants had an Axis I diagnosis; in Keefer (2001), 77% had an Axis I diagnosis, and participants were excluded if they had bipolar I or II, schizophrenia or other psychoses, or if they were actively suicidal. Co-morbidities were not stated in Forbes (2000).

Interventions

Blanchard (1993) used progressive muscle relaxation, on an individual basis with two sessions per week for the first two weeks and then once a week for six additional weeks; regular home practice was emphasised with an audiotape to guide this. Keefer (2001) used relaxation response meditation, in six weekly 30-minute treatment sessions.

The following comparisons were included:

- Relaxation versus symptom monitoring only: two studies (Blanchard 1993; Keefer 2001).
- Relaxation versus another intervention
    - Relaxation versus hypnotherapy (Forbes 2000).

Outcomes

The outcomes reported were:

1. Global symptoms:
    a) Global improvement in symptoms (number of patients) (Blanchard 1993; Forbes 2000; Keefer 2001)
    b) Global symptom score:
        - Global improvement of IBS symptoms (mean Composite Primary Symptom Reduction [CPSR] score; CPSR represents proportional reduction in score from baseline; scale range -1 to +1; Blanchard 1993; Keefer 2001).

2. Individual symptoms:
    a) Pain
        - Pain score (0 to 4 recorded over 28 days where 0=absent to 4=debilitating; i.e. maximum 112) reported by Blanchard (1993).

METHODOLOGICAL QUALITY

The quality assessment for included trials is shown in Appendix D.

An adequate method of randomisation was reported in one study (computer-generated random numbers; Forbes 2000); the other studies did not state the method. Allocation concealment was also not reported. The patients were not blinded (because of the type of intervention). No study described an *a-priori* power calculation. The three studies included in the review demonstrated baseline comparability of the groups, although the baseline scores for Blanchard (1993) were higher for the relaxation group on abdominal pain (mean score 31.2 (SD 25.1) compared with 24.4 (21.4) for the symptom monitoring group). This was not a statistically significant difference (Figure 1).

Figure 1: Baseline pain scores

All the participants were followed up in Forbes (2000). There were 20% or fewer drop-outs overall in one study (Keefer 2001): 3/16 dropped out (19%) (2/8 (25%) from the intervention group and 1/8 from the control group). 7/23 dropped out (30.4%) in Blanchard (1993), 6/14 (43%) from the intervention group and 1/9 (11%) from the control group; this study was regarded with caution, as this large and unequal drop-out could have introduced a bias.

RESULTS

A. Relaxation versus symptom monitoring only

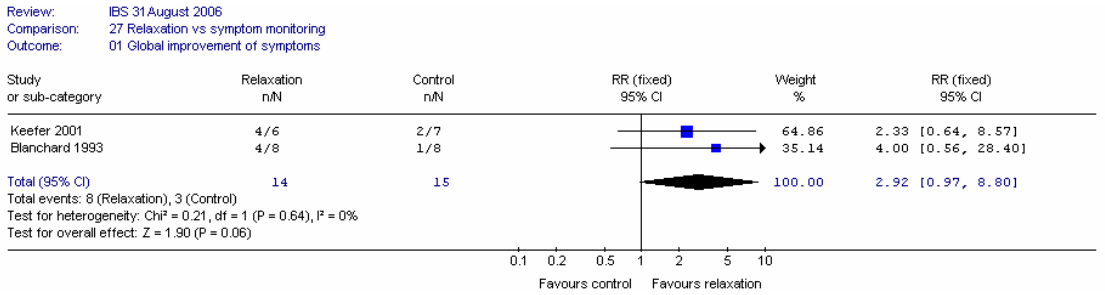
There were two studies that compared relaxation with symptom monitoring in people with IBS (Blanchard 1993; Keefer 2001).

1. Global symptoms

a) Number of patients with global improvement in symptoms

This outcome was reported by Blanchard (1993) and Keefer (2001).

Figure 2: Global improvement of symptoms

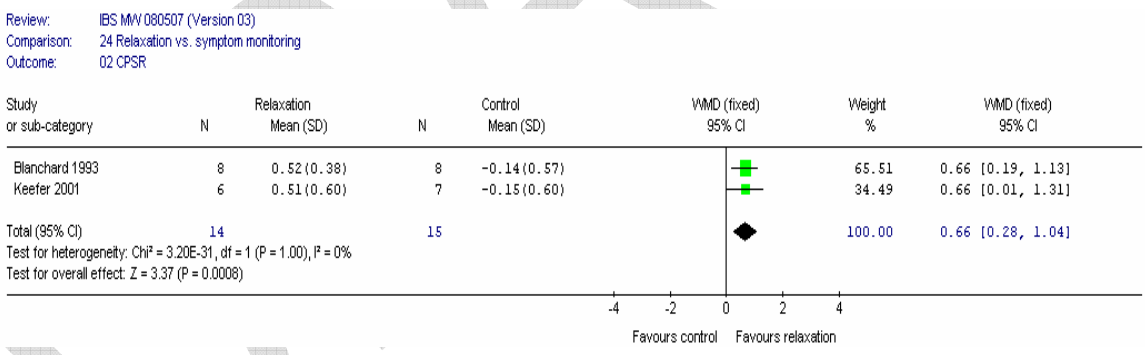


Meta-analysis of two studies in 29 patients showed a large effect, favouring relaxation, but the confidence interval was wide, such that the results are not significant. We noted that there was also attrition bias for the Blanchard (1993) study.

b) Global symptom score

The global improvement of IBS symptoms (mean Composite Primary Symptom Reduction [CPSR] score; CPSR represents proportional reduction in score from baseline; scale -1 to +1) was reported by Blanchard (1993) and Keefer (2001). There was a large statistically significant improvement in symptoms for the relaxation group, but the confidence interval was also wide. We noted that there was also attrition bias for the Blanchard (1993) study, and the other study, Keefer (2001), was small (13 patients).

Figure 3: Global symptom score (CPSR)

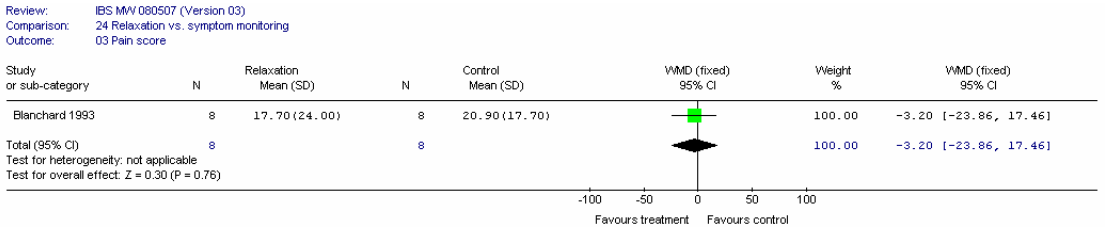


2. Individual symptoms

a) Pain

A pain score (0-4 recorded, over 28 days, where 0=absent and 4=debilitating, i.e. maximum 112) was reported by Blanchard (1993). There was no significant difference between interventions.

Figure 4: Pain score

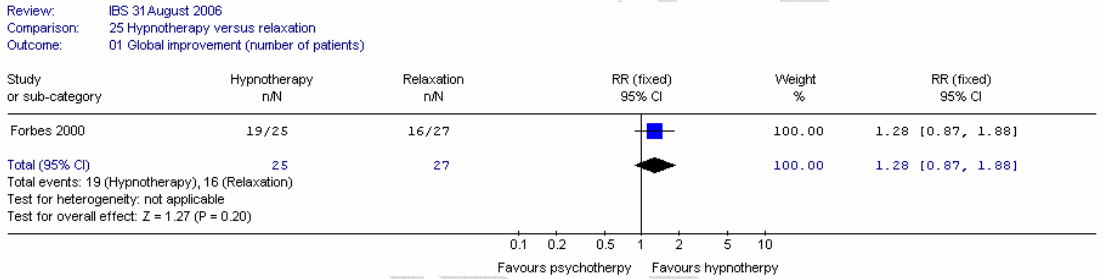


B. Hypnotherapy versus relaxation

1. Global symptoms

Global improvement in symptoms (number of patients) was reported by Forbes (2000) at 12 weeks. There was no significant difference between interventions.

Figure 5:



EVIDENCE STATEMENTS

1. There is insufficient evidence to show if there is a difference between relaxation and symptom monitoring, in the number of people with global improvement of symptoms, in people with long term IBS, at least half of whom had psychiatric co-morbidities.

2. There is a limited amount of weak evidence to show a large, significant improvement in global symptom score for people receiving relaxation, compared with symptom monitoring, in people with long term IBS, at least half of whom had psychiatric co-morbidities.

3. There is limited evidence to show no significant difference in pain score between relaxation and symptom monitoring, in people with long term IBS, at least half of whom had psychiatric co-morbidities.

4. There is a fair evidence to show no significant difference between relaxation and hypnotherapy in the number of people with global improvement of symptoms.

Evidence to recommendation

The GDG decided there is insufficient evidence to make a recommendation. This is discussed in the evidence to recommendation statement for relaxation and biofeedback (Section 9.3).

9.2 Biofeedback

SELECTION CRITERIA

The selection criteria described in the general methodology section were used, but some were specific to this review and are reported below.

Types of intervention

Both multiple and single component therapies were eligible for inclusion.

Search strategy for identification of studies

Searches were performed on the following core databases: MEDLINE, EMBASE, CINAHL and *The Cochrane Library* (1966 to current day with guidance from the GDG). Additional databases were not searched for this review. Biofeedback, aloe vera and reflexology were combined into one search. The search strategies are listed in Appendix B.

The search strategy identified 560 studies. The titles and abstracts of these studies were assessed. Fifty-four studies were identified as being potentially relevant to the reviews and the papers for these were retrieved in full. Four studies met the inclusion criteria for this review, two of which were reports of the same trial (Blanchard 1992; Meissner 1997). The reference lists of these studies were inspected for further potential papers, but none were identified. The 17 excluded studies, with reasons for exclusion, are listed in the Appendix E.

DESCRIPTION OF STUDIES

Study Design

There were four randomised trials in this review, reported in three papers (Blanchard 1992; Leahy 1997; Neff 1987); two trials were from the same paper (Blanchard 1992), and one was reported only as an abstract (Leahy 1997). All the studies but one took place in the US. Leahy (1997) was carried out in the UK.

Population

All patients had a diagnosis of IBS and were treated in the secondary care setting in which the study took place. There was a higher proportion of women. The age range was 21 to 76 years.

Patients in the Leahy study were said to be resistant to conventional medical therapy. The other studies did not report whether the IBS was refractory.

Interventions

One study (Leahy 1997) evaluated a single intervention, using a computer-aided gut-directed biofeedback apparatus to teach relaxation for IBS patients when troubled by symptoms. Patients

were randomised to biofeedback or counselling. Biofeedback patients received four half-hour sessions.

Three trials (Blanchard 1992 x 2; Neff 1987) evaluated multi-component therapy, which used a combination of educational information, progressive relaxation therapy, thermal biofeedback treatment and training in stress coping strategies. This was offered on an individual basis. The combination treatment consisted of twelve one-hour sessions spread over eight weeks.

In Blanchard (1992a), the same therapist delivered the treatments, but in Blanchard (1992b) eight different therapists took part.

In the two Blanchard 1992 trials, the patients were matched into triads, based on gender, age and predominant GI symptoms, and randomly assigned to multi-component biofeedback, attention placebo or symptom monitoring. Neff (1987) randomly assigned patients to multi-component biofeedback and symptom monitoring.

Comparisons

All the comparative studies used symptom monitoring or attention placebo controls. The latter was used in Blanchard (1992). A combination of two procedures was used: 'pseudo meditation' (in which patients were asked not to relax) and biofeedback using suppression of alpha-waves in the EEG (this is not associated with the relaxed state).

In the symptom monitoring control group, patients simply monitored their symptoms for the duration of the intervention. The symptom monitoring (control) group were offered treatment at a later stage.

The following comparisons were reported:

- Single component biofeedback versus counselling then both groups had biofeedback (Leahy 1997)
- Multi-component biofeedback versus symptom monitoring (Blanchard 1992 x2; Neff 1987)
- Multi-component biofeedback versus attention control (Blanchard 1992 x2).

METHODOLOGICAL QUALITY OF INCLUDED STUDIES

None of the RCTs reported details of the method of randomisation or allocation concealment. Patients were matched on age, gender and primary GI symptoms before randomisation in the Blanchard (1992) study. Patients in the Neff (1987) study were similar at baseline for age, duration of IBS, and years of education, but there were differences in the number of IBS-D patients: 5/10 in the biofeedback group and 2/9 in the control group.

In Blanchard (1992a) all patients completed the trial, 1/9 dropped out from the control group of the Neff study, and in Blanchard (1992b), 7/31 (22%), 8/30 (27%) and 10/31 (32%) dropped out of the study for multi-component, attention placebo and symptom monitoring respectively. Therefore the second Blanchard trial is at higher risk of bias and will be considered in sensitivity analyses as appropriate.

RESULTS

A. Single component biofeedback

In an abstract, Leahy (1997) reported that counselling had no effect on symptom score, but did not give separate results for the group randomised to biofeedback.

B. Multi-component biofeedback

Three randomised trials (Blanchard 1992a and b; and Neff 1987) in 30 and 115 patients, and 19 patients respectively gave a multi-component therapy as the biofeedback intervention.

1. Global symptoms

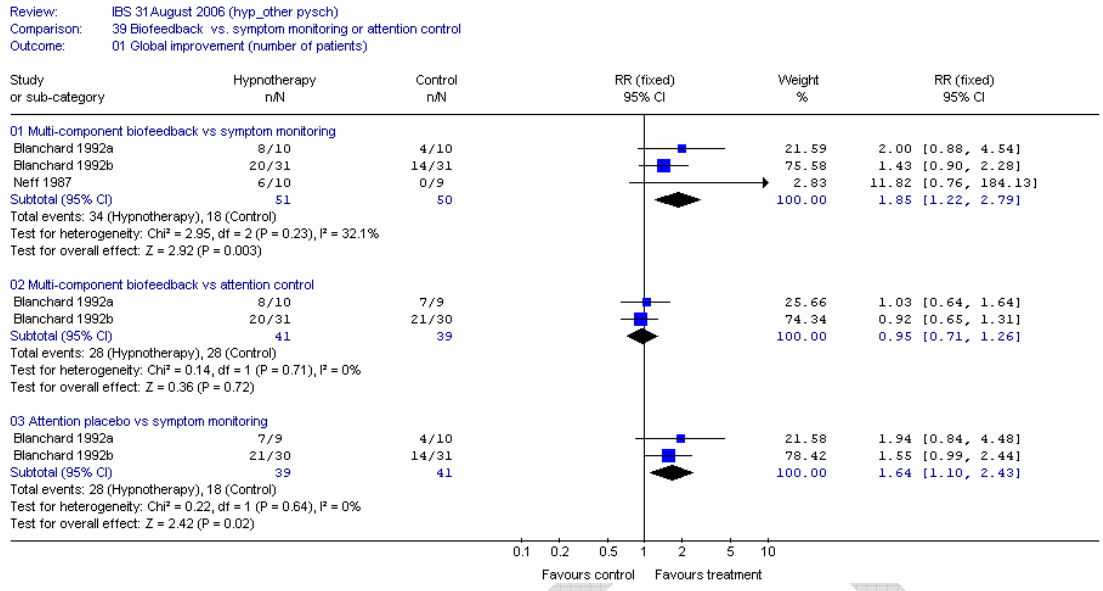
All studies reported a composite primary symptom reduction score (CPSR): firstly, each patient recorded in a daily diary a symptom score, comprising abdominal pain, tenderness, diarrhoea, constipation, flatulence, belching and nausea. This was used to calculate a reduction score using the formula:

(baseline symptom score – end of treatment score) / baseline symptom score *100.

a) Global improvement in symptoms (number of patients)

The RCTs reported the number of patients with an improvement in global symptoms; the Blanchard (1992) trials reported rater-assessments, but the patient assessment results were selected for the Neff (1987) study. Meta-analysis of three trials in 101 patients showed a statistically significant improvement in symptoms for biofeedback compared with symptom monitoring; RR 1.85 (95%CI 1.22, 2.79), with insignificant heterogeneity (I^2=32%, p=0.23). This corresponded to a number needed to treat of 4 (95%CI 3, 8), for a control group rate of 0 to 45%. However, there was no significant difference between biofeedback and attention placebo. The comparison of attention placebo versus symptom monitoring was also significant. We noted that the Blanchard (1992b) study had about 30% dropouts. A sensitivity analysis without this study for the comparison of biofeedback with symptom monitoring resulted in more heterogeneity and changed the relative risk to 3.14 (95%CI 1.35, 7.31).

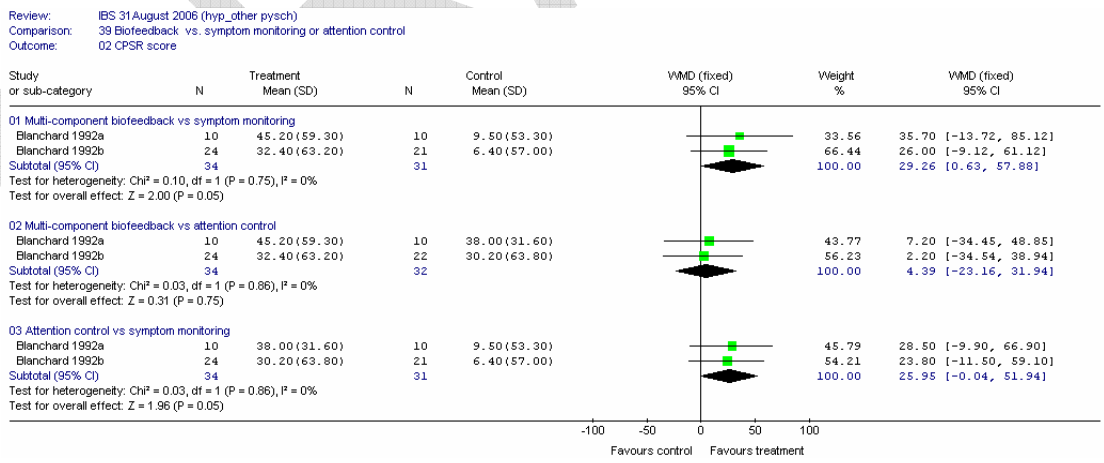
Figure 1



b) Global improvement of symptoms

The two trials within Blanchard (1992) reported the scores on the CPSR. There was a statistically significant difference, favouring multi-component feedback compared with symptom monitoring, but not in comparison with attention control, although the confidence intervals were fairly wide. We noted that around 30% of the patients in Blanchard (1992b) had missing data and we have assumed the numbers of patients in the analysis are the values for completers only.

Figure 2



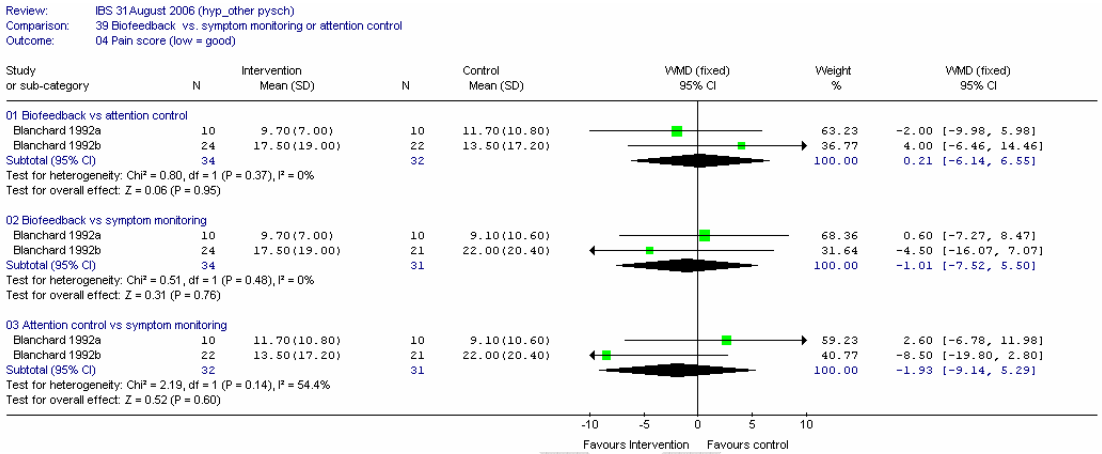
2. Individual symptoms

Neff (1987) reported means for these outcomes, but no standard deviations or p-values were given, so the rest of this review uses the results from Blanchard (1992).

a) Pain

The study reported daily abdominal pain and discomfort symptom scores on a scale of 0 to 4, recorded as weekly scores (i.e. maximum of 28). The confidence intervals were too wide to draw conclusions.

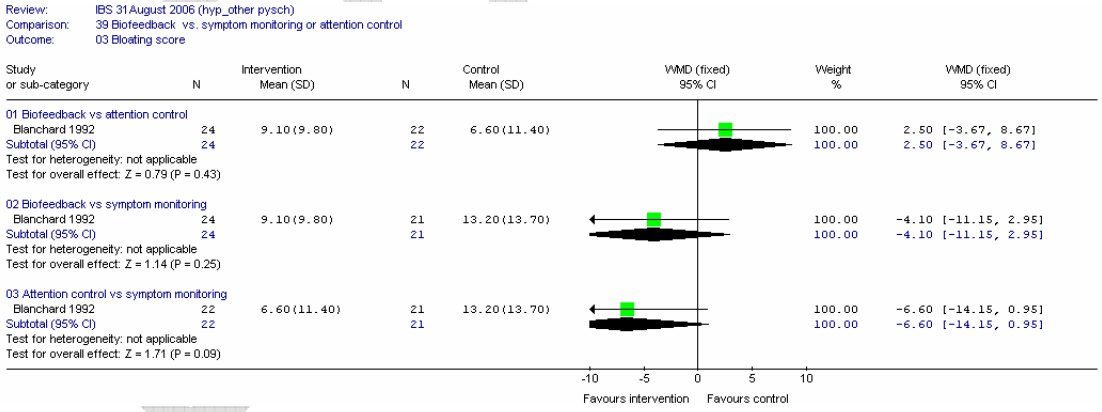
Figure 3



b) Bloating

The second study reported bloating scores. Generally the confidence intervals were wide, but the attention placebo gave significantly less bloating than the symptom monitoring.

Figure 4

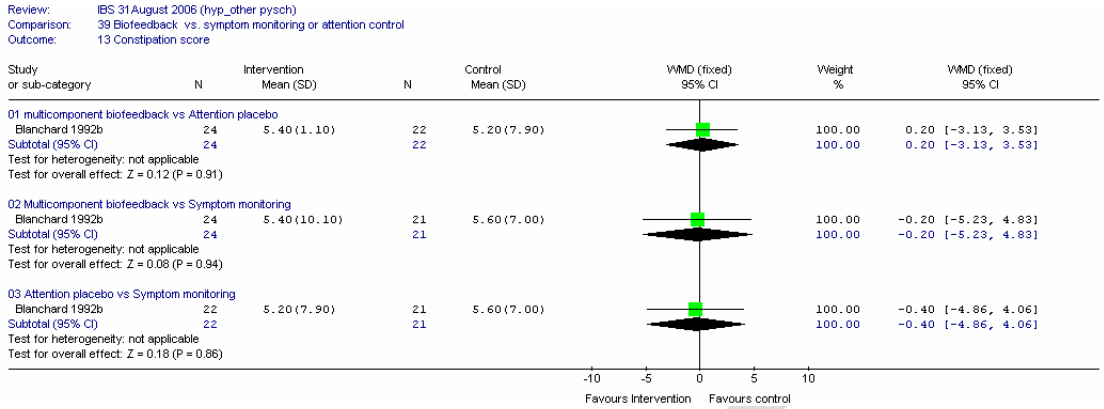


c) Bowel Habit

i. Constipation

The second study reported constipation scores. The scale used was 0 to 4 and the weekly average was used (i.e. maximum of 28). Generally the confidence intervals were too wide to draw conclusions.

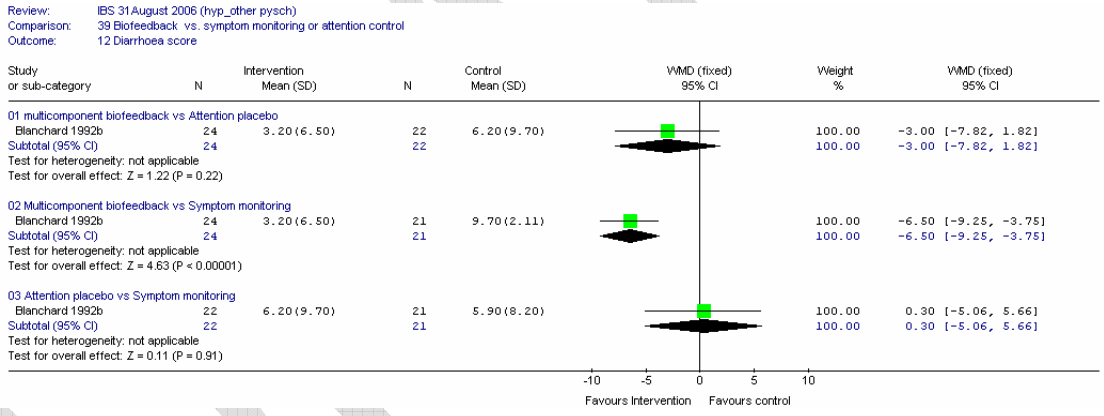
Figure 5



ii. Diarrhoea

The second study reported diarrhoea scores. The scale used was 0 to 4 and the weekly average was used (i.e. maximum of 28). Generally the confidence intervals were wide, but the multi-component biofeedback gave significantly lower diarrhoea score than the symptom monitoring.

Figure 6



GDG DISCUSSION

The GDG noted that multi-component biofeedback (consisting of education, progressive relaxation therapy, thermal biofeedback treatment and training in stress coping strategies) is effective for people with IBS in comparison with symptom monitoring. However, the attention placebo of pseudo meditation and alpha wave EEG biofeedback had similar efficacy for improving global symptoms. The GDG suggested that actively involving people in the management of their chronic condition may have a beneficial effect. They also noted that spending time with patients and taking them seriously is usually valuable, and that behavioural treatments are difficult to unravel.

EVIDENCE STATEMENTS

1. There is limited weak evidence to show a statistically significant improvement in global symptoms for biofeedback compared with symptom monitoring, although the confidence interval was fairly wide. There was no difference between biofeedback and attention placebo.

2. There was insufficient evidence to determine the effects of biofeedback on pain, bloating and constipation.

3. There is limited weak evidence to show a statistically significant improvement for reduction in diarrhoea for biofeedback compared with symptom monitoring, although the confidence interval was fairly wide. There was no significant difference between biofeedback and attention placebo and between symptom monitoring and attention placebo but there was much uncertainty due to wide confidence intervals.

EVIDENCE TO RECOMMENDATION

The GDG decided there is insufficient evidence to make a recommendation. This is discussed in the evidence to recommendation statement for relaxation and biofeedback (Section 9.3).

9.3 Evidence to recommendation: relaxation and biofeedback

The GDG took into consideration the limited clinical effectiveness evidence for relaxation and biofeedback. They noted that the relaxation review showed significant improvement in global symptoms for relaxation compared with symptom monitoring, but the trials were small and one of them had a large attrition bias. The biofeedback review compared biofeedback with symptom monitoring and with attention control: there was a significant effect on global symptoms in comparison with the former, but not with the latter and this led the GDG to conclude that attention may be an important factor for biofeedback.

The GDG considered the clinical evidence to be too limited, either to carry out cost effectiveness analyses or to make recommendations for practice. However, they considered these therapies to be worth following up, particularly in view of recent developments in computer-aided biofeedback techniques and positive patient experience within the GDG indicating a preference towards relaxation. Therefore, the GDG proposed a recommendation for research, involving a comparison of computer-aided biofeedback, relaxation and attention control. The research recommendation is given in chapter 12.

9.4 Psychotherapy

SELECTION CRITERIA

The selection criteria described in the general methodology section were used, except that crossover studies were excluded as inappropriate due to the carry-over effect of the interventions.

The following comparisons were to be included:

- Psychotherapy versus waiting list control/symptom monitoring
- Psychotherapy versus usual medical care
- Psychotherapy plus another intervention versus the other intervention alone
- Psychotherapy versus another intervention.

SEARCH STRATEGY FOR IDENTIFICATION OF STUDIES

Searches were performed on the following core databases: MEDLINE, EMBASE, CINAHL, and *The Cochrane Library* (1966 to current day with guidance from the GDG). Additionally, the PSYCINFO database was searched for this review.

The search strategies are the same as those for hypnotherapy, as these were searched together. Details of the search strategies are lisetd in Appendix B. The titles and abstracts of the studies identified by the searches were assessed. Fifteen were identified to be potentially relevant to the reviews and these papers were retrieved in full. The reference lists of the retrieved studies were inspected for further potential papers, but none were identified. Twelve studies were excluded and are listed in Appendix E, along with reasons for exclusion.

CHARACTERISTICS OF INCLUDED STUDIES

Study Design

Three randomised trials were included (Creed 2003; Guthrie 1991; Svedlund 1983), all in secondary care. Two of these were in the UK, the other in Sweden.

Population

The studies included patients between the ages of 17 and 75 years, although each had slightly different inclusion criteria and mean age of participants (Svedlund 1983: mean age was around 34 years, range 17 to 59 years; Guthrie 1991: mean around 48 years, range 20 to 75 years; Creed 2003: mean around 40 years, range 18 to 65 years). All the studies included more women than men.

IBS was stated, or implied, to be refractory in all of the studies. The patients in Guthrie (1991) had had IBS for more than 1 year (median around 4 years, range 1 to 20 years); their symptoms had not improved with medical treatment (bulking agents and/or antispasmodics) over six

months. The patients in Creed (2003) had had IBS for more than six months; they had failed to respond to usual medical treatment. The patients in Svedlund (1983) had had IBS for at least a year, range 1 to 40 years, but their response to previous treatment was not stated.

Only one study gave details about IBS characteristics: Creed (2003) reported that the patients had severe abdominal pain (over 60 on a 100 mm visual analogue scale [VAS]); 29% of the patients had diarrhoea-predominant IBS; 23% were constipation-predominant; and 48% had 'general' IBS.

In two of the studies, around half the participants currently had a psychiatric diagnosis. Of the patients in Guthrie (1991), 30% had major depression and a further 18% had anxiety states; in Creed (2003), 47% had a psychiatric diagnosis (mainly anxiety or depression). In Svedlund (1983), 29% had previously had depression and a further 41% had had other mental disorders. It was unclear if this was their current diagnosis.

Svedlund (1983) stated that the patients were less representative of the general IBS population because they had to be prepared to participate in an extended socio-psychological investigation. Creed (2003) reported that the patients all had severe symptoms, but within this group were broadly representative, and Guthrie (1991) recruited patients from a tertiary referral centre, where there is likely to be a higher proportion with abuse and associated psychological problems.

None of the studies reported the number of participants with bloating or whether the symptoms were post-infective. Creed (2003) described IBS as severe. Guthrie (1991) reported that gastroenterologists assessment of severity was median 5 (range 2 to 8) on scale 0 to 9. Svedlund (1983) did not report severity.

Interventions

All the studies examined the effect of psychotherapy on IBS symptoms. Two studies (Svedlund 1983; Guthrie 1991) compared psychotherapy plus medical therapy versus medical therapy alone; the third (Creed 2003) compared psychotherapy versus medical therapy and also had a second comparison with the SSRI antidepressant, paroxetine.

In Svedlund (1983), all patients received the same medical treatment but those in one group also received dynamically oriented individual psychotherapy in ten hour-long sessions spread over three months. In Guthrie (1991), patients received the same medical treatment but patients in one group also received dynamic psychotherapy in seven interviews over three months, plus a relaxation tape to use at home. At the end of the 3 month period, patients in the control group were given psychotherapy. Creed (2003) randomised patients into three groups: psychodynamic interpersonal therapy (8 sessions over 3 months); 20mg daily of the SSRI antidepressant

paroxetine for 3 months; or 'usual care', in which 'patients continued to be seen either by their gastroenterologist and/or general practitioner, using whatever management was deemed appropriate' (Creed 2003). Other medical management was stopped during the trial period in the paroxetine and psychotherapy groups. In the follow-up period, patients were allowed other treatments, principally antidepressants.

Comparisons

The following comparisons were included:

- Psychotherapy plus medical care versus medical care only (Svedlund 1983; Guthrie 1991)
- Psychotherapy versus usual care (Creed 2003)
- Psychotherapy versus another intervention (antidepressant: SSRI – paroxetine) (Creed 2003).

METHODOLOGICAL QUALITY

The quality assessment for included trials is shown in the Appendix D.

The method of randomisation was adequate in Creed (2003) (computer generated random numbers) but not stated in either Svedlund (1983) or Guthrie (1991). Allocation concealment was adequate in Creed (2003) (randomisation list held by study administrator) but not stated in either Svedlund (1983) or Guthrie (1991). The patients were not blinded in any study (because of the type of intervention). The GDG did not consider blinding to be important for this review. Creed (2003) reported an *a priori* power calculation but the other two studies did not.

Svedlund (1983) and Creed (2003) demonstrated baseline comparability between the groups. The groups were mainly comparable in Guthrie (1991), except there was a higher proportion of males in the control group than the intervention group (17/49 vs. 8/53, $p<0.05$). Svedlund (1983) reported significant differences in the assessors rating of pain (however, this was not significantly different for the self-rating, which we used).

There were fewer than 20% drop-outs in all the studies. Svedlund (1983) reported 2 out of 101 participants dropped out. Guthrie (1991) reported that 7 of 53 participants dropped out of the treatment group plus 6 of 49 controls; data were available at 3 months for all but 2 participants (2% drop out), despite the withdrawal from treatment. In Creed (2003) there were missing data: 16% (14/86) in the paroxetine group; 14% (12/85) psychotherapy; 0% in the routine care group did not start the trial. A further 29/86 (34%) in the paroxetine group and 14/85 (16%) in the psychotherapy arm discontinued treatment, but these patients still appear to have been followed. Overall, loss to follow-up at three months was 12/86 (14%) for paroxetine, 11/85 (13%) psychotherapy and 7/86 (8%) usual care arm. At 15 months the authors contacted more of the patients. The authors reported that there were no significant differences at baseline between those who did and did not complete the treatments. For the 3 month pain score and SF36

outcome measures respectively, the patients included in the analysis were 74 and 59 (69%) paroxetine; 74 and 58 (68%) psychotherapy and 79 and 63 (73%) usual care, but some of these patients had discontinued treatment. We decided to include the results from this study, with some reservations, especially about the paroxetine arm and about the SF36 results. The study also recorded the number of patients with an improvement in global symptoms, based on the results from 74, 74 and 80 patients respectively. The GDG decided that this outcome was more representative because patients that dropped out due to side effects would not have rated their global symptoms as improved. The follow-up period allowed the patients to have paroxetine in all arms: 42% in paroxetine group; 19% in psychotherapy, and; 22% in the usual care group, i.e. the follow-up for the comparison of psychotherapy and paroxetine should be considered to be partly confounded. In addition, 10% of the usual care group were given psychological treatment. Therefore we did not report the results for the follow-up period for the comparison psychotherapy versus paroxetine, and the comparison psychotherapy versus usual care was also considered with caution.

Overall, we considered that none of the studies were at high risk of bias. Creed (2003) was treated with caution for the outcomes pain and SF36 because of missing data and non compliance. We also noted there was some confounding in the follow-up period.

RESULTS

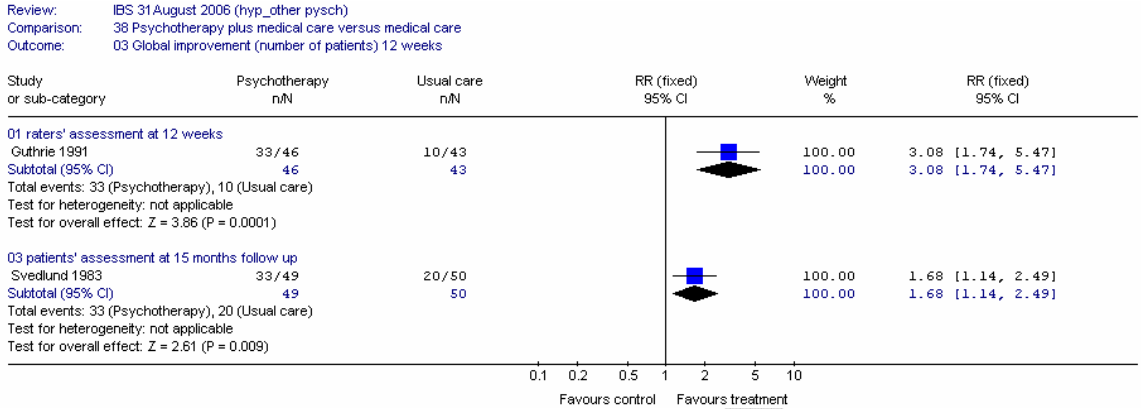
A. Psychotherapy plus medical therapy versus medical therapy only

1. Global symptoms

a) Global improvement in symptoms (number of patients)

Two studies reported the numbers of patients with an improvement in global symptoms: Guthrie (1991) gave the numbers as assessed by gastroenterologists at the end of treatment (12 weeks), and; Svedlund (1983) reported the patients' self-assessment at 15 months follow-up (treatment lasted three months). There are significantly more patients with global improvement at both times. The GDG preferred to use the patient assessment in all reviews. At 15 months follow-up, the number needed to treat was 4 (95% 3, 13), for a control group rate of 40%. [The rater assessed result at 12 weeks corresponded to an NNT of 3 (95%CI 2, 4) for a control group rate of 23%].

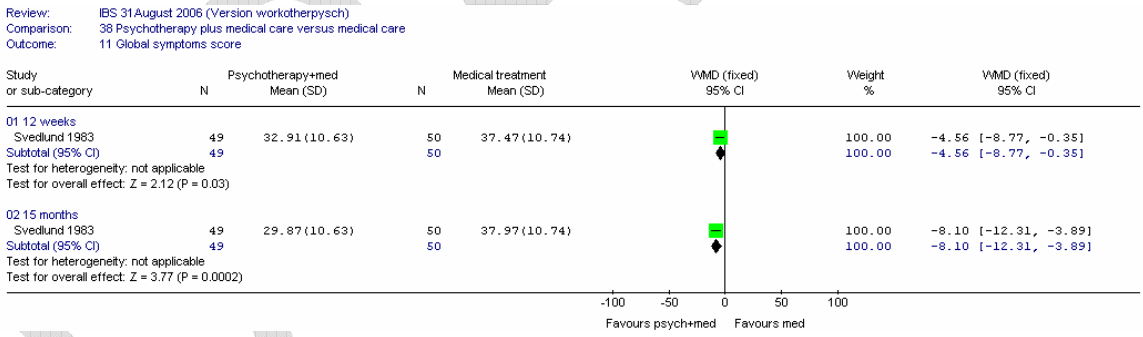
Figure 1:



b) Global symptom score

Svedlund (1983) reported a patient-rated global symptom score at 12 weeks and 15 months follow-up; this score rated somatic symptoms (19 items; each rated on a 7-point scale 0=absent to high=extremely; i.e. lower is better. It was unclear what the maximum of the scale was but it is assumed to be 6. This gave an overall maximum of 114). There was a small statistically significant difference at 12 weeks, favouring psychotherapy plus medical treatment, which increased to -8.10 (95%CI -12.31, -3.89) at 15 months follow-up. The control group score was 38.0.

Figure 2:

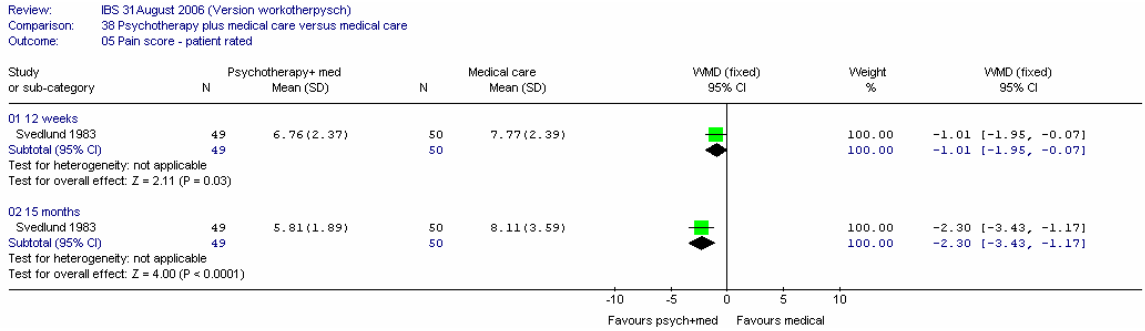


2. Individual symptoms

a) Abdominal pain

Svedlund (1983) reported a patient-rated pain score at 12 weeks and 15 months follow-up. It was unclear what the maximum of the scale was but the baseline was about 10 units. There was a small statistically significant difference at 12 weeks, favouring psychotherapy plus medical treatment, which increased to -2.30 (95%CI -3.43, -1.17) at 15 months follow-up. The control group score was 8.11.

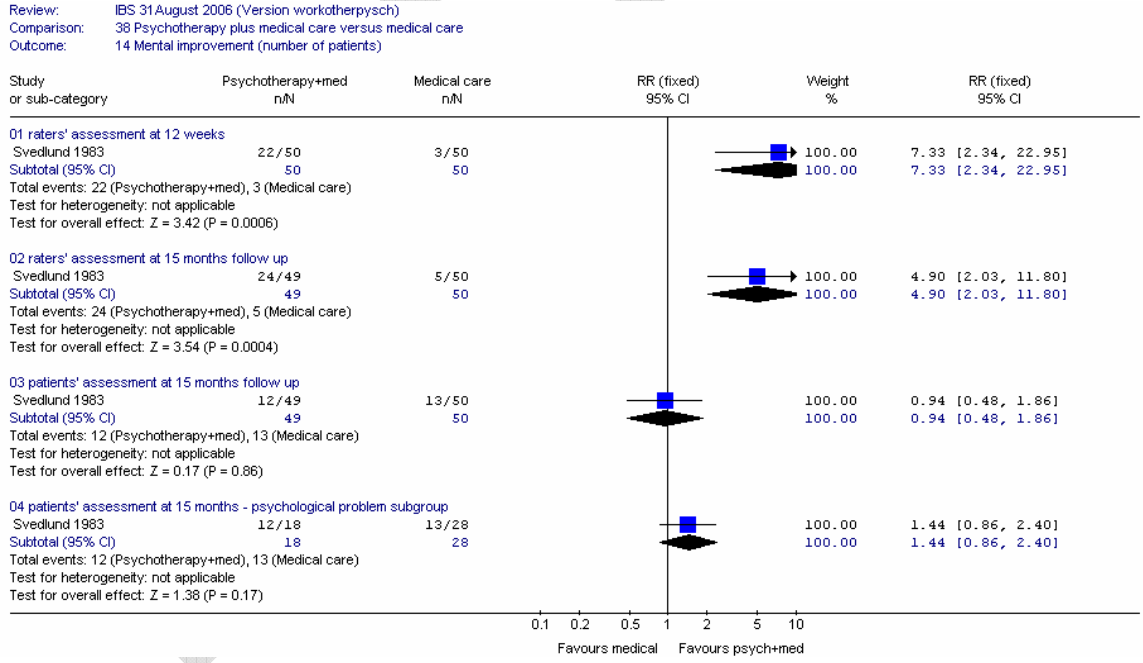
Figure 3:



3. Mental health outcomes (overall mental health; depression; anxiety)

Svedlund (1983) reported the number of patients with improved mental symptoms, as assessed by raters at 12 weeks and by raters and patients at 15-month follow-up. There were significantly more patients improving according to the raters, but the patients' rating showed no significant changes. The authors reported that several patients denied having mental complaints at baseline.

Figure 4:



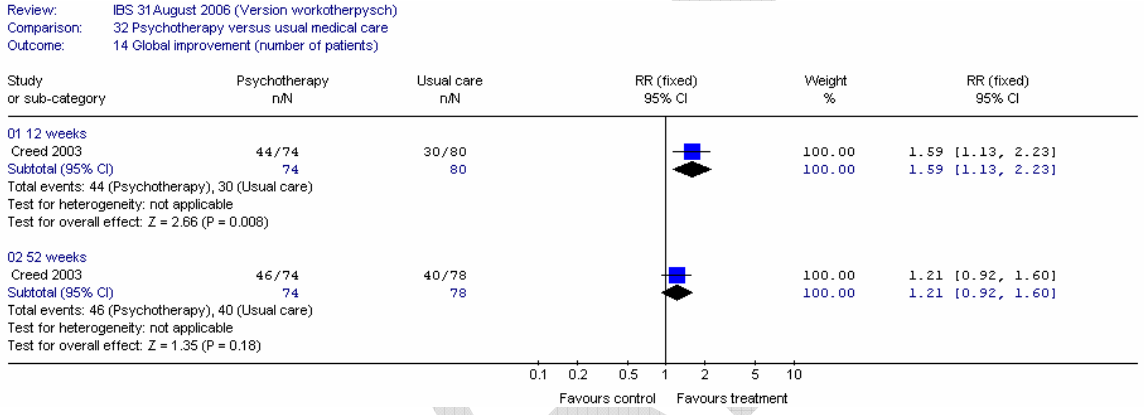
Guthrie (1991) reported a significant improvement, favouring the psychotherapy group, in the median scores on the Hamilton depression scale ($p<0.001$) and the Clinical anxiety scale ($p<0.01$), as assessed by the psychiatrist.

B. Psychotherapy versus usual medical therapy

1. Global symptoms

Global improvement in symptoms (number of patients) was reported by Creed (2003) at 12 and 52 weeks. There were significantly more patients with global improvement in the psychotherapy group compared to usual care, at 12 weeks: RR 1.59 (95%CI 1.13, 2.23). This corresponded to an NNT of 5 (95%CI 3, 15), for a control group rate of 38%. However, there was no significant difference at 12 months follow-up. We noted, however, that 10% of the usual therapy patients were given psychotherapy in the follow-up period, which may have reduced the relative effectiveness of the psychotherapy arm.

Figure 5:

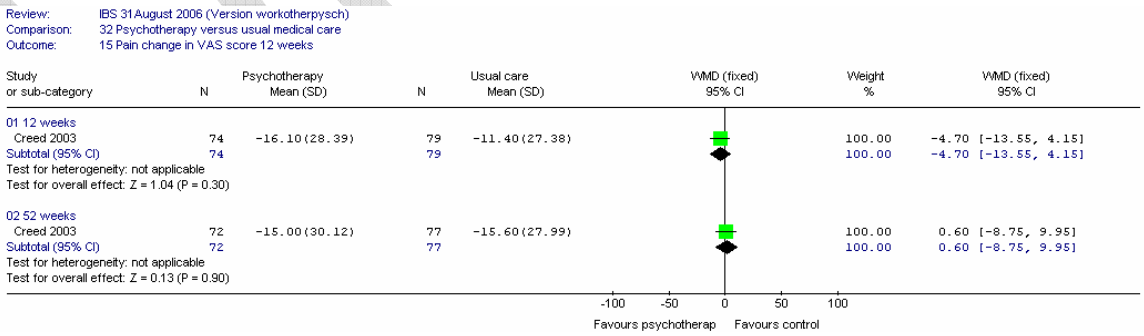


2. Individual symptoms

a) Pain

Pain (change in VAS score on a scale of 100 mm) was reported by Creed (2003) at 12 and 52 weeks. There was no significant difference between interventions at either time.

Figure 6:



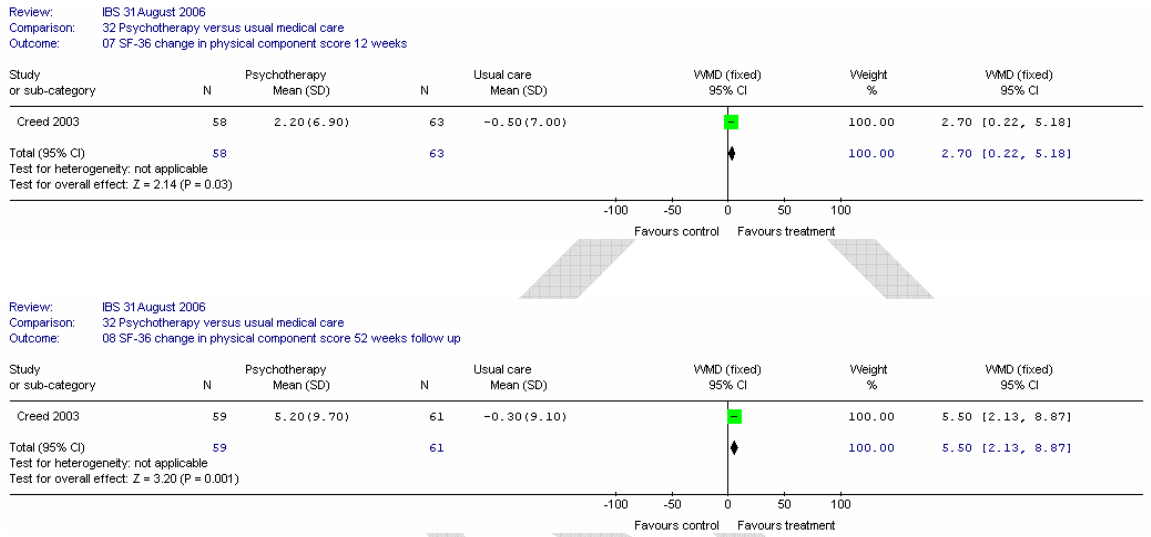
3. Quality of life

Creed (2003) measured the health-related quality of life using SF-36, recording both the physical and mental components. We noted that there was about 30% of missing data for these outcomes at three months follow-up.

a) Physical component

The physical component change score was reported at 12 weeks and at 52 weeks. On this 0 to 100 scale, an increase is a benefit and a negative change score is a worsening. There was a small statistically significant improvement favouring psychotherapy at 12 weeks, which increased slightly at 52 weeks to mean difference 5.50 (95%CI 2.13, 8.87) for a control group value of 38.1.

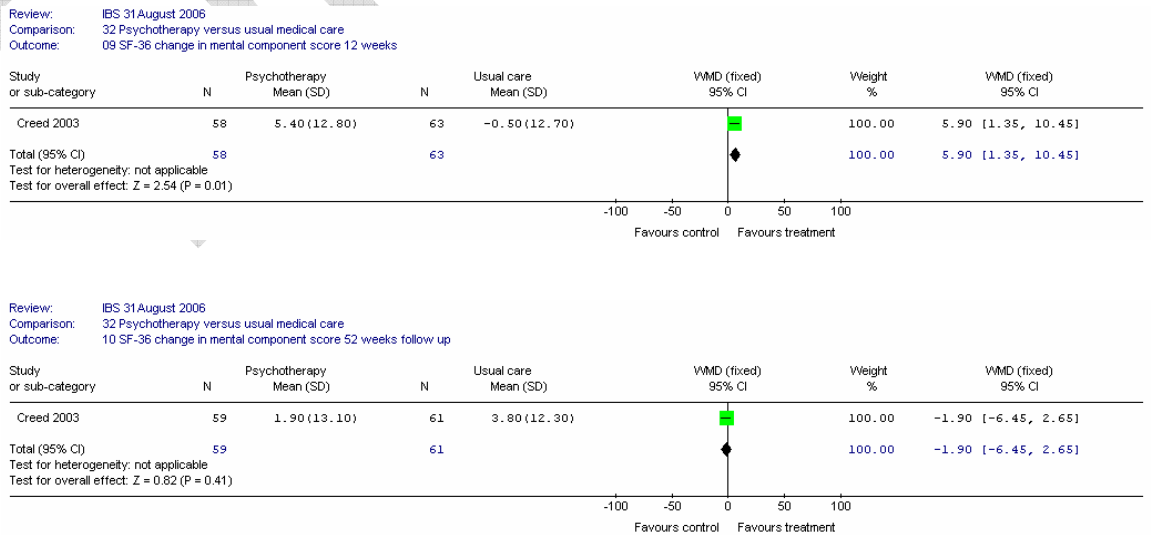
Figure 7:



b) Mental component

The SF-36 mental component change score was reported by Creed (2003) at 12 weeks and at 52 weeks. There was a small statistically significant difference at 12 weeks, but no significant difference at one year.

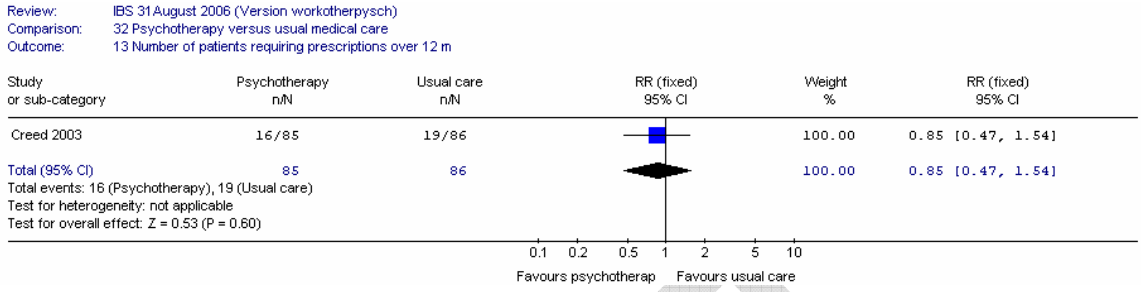
Figure 8:



4. Number of patients receiving prescriptions for antidepressants in follow up year

Creed (2003) compared the number of patients receiving prescriptions for antidepressants in follow-up year. There was no significant difference between interventions.

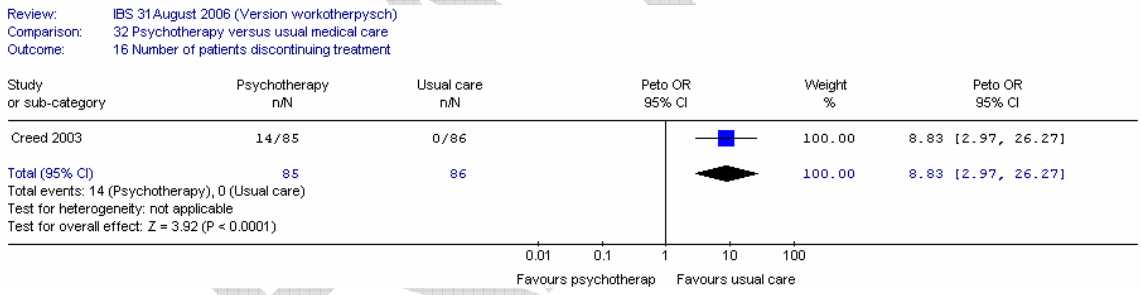
Figure 9:



5. Number of patients discontinuing treatment

Creed (2003) also reported the number of patients in each group who discontinued treatment. There was a large, statistically significant difference between interventions, favouring usual care.

Figure 10:



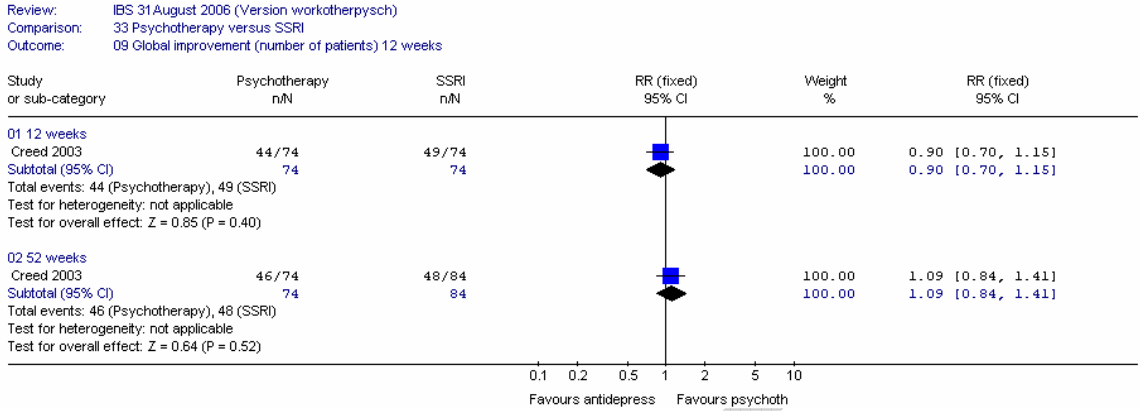
C. Psychotherapy versus antidepressant medication (SSRI - paroxetine)

1. Global symptoms

a) Global improvement in symptoms (number of patients)

The numbers of patients improved were reported by Creed (2003) at 12 weeks and at 52 weeks. There was no significant difference at either time, although we noted that the 52 week results are likely to be confounded by the use of antidepressants in both arms.

Figure 11:



2. Individual symptoms

a) Pain

Pain (change in VAS score) was reported by Creed (2003) at 12 weeks. There was no significant difference between interventions.

Figure 12:

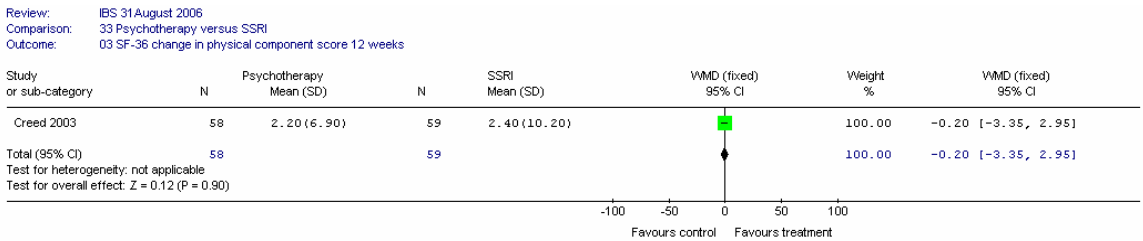
3. Quality of life

Creed (2003) measured the health-related quality of life using SF-36, recording both the physical and mental components. We noted that there was about 30% of missing data for these outcomes at three months follow-up.

a) Physical component

The physical component change score was reported at 12 weeks. There was no significant difference between interventions.

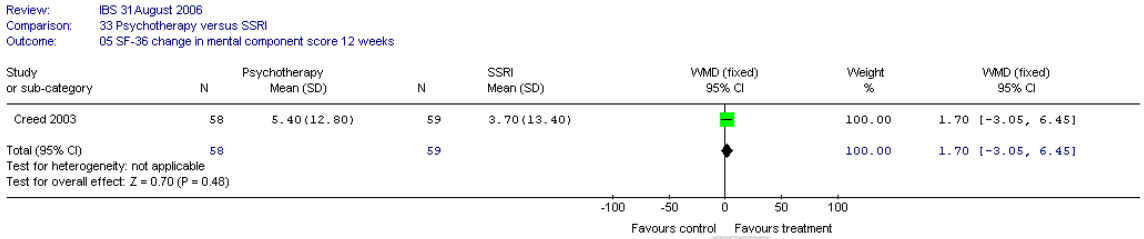
Figure 13:



b) Mental health outcomes

The SF-36 mental component change score was reported by Creed (2003) at 12 weeks. There was no significant difference between interventions.

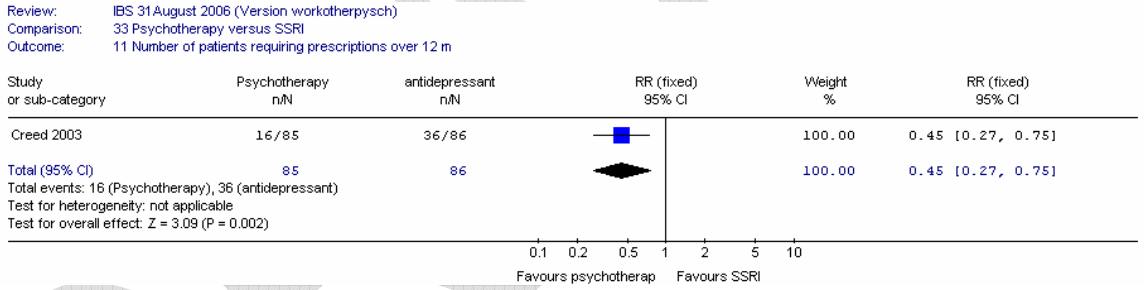
Figure 14:



4. Number of patients receiving prescriptions for antidepressants in follow up year

Creed (2003) compared the number of patients receiving prescriptions for antidepressants in follow-up year. There was a statistically significant difference between interventions, favouring psychotherapy: RR 0.45 (95%CI 0.27, 0.75). This corresponded to a number needed to harm of 5 (95%CI 3, 10), for an antidepressant group rate of 42%.

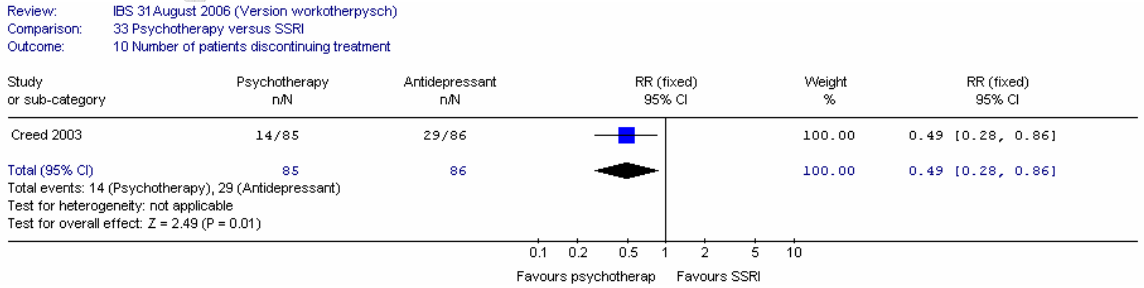
Figure 15:



5. Number of patients discontinuing treatment

Creed (2003) also reported the number of patients in each group who discontinued treatment. There was a statistically significant difference between interventions, favouring psychotherapy. This gave an NNH of 6 (95%CI 4, 20), for an antidepressant group rate of 34%.

Figure 16:



ECONOMIC LITERATURE FOR PSYCHOTHERAPY

One relevant health economic analysis was identified on the cost-effectiveness of psychotherapy in the treatment of IBS. Creed (2003) was a trial based economic evaluations conducted in the UK which recruited patients from secondary and tertiary care with severe IBS. This study aimed to assess whether psychotherapy would be superior to usual care in reducing abdominal pain and improving quality of life and whether these improvements could be achieved at no additional cost due to treatment costs being offset by reduced health care costs. It also included a comparison of SSRIs with usual care. The patient population considered were secondary and tertiary care patients with severe IBS who had not responded to usual treatment. The included patients had a mean duration of IBS of 8 years. This study was considered to be relevant to patients with refractory IBS only. The psychotherapy intervention consisted of 8 sessions over 3 months delivered by trained therapists. After three months, patients in the psychotherapy arm returned to their GP and received usual care for one year during which time they were followed-up. In the comparator arm patients received usual care from either their gastroenterologist or their GP for the three month treatment period and the following year of follow-up. The primary outcome was abdominal pain measured on a VAS of severity with secondary outcomes considering days with pain, overall change in symptoms and HRQofL measured by the SF-36. Direct health care costs per week were estimated for the intervention and follow-up periods. This included hospital costs (inpatient days, outpatient, day-patient and A&E attendances), primary care costs (GP surgery and home visits, practice nurse and practice based counsellor visits), domiciliary care services (NHS and PSS) and day centres, use of alternative therapies and prescribed medications. These were adjusted to allow for any differences before baseline and bias corrected 95% confidence intervals were presented. The cost of providing psychotherapy was not presented separately from the other direct health care costs.

There number of patients with an improvement in global symptoms was significantly higher for psychotherapy at the end of treatment compared to usual care. The clinical outcomes from this trial have been summarised in detail in the clinical effectiveness review. Direct health care costs were significantly increased for psychotherapy compared to usual care during the intervention period and were significantly decreased during the following year. There was no significant increase in direct health care costs over the 15 month trial period.

This study was a partial economic evaluation as it did not assess the incremental cost of any benefit achieved in the form of a cost-effectiveness ratio. The evidence provided by this study was considered to be indirect as the patients were recruited from secondary and tertiary care and costs may differ for refractory patients managed in primary care. No potential areas of significant bias were identified. Direct health care costs were significantly increased by psychotherapy during the intervention period and they were significantly increased during the follow-up period. However, the study was powered to detect a specific change in clinical rather

than cost outcomes. As this study did not provide an estimate of the cost per QALY for psychotherapy compared to usual care, it was not particularly useful in determining whether recommending psychotherapy for use in the NHS would result in the efficient use of NHS resources.

COST-EFFECTIVENESS ANALYSIS FOR PSYCHOTHERAPY

The section describes the health economic analysis undertaken to inform recommendations on the use of psychotherapy as one-off intervention in the management of IBS. The general methods used in the economic analysis for all management interventions are described in detail in Chapter 5 and the model inputs and assumptions relevant to this particular intervention are described below.

- The effectiveness of psychotherapy in addition to usual care compared to usual care alone in people with refractory IBS was based on the number of patients with an improvement in global symptoms (at the end of treatment) for psychotherapy vs usual care (RR = 3.08, 95%CI 1.74 – 5.47, based on Guthrie 1991).
- We assumed that the relative risk of response had fallen to 1.68 (95% CI 1.14 – 2.49) by 15 months based on follow-up data from Svedlund (1983).
- The evidence included in the clinical effectiveness review did not allow a subtype specific estimate of clinical effectiveness to be estimated. Therefore it was assumed that psychotherapy is equally effective in all IBS subtypes although it should be noted that the trials were carried out in patients with refractory IBS and a significant proportion of the trial population had a current or previous psychiatric diagnosis.
- It was assumed that psychotherapy is given over 12 weeks as this was the duration used in RCTs.
- The costs of psychotherapy were estimated from the number and duration of sessions and the unit cost for face-to-face time with a psychotherapist. The mean duration of psychotherapy from the three RCTs (Svedlund 1983; Guthrie 1991; Creed 2003) was 9.9 hours. The cost of face-to-face time with a psychotherapist was based on the reference cost for counselling services in primary care (£48 per hour) on advice from GDG members that psychotherapy is provided by counsellors and nurses in the NHS at present. This gave a total cost of £471 (range £348 - £672) over 12 weeks.

In the Creed (2003) economic analysis, there was a statistically significant lower cost per week for psychotherapy vs usual care (-£8.11 to -£0.04 95% CI) in the year following the intervention period (costs have been uplifted to reflect current prices). We took the mid-point of this interval which gave a cost per week of £-4.08 for psychotherapy compared to usual care in the year following treatment. This was applied in the basecase analysis for psychotherapy resulting in cost savings of £212 over the year following intervention.

The results of the Creed (2003) study also suggested that there was a reduction in service use during the intervention period, as whilst the weekly costs during this period were significantly higher for psychotherapy compared to usual care (£1.23 to £15.30), these were not comparable to the cost of providing psychotherapy which would be expected to have a mean cost of £40 per week based on the number and duration of sessions provided in this study and the unit costs presented above. This suggested that there was a significant reduction in other health care use during the intervention period. As it was not possible to separate the costs of psychotherapy from the costs offsets due to lower resource use during the intervention period of the Creed (2003) study, we have based the intervention cost on the estimate described above. However, as it seems reasonable that patients will access NHS services less whilst they are receiving an effective intervention, we have applied the reduction in resource use seen in the follow-up period as a cost off-set during the intervention period. The direct costs measured by Creed (2003) during the intervention period have been considered in a sensitivity analysis.

Modelled response rates

In the basecase scenario the response rate of 25% in the no treatment arm was taken from the mean placebo arm response rate from the behavioural therapy trials. This represents the group of patients whose symptoms improve under usual care. The RR for an improvement in global symptoms for psychotherapy vs no treatment at the end of treatment is 3.08; therefore the response rate in the intervention arm is 78% after 12 weeks. The response rate has fallen to 43% by 15 months based on the 15 month follow-up data from Svedlund (1983). The time-frame of the analysis was limited to 15 months, with no further costs or benefits accrued beyond this time-point, as this was the longest follow-up available for psychotherapy in IBS.

Figure 17: Response rate in the basecase analysis

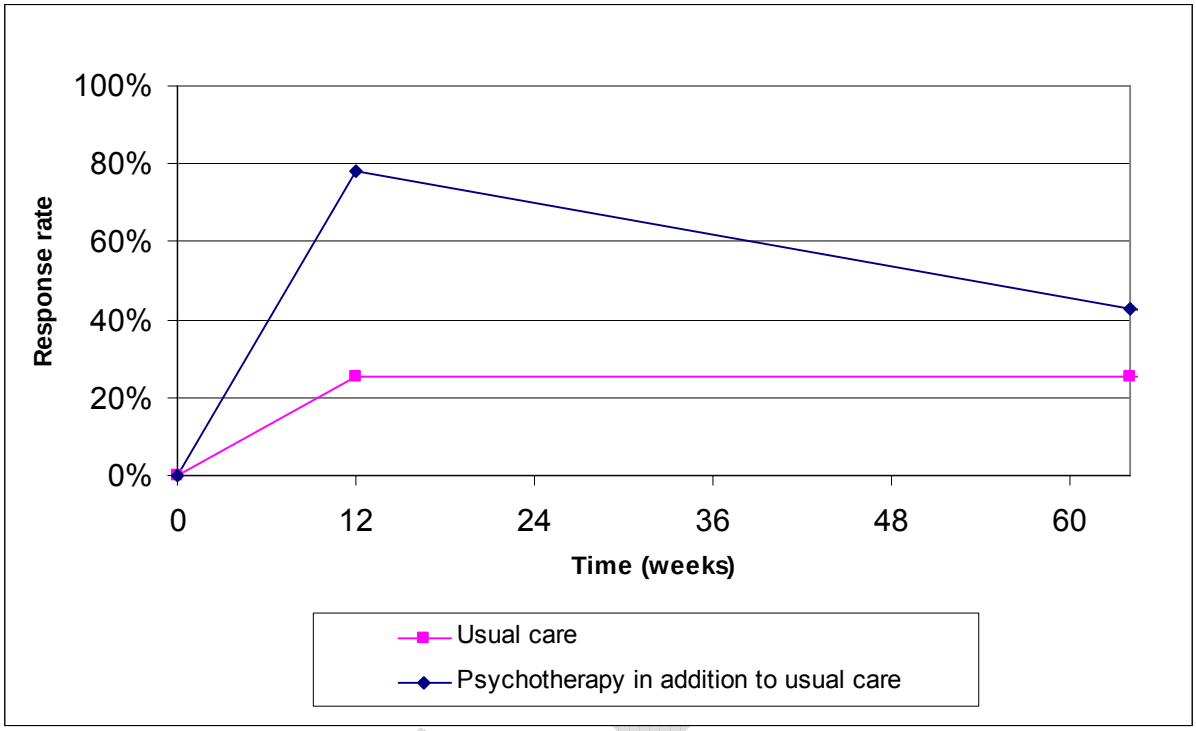


Table 1: Intervention specific parameters – Psychotherapy

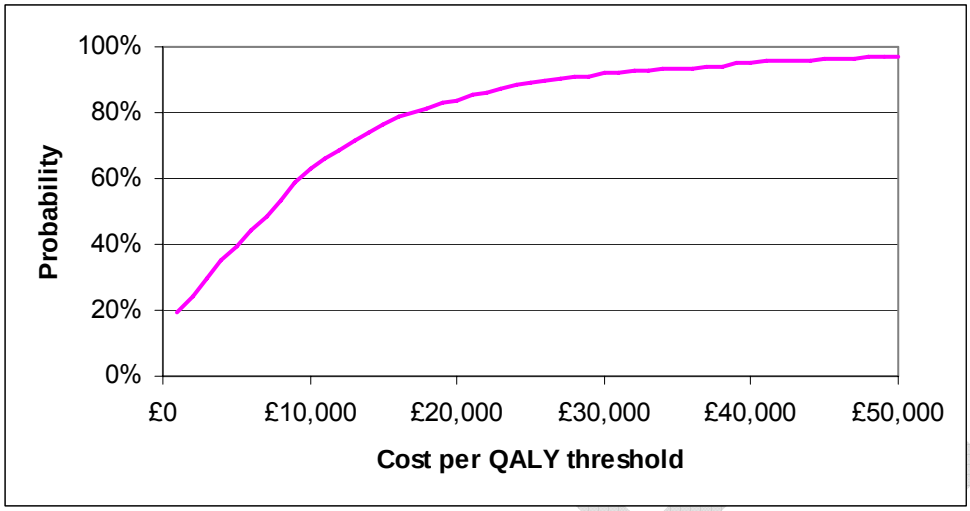
Description	Value	Evidence
RR of response for intervention vs placebo (at end of treatment)	3.08 (1.74 – 5.47)	Guthrie (1991)
RR of response for intervention vs placebo (at 15 months)	1.68 (1.14 – 2.49)	Svedlund (1983)
Cost for psychotherapy	£471 (range £348 - £672) over 12 weeks	Weighted mean duration across studies and unit cost form Netten (2006)
Cost-offset due to reduced resource use during intervention and 1 year after	-$4.70 per week (-£8.11 to -£0.04) Equiv to -£4.08 at current UK prices*	Creed (2003)

* Uplifted to 05/06 prices using Hospital and Community Health Services Pay and Prices Index, Netten (2006)

Psychotherapy in addition to usual care for 100 patients with refractory IBS is estimated to gain an additional 2.94 QALYs for an additional cost of £21,035 compared to usual care alone under the basecase assumptions. The incremental cost per QALY is therefore £7,160. The probabilistic sensitivity analysis considers the uncertainty in this basecase estimate due to the uncertainty in the parameters used to estimate the cost-effectiveness. The CEAC in Figure 18 shows that given the parameter uncertainty, psychotherapy in additional to usual care has a

84% probability of having a cost per QALY under £20,000 and a 92% probability of having a cost per QALY under £30,000, compared to usual care alone.

Figure 18: CEAC for psychotherapy in addition to usual care compared to usual care alone in patients with refractory IBS



The incremental cost-effectiveness is dependent on the probability of an improvement for patients who receive usual care. When we applied a lower response rate of 9% in the usual care arm, the cost per QALY was increased to £14,629. As this sensitivity analysis significantly increased the cost per QALY estimate, the probabilistic sensitivity analysis was re-run using this lower response rate for the comparator arm. The mean cost per QALY from the 1000 samples was £17,577 and the cost per QALY had a 51% probability of being under £20,000 per QALY and a 62% probability of being under £30,000 per QALY.

The threshold analysis showed that a response to treatment would need to provide more than 0.026 QALYs per annum to give a cost per QALY of under £20,000 in the basecase analysis. When the utility gain associated with a response to treatment was increased to 0.135 (equivalent to the QALY gain expected for a complete remission of symptoms) the cost per QALY was significantly lower at £3,782.

When we assumed no fall-off in response up to 52 weeks post-intervention, the cost per QALY was £5,000. This would be further reduced by any continued response beyond 52 weeks. When we assumed that there was no significant difference between psychotherapy and usual care at 12 months, the cost per QALY increased to £9,062.

When we estimated the incremental cost during the intervention and follow-up period directly from those measured in Creed (2003), psychotherapy was cost saving compared to usual care and resulted in greater QALY gain, dominating usual care. When we excluded the reduction in resource use observed in the Creed (2003) study from the analysis, the incremental cost of

psychotherapy increased significantly to £47,154 and the cost per QALY increased to £16,051. As this is a significant increase in the cost per QALY, the probabilistic analysis was re-run under this assumption. In this conservative estimate the cost per QALY for psychotherapy in addition to usual care compared to usual care alone had a 57% probability that of being under £20K and a 77% probability of being under £30K.

Table 2: Sensitivity results for psychotherapy in addition to usual care compared to usual are alone for 100 patients with refractory IBS (all subtypes)

Scenario	Usual care		Behavioural intervention and usual care		Incremental
	Cost	QALY	Cost	QALY	Cost per QALY
Basecase	£0	2.02	£21,035	4.96	£7,160
Lower response rate in comparator arm (9%)	£0	1.30	£21,035	2.74	£14,629
No fall-off in effect for 1 year	£0	2.02	£21,035	6.23	£5,000
Effect falls off over 12 months	£0	2.02	£21,035	4.34	£9,062
No resource use reduction	£0	2.02	£47,154	4.96	£16,051
Costs as measured in Creed (2003)	£0	2.02	-£11,307	4.96	-£3,849 Psychotherapy dominates
High utility gain of 0.135	£0.00	3.83	£21,035	9.39	£3,782
Threshold analysis on lowest utility	A cost per QALY of £20,000 is reached when the QALY gain associated with responding to treatment lies between 0.025 and 0.026.				

Further analyses on the cost-effectiveness of psychotherapy compared to other behavioural interventions are given in section 9.7.

EVIDENCE STATEMENTS

For this review, the evidence was assessed using the GRADE process and tables are shown in Appendix F. The following evidence statements are derived from the GRADE tables.

1. There is fair evidence to show a significant global improvement in symptoms after 12 weeks and after 15 months, for dynamic psychotherapy in addition to medical therapy compared with medical therapy alone, given in secondary care to patients with long term or refractory IBS, approximately half of whom had psychological co-morbidities.

2. There is fair evidence to show a significant global improvement in symptoms after 12 weeks, for psychodynamic interpersonal therapy compared with medical treatment, given in

secondary care to patients with refractory IBS, approximately half of whom had psychological co-morbidities.

3. There is weak evidence to show no significant global improvement in IBS symptoms after 12 months follow up, for psychodynamic interpersonal therapy compared with medical treatment, given in secondary care to patients with long term IBS, many of whom had had psychological co-morbidities. This fall-off in effect may have been caused by confounding in the control arm.

4. There is moderately good evidence to show a significant decrease in pain after 12 weeks and 15 months, for dynamic psychotherapy in addition to medical therapy compared with medical therapy alone, given in secondary care to patients with long term IBS, many of whom had had psychological co-morbidities.

5. There is fair evidence to show no significant reduction in pain after 12 weeks and 12 months follow up, for psychodynamic interpersonal therapy compared with medical treatment, given in secondary care to patients with refractory IBS, approximately half of whom had psychological co-morbidities.

6. There is weak evidence to show no significant difference in the patients' assessment of their mental health at 15 months, between patients given dynamic psychotherapy in addition to medical therapy compared with medical therapy alone, either for all patients or for a subgroup with a psychological co-morbidity history.

7. There is weak evidence to show a small, significant improvement in the physical component of the SF36 quality of life score after 12 weeks and 12 months follow up, and a small significant difference in the mental health score after 12 weeks, for psychodynamic interpersonal therapy compared with medical treatment, given in secondary care to patients with refractory IBS, approximately half of whom had psychological co-morbidities. There was no significant difference in the mental health score at 12 months follow up.

8. There is weak evidence to show no significant difference in the number of patients requiring a prescription for antidepressants over 12 months, for psychodynamic interpersonal therapy compared with medical treatment, given in secondary care to patients with refractory IBS, approximately half of whom had psychological co-morbidities.

9. There is weak evidence to show significantly more patients discontinued treatment for psychodynamic interpersonal therapy compared with medical treatment, given in secondary care to patients with refractory IBS, approximately half of whom had psychological co-morbidities.

10. There is fair evidence to show no significant difference in global improvement in symptoms, pain and quality of life (physical and mental) after 12 weeks, between psychodynamic interpersonal therapy compared with an SSRI, given in secondary care to patients with refractory IBS, approximately half of whom had psychological co-morbidities.

11. There is weak evidence to show that significantly fewer patients required a prescription for antidepressants over 12 months, for psychodynamic interpersonal therapy compared with an SSRI, given in secondary care to patients with refractory IBS, approximately half of whom had psychological co-morbidities.

12. There is weak evidence to show significantly fewer patients discontinued treatment for psychodynamic interpersonal therapy compared with an SSRI, given in secondary care to patients with refractory IBS, approximately half of whom had psychological co-morbidities.

HEALTH ECONOMIC STATEMENT

Evidence from a trial based economic evaluation in secondary and tertiary care patients with a high level of NHS service use at baseline showed that direct health care costs are lower in the year following treatment for 3months of psychotherapy compared to 3 months of usual care. Health care costs were significantly higher during the intervention period for psychotherapy compared to usual care. This evidence is unlikely to be applicable to primary care patients except those with refractory IBS.

Evidence from a decision analytic model showed that the addition of psychotherapy to usual care is cost-effective in individuals with refractory IBS although the cost-effectiveness was sensitive to uncertainty around the proportion of patients experiencing an improvement in global symptom score with usual care alone. It was also sensitive to the whether or not there was any reduction in health care service use during and following treatment

A decision analytic model was used to carry out an incremental analysis for the three behavioural therapies. This was an indirect comparison based on the effectiveness of each behavioural therapy compared to usual care and therefore may be biased. Psychotherapy was had a 91% probability of being the most cost-effective intervention under the basecase assumptions. However, when assuming that psychotherapy does not result in lower resource use, psychotherapy had a 56% probability of being the most cost-effective intervention with CBT having a 16% probability and hypnotherapy having a 29% probability.

GDG DISCUSSION

Despite the prevalence of psychiatric comorbidities in the trials for this review, the GDG considered that dynamic psychotherapy could be a useful option for all people with refractory

IBS, and had potential to be a first line therapy. The GDG therefore decided to include pyschotherapy in one of its top five research recommendations, with the potential for this intervention to be considered as a first line therapy option.

EVIDENCE TO RECOMMENDATION

The evidence to recommendation statement for psychotherapy, CBT and hypnotherapy is detailed in section 9.8.

The combined guideline recommendation for psychotherapy, CBT and hypnotherapy is also stated in section 9.8.

9.5 Cognitive behavioural therapy

SELECTION CRITERIA

The selection criteria described in the general methodology section were used, except that crossover studies were excluded as inappropriate due to the carry-over effect of the CBT interventions.

The following comparisons were to be included:

- CBT versus waiting list control or symptom monitoring only
- CBT type 1 versus type 2 (e.g. stress management versus contingency management)
- CBT individual versus CBT group
- CBT + another intervention (e.g. medical therapy) versus the other intervention alone
- CBT versus medical treatment.

SEARCH STRATEGY FOR IDENTIFICATION OF STUDIES

Searches were performed on the following core databases: MEDLINE, EMBASE, CINAHL, and *The Cochrane Library* (1966 to current day with guidance from the GDG). Additionally, the PSYCINFO database was searched for this review. The search strategies are listed in Appendix B.

Study Design

Seventeen parallel randomised trials were included (Bennett 1985; Bergeron 1983; Blanchard 1993; Bogalo 2006; Boyce 2003; Corney 1991; Drossman 2003; Fernandez 1998; Gong 2002; Greene 1994; Heymann-Monnikes 2000; Kennedy 2005; Lynch 1989; Payne 1995; Tkachuk 2003; Toner 1998; Vollmer 1998). Further details are given in the included studies table.

Six studies had more than one arm: Bergeron (1983) (stress management, relaxation, biofeedback); Boyce (2003) (CBT, relaxation, routine medical care); Drossman (2003) (half of the patients were randomised to CBT or attention control; the other half to desipramine or

placebo tablet; the two halves were divided randomly initially); Fernandez (1998) (stress management, contingency management, conventional medical treatment or placebo); Payne (1995) (CBT, self help group or waiting list control); Vollmer (1998) (CBT in a group, CBT individually or symptom monitoring waiting list control). Thus, there were 28 possible comparisons for this review. We did not include the comparison with desipramine because this drug is not licensed for use in the UK.

Two studies were reported only as abstracts (Bergeron 1983; Gong 2002). The former had no data reported. Three studies were RCTs with limited or incomplete data (Bennett 1985; Toner 1998; Bogalo 2006). The Bennett study gave little detail (e.g. it was unclear how many patients were assigned to each group; no primary data were given; only p values for ANOVAs). The Toner (1998) study was briefly reported as part of a larger article. This study enrolled 101 individuals with IBS, who were randomly allocated to group CBT, a psychoeducational group treatment (education about the condition and support) or usual medical treatment. No primary outcome data were reported. Bogalo (2006) appeared to use data from a randomised trial. However, this paper only reported outcomes for the intervention group not the controls. For the rest of this review, only the 14 studies with sufficient data are reported.

The studies were carried out in the UK (Corney 1991; Kennedy 2005), Europe, Canada, the USA and China. Trials lasted between 6 and 12 weeks (the duration of the Gong (2002) study was not stated). One study was conducted in primary care (Kennedy 2005); seven were in secondary care (Blanchard 1993; Corney 1991; Drossman 2003; Fernandez 1998; Gong 2002; Heymann-Monnikes 2000; Lynch 1989); one study (Boyce 2003) recruited equal numbers of patients through gastroenterology clinics and through newspaper advertisements, and the others did not report the setting. The total number of patients in the studies ranged from 20 to 431, with three studies including more than 100 patients (Boyce 2003; Drossman 2003; Kennedy 2005). All but four studies (Boyce 2003; Drossman 2003; Gong 2002; Kennedy 2005) had fewer than 25 patients in the treatment arm.

Population

All the studies included only patients with IBS, apart from Drossman (2003), for which 78% of the patients had IBS. None of the studies reported the number of patients with bloating or whether the symptoms were post-infective. The mean age of patients across studies was around 40 years, with those aged between 16 and 70 years included. All the studies included more women than men.

Four studies reported or implied that the patients had refractory IBS (Greene 1994; Heymann-Monnikes 2000; Lynch 1989; Tkachuk 2003): Tkachuk (2003) stated that the patients had refractory IBS; Lynch (1989) had patients referred from gastroenterology clinics and had duration of IBS of around 9 years; Heymann-Monnikes (2000) had tertiary referral patients. The

patients in Greene (1994) had had IBS for 14.5 years. Boyce (2003) reported that about 50% of patients had received medication for IBS. The other studies did not give any information about IBS duration.

Most studies reported whether the patients had an Axis I diagnosis (e.g. major depression; schizoaffective disorder; paranoid state) or other psychiatric or psychological co-morbidities:

- Heymann-Monnikes (2000) stated that patients were excluded if they had any mental disorder.
- Drossman (2003) reported that no patients had psychiatric disorders, but almost half had a history of physical or sexual abuse.
- Boyce (2003) excluded patients if they had major current psychotic illness, used psychological treatment, or antidepressants or antipsychotics.
- Two studies excluded patients with serious psychiatric disorders (Lynch 1989 (implied); Vollmer 1998).
- Five studies stated that the majority of patients had an Axis I diagnosis (Blanchard 1993, 50-73%; Greene 1994, 90%; Payne 1995, 80-92%; Tkachuk 2003, 68%; Vollmer 1998, 82-90%).
- Three studies mentioned that the patients had received psychiatric treatments: in Fernandez (1998) 49% had had psychiatric treatment; in Kennedy (2005) 43% had consulted a doctor because of a psychological problem; in Lynch (1989) 6/21 (29%) patients used psychotropic drugs.
- Corney (1991) had over 50% of the patients with one or more social problems.
- The remaining studies (Bergeron 1983; Gong 2002) did not mention Axis I diagnoses or psychiatric complaints/treatments.

Overall, therefore, eight studies can be considered to be representative or partly representative of the IBS population with concurrent psychiatric or psychological illnesses (Blanchard 1993; Fernandez 1998; Greene 1994; Kennedy 2005; Lynch 1989; Payne 1995; Tkachuk 2003; Vollmer 1998). Three studies can be considered to be in patients with IBS who do not have concurrent psychiatric or psychological illnesses (Heymann-Monnikes 2000; Drossman 2003; Boyce 2003). We noted that 15 to 20% of patients in primary care have a co-existing psychiatric condition and approximately half of those in secondary care.

Interventions

Twelve studies described some form of CBT: Boyce (2003); Corney (1991); Drossman (2003); Fernandez (1998) (one group had stress management sessions involving progressive muscle relaxation; another had contingency management sessions involving contingency contract for new behaviours; self-observation, shaping, stimulus control, neutralising inadequate habits and breaking learned illness behaviour, social skills training); Gong (2002); Greene (1994); Heymann-Monnikes (2000); Kennedy (2005); Lynch (1989); Payne (1995); Tkachuk (2003);

Vollmer (1998). Two studies gave relaxation training (Bergeron 1983; Blanchard 1993).

The CBT interventions differed in the methods used (group or individual; administered by nurse practitioner or other professional); the number of sessions given (6 to 12), and; the duration of the study (6 to 12 weeks in the studies that stated this).

CBT was defined in different ways in different papers. Two studies had therapy delivered by nurses (Corney 1991; Kennedy 2005). Details are given in the included studies table (Appendix D).

It was decided to combine all CBT, behavioural therapy (BT) and cognitive therapy (CT) interventions under the general heading of CBT.

CBT was compared with relaxation training; symptom monitoring; self-help support groups; medical therapy or placebo. Two studies had placebo as a comparator (Drossman 2003; Fernandez 1998). Drossman (2003) randomised the patients into two groups and then randomised one group to CBT and attention control and the other group to desipramine and placebo desipramine. We decided to classify the CBT-attention control comparison as placebo and treat the desipramine placebo as no treatment. Fernandez (1998) had a placebo condition consisting of giving the patient exercises to visualise bowel function; and prompting their own capacity for self regulation through thought.

For the purposes of this review, we combined the comparators waiting list control, symptom monitoring, no treatment and placebo condition. The following comparisons were included:

1. CBT versus a waiting list control group, symptom monitoring only or placebo: nine studies, 12 comparisons (Blanchard 1993; Drossman 2003 x2; Fernandez 1998 x2; Gong 2002; Greene 1994; Lynch 1989; Payne 1995; Tkachuk 2003; Vollmer 1998 x2):
    - CBT versus waiting list control (Lynch 1989)
    - CBT versus symptom monitoring (Blanchard 1993; Greene 1994)
    - CBT versus waiting list control including symptom monitoring (Payne 1995; Tkachuk 2003; Vollmer 1998 x2)
    - CBT versus an attention control condition involving symptom monitoring plus education plus access to a therapist (Drossman 2003)
    - CBT versus placebo condition (Fernandez 1998 x2)
    - CBT versus no treatment (Drossman 2003; Gong 2002);
2. CBT + another intervention versus the other intervention alone:
    - CBT + mebeverine versus mebeverine (Kennedy 2005)
    - CBT (multicomponent behavioural therapy) + optimised medical treatment versus optimised medical treatment alone (Heymann-Monnikes 2000);

3. CBT 1 versus CBT 2 (three studies):
    - Stress management versus relaxation (Bergeron 1983 – no data)
    - CBT versus relaxation (Boyce 2003)
    - Stress management versus contingency management (Fernandez 1998);
4. CBT individual therapy versus CBT group therapy:
    - Vollmer (1998);
5. CBT versus another intervention:
    - CBT versus biofeedback (Bergeron 1983 – no data)
    - CBT versus support group (Payne 1995)
    - CBT versus psychoeducational group (Toner 1998 – no data);
6. CBT versus routine medical treatment (five studies, six comparisons):
    - CBT versus fluphenazine (anti-anxiety), mebeverine and fybogel (Bennett 1985)
    - CBT vs 'routine medical care' (Boyce 2003 x2; Corney 1991; Fernandez 1998 x2).

Six studies stated that the patients were allowed to continue their IBS medical treatment: Fernandez (1998), although 50% did not take the medication properly; in Heymann-Monnikes (2000), 9/12 in the BT group and 11/12 in symptom monitoring had concurrent medication for IBS; Kennedy (2005); Lynch (1989), 10/21 had analgesics at recruitment and 6 used Metamucil or similar bulking agents; Tkachuk (2003); Vollmer (1998), no patients were excluded because of their ongoing IBS drug treatment. Gong (2002) reported that all patients received selective gastrointestinal calcium antagonists.

One study (Boyce 2003) stated that the 'vast majority' were not taking concurrent medication. The rest did not state the concurrent medications for IBS.

In view of the use of other IBS medication in both arms of the CBT versus placebo/symptom monitoring comparisons, we decided to combine interventions 1 and 2 as subgroups because they each could be considered to be variations of CBT versus no treatment/symptom monitoring. Furthermore, the GDG advised that CBT treatment would not interact with other medical treatments. We decided that if subgroup analysis were to be used, the attention control and placebo condition (Fernandez 1998; Drossman 2003) should be considered as a separate group to the other comparators.

Outcomes

The outcomes examined were:

1. Global symptoms:
    a) Global improvement in symptoms (number of patients)
    b) Global symptom score.
2. Individual symptoms:
    a) Pain

b) Bloating
c) Bowel habits.

3. Adverse events
4. Quality of life
5. Number of patients withdrawing from the study
6. Mental health outcomes (overall mental health; depression; anxiety)

Five studies recorded longer term follow up: Vollmer (1998) at 12 weeks; Corney (1991) at 40 weeks; Boyce (2003) and Kennedy (2005) both at 26 and 52 weeks; Fernandez (1998) at 52 weeks.

The following outcome measures were recorded:

Table 1.

Outcome measure	Measured at treatment end (weeks)	Measured at follow up (weeks)
Global scores		
Global IBS symptom score (Bowel symptom severity scale 0-48 scale; high = severe)	Boyce 2003 (8)	Boyce 2003 (26) Boyce 2003 (52)
Global IBS symptom score (satisfaction, global wellbeing, diary pain scores, health related quality of life); high score = good; maximum unclear	Drossman 2003 (12)	
Global IBS symptom score (7 symptoms daily for 2 weeks each scored 0-4 from not a problem to debilitating symptom intensity; high score = bad)	Greene 1994 (8)	
Global IBS symptom score (20 items over 14 days); high score = bad	Heymann-Monnikes 2000 (10)	
Global IBS symptom score (<75=normal; 75-174 mild; 175-299 moderate; 300-500 severe symptoms)	Kennedy 2005 (6)	Kennedy 2005 (26) Kennedy 2005 (52)
Global IBS symptom score (pain, discomfort, diarrhoea, constipation each rated 0=no symptoms to 6=very severe symptoms)	Lynch 1989 (8)	
Global improvement of IBS symptoms (mean Composite Primary Symptom Reduction [CPSR] score; CPSR represents % reduction in score from baseline); i.e. high = bad	Blanchard 1993 (8) Greene 1994 (8) Payne 1995 (8) Vollmer 1998 (10)	Vollmer 1998 (12)
Global improvement of IBS symptoms (mean score) VAS (1=very much better to 7=very much worse; 4=no change)	Heymann-Monnikes 2000 (10)	

Global improvement of IBS symptoms (no. patients)	Blanchard 1993 (8) Fernandez 1998 (10) Gong 2002 (duration of treatment not stated) Greene 1994 (8) Lynch 1989 (8) Payne 1995 (8) Tkachuk 2003 (9) Vollmer 1998 (10)	Fernandez 1998 (52)
Pain scores		
Pain score (0=not a problem; 4=debilitating symptoms) daily for 4 weeks	Blanchard 1993 (8)	
Pain score (VAS score); high = bad.	Corney 1991 (16)	Corney 1991 (40)
Pain score (McGill average daily pain); high score = bad	Drossman 2003 (12)	
Pain score (0=not a problem; 1=mild; 2=moderate; 3=severe; 4=debilitating; scores totalled for 1 week); high score = bad	Fernandez 1998 (10)	
Pain score (scored 0-4 daily for 2 weeks); high score = bad	Greene 1994 (8)	
Pain score (0=no pain; 6=very severe pain)	Lynch 1989 (8)	
Pain score (0=not a problem; 4=intense and incapacitating)	Tkachuk 2003 (9) Vollmer 1998 (10)	
Pain score (0=not a problem; 4=debilitating symptoms) daily for 4 weeks	Blanchard 1993 (8)	
Bloating		
Bloating score (0=no symptom; 6=very severe symptom)	Greene 1994 (8) Lynch 1989 (8)	
Bloating score (0=not a problem; 4=intense and incapacitating)	Tkachuk 2003 (9)	
Bloating score (0=not a problem; 4=debilitating symptoms)	Vollmer 1998 (10)	
Bowel habits		
Constipation (VAS score); high = bad	Corney 1991 (16)	Corney 1991 (40)
Constipation (0=not a problem; 4=debilitating symptoms)	Greene 1994 (8)	
Constipation (0=no symptom; 6=very severe symptom)	Lynch 1989 (8)	
Diarrhoea (VAS score); high=bad	Corney 1991 (16)	Corney 1991 (40)
Diarrhoea (0=not a problem; 4=debilitating symptoms)	Greene 1994 (8)	
Diarrhoea (0=no symptoms; 6=very severe symptoms)	Lynch 1989 (8)	
Mental health		
Dysfunctional cognitions (Cognitive Scale for Functional Bowel Disorders); scale 25-175; high=bad	Tkachuk 2003 (9)	
Mental health (max = 100)	Tkachuk 2003 (9)	

Psychological distress (Clinical Interview Schedule); 0-48; high=bad		Corney 1991 (40)
Overall anxiety and psychological distress (Anxiety, State-Trait Anxiety Inventory [STAI]); Scale range 20-80; high = bad	Greene 1994 (8) Heymann-Monnikes 2000 (10) Payne 1995 (8) Tkachuk 2003 (9)	
Psychological distress (HADS); range 0-56; high=bad	Boyce 2003 (8) Kennedy 2005 (8)	Boyce 2003 (26) Boyce 2003 (52) Kennedy 2005 (26) Kennedy 2005 (52)
Beck depression inventory (scale maximum 63; high=bad)	Greene 1994 (8) Heymann-Monnikes 2000 (10) Lynch 1989 (8) Payne 1995 (8) Tkachuk 2003 (9)	
Quality of life		
Disruption of daily life (0=no symptom; 6=very severe symptom)	Lynch 1989 (8)	
Physical health (SF-36 Physical Composite Scale); high = bad; scale max 100	Tkachuk 2003 (9)	
Quality of life (IBS-QOL) ; high score = good; max 84	Drossman 2003 (12)	
Quality of life (GLQI score); max score 144; high=good	Heymann-Monnikes 2000 (10)	
Work and social adjustment score (handicap in work, home, leisure and relationships; 0=not affected; 8 severely affected for each area; maximum total 40)	Kennedy 2005 (6)	Kennedy 2005 (26) Kennedy 2005 (52)
Other		
Satisfaction (responder = satisfaction 3 or more on a scale where each of 8 items were rated 1=strongly disagree to 5=strongly agree)	Drossman 2003 (12)	

Where necessary, linear scales that had a maximum value corresponding to a good outcome were inverted by subtracting the mean value from the maximum and using the same standard deviation. Studies could then be combined in a meta-analysis.

METHODOLOGICAL QUALITY

The results of the quality assessment for included trials are shown in Appendix D.

An adequate method of randomisation was reported in two studies (Drossman 2003 – computer generated; Kennedy 2005 – random number tables); the other studies did not state the method.

Allocation concealment was adequate in two studies (Drossman 2003 and Kennedy 2005 – independent third party); the other studies did not report allocation concealment.

Because of the type of intervention, the patients were not blinded. However, the GDG decided that blinding was not important for this review.

Two studies (Drossman 2003; Kennedy 2005) described an *a-priori* power calculation. All studies included in the review demonstrated baseline comparability of the groups apart from the two that were reported only as abstracts (Bergeron 1983; Gong 2002).

All the patients were followed up in four studies (Gong 2002; Greene 1994; Payne 1995; Tkachuk 2003). There were fewer than 20% missing data in five studies (Corney 1991: 2%; Drossman 2003: 7%; Heymann-Monnikes 2000: 7%; Kennedy 2005: 11%; Vollmer 1998: 6%).

There was more than 20% missing data at the end of treatment in five studies (Bennett 1985; Blanchard 1993; Boyce 2003; Fernandez 1998; Lynch 1989):

- Bennett (1985) reported 28% missing data
- Blanchard (1993) reported 6 drop-outs from relaxation group; 1 from controls; the 7 drop-outs out of the original 16 participants (44%) were replaced to give 16 participants (so not an ITT analysis); dropouts were unequal between the groups
- Boyce (2003) reported that 66 of the original 105 participants were left at the end of treatment (8 weeks; 63% left; 37% drop-out); within groups drop outs were 13/35 (37%) in the CBT group, 16/35 (46%) in the relaxation arm and 9/34 (26%) in the medical therapy group
- Fernandez (1998) reported that 33 patients dropped out at the end of treatment (16/23 (70%) from the placebo group; 6/21 (29%) for stress management; 7/23 (30%) for contingency management and 4/23 (17%) on medical treatment), i.e. 48% drop-out overall
- Lynch (1989) reported 6/27 missing data (22%; not stated from which group) and dropouts were replaced to achieve 21 patients in all.
- Drop-out was unclear in the remaining study (Bergeron 1983).

Of the five studies that reported longer term follow-up:

- Boyce (2003) reported that 52/105 patients were followed-up at one year (50% missing data)
- Fernandez (1998) had 53% missing data at 12 months
- Kennedy (2005) reported 28% and 36% loss to follow up in the CBT+ mebeverine and mebeverine groups respectively at 3 months; 26% and 24% at 6 months, and 27% and 25% at 12 months for the primary outcome (IBS symptom score)
- Corney (1991) appeared to lose one patient to follow-up at 9 months
- Vollmer (1998) had 45% loss to follow up at 3 months.

Overall, we regarded the comparisons with placebo in Fernandez (1998) as having high potential for bias and these were not included in the analysis. The other comparisons in Fernandez (1998), Blanchard (1993), Boyce (2003) and Lynch (1989) were treated with caution, especially the relaxation arm of the Boyce study. Sensitivity analyses were carried out as appropriate. We also noted that Drossman (2003) had a population in which only 78% of patients had IBS. This study was similarly treated with caution. At follow-up, Fernandez (1998), Boyce (2003) and Vollmer (1998) were treated as having high potential for bias, and Kennedy (2005) had some potential for bias.

RESULTS

A. CBT versus waiting list control group, placebo or symptom monitoring only; and CBT + IBS medication versus IBS medication alone

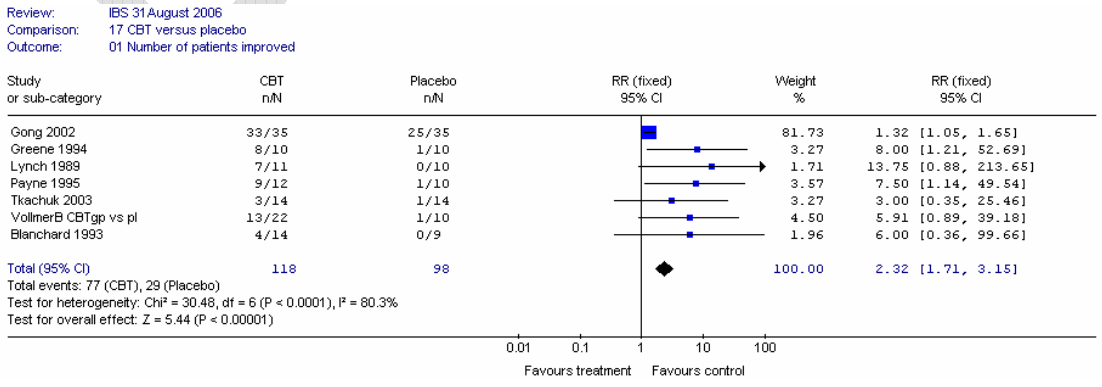
There were nine studies included in the analysis that compared CBT with a waiting list control group; symptom monitoring only, or; placebo condition in patients with IBS (Blanchard 1993; Drossman 2003; Fernandez 1998; Gong 2002; Greene 1994; Lynch 1989; Payne 1995; Tkachuk 2003; Vollmer 1998). Two studies compared the combination of IBS medication and CBT with IBS medication alone (Heymann-Monnikes 2000; Kennedy 2005). Heymann-Monnikes (2000) compared CBT plus optimised medical treatment versus optimised medical treatment alone. Kennedy (2005) investigated the addition of CBT to mebeverine in each arm.

1. Global symptoms

a) Number of patients with global improvement of symptoms

Eight studies with 217 patients compared CBT with symptom monitoring; no treatment, or; attention control (Blanchard 1993; Fernandez 1998; Gong 2002; Greene 1994; Lynch 1989; Payne 1995; Tkachuk 2003; Vollmer 1998 [individual and group CBT interventions]) for the outcome of global improvement in terms of the number of patients improved at the end of treatment. For this outcome measure the two CBT groups were combined in the Vollmer (1998) study.

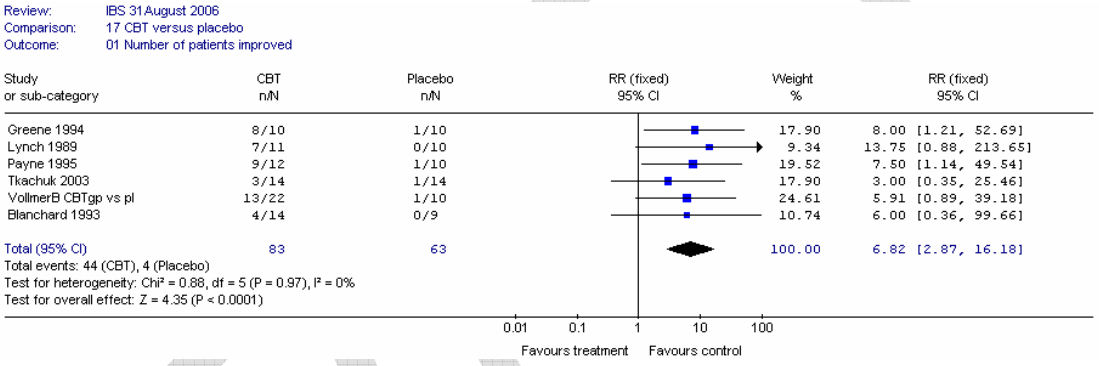
Figure 1



The relative risk analysis (Figure 1) showed significant heterogeneity (I^2=80%, p<0.0001), attributable to Gong (2002). This was a larger study in which nearly all the patients improved with CBT and many with no treatment. A sensitivity analysis of the relative risk without Gong (2002), gave no heterogeneity (I^2=0%, p=0.99) and the result was statistically and clinically significant (Figure 2). It was not clear why Gong (2002) should be so different, however, we noted that, whilst the majority of studies had patients with a psychiatric diagnosis or treatment, the exception was Gong (2002) (not stated). In addition, Gong (2002) was an abstract and all patients received selective GI calcium antagonists; the comparator was no treatment.

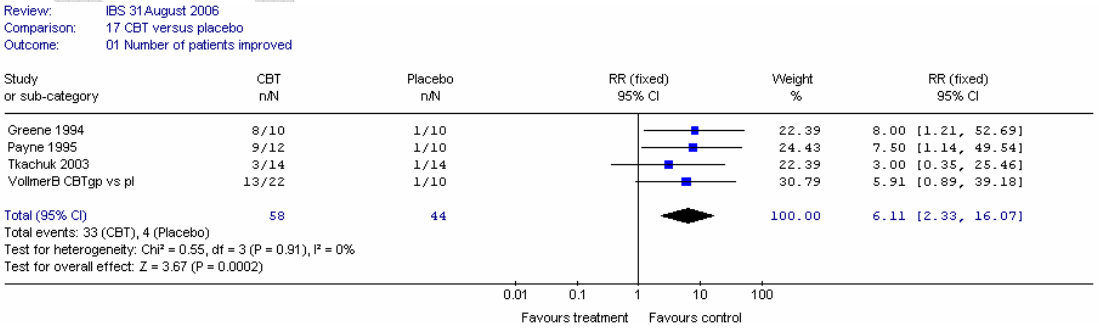
The RR was 6.82 (95%CI 2.87, 16.18), for the meta-analysis of 6 studies in 146 patients. This corresponded to a number needed to treat (NNT) of 3 (95%CI 2, 3), for a baseline risk of 0 to 10%.

Figure 2



Due to the high drop-out rates, a further sensitivity analysis was conducted excluding data from Blanchard (1993) and Lynch (1989). This made a slight difference (Figure 3) and therefore this figure was reported in the GRADE tables and used in the health economic modelling. This gave an NNT of 3 (95%CI 2, 4) for a control group risk of 7 to 10%.

Figure 3

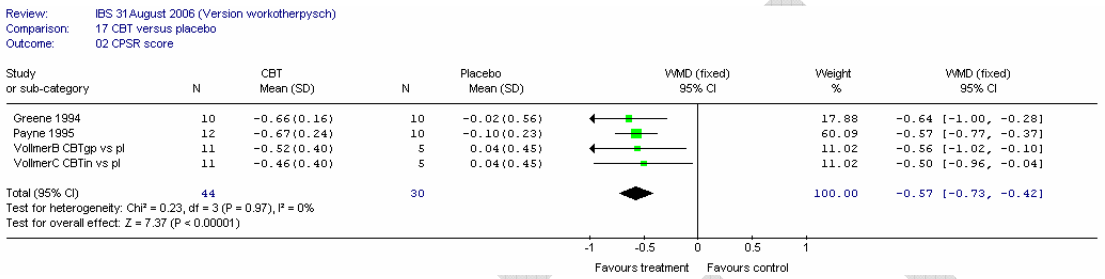


One study (Fernandez 1998) reported global improvement in terms of the number of patients improved at 1 year follow-up. This was likely to be flawed because of the high drop-out rate for the no treatment group and is not reported here.

b) Global symptom improvement score (CPSR)

Four studies (Blanchard 1993; Greene 1994; Payne 1995; Vollmer 1998) reported outcomes in terms of a global IBS change score, the 'Composite Primary Symptom Reduction (CPSR) score' (including measurements of pain, tenderness, diarrhoea, constipation). The scale ranged from -1 to +1, so for example -0.66 represented a 66% improvement from baseline; 0.04 represented a 4% worsening. There was a statistically significant difference in symptom score of: -0.57 (95%CI -0.73, -0.42), which is clinically significant.

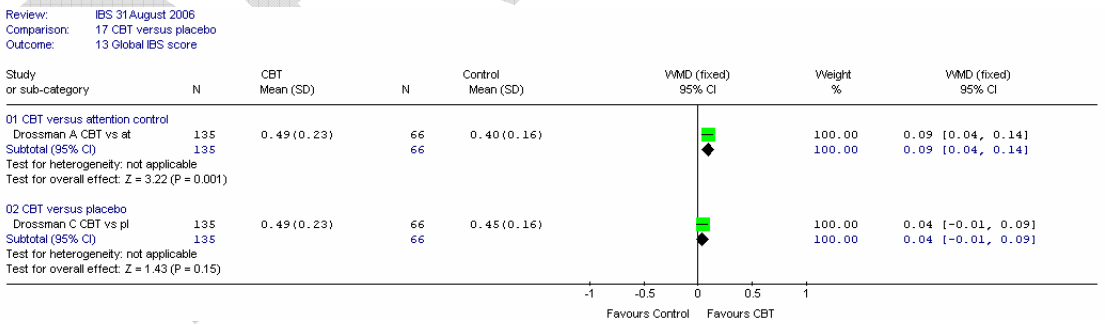
Figure 4



c) Global symptom score (scale: high is good)

One large study included a global IBS score based on 'satisfaction, global wellbeing, diary pain scores, and health related quality of life' (Drossman 2003). For this study, CBT was significantly better than attention control, MD 0.09 (95%CI 0.04, 0.14), but was not significantly different from the no treatment placebo for desipramine; MD 0.04 (95%CI -0.01, 0.09). However, the range for the composite scale was unclear, so the clinical significance could not be assessed.

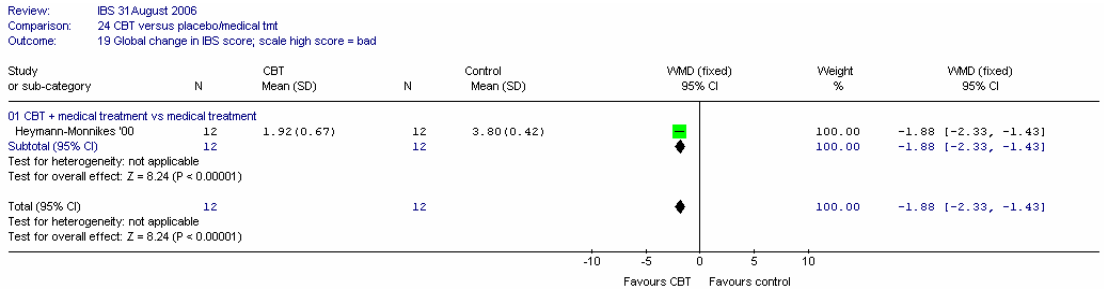
Figure 5



d) Global change in symptom score

Heymann-Monnikes (2000) also reported the change in overall wellbeing compared to pre-treatment on a visual analogue scale ranging from: 1=very much better, to; 7=very much worse, with; 4 indicating no change. This was a statistically significant improvement for the CBT + medical treatment compared with medical treatment alone.

Figure 6



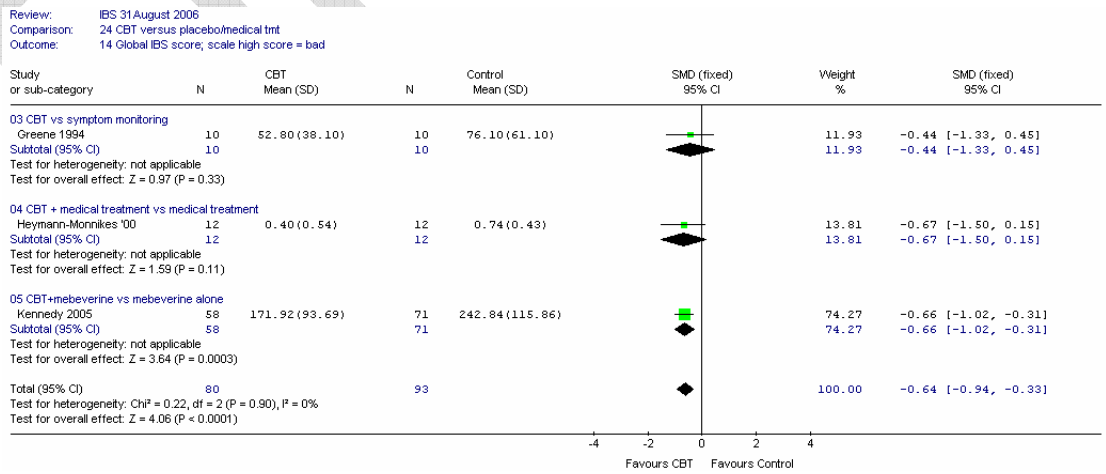
e) Global symptom score (scale: high = severe)

Another study (Lynch 1989) described an IBS score in terms of 'pain, discomfort, diarrhoea, and constipation, each rated 0 (no symptoms) to 6 (very severe symptoms)'. The treated patients had a reduction of 2.16 points compared with 0.36 points in the waiting list group (no SDs reported, p<0.05).

A further study (Greene 1994) of CBT versus symptom monitoring reported an IBS score based on 7 symptoms daily for 2 weeks each scored 0 to 4 (severe). The Heymann-Monnikes (2000) comparison of CBT+ medical treatment vs medical treatment alone reported a global symptom score derived from 20 items scored over 14 days. Kennedy (2005) reported the global IBS symptom score for patients receiving CBT plus mebeverine versus mebeverine alone. On the scale used, a score of <75 represented normal; 75-174 mild symptoms; 175-299 moderate symptoms and 300-500 severe symptoms.

Meta-analysis of these studies using the standardised mean difference showed a statistically significantly lower (better) global symptom scores for CBT compared with placebo.

Figure 7

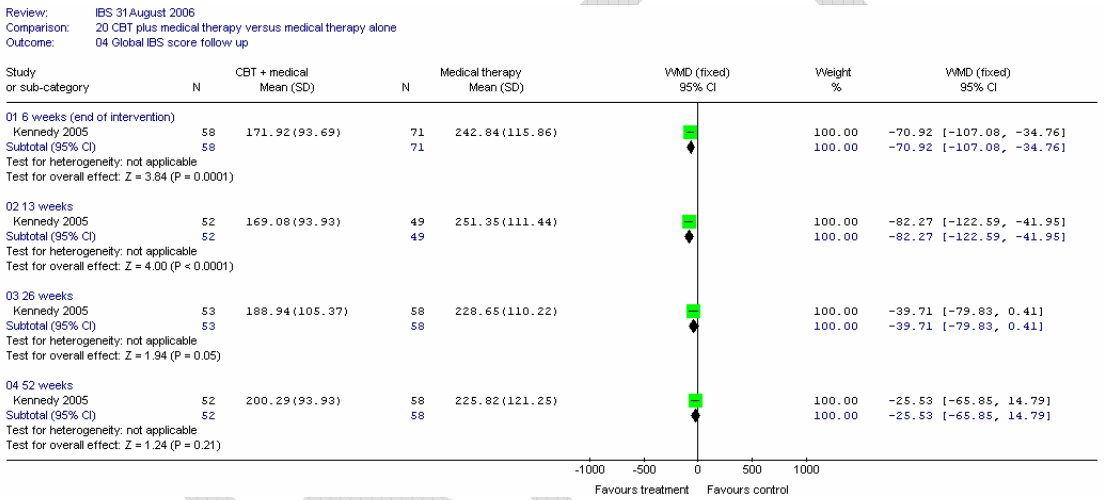


For the specific comparison of CBT plus mebeverine versus mebeverine alone, there was a statistically significant improvement; mean difference: -71 (95%CI -107, -35) on a scale of 0 to 500.

Follow-up in global symptom scores

Kennedy (2005) (CBT + mebeverine versus mebeverine alone) also reported this outcome at follow-up at 13; 26, and; 52 weeks. At 13 weeks there was a statistically significant difference in favour of CBT + mebeverine; MD: -82 (95%CI -123, -42); at 26 weeks there was a borderline significant difference between interventions; MD: -40 (95%CI -80, 0.4; p=0.05), and there was no significant effect at 52 weeks; MD: -26 (95%CI -66, 15). The data were extracted from a graph, but the latter two results do not agree with the 'estimated treatment effects' (-14 and 3 respectively) reported in table 10 of the paper. There was close agreement between the graph and the table for the effect size at the end of treatment and fairly close agreement at 13 weeks (table: -68 and -71 respectively). We have used the results from the graph because the table was said to be 'estimated'.

Figure 8



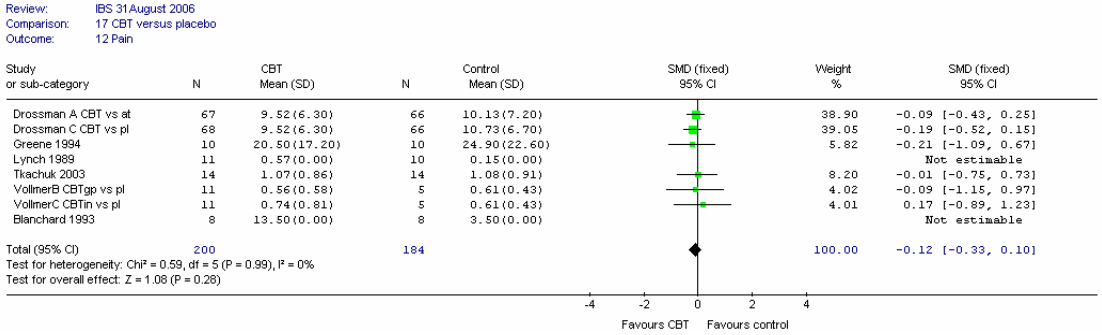
2. Individual symptoms

a) Pain

Seven studies (Blanchard 1993; Drossman 2003; Fernandez 1998; Greene 1994; Lynch 1989; Tkachuk 2003; Vollmer 1998) reported pain score outcomes. However, different pain scoring scales were used: Blanchard (1993): 0-4 scale daily added up over 4 weeks; Drossman (2003) used the McGill pain score (items scored 0-3, averaged, and added over 2 weeks); Fernandez (1998): 0 to 4 scale daily added up over 1 week; Greene (1994): 0 to 4 scale daily added up over 4 weeks; Lynch (1989) used a score ranging from 0 to 6; Tkachuk (2003) and Vollmer (1998) used a score ranging from 0 to 4 daily. In all cases, the maximum of the scale corresponded to severe pain.

The studies were combined in a meta-analysis (omitting Fernandez (1998) due to high drop-out rates) using standardised mean differences. There was no significant difference between CBT and control for pain score.

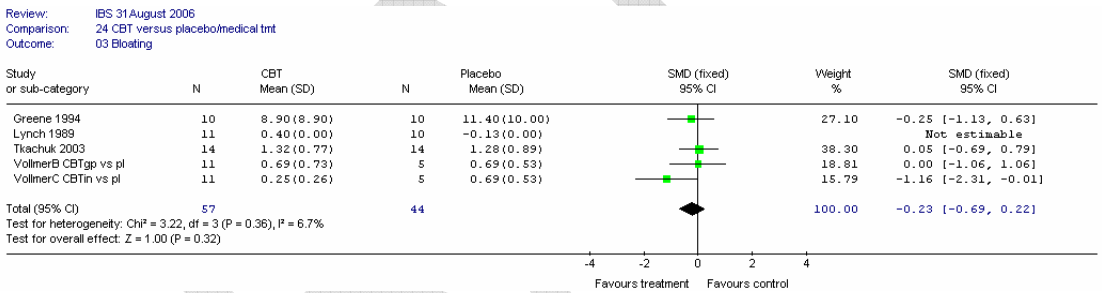
Figure 9



b) Bloating

Bloating was reported by Greene (1994) on a 0-4 daily scale added up over 4 weeks, i.e. maximum 112; Lynch (1989) on a 0-6 scale; Tkachuk (2003) on a 0-4 scale daily, and; Vollmer (1998) (group and individual CBT; on a 0-4 scale daily). In each case, the maximum of the scale corresponded to severe bloating. The studies were combined using standardised mean differences.

Figure 10



There was no significant difference between interventions in the bloating score.

c) Bowel habits

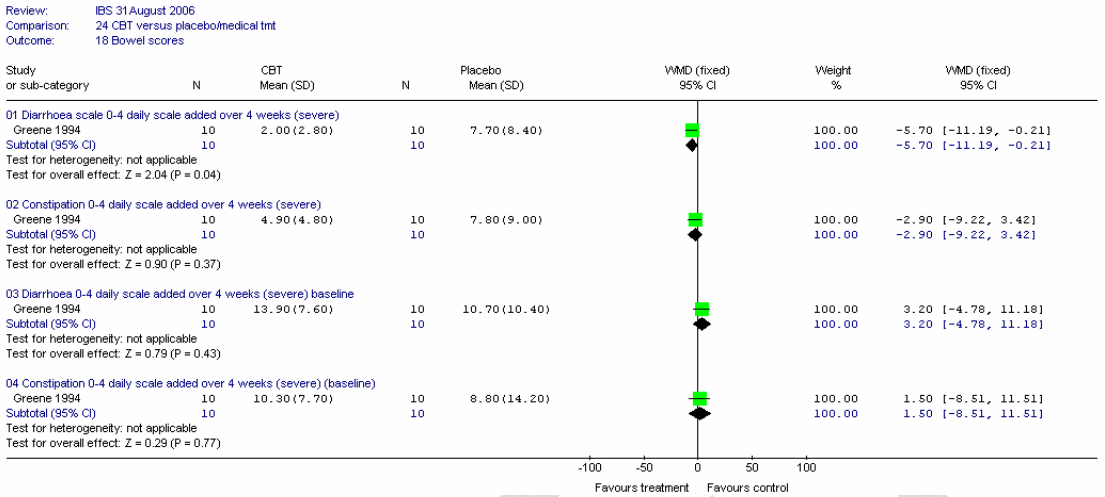
Ratings of constipation and diarrhoea were reported by Greene (1994) on a 0-4 scale daily added up over 4 weeks, i.e. maximum 112, and; Lynch (1989) on a 0-6 scale. In each case, the maximum of the scale corresponded to severe symptoms.

Both studies reported mean scores at baseline and after the intervention period. However, Lynch (1989) did not report standard deviations and was not analysed further.

In Greene (1994), baseline constipation scores were 10.3 (SD 7.7) in the CBT group compared with 8.8 (SD 14.2) in the placebo group. Baseline diarrhoea scores were 13.9 (SD 7.6) compared with 10.7 (SD 10.4). These are not significant differences.

Final scores at eight weeks showed a fairly small, statistically significant difference in the diarrhoea score (Figure 11). There was no significant difference in the constipation score.

Figure 11



3. Adverse events

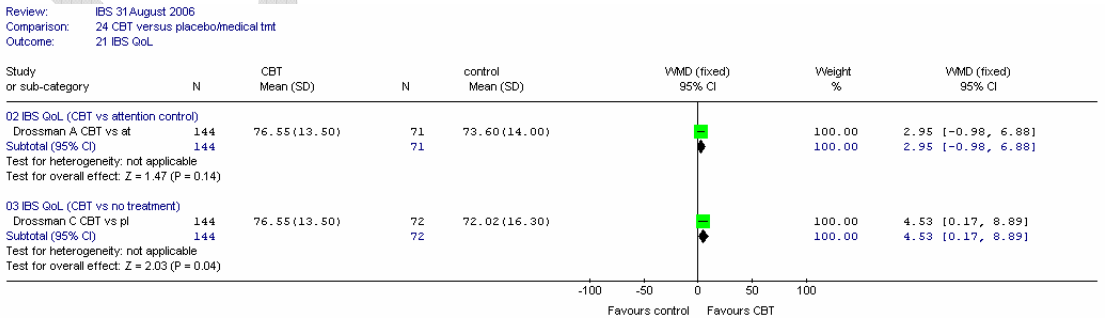
These were not reported in any of the studies.

4. Quality of life

The IBS-QOL scale (maximum 84; high is good) was used to report outcomes in Drossman (2003), whilst a scale of 'disruption of daily life' was used in Lynch (1989), although no standard deviations were reported.

In Drossman (2003), there was a small statistically significant difference between CBT and no treatment on the IBS QoL scale. There was no significant difference between CBT and attention control.

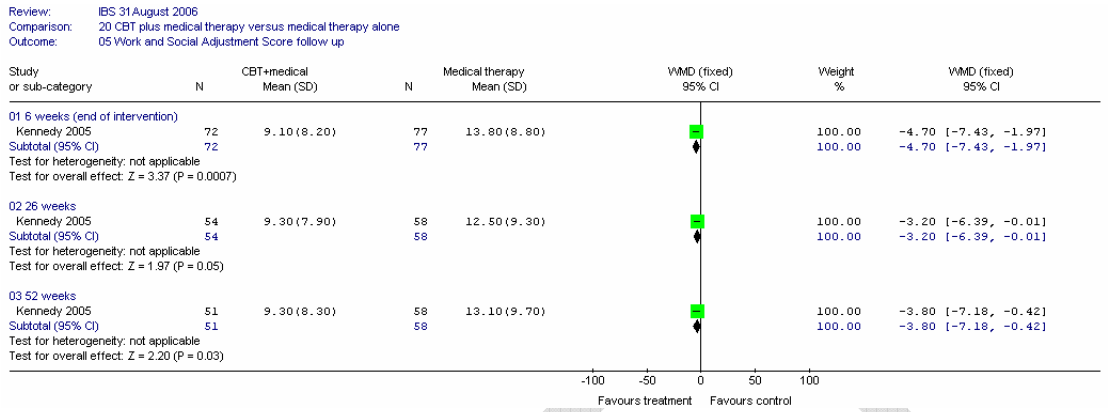
Figure 12



Kennedy (2005) (CBT+mebeverine versus mebeverine alone) also reported on a global 'Work and social adjustment score' (handicap in work, home, leisure and relationships; 0=not affected; 8=severely affected for each area; maximum total 40). This outcome was also

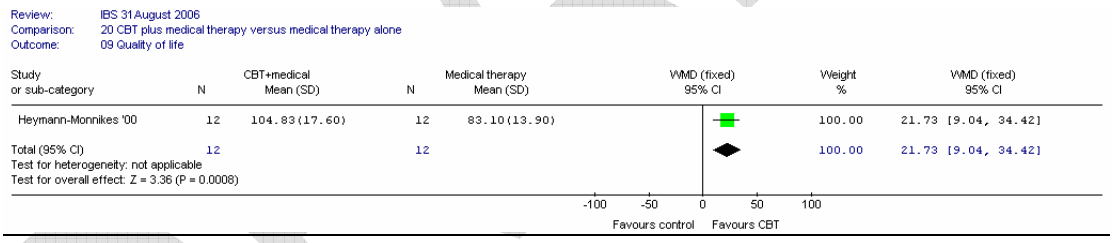
reported at 26 and 52 weeks follow-up. There was a statistically significant improvement in this score that was maintained over the 52 weeks of follow-up. The difference was fairly small though: MD at 6 weeks -4.70 (95%CI -7.43, -1.97) on a scale of 0 to 40.

Figure 13



Heymann-Monnikes (2000) (CBT + medical treatment versus medical treatment) reported scores on the GI quality of life instrument (scale maximum 144; high is good). There was a statistically and clinically significant improvement in quality of life for the CBT group.

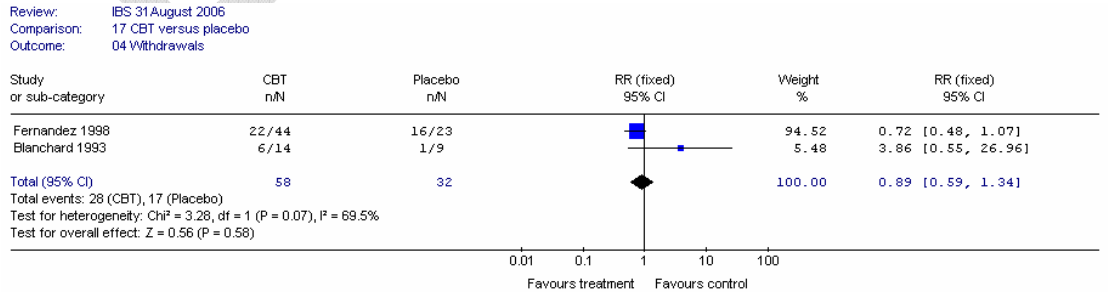
Figure 14



5. Number of patients withdrawing from study

Blanchard (1993) and Fernandez (1998) reported withdrawals from the study.

Figure 15



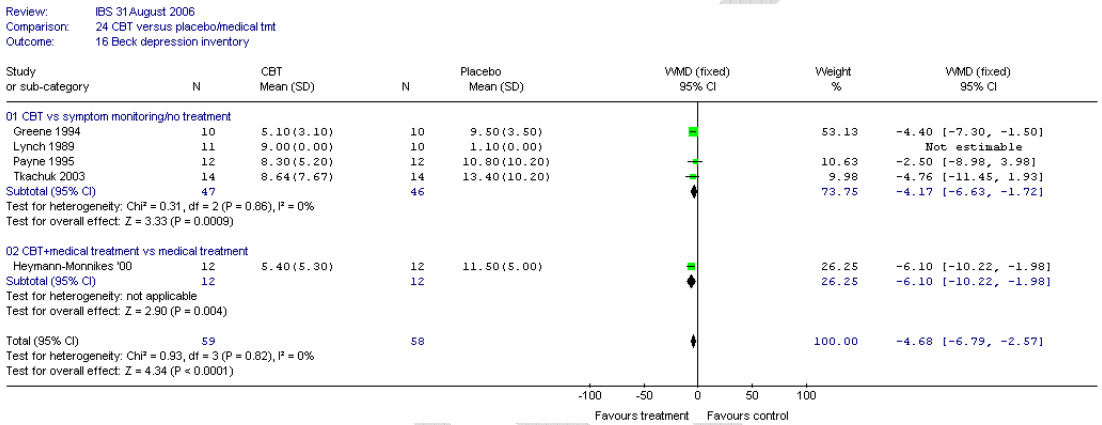
6. Mental health outcomes

Five studies (Greene 1994; Heymann-Monnikes 2000; Lynch 1989; Payne 1995; Tkachuk 2003) reported Beck depression inventory scores.

a) Beck depression inventory score

There was a statistically significant improvement in Beck Depression scores (scale maximum 63; high=bad), favouring CBT; WMD -4.68 (95%CI -6.79, -2.57), but the difference was fairly small. There was no heterogeneity between studies (I^2=0%, p=0.82).

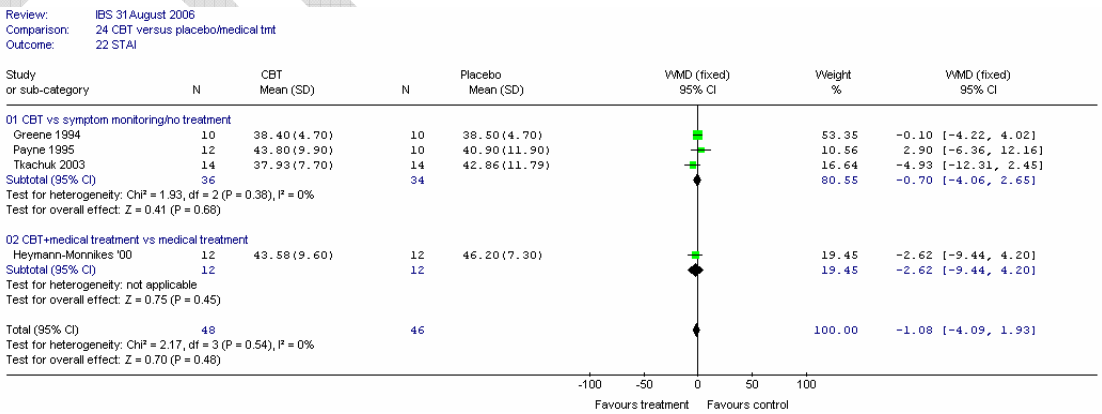
Figure 16



b) Overall anxiety and psychological distress: State-Trait Anxiety Inventory (STAI).

Four studies (Greene 1994; Heymann-Monnikes 2000; Payne 1995; Tkachuk 2003) reported anxiety using the State-Trait Anxiety Inventory (STAI) (scale range 20-80; high = bad). There was no significant difference between CBT and control.

Figure 17

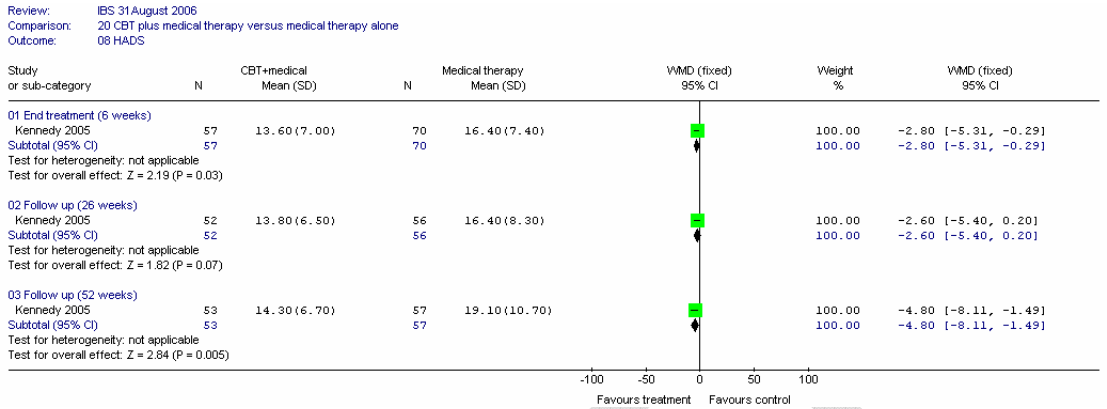


c) Psychological distress (HADS)

Kennedy (2005) (CBT plus mebeverine versus mebeverine) reported the HADS score (range 0 to 56; high=bad) at the end of treatment (6 weeks) and at follow-up at 26 and 52 weeks.

There was a small statistically significant difference favouring CBT which was maintained over 52 weeks; MD at 6 weeks: -2.80 (95%CI -5.31, -0.29).

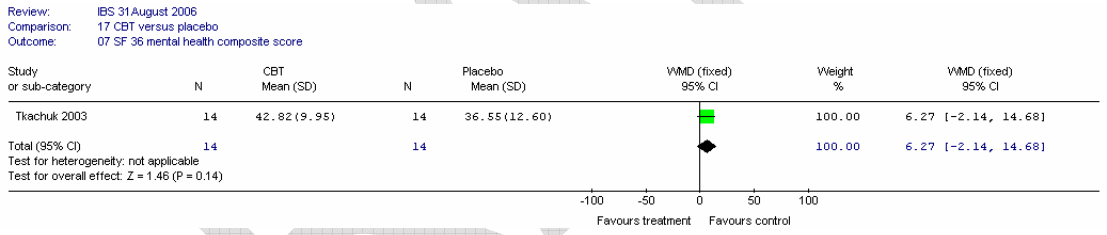
Figure 18



d) SF-36 mental health composite

One study (Tkachuk 2003) reported the SF-36 mental health composite score (maximum 100, high = bad). There was no significant difference between interventions.

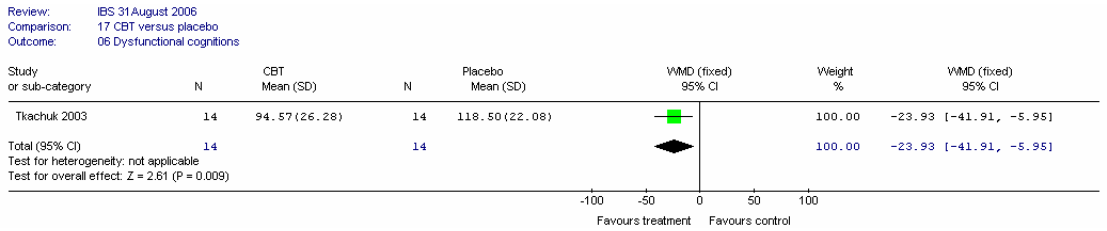
Figure 19



e) Dysfunctional cognitions score

One study (Tkachuk 2003) reported dysfunctional cognitions (scale 25-175; high=bad). This study showed a statistically significant improvement for the CBT patients compared with waiting list control with symptom monitoring. We noted that this study had the majority of patients with an Axis I diagnosis.

Figure 20



B. CBT type 1 versus type 2 (e.g. stress management versus contingency management)

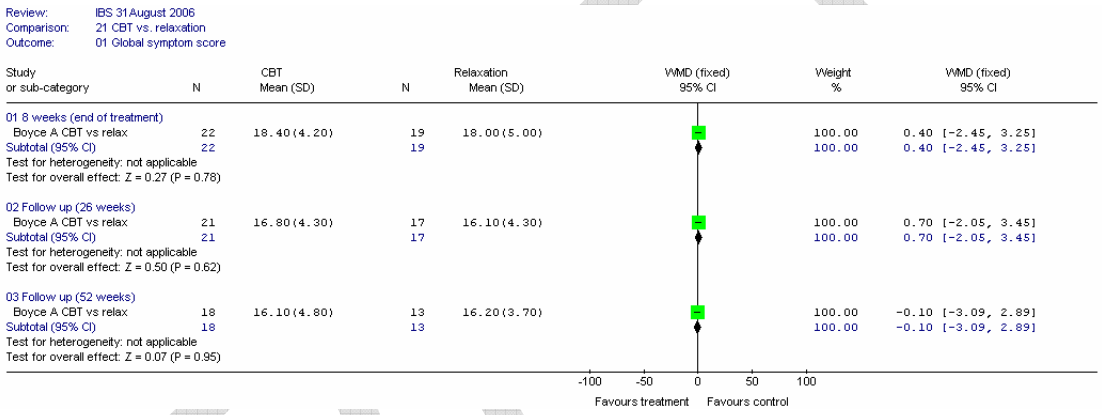
Boyce (2003) compared CBT with relaxation. Fernandez (1998) compared stress management with contingency management. Payne (1995) compared CBT with self-help groups.

B1. CBT versus relaxation

1. Global symptoms

Boyce (2003) reported Global IBS symptom score (symptom severity on a 0 to 48 scale) at the end of treatment (8 weeks) and at follow-up at 26 and 52 weeks. There was no significant difference between interventions at any time. We noted that there were large numbers of drop-outs, especially in the relaxation arm.

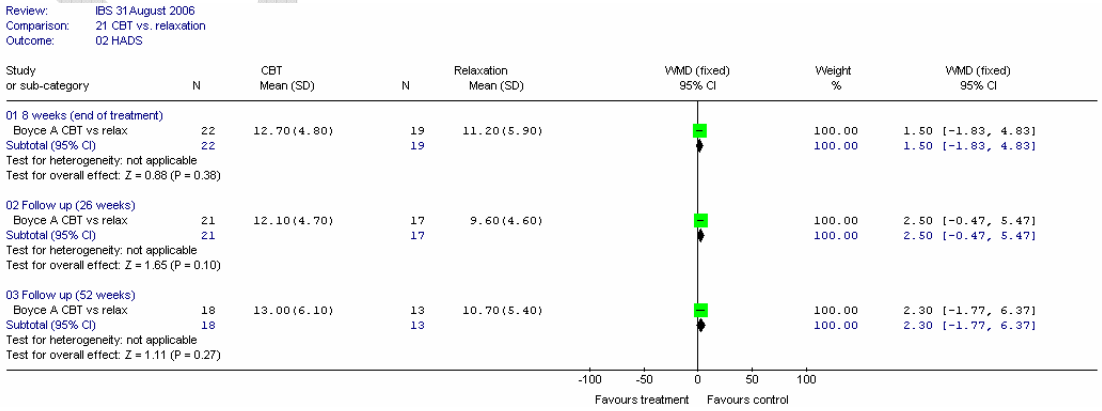
Figure 21



2. Mental health outcomes

Boyce (2003) reported the HADS score (0-56; high=bad) at the end of treatment (8 weeks) and at follow-up at 26 and 52 weeks. There was no significant difference between interventions.

Figure 22

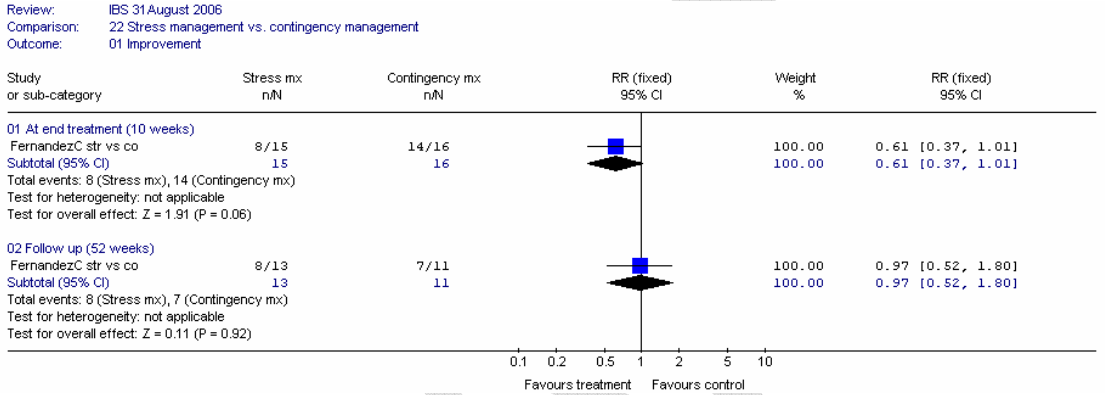


B2. Stress management versus contingency management

1. Global symptoms

Fernandez (1998) found that 8/15 of the stress management group and 14/16 of the contingency management group improved at the end of treatment (10 weeks). This study also reported global improvement in terms of the number of patients improved at 1 year follow-up: 8 of the 13 remaining patients in the stress management group versus 7 of 11 patients in the contingency management group. At both durations the confidence intervals were fairly wide and there was no statistically significant difference between interventions, however, at the end of treatment stress management was favoured.

Figure 23

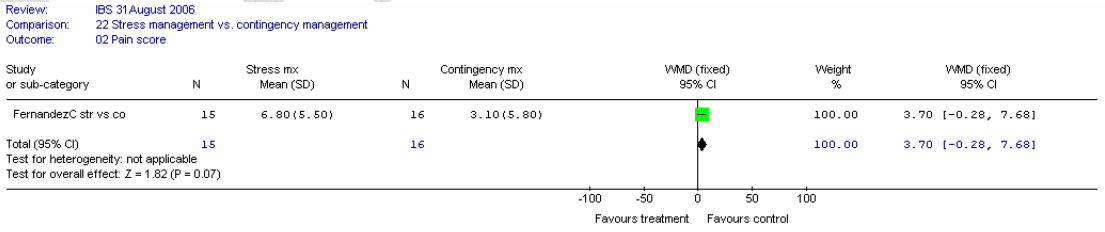


2. Individual symptoms

a) Pain

Fernandez (1998) reported mean pain scores on a scale of 0 to 4 (scores totalled for 1 week). There was no significant difference between interventions. No other individual symptoms were reported.

Figure 24



3. Number of patients withdrawing from study

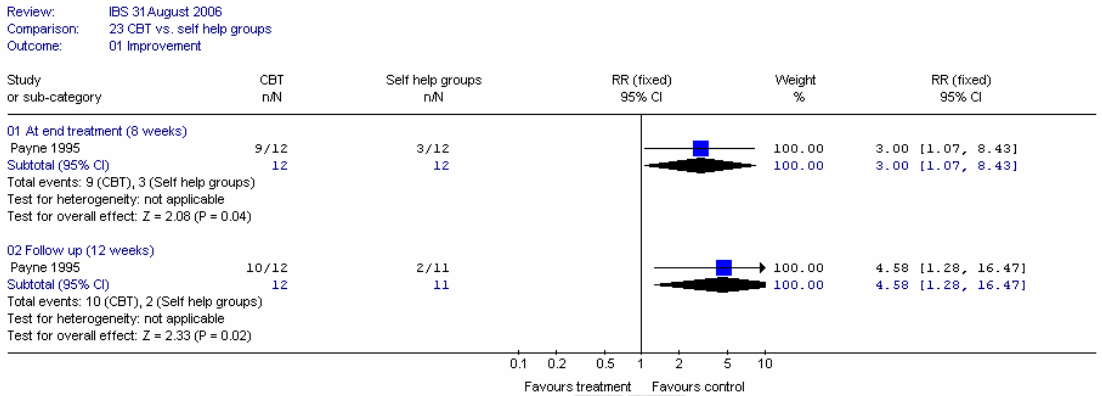
Fernandez (1998) reported 6/21 patients withdrawing from the stress management group compared with 7/23 for contingency management.

B3. CBT versus self help groups

1. Global symptoms

At the end of treatment (8 weeks), Payne (1995) reported that 9/12 CBT patients and 3/12 self-help group patients were improved after treatment. At follow-up (12 weeks) 10/12 CBT patients and 2/11 self-help group patients were improved. At both times there was a statistically significantly better result for the CBT group, but confidence intervals were wide.

Figure 25

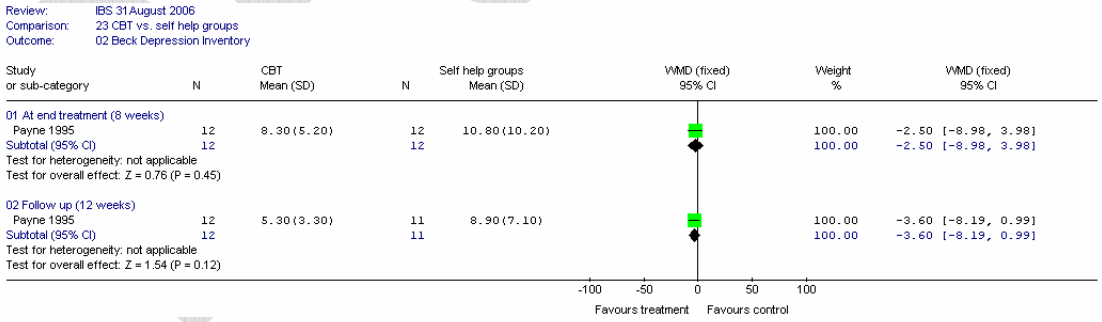


2. Mental health outcomes

a) Beck Depression Inventory

Payne (1995) reported Beck Depression Inventory scores (scale maximum 63; high=bad) at the end of treatment (8 weeks) and at follow-up at 12 weeks. There was no significant difference at either time.

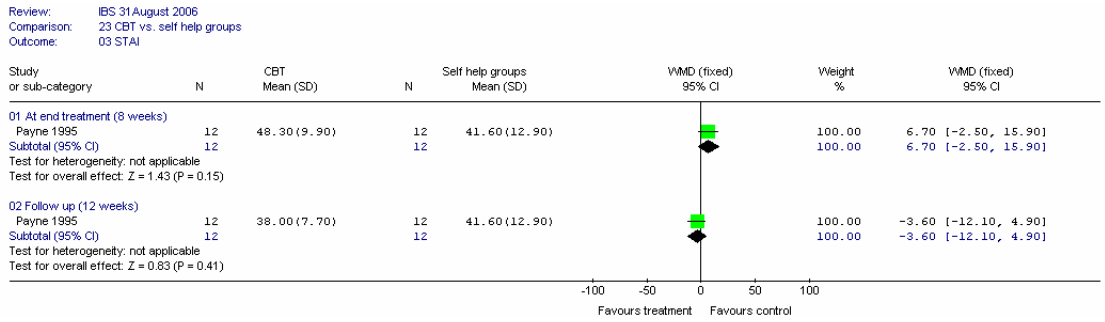
Figure 26



b) Overall anxiety and psychological distress: State-Trait Anxiety Inventory (STAI)

Payne (1995) reported STAI scores (20 to 80; high = bad) at the end of treatment (8 weeks) and at follow-up at 12 weeks. There was no significant difference between interventions.

Figure 27



C. CBT individual versus group

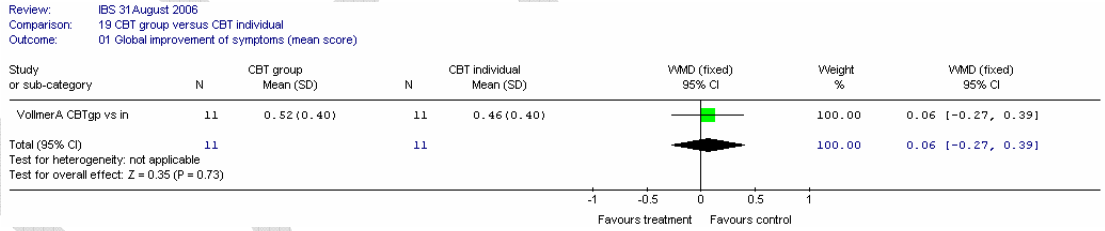
One study (Vollmer 1998) compared CBT on an individual basis with CBT on a group basis. Outcomes reported were global improvement in symptoms (mean score); global improvement in symptoms (number of patients); pain score, and; bloating score (0=not a problem; 4=debilitating symptoms).

1. Global outcomes

a) Global improvement in symptoms score

Vollmer (1998) reported the mean global improvement in symptoms score (CPSR; scale -1 to +1) for CBT group patients compared with individual CBT at the end of treatment. There was no significant difference between intervention, but the confidence interval was fairly wide, leading to uncertainty. No standard deviations were given for the follow-up scores.

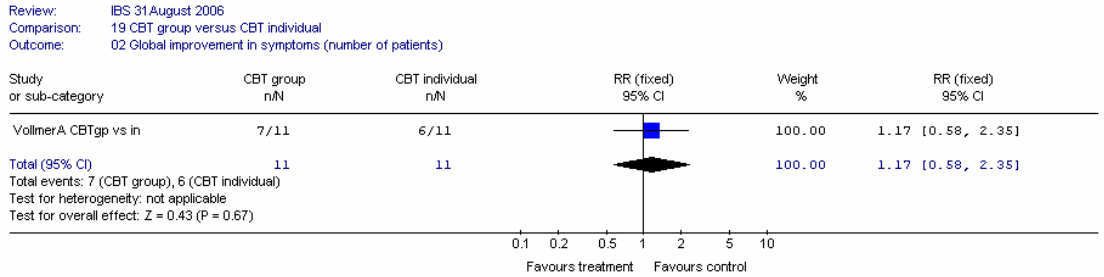
Figure 28



b) Global improvement in symptoms (number of patients)

Vollmer (1998) reported 7/11 patients improved with group CBT compared with 6/11 for individual CBT. There was no significant difference between intervention, but the confidence interval was fairly wide, leading to uncertainty.

Figure 29

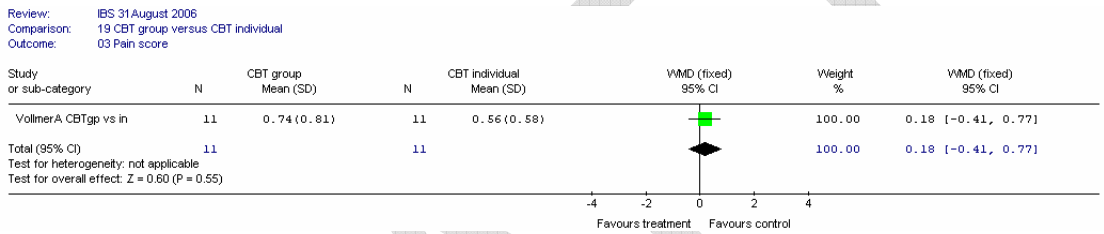


2. Individual symptoms

a) Pain

The mean pain score (scale 0 to 4) showed no significant difference between interventions.

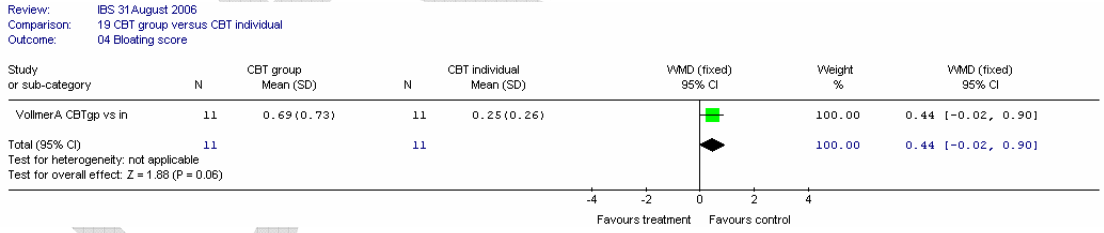
Figure 30



b) Bloating

The mean bloating score showed no significant difference between CBT group therapy and individual therapy, although individual therapy was favoured.

Figure 31



D. CBT versus medical therapy

Boyce (2003) compared CBT or relaxation with routine medical care. Corney (1991) compared behavioural psychotherapy (nurse behaviour therapist 6-15 one-hour sessions) with 'conventional medical treatment'. Fernandez (1998) compared stress management or contingency management with 'conventional medical treatment'.

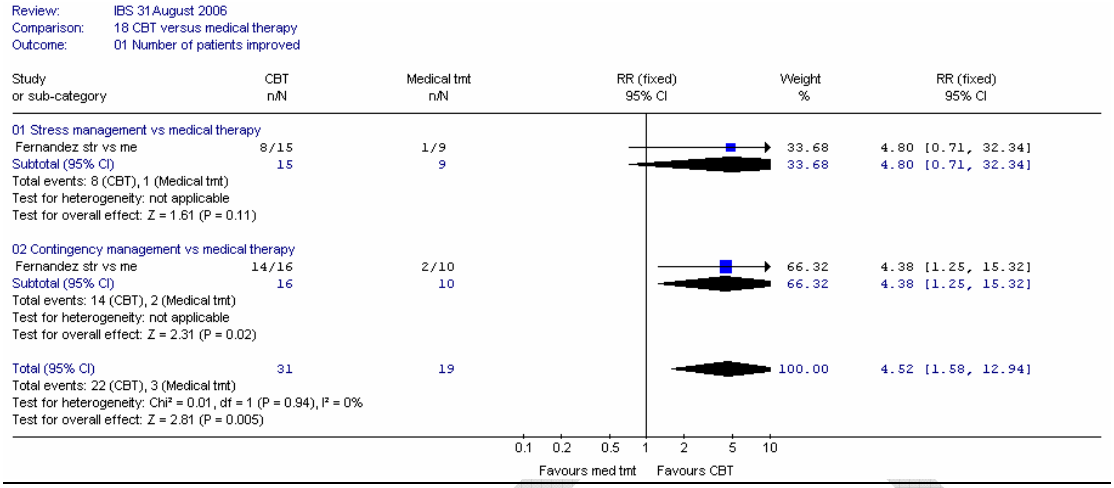
1. Global outcomes

a) Number of patients with improvement in global symptoms

One study (Fernandez 1998) reported the number of patients improved. Meta-analysis showed a statistically significant improvement for CBT compared with medical treatment, but

the confidence intervals were wide. At 52 week follow-up there were too many withdrawals for this to be reliable.

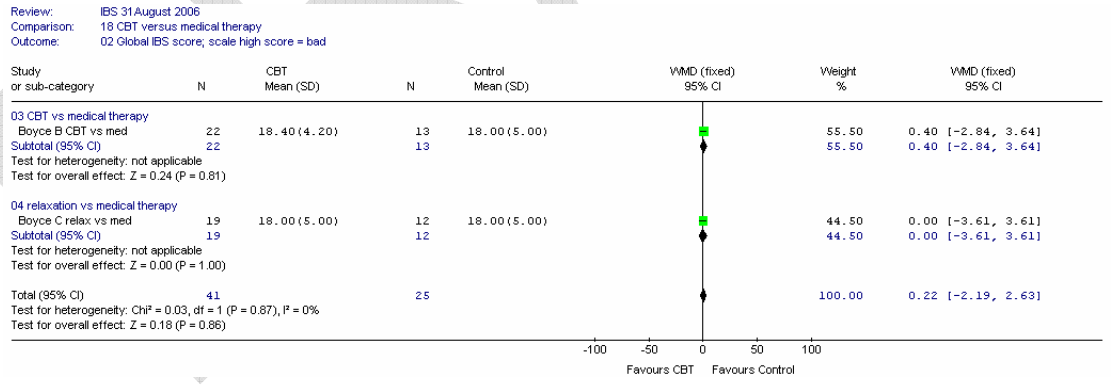
Figure 32



b) Global symptom score

Boyce (2003) (CBT or relaxation versus medical care) reported Global IBS symptom score (symptom severity on a 0 to 48 scale) in 66 patients at the end of treatment (8 weeks) and at follow-up at 26 and 52 weeks. At 8 weeks, there was no significant difference between interventions, although we noted that the drop-out rates were fairly high, especially for the relaxation arm of the study.

Figure 33

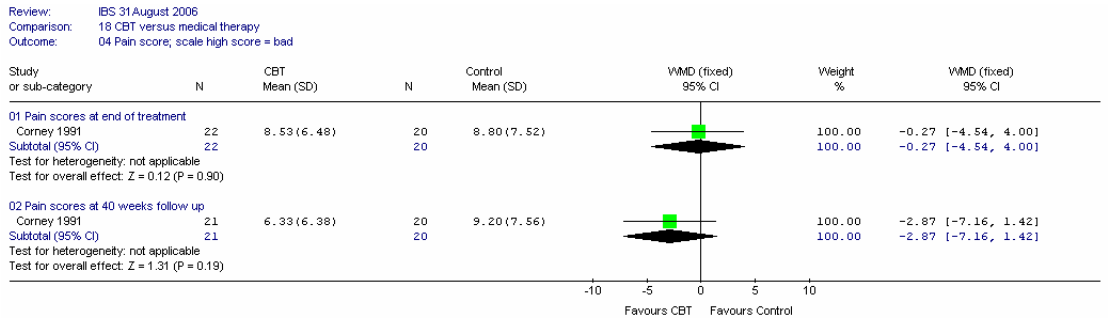


2. Individual symptoms

a) Pain

Corney (1991), in 42 patients, reported pain on a visual analogue scale (VAS) (the scale was unclear, but may be 0 to 8 scale in 3 dimensions) at the end of treatment (16 weeks) and at follow-up (40 weeks). There was no significant difference between interventions at either time, but the confidence intervals were fairly wide.

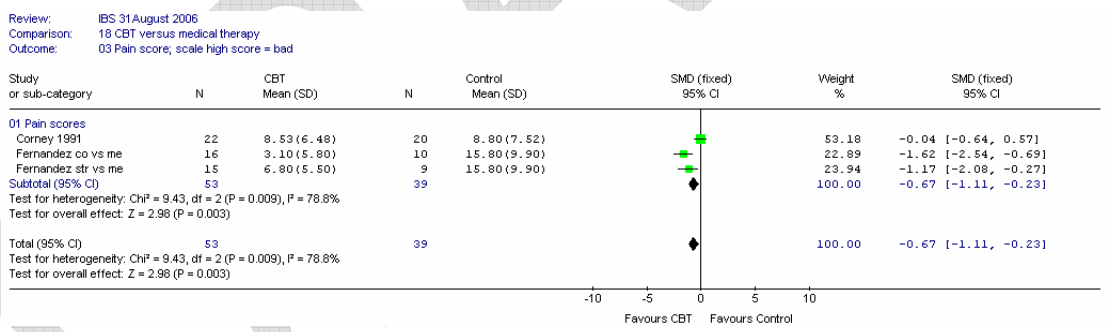
Figure 34



Fernandez (1998), in 50 patients, reported a pain score rated 0 (not a problem) to 4 (debilitating). There were significant differences between both active treatment groups and the medical treatment control group (p<0.001 for the contingency management group and p<0.022 for the stress management group). We noted that around 30% of each CBT group was missing data and 26% of the control group.

We combined these studies in a meta-analysis using standardised mean differences and found significant heterogeneity (I^2=79%, p=0.009). The source of heterogeneity was not clear, although one difference is that the CBT intervention in Corney (1991) was behavioural psychotherapy.

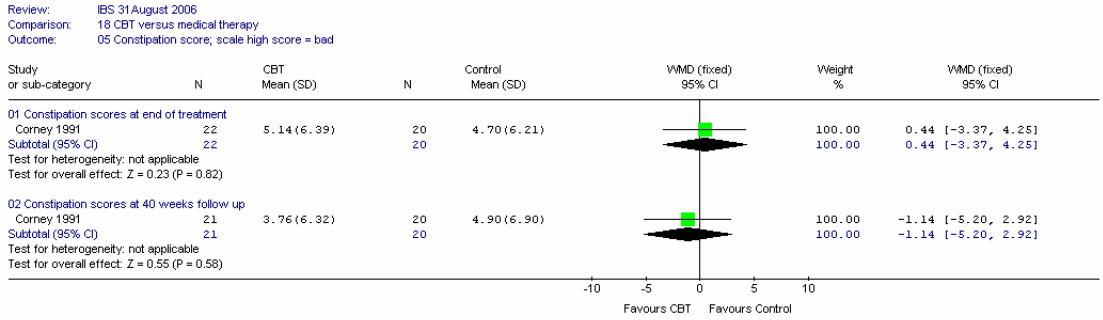
Figure 35



b) Bowel habits

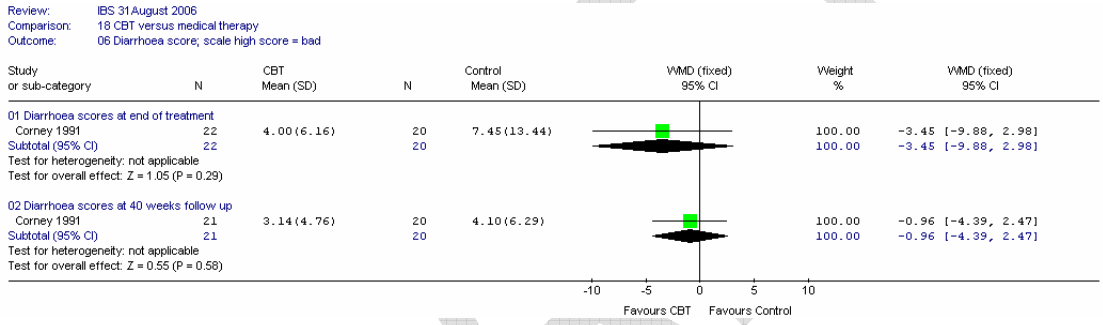
Corney (1991) reported constipation and diarrhoea on a visual analogue scale (VAS) at end of treatment (16 weeks) and at follow-up (40 weeks). The scale was unclear. There was no significant difference between interventions, although the confidence interval may have been wide.

Figure 36



For diarrhoea scores there was no significant difference, but the confidence interval was probably wide, depending on the scale.

Figure 37



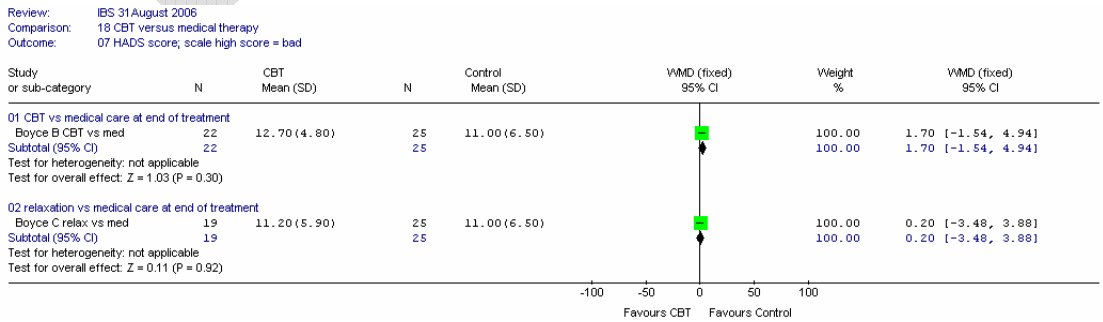
c) Number of patients withdrawing from study

Fernandez (1998) reported 6/21 withdrawals from the stress management group, 7/23 from the contingency management group and 4/23 from the medical treatment group.

d) Mental health outcomes

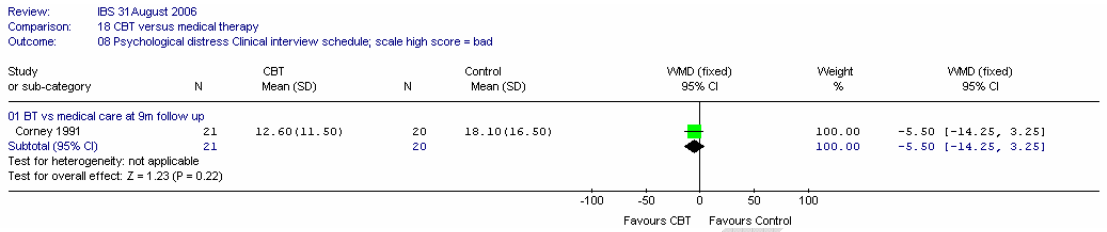
Boyce (2003) (CBT versus medical care) reported the psychological distress on the HADS scale (0-56, high is bad) at the end of treatment (8 weeks) and at follow-up at 26 and 52 weeks. At 8 weeks, there was no significant difference between interventions.

Figure 38



Corney (1991) reported psychological distress at 9 months follow up using the Clinical Interview Schedule (0-48, high=bad). There was no significant difference between interventions.

Figure 39



ECONOMIC LITERATURE FOR CBT

One relevant health economic analysis was identified on the cost-effectiveness of CBT in the management of IBS. Kennedy (2006) was a trial based economic evaluation conducted in the UK, which recruited patients from primary care with IBS symptoms of moderate or greater severity following 2 weeks of GP care and 4 weeks of mebeverine. Patients were randomised to receive either CBT plus mebeverine or mebeverine alone. CBT consisted of six 50-minute sessions delivered by face-to-face contact with a trained nurse. The primary effectiveness measure was global IBS symptom score. Direct and indirect costs were measured and cost-effectiveness acceptability curves were used to describe the probability that CBT plus mebeverine would be more cost-effective than mebeverine alone for various willingness to pay thresholds for a 10 unit change in global IBS symptom score.

The addition of CBT produced significantly better global IBS symptom scores at 3 months but the effect had diminished and was no longer significant after 6 and 12 months of follow-up. Similar results were observed in the secondary effectiveness measures and further details of the clinical outcomes have been given in the clinical effectiveness review. The mean intervention cost of CBT was £308 per patient. The addition of CBT did not reduce service costs at 3, 6 or 12 months. It is unclear whether service costs included intervention costs but given that the mean service costs at 3 months were less than £308 in both arms it is likely that they excluded the intervention cost. The CEACs presented show that CBT has a low probability (<25%) of being cost-effective when willingness to pay thresholds for a 10 unit change in global IBS symptom score are below £100. As this study did not provide an estimate of the cost per QALY for the addition of CBT to antispasmodic therapy, it was not particularly useful in determining whether recommending CBT for use in the NHS would result in the efficient use of NHS resources.

COST-EFFECTIVENESS ANALYSIS FOR CBT

This section describes the health economic analysis undertaken to inform recommendations on the use of CBT as a one-off intervention in the management of IBS. The general methods used

in the economic analysis for all management interventions are described in detail in Chapter 5 and the model inputs and assumptions relevant to this particular intervention are described below.

- The effectiveness of CBT in addition to usual care compared to usual care alone in people with refractory IBS was based on the number of patients with an improvement in global symptoms (at the end of treatment) for CBT vs no treatment, symptom monitoring or attention control. (RR 6.11 (95%CI 2.33, 16.07) for baseline rate of 9%, from Figure 3 of CBT review).
- We assumed that the response rate for CBT fell by 55% over the first 6 months and that there was no significant difference between CBT and usual care by the end of 12 months. This assumption was based on follow-up data for global symptom score from the study by Kennedy (2005). The mean difference, after adjustment for baseline difference, was used to scale the response rate after the end of treatment.
- The evidence included in the clinical effectiveness review did not allow a subtype specific estimate of clinical effectiveness to be estimated. Therefore it was assumed that CBT is equally effective in all IBS subtypes.
- CBT was assumed to be given over 12 weeks with alternative durations of 6 and 8 weeks considered in a sensitivity analyses, in which the costs are assumed to remain constant, but the effect is achieved over a shorter intervention period (i.e. the same number of sessions given at the same cost over a shorter time-frame).
- A 15 month time-frame was used so that the cost-effectiveness could be compared to against other behavioural therapies for which there was 15 month efficacy data.

Modelled response rates

In the basecase scenario the response rate of 25% in the no treatment arm was taken from the mean placebo arm response rate from the behavioural therapy trials. This represents the group of patients whose symptoms improve without any specific intervention. The RR for an improvement in global symptoms for CBT vs no treatment at the end of treatment is 6.11; therefore the modelled response rate in the intervention arm is 100% at the end of treatment (12 weeks). As shown in Figure 40, the response rate in the CBT arm decreases to 59% by 6 months and 25% by one year, based on the assumptions regarding fall-off in effectiveness described above.

We have also considered a maintained benefits scenario in which the response to CBT was assumed to be maintained for the one year after the end of treatment but we assumed no further benefit beyond that point.

The cost of CBT was calculated using the mean number and duration of sessions from the studies used to calculate the RR, giving a mean duration of 6.6 hours of CBT (excluding Payne

(1995) which did not provide sufficient information). To this we applied the unit cost for face-to-face time with a Cognitive Behavioural Therapist of £57 per hour (PSSRU 2006), which gave a total mean cost of £375 (95%CI £167 - £582).

The study by Kennedy (2005) found no significant difference in direct health care costs at 3, 6 or 12 months for CBT plus mebeverine compared to mebeverine alone in patients with severe symptoms after 3 months of mebeverine. It is likely that significant reductions in resource use would only be observed in patients who are high service users at baseline and who then experience a reduction in symptoms as a result of therapy. It is likely that the population included in the Kennedy (2005) study were not high service users since they were recruited from primary care after a failure to respond to only one intervention. This is in contrast with the Creed (2003) study which recruited patients from secondary and tertiary gastroenterology clinics who had a median of 6 visits to the doctor in the past 6 months, median symptom duration of 8 years and a median of 30 days with pain in the past 30 days. If an indirect comparison is made between CBT and psychotherapy, the odds ratios at the end of treatment suggest that CBT is at least as effective as the psychotherapy delivered in the Creed (2003) study (CBT compared to usual care OR=13.54, 95%CI 4.12-44.48, and psychotherapy vs usual care OR=2.44, 95%CI 1.28 – 4.67). It is therefore possible that similar reductions in resource use would be observed for CBT if the population were restricted to high service users. However, as there is no direct evidence for this we have excluded any reduced resource use for CBT in the basecase analysis. It was included in a sensitivity analysis by applying the reduction in resource use observed during the follow-up period of the Creed (2003) study for psychotherapy compared to usual care (£-4.08 per week, 95%CI-£8.11 to -£0.04) indirectly to CBT.

Figure 40: Response rate in the basecase analysis

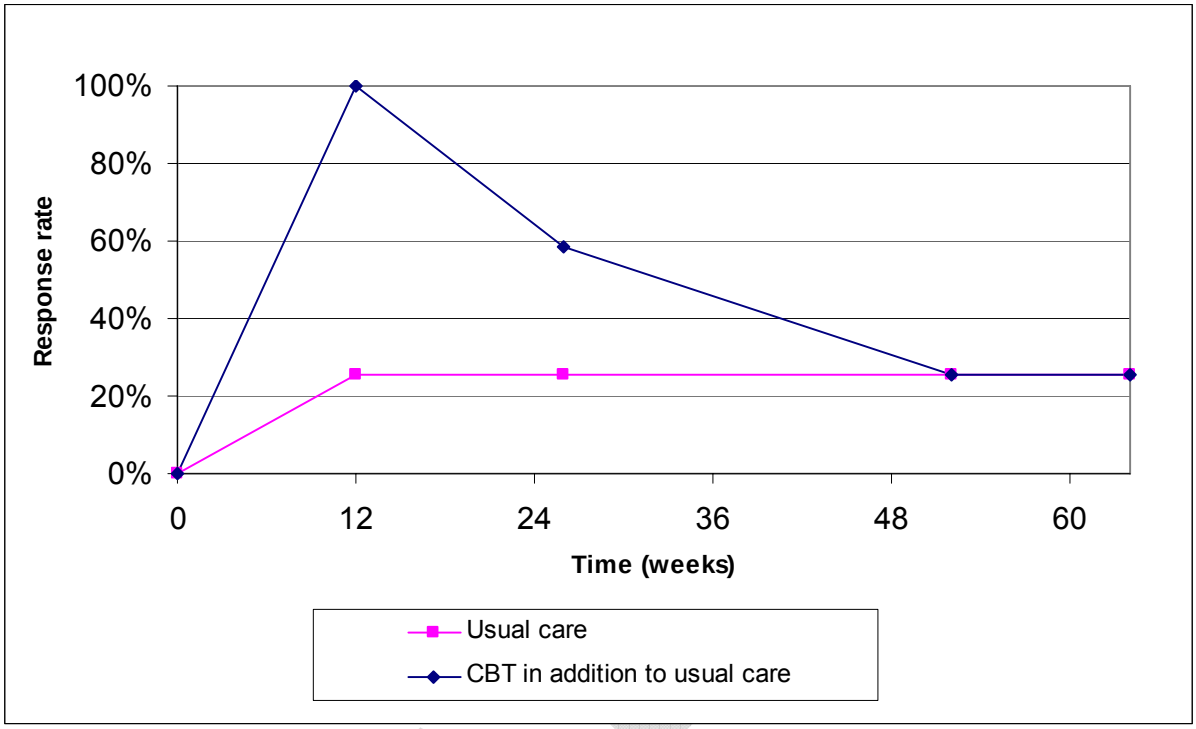
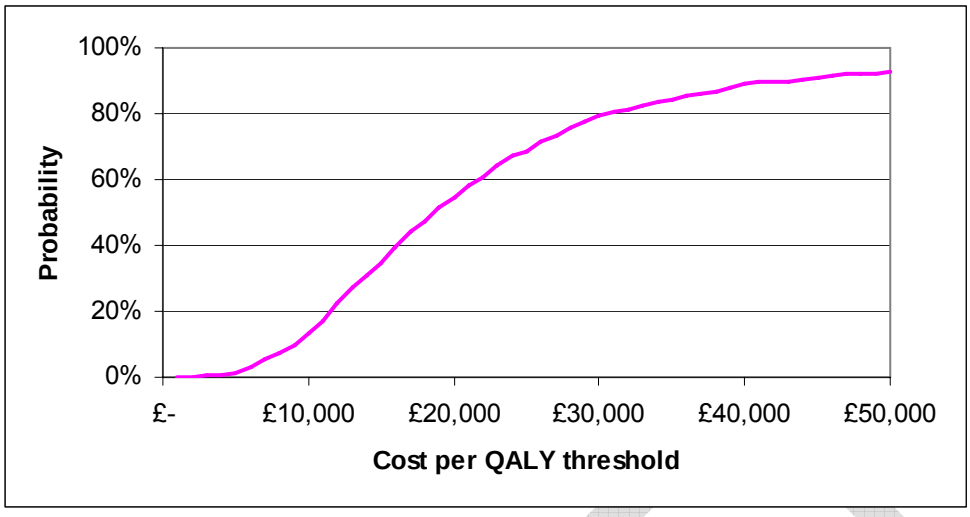


Table 2: Intervention specific parameters – CBT

Description	Value	Evidence
RR of response for intervention vs placebo (at end of treatment)	6.11 (2.33 – 16.07)	Meta-analysis of RCT evidence for improvement in global symptoms
Fall-off in effect at 6 months compared to end of treatment	56% (47% to 66%)	Kennedy (2005), global symptom score
Fall-off in effect at 12 months compared to end of treatment	100% (Fixed)	Kennedy (2005), global symptom score
CBT cost: equiv to 6.6 hours per patient	£375 (£167 - £582).	Weighted mean duration across studies and unit cost from Netten (2006)

CBT in addition to usual care for 100 patients with refractory IBS is estimated to gain an additional 2.24 QALYs for an additional cost of £37,460 compared to usual care alone under the basecase assumptions. The incremental cost per QALY is therefore £16,732. The probabilistic sensitivity analysis considers the uncertainty in this basecase estimate due to the uncertainty in the parameters used to estimate the cost-effectiveness. The CEAC in Figure 41 shows that given the parameter uncertainty, CBT in additional to usual care has a 55% probability of having a cost per QALY under £20,000 and a 79% probability of having a cost per QALY under £30,000, compared to usual care alone.

Figure 41: CEAC for CBT in addition to usual care compared to usual care alone in patients with refractory IBS



When we assumed that CBT is given over 6 or 8 weeks but at the same cost as in the basecase, the cost per QALY was £15, 771 or £16,079 respectively as the QALY gain was marginally increased (2.38 for 6 weeks and 2.33 for 12 weeks, compared to 2.24 in the basecase). However, it should be noted that in this sensitivity analysis it was assumed that the response rate in the placebo arm was also achieved over a shorter duration, so that the RR was applied at the end of the intervention period to the same baseline response rate of 25%. These results suggest that assuming a 12 week intervention period in the basecase may have slightly underestimated the cost-effectiveness of CBT but it didn't significantly bias the cost per QALY estimate.

The RR for an improvement in global symptoms for CBT has been applied to a 25% response rate in the comparator arm giving a 100% response rate at 12 weeks for CBT. However, in the CBT trials, the mean response rate in the control arm was 9%. The sensitivity analysis using this lower response rate in the comparator arm gave a cost per QALY of £27,129. As this sensitivity analysis significantly increased the cost per QALY estimate, the probabilistic sensitivity analysis was re-run using this lower response rate for the comparator arm. The mean cost per QALY from the 1000 samples was £25,940 and the cost per QALY had a 31% probability of being under £20,000 per QALY and a 48% probability of being under £30,000 per QALY.

The threshold analysis on utility gain showed that the response to treatment would need to provide more than 0.059 QALYs per annum to give a cost per QALY of under £20,000 in the basecase analysis. When the utility gain associated with a response to treatment was increased to 0.135 (equivalent to the QALY gain expected for a complete remission of symptoms) the cost per QALY was significantly lower at £8,837.

When we assumed no fall-off in response up to 52 weeks post-intervention the cost per QALY was £6,317. This estimate would be further reduced by any continued response beyond 52 weeks. When we assumed that there was no significant difference between CBT and usual care from 6 months, the cost per QALY increased to £28,184. Whilst these two scenarios represent extreme possibilities for the estimated fall-off in response, they demonstrate that the cost-effectiveness is sensitive to the rate of fall-off in response after the end of intervention.

When we assumed that the reduction in resource use observed in the one year after psychotherapy from the Creed (2003) study could also be expected in patients receiving CBT, the incremental cost for CBT reduced to £11,342 and the cost per QALY reduced to £5,066.

Table 3: Sensitivity results for CBT in addition to usual care compared to usual care alone for 100 patients with refractory IBS (all subtypes)

Scenario	**Usual care**		**Behavioural intervention and usual care**		**Incremental**
	Cost	QALY	Cost	QALY	Cost per QALY
Basecase	£0	2.02	£37,460	4.26	£16,732
Intervention given over 6 weeks	£0	2.13	£37,460	4.50	£15,771
Intervention given over 8 weeks	£0	2.09	£37,460	4.42	£16,079
Lower response rate in comparator arm (9%)	£0	0.72	£37,460	2.10	£27,129
No fall-off in effect for 1 year	£0	2.02	£37,460	7.95	£6,317
Effect falls off over first 6 months	£0	2.02	£37,460	3.35	£28,184
Resource use reduction from Creed (2003) study	£0	2.02	£11,342	4.26	£5,066
High utility gain of 0.135	£0.00	3.83	£37,460	8.07	£8,837
Threshold analysis on lowest utility	A cost per QALY of £20,000 is reached when the QALY gain associated with responding to treatment lies between 0.059 and 0.060.				

Further analyses on the cost-effectiveness of CBT compared to other behavioural interventions are given in section 9.7.

EVIDENCE STATEMENTS

For this review, the evidence was assessed using the GRADE process and tables are shown in Appendix F. The following evidence statements are derived from the GRADE tables.

1. There is good evidence to show a significant global improvement in symptoms for CBT when compared with no treatment/symptom monitoring, mainly in patients with psychiatric co-morbidities and refractory IBS.

2. There is moderately good evidence to show a borderline global improvement in symptom score for CBT in addition to mebeverine compared with mebeverine alone, at 26 weeks follow up, but there is no significant difference at 52 weeks, in primary care patients with about 50% psychiatric co-morbidities and IBS that did not respond to three months treatment with mebeverine.

3. There is moderately good evidence to show no significant difference in pain and bloating for CBT when compared with no treatment/symptom monitoring in patients, most of whom had psychiatric co-morbidities

4. There is limited evidence to show no significant effect on constipation, but a small, significant improvement in diarrhoea for CBT when compared with no treatment/symptom monitoring in patients, most of whom had psychiatric co-morbidities

5. There is weak evidence to show no significant difference in quality of life (IBS QoL) for CBT when compared with no treatment/symptom monitoring in patients with psychiatric co-morbidities

6. There is moderately good evidence to show a significant global improvement in symptom score when CBT is added to mebeverine when compared with mebeverine alone.

HEALTH ECONOMIC STATEMENT

Evidence from a trial based economic evaluation showed that the addition of CBT to antispasmodic therapy does not result in lower service costs at 3, 6 or 12 months in individuals with symptoms of moderate or greater severity after 2 weeks of GP care and 4 weeks of mebeverine.

Evidence from a decision analytic model showed that the addition of CBT to usual care is cost-effective in individual with refractory IBS although the cost-effectiveness was sensitive to uncertainty around the proportion of patients experiencing an improvement in global symptom score with usual care alone.

GDG DISCUSSION

The majority of people in the randomised trials had psychiatric co-morbidities and it is the view of the GDG that these could have skewed data when seeking to apply trial findings to the IBS population as a whole.

Generally, CBT has a positive benefit in improving global symptom scores for people with IBS in the trials. Meta-analysis demonstrates the benefit of CBT in producing an initial big treatment effect. The GDG view is that people with IBS are likely to feel that they are coping better with their symptoms, whilst recognising the potential for a treatment tail off. Even though there is some evidence that there is sustainable treatment effect, tail-off is usually addressed by a top up session.

CBT has not generally been used as a first line therapy for the management of IBS, but the GDG agreed that this needs to be investigated further. The GDG therefore decided to include CBT in one of its top five research recommendations.

EVIDENCE TO RECOMMENDATION

The evidence to recommendation statement for psychotherapy, CBT and hypnotherapy is detailed in section 9.8.

The combined guideline recommendation for psychotherapy, CBT and hypnotherapy is also stated in section 9.8.

9.6 Hypnotherapy

SELECTION CRITERIA

The selection criteria described in the general methodology section were used, except that crossover studies were excluded as inappropriate due to the carry-over effect of the hypnotherapy interventions.

The following comparisons were included:

- Hypnotherapy versus waiting list control, or symptom monitoring only
- Hypnotherapy versus usual medical care
- Hypnotherapy individual versus hypnotherapy group
- Hypnotherapy versus another intervention (e.g. psychotherapy or relaxation).

SEARCH STRATEGY FOR IDENTIFICATION OF STUDIES

Searches were performed on the following core databases: MEDLINE, EMBASE, CINAHL, and *The Cochrane Library* (1966 to current day with guidance from the GDG). Additionally, the

PSYCINFO database was searched for this review. The search strategies are listed in Appendix B.

The titles and abstracts from the search strategy were assessed. Nineteen were identified to be potentially relevant to the review and these papers were retrieved in full. The reference lists of the retrieved studies were inspected for further potential papers, but none were identified. The 13 excluded studies are listed in Appendix E, along with reasons for exclusion.

Study Design

Six parallel group design randomised trials were included (Forbes 2000; Galovski 1998; Harvey 1989; Palsson 2002; Roberts 2006; Whorwell 1984). Further details are given in the included studies table.

Four of the studies were carried out in the UK (Forbes 2000; Harvey 1989; Roberts 2006; Whorwell 1984). The remaining studies were carried out in the USA (Galovski 1998; Palsson 2002). Trials lasted between 6 and 12 weeks. One study was conducted among patients recruited from primary care (Roberts 2006); the others were in secondary care.

The total number of patients in the studies ranged from 12 to 81. Only two studies included more than 25 patients in a treatment arm (Forbes 2000; Roberts 2006). Forbes included 25 and 27 patients in the two treatment arms respectively. In Roberts (2006) a power calculation was done, which suggested that 50 patients per group would be needed; however, the study only recruited 40 patients in one arm and 41 patients in the other, so it was underpowered. On the basis of this power calculation, it is likely that all the studies are underpowered.

Population

All the studies included only patients with IBS. None of the studies reported the number of patients with bloating or whether the symptoms were post-infective, and it was unclear if the patients had pain at baseline. The mean age of patients was around 40 years, with those aged between 18 and 65 years included. All the studies included more women than men.

IBS was stated, or implied, to be refractory all of the studies. The patients in Forbes (2000) had had IBS for more than six months and the inclusion criteria required that they had failed on conventional treatments, with the exception of antidepressants. Palsson (2002) stated that the patients all had symptoms refractory to standard medical management. Galovski (1998) had patients with a mean duration of IBS symptoms of six years (range 0.5 to 17years). Harvey (1989) did not report the duration of symptoms, but stated that the patients had refractory IBS. Roberts (2006) included primary care patients with IBS for more than six weeks, who were said to have failed conventional management. Whorwell (1984) included patients with severe

refractory IBS who had not responded to any therapy over at least one year (the mean number of therapies previously tried per patient was six).

The patients in Forbes (2000) and Roberts (2006) were allowed to continue pre-existing therapy for IBS, including antispasmodics and antidepressants; those in Palsson (2002) discontinued their IBS medication. Continued medication use was not stated in Galovski (1998), Harvey (1989), or Whorwell (1984).

In Galovski (1998), 67% of patients had an Axis I diagnosis; one patient with bipolar disorder with a current manic state was excluded. Forbes (2000) stated that 19/52 (37%) of patients were considered to be psychiatric cases according to the GHQ. Harvey (1989) reported that 8/22 (36%) had psychological problems (GHQ≥5). Patients requiring psychotropic medications were excluded from Palsson (2002). Psychiatric co-morbidities were not stated in the other two studies (Roberts 2006; Whorwell 1984).

Interventions

The hypnotherapy interventions were all 'gut-directed hypnotherapy' based on the methods described by Whorwell in 1984. All the trials assessed individual therapy; in one trial the comparator was group hypnotherapy (Harvey 1989). The studies varied in how hypnotherapy was delivered: Roberts (2006) had 5 weekly half-hour sessions and follow-up data were available at 3, 6 and 12 months (not end of therapy). Harvey (1989) had four 40-minute sessions over 7 weeks; Palsson (2002) had seven 45-minute sessions over 12 weeks; Forbes (2000) had six 30-minute sessions over 12 weeks, and; Whorwell (1984) had seven 30-minute sessions over 3 months.

Hypnotherapy was compared with relaxation training, psychotherapy, symptom monitoring, waiting list control, and usual care. In one trial (Harvey 1989), hypnotherapy in groups was compared with individual therapy. In the Whorwell (1984) trial, hypnotherapy was compared with 'psychotherapy', but author communication described this as 'supportive listening', more akin to attention control than psychotherapy. In Roberts (2006), IBS medication was continued in both groups, so that their comparison, hypnotherapy versus usual management, was, in reality, hypnotherapy versus no treatment. It was agreed to combine the comparators, waiting list control, attention control, symptom monitoring and no treatment / usual care.

The following comparisons were included:

- Hypnotherapy versus: a waiting list control group; attention control; symptom monitoring only, or; usual care (four studies: Galovski (1998); Palsson (2002); Roberts (2006); Whorwell (1984)):
    - Hypnotherapy versus waiting list control (Palsson 2002)
    - Hypnotherapy versus symptom monitoring (Galovski 1998)

  - Hypnotherapy versus usual management (conventional medication in primary care) (Roberts 2006)
  - Hypnotherapy versus attention control + placebo tablet (both therapies delivered by same therapist) (Whorwell 1984);
- Group hypnotherapy versus individual hypnotherapy:
  - Harvey (1989);
- Hypnotherapy versus another intervention:
  - Hypnotherapy versus audiotape on relaxation (tape produced by same therapist) (Forbes 2000).

METHODOLOGICAL QUALITY

The results of the quality assessment for included trials are shown in Appendix D.

One study (Forbes 2000) reported an adequate method of randomisation (computer-generated random numbers); the other studies did not state the method. Allocation concealment was partially adequate in one study (Roberts 2006, sealed envelopes); the other studies were unclear. The patients were not blinded (because of the type of intervention). However, the GDG did not consider this to be important for the behavioural interventions. One study (Roberts 2006) described an *a-priori* power calculation, but did not meet the required number of patients during recruitment.

The comparability of groups at baseline varied amongst the studies:

- Two studies demonstrated baseline comparability of the groups (Forbes 2000; Galovski 1998)
- Two were mainly comparable:
  - Roberts (2006) reported that there were more males in the intervention group (8/40 versus 4/41); and there were some differences in baseline quality of life scores (on three of eight subscales, p value not given)
  - Whorwell (1984) reported that bowel habit was more severely disordered in patients receiving hypnotherapy than in control patients (intervention group baseline score 17.2 versus controls 12.8; where abnormality of bowel habit was scored 0=none, 1=mild, 2=moderate or 3=severe, and scores totalled over 7 days, i.e. scale from 0 to 21, p=0.005 for baseline difference);
- Two did not state the comparability for the randomised population (Harvey 1989; Palsson 2002).
  - However, Palsson (2002) gave baseline pain and bloating scores and the proportion of hard/loose stools only for completers, and these were not comparable across groups (more severe pain and bloating and lower proportion of hard/loose stools for the intervention group).

All the patients were followed up in two studies (Galovski 1998; Whorwell 1984). There were 20% or fewer drop-outs overall in two studies (Harvey 1989; Forbes 2000). In Harvey (1989), 3 out of 36 [8%] were missing and Forbes (2000) had 7/52 missing data for symptom diaries, but only 25/52 (48%) complied with the follow up for psychological outcomes. One study (Palsson 2002) had more than 20% missing data in the control group: the 6 drop-outs in the study were all from the control group (i.e. 40% drop-out in this group), however, the study stated that the drop outs were related to non-treatment related causes such as relocation, scheduling difficulties and unrelated medical problems. Nevertheless we regarded this study with caution because this unequal drop-out could still have introduced a bias. In the other study (Roberts 2006), data were missing for 18% of patients at 3 months; 17% at 6 months and 35% at 12 month follow-up. However, the study stated that analysis indicated that the missing data were 'missing completely at random', so that the results for the missing data would not be significantly different from those that completed the study.

Overall, there is a risk of bias in the Palsson (2002) study for the pain and bloating outcomes, and the uneven drop-out rates between the groups should be taken into consideration (40% drop-out among controls versus none from the intervention group) and the differences at baseline. Forbes (2000) was considered at high risk for the psychological outcomes. The Roberts (2006) 12 month follow-up data should be regarded with caution, also due to the fairly high drop-out rate (35%). The difference in baseline for bowel habit should be taken into consideration in the Whorwell (1984) study.

RESULTS

A. Hypnotherapy versus waiting list control group, attention control, symptom monitoring only or usual management

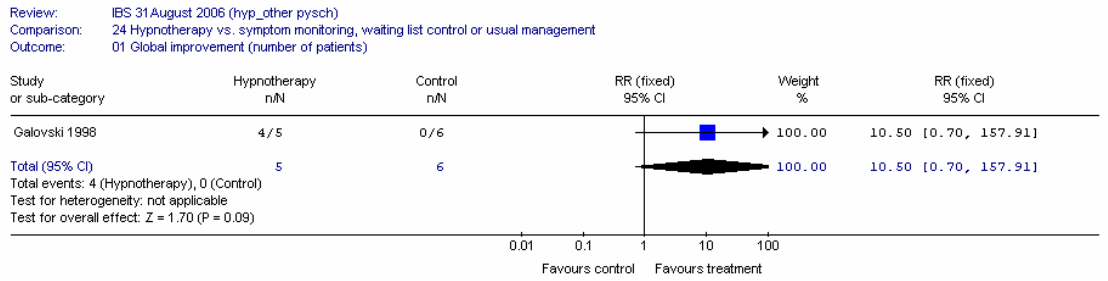
Four studies compared hypnotherapy with a waiting list control group; attention control; symptom monitoring only, or; usual management in patients with IBS (Galovski 1998; Palsson 2002; Roberts 2006; Whorwell 1984).

1. Global symptoms

a) Number of patients with global improvement in symptoms

This outcome was reported by Galovski 1998 at 6 weeks for hypnotherapy versus symptom monitoring in 11 patients.

Figure 1



The confidence interval was too wide to determine if there is an effect (but see next section for further evidence on global improvement of symptoms – number of patients).

b) Global improvement of symptoms score

The Whorwell (1984) study in 30 patients reported the overall improvement of symptoms and general wellbeing, scored weekly on a scale of 0 to 3 (where 0 is no improvement and 3 is maximum improvement). From a baseline score of 0 in both groups, patients in the hypnotherapy group increased to a mean weekly value of 2.95 and those in the psychotherapy group increased to 0.52, i.e. a difference of 2.43. This was reported to be statistically significant ($p<0.0001$), i.e. a large effect.

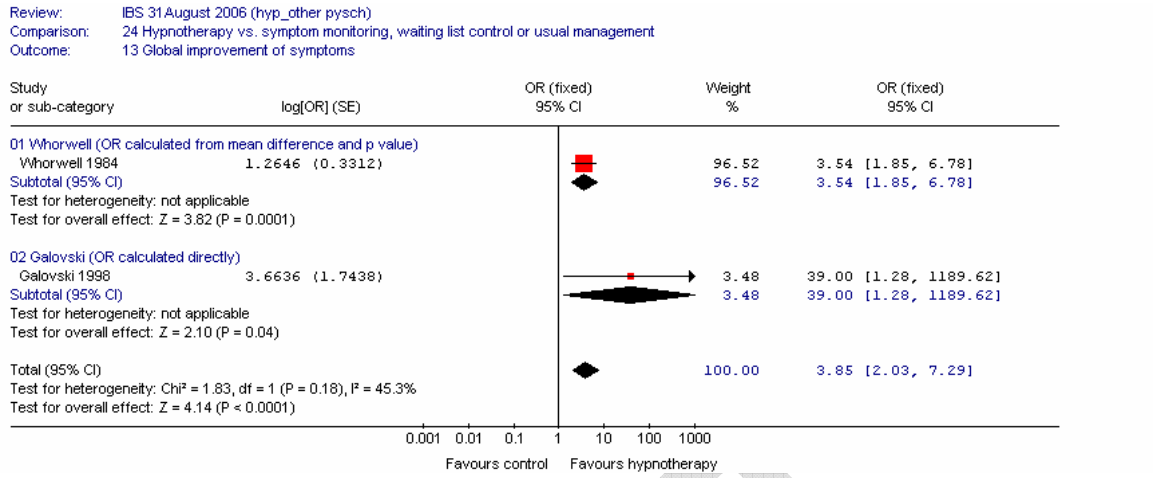
Chinn (2000) introduced a statistical approach that re-expresses standardised mean differences as odds ratios, according to the following simple formula:

$$\log OR = (\pi/\sqrt{3})\ SMD$$

The standard error of the standardised mean difference can be converted to the standard error of the log odds ratio by multiplying by $\pi/\sqrt{3} = 1.8140$. We carried out this procedure for Whorwell (1984) in order to combine the data with those of Galovski (1998). This involved calculation of the standard error from the p value, conversion of the mean difference to standardised mean difference by dividing both MD and standard error by the standard deviation and then converting to log OR.

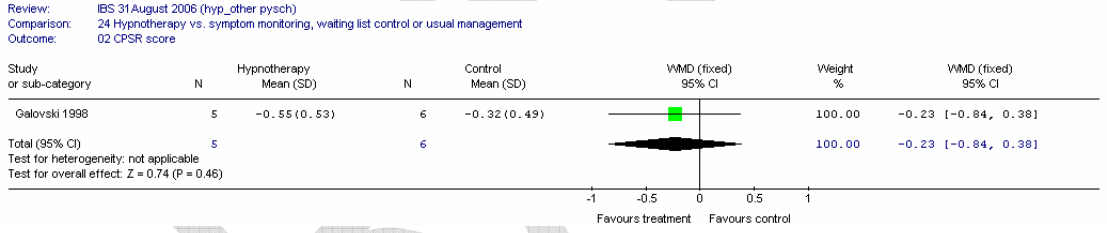
Meta-analysis of the two studies, in 41 patients, gave a pooled odds ratio of 3.85 (95%CI 2.03, 7.29), with non-significant heterogeneity (I^2=45%, p=0.16). This was statistically significant, in favour of hypnotherapy.

Figure 2: Meta-analysis for global improvement of symptoms (number of patients)



Galovski (1998) reported the global improvement of IBS symptoms at six weeks in 11 patients using the Composite Primary Symptom Reduction (CPSR) score; CPSR represents the proportional reduction in the score from baseline; scale -1 to +1. The confidence interval was too wide to determine if there was a difference between interventions.

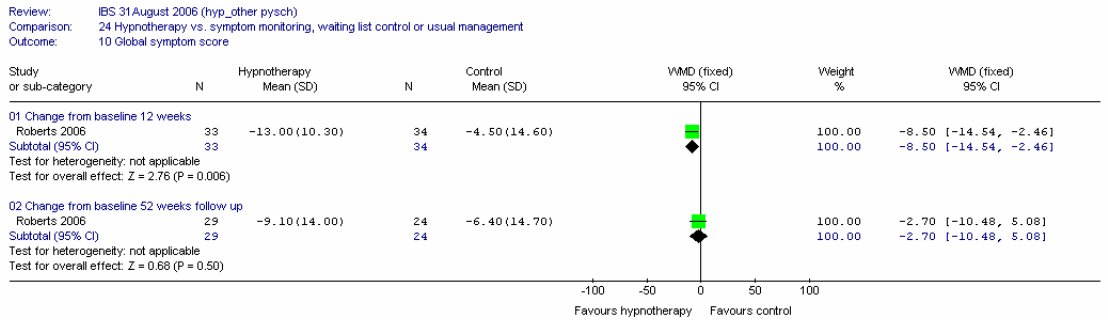
Figure 3



c) Global symptom score

The change over baseline in global symptom score was reported by Roberts (2006) at 12 weeks (about 7 weeks after the end of treatment) for hypnotherapy versus usual IBS care in 81primary care, refractory patients and at 26 and 52 weeks follow-up. 26 week standard deviations were not given, although the means were, and we noted that there was 35% missing data at 52 weeks (although the authors showed this to be missing-at-random, which made the results more acceptable). There was a statistically significant improvement in symptom score at 12 weeks, favouring hypnotherapy. The scale was not given, but reference was made to a questionnaire using 22 items each rated at 1-7 (7=high) (Wiklund 2003). This would have meant a maximum score of 154, but this was not entirely clear. The baseline scores were about 40, so a change of 8.5 units seems a reasonable effect size. At six months, the decreases in symptom score were 10 and 8 for the intervention and control groups respectively, i.e. a change of -2 units. At 12 months (follow-up) the change in symptom score was -2.70 (95%CI -10.48, 5.09), i.e., no longer significant.

Figure 4



2. Individual symptoms

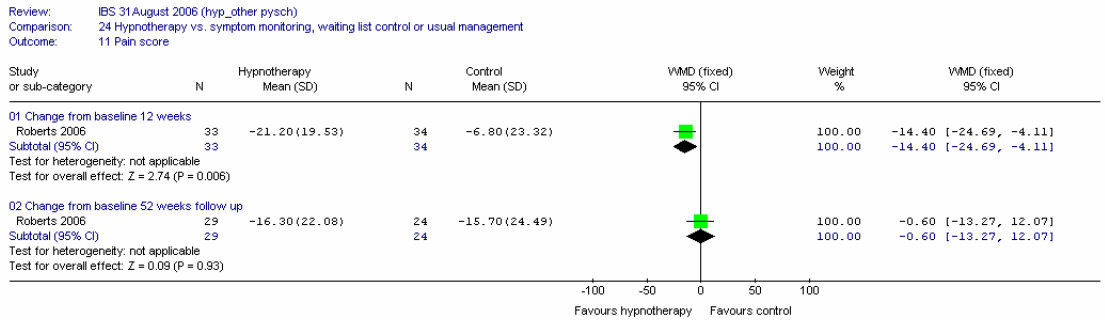
a) Pain

A pain score was reported by three studies (Palsson 2002; Roberts 2006; Whorwell 1984), all at 12 weeks. Palsson (2002) compared hypnotherapy versus waiting list control in 30 patients; neither had concurrent IBS medical treatments, and recorded pain score on a scale of 0 to 4 recorded over 14 days, where 0=none, 1=mild, 2=moderate, 3=severe and 4=incapacitating, i.e. maximum 56. We noted that this study had 40% missing data in the control group, in addition, there was a significant difference in the baseline pain score for completers in the intervention group was of 7.9 units, which was large compared to the difference in effect size (11.8 units). Therefore the results from this study were considered to be potentially biased and are therefore not reported here.

Roberts (2006) showed a significant difference in the pain score of -14.40 (95%CI -24.69, -4.11) at 3 months, but this was no longer significant at 12 months. The baseline scores were 53-55. Again there was 35% missing data, said to be missing-at-random.

Whorwell (1984) recorded a pain score (0-3 recorded over 7 days, where 0=none, 1=mild, 2=moderate, 3=severe, i.e. maximum 21). From a baseline score of 13 in both groups, patients receiving hypnotherapy reduced their mean score to 2.2 (i.e. a fall of 10.8), while those on psychotherapy had a mean score of 11.6 at 12 weeks (i.e. a fall of only 1.4); no standard deviations were given, but the difference between groups of -9.4 was reported to be statistically significant (p<0.0001).

Figure 5



b) Bloating

Two studies reported a bloating score at 12 weeks (Palsson 2002; Whorwell 1984). Palsson (2002) used a scale of 0 to 4 recorded over 14 days, where 0=none, 1=mild, 2=moderate, 3=severe and 4=incapacitating. However, the baseline values for bloating were much lower for the control group (data given for completers only, mean 13.6 at baseline) than the intervention group (mean 20.3 at baseline), and there was 40% missing data in the control group. The study was therefore considered to be confounded for this outcome and was not considered further.

Whorwell (1984) measured a bloating score (0-3 recorded over 7 days, where 0=none, 1=mild, 2=moderate, 3=severe). From a baseline score of around 16, patients receiving hypnotherapy reduced their mean score to 3.2 (i.e. a fall of 12.8), while those receiving supportive listening ('psychotherapy') had a mean score of 13.2 at 12 weeks (i.e. a fall of only 2.8); no standard deviations were given, but the difference between groups of -10.0 was reported to be statistically significant (p<0.0001).

c) Bowel habit

Roberts (2006) reported scores for constipation and diarrhoea. There was a non-significant difference (Figure 6), favouring hypnotherapy, in the diarrhoea score of –7.90 (95%CI -16.29, 0.49) at 3 months, but very little difference at 12 months. The baseline scores were about 33. Again there was 35% missing data, said to be missing-at-random. For constipation, there was no significant effect at any time (Figure 7). Baseline scores were around 38.

Figure 6

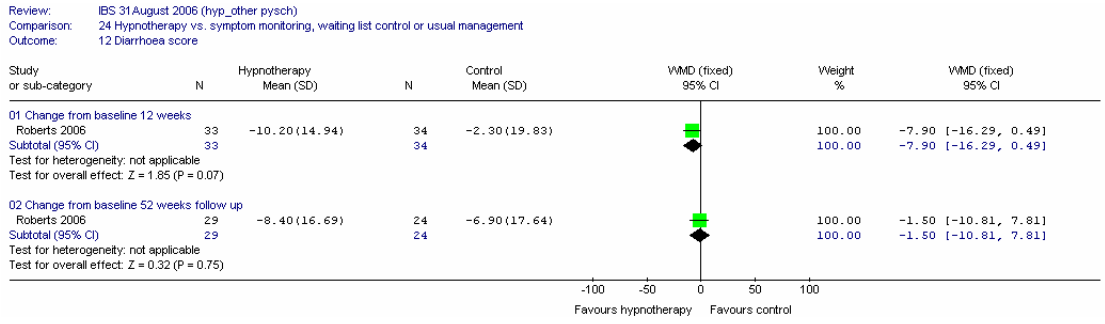
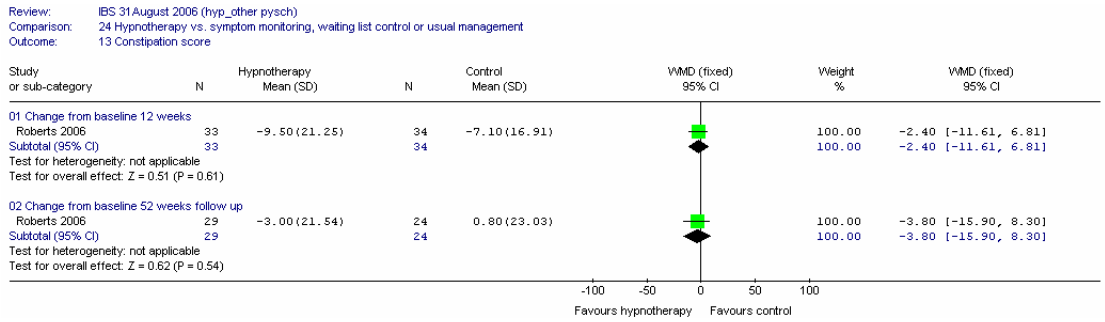


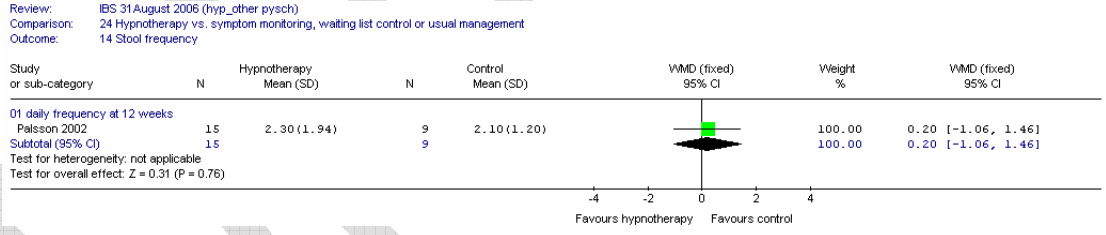
Figure 7



Abnormality of bowel habit was reported by Whorwell (1984). At baseline, this was more severely disordered in patients on hypnotherapy than in control patients (intervention group baseline score 17.2 versus psychotherapy 12.8 (i.e. baseline difference of 4.4); where abnormality of bowel habit was scored 0=none, 1=mild, 2=moderate or 3=severe, and scores totalled over 7 days, i.e. scale from 0-21, p=0.005 for baseline difference). The score fell from 17.2 to 1.6 (i.e. 15.6) in the hypnotherapy group compared with from 12.8 to 11.8 (i.e. 1.0) on psychotherapy (p<0.0001). The large baseline difference may have confounded this outcome measure.

Palsson (2002) reported stool frequency. There was no significant difference in the baseline values, or at 3 months.

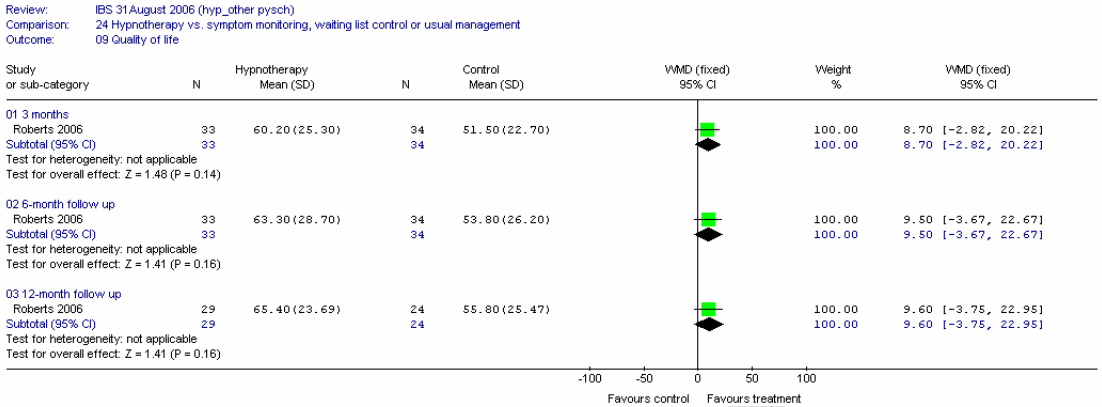
Figure 8



3. Quality of life

IBS-specific quality of life (high = good) was reported by Roberts (2006) at 3 months (about 7 weeks after end of treatment) in 81 patients and at 6 and 12 month follow-up. There was no significant difference at any time, although the difference in QoL score did not appear to change over time. Again the scale was not given, but reference to the Wiklund (2003) study suggested that the scale was 26 items with a 7 point Likert scale, giving a possible maximum of 182. Baseline scores were about 50.

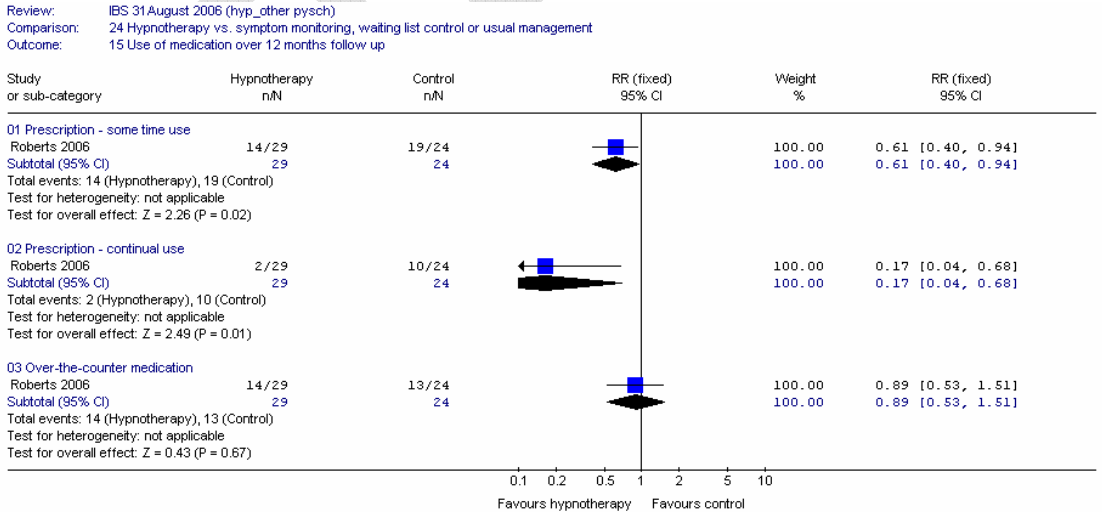
Figure 9



4. Use of IBS medication

One study (Roberts 2006) gave the self-reported use of prescription medication, either sometime, or continual, and over-the-counter medication (including antispasmodics, anti-motility agents, probiotics, herbal juices and teas, and incontinence pads) over the 12 months follow-up period. There were significantly more patients using prescription medication at some time during the 12 months; RR 0.61 (95%CI 0, 40, 0.94). This corresponded to an NNT of 4 (95%CI 2, 14), for a control group risk of 79%. There was no significant difference in the over-the-counter medication use.

Figure 10



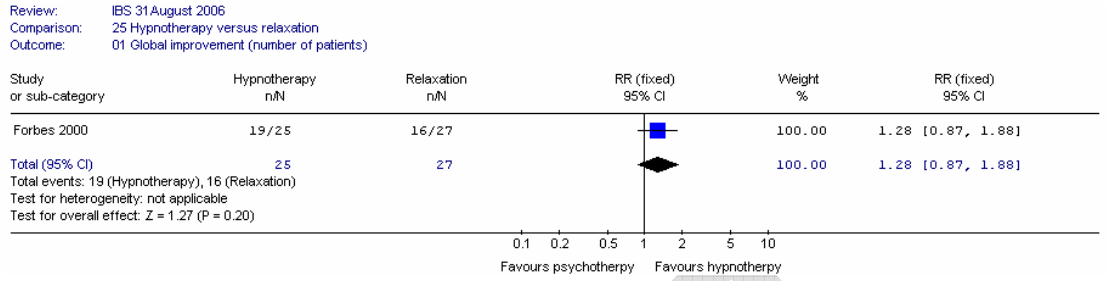
B. Hypnotherapy versus another intervention (relaxation)

Forbes (2000) compared hypnotherapy with relaxation in 52 patients. We noted that in both studies the two types of therapy were delivered by the same person, which could have introduced a therapist effect.

1. Global symptoms

Global improvement in symptoms (number of patients) was reported by Forbes (2000) at 12 weeks. There was no significant difference between interventions.

Figure 11



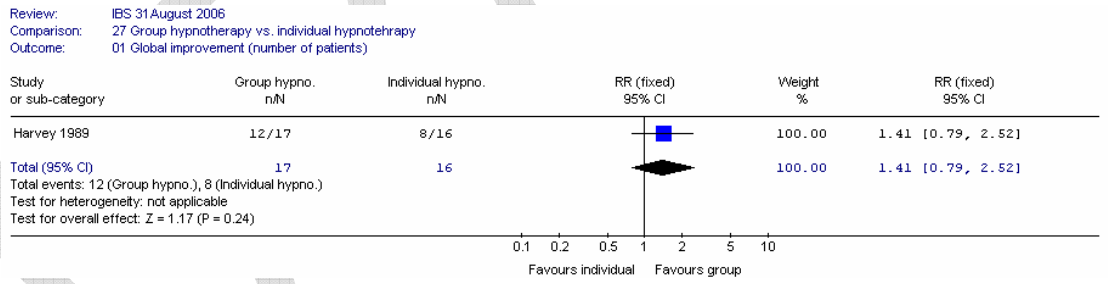
C. Group hypnotherapy versus individual hypnotherapy

One study in 33 patients (Harvey 1989) compared hypnotherapy on an individual basis versus hypnotherapy on a group basis (6 to 8 patients); the outcome reported was the global improvement in symptoms (number of patients). There was no significant difference between interventions.

1. Global outcomes

Global improvement in symptoms (number of patients)

Figure 12



ECONOMIC LITERATURE FOR HYPNOTHERAPY

No relevant health economic analyses were identified on the cost-effectiveness of hypnotherapy in the management of IBS.

COST-EFFECTIVENESS ANALYSIS FOR HYPNOTHERAPY

This section describes the health economic analysis undertaken to inform recommendations on the use of hypnotherapy as a one-off intervention in the management of IBS. The general methods used in the economic analysis for all management interventions are described in detail in Chapter 5 and the model inputs and assumptions relevant to this particular intervention are described below.

- The effectiveness of hypnotherapy in addition to usual care compared to usual care alone in people with refractory IBS was based on the number of patients with an improvement in global symptoms (at the end of treatment) for hypnotherapy vs waiting list control, symptom monitoring, attention control or usual care. (OR 3.85, 95%CI 2.03- 7.29, from meta-analysis of Whorwell (1984) and Galvoski (1998), giving a RR of 2.23, 95% CI 1.16 – 2.80, for a 25% response rate in the control arm).
- We assumed that there is no further benefit after 12 months based on a non significant difference in mean global symptom score at 12 months (Roberts 2006). A linear fall-off was assumed between the end of treatment and 12 months. A sensitivity analysis assuming no further benefit after 6 months was carried out as the mean difference in global symptom score is similar at 6 months and 12 months but it is not possible to calculate statistical significance from the data presented for 6 months (Roberts 2006).
- The evidence included in the clinical effectiveness review did not allow a subtype specific estimate of clinical effectiveness to be estimated. Therefore it was assumed that hypnotherapy is equally effective in all IBS subtypes.
- Hypnotherapy was assumed to be given over 12 weeks as this was the duration of intervention in the Whorwell (1984) and Galovski (1998) studies.
- A 15 month time-frame was used so that the cost-effectiveness could be compared to against other behavioural therapies for which there was 15 month efficacy data.

Modelled response rates

In the basecase scenario the response rate of 25% in the no treatment arm is taken from the mean placebo arm response rate from the behavioural therapy trials. This represents the group of patients whose symptoms improve without any specific intervention. The RR for an improvement in global symptoms for hypnotherapy vs no treatment at the end of treatment is 2.23, therefore the response rate in the intervention arm is 57% at the end of treatment (12 weeks). As shown in Figure 13, the response rate in the hypnotherapy arm has decreased to 46% by 6 months and 25% by one year, based on the assumptions regarding fall-off in effectiveness described above.

We have also considered a maintained benefits scenario in which the response to hypnotherapy is maintained for the one year after the end of treatment but there is no further benefit beyond this point.

There was no NHS reference cost available for hypnotherapy, even though it is funded in some regions of the NHS. A typical salary for a hypnotherapist falls within the Agenda for Change band 6 (based on personal communication from Peter Whorwell). This is the same salary used in estimating the reference cost for counsellors, on which the cost estimate for psychotherapy has been based. We have assumed that hypnotherapists have a similar working pattern to counsellors undertaking psychotherapy in terms of the proportion of their time that is spent on

direct client contact and the proportion that is spent on research, administration, education and other activities. Therefore the cost per hour for hypnotherapy has been taken to be equivalent to the cost per hour for psychotherapy. The costs of hypnotherapy were based on the mean number and duration of sessions used in the Whorwell (1984) and Galoviski (1998) studies, weighted by their contribution to the meta-analysis. This gave a mean duration of 3.6 hours of hypnotherapy. As there were only two studies used to estimate the RR, the cost range was based on the range from the various studies included in the clinical effectiveness review (2.2 – 4.9 hours). This gave a total cost for hypnotherapy of £171, (range £105 - £237).

For hypnotherapy there was evidence from Roberts (2006) that hypnotherapy resulted in a significant reduction in the use of prescriptions in the 1 year following intervention: RR of 0.61 (0.40 – 0.91) for any prescription use and RR of 0.17 (0.04 to 0.68) for continual prescription use for hypnotherapy compared to control. We have assumed no reduced resource use in the basecase analysis as reduced prescription rates are unlikely to have a significant cost impact. It was included in a sensitivity analysis by applying the reduction in resource use observed during the follow-up period of the Creed (2003) study for psychotherapy compared to usual care (£-4.08 per week, 95%CI-£8.11 to -£0.04) indirectly to hypnotherapy. This is plausible given that the odds ratio for an improvement in global symptom score at the end of treatment is larger for hypnotherapy compared to usual care (3.85, 95% CI 2.03 – 7.29) than the odds ratio observed for psychotherapy vs usual care in the Creed (2003) study (OR=2.44, 95%CI 1.28 – 4.67).

Figure 13: Response rate in the basecase analysis

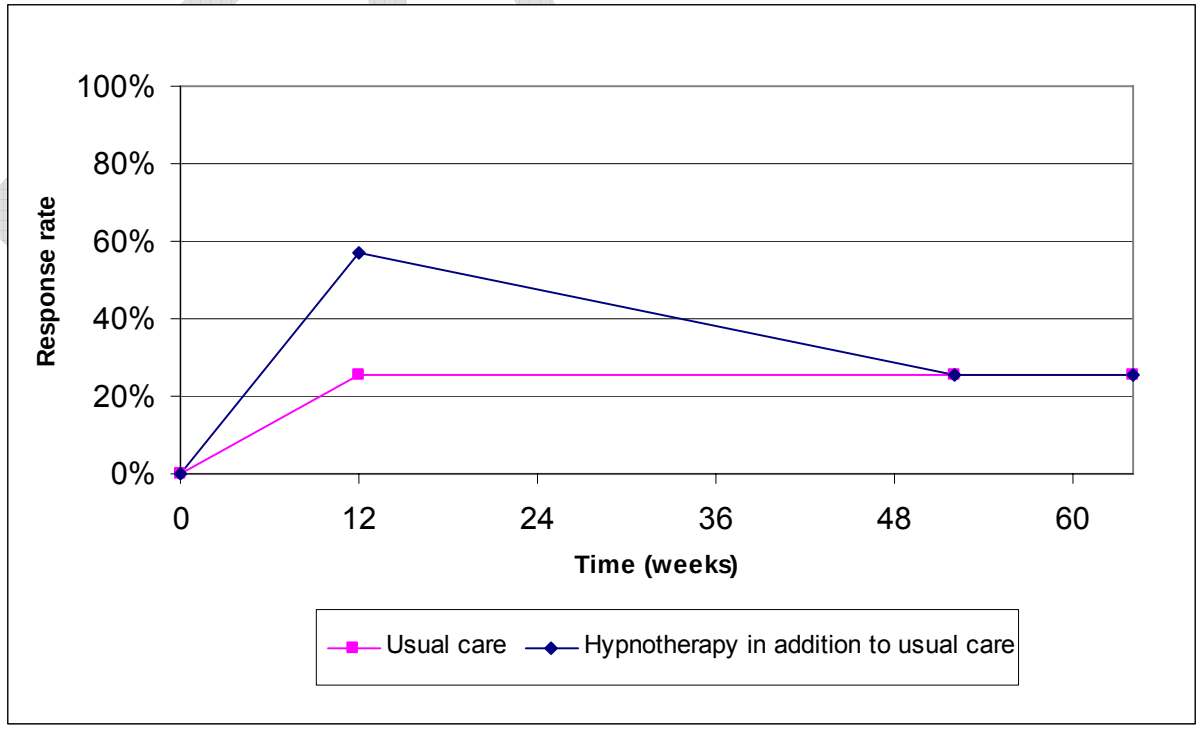
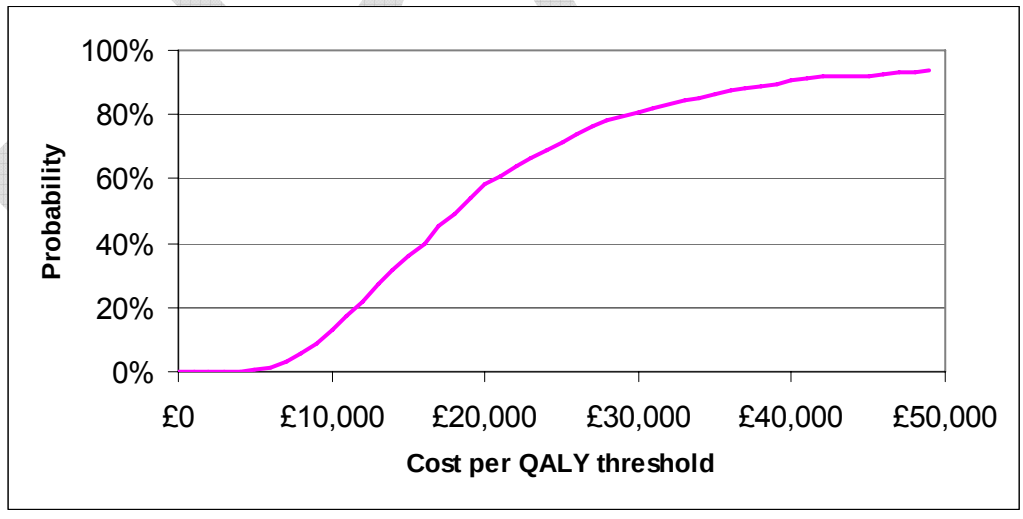


Table 1: Intervention specific parameters – Hypnotherapy

Description	Value	Evidence
RR of response for intervention vs placebo (at end of treatment)	2.23 (1.61 – 2.80)	Meta-analysis of RCT evidence for improvement in global symptoms
Fall-off in effect at 12 months compared to end of treatment	100%	Roberts (2006) global symptom score
Hypnotherapy cost: equiv to 3.6 hours per patient	£171, (range £105 - £237)	Weighted mean duration across studies and unit cost from Netten (2006)

Hypnotherapy in addition to usual care for 100 patients with refractory IBS is estimated to gain an additional 1.12 QALYs for an additional cost of £17,092 compared to usual care alone under the basecase assumptions. The incremental cost per QALY for is therefore £15,300. The probabilistic sensitivity analysis considers the uncertainty in this basecase estimate due to the uncertainty in the parameters used to estimate the cost-effectiveness. The CEAC in Figure 14, shows that given the parameter uncertainty, hypnotherapy in additional to usual care has a 59% probability of having a cost per QALY under £20,000 and a 81% probability of having a cost per QALY under £30,000, compared to usual care alone.

Figure 14: CEAC for hypnotherapy in addition to usual care compared to usual care alone in patients with refractory IBS



The incremental cost-effectiveness is dependent on the probability of an improvement for patients who receive usual care. When we applied a lower response rate of 9% in the usual care arm, the cost per QALY was increased to £25,809. It should be noted that the odds ratio rather than the RR was kept constant for this analysis as this was the efficacy estimate available from the clinical effectiveness review. As this sensitivity analysis significantly increased the cost per

QALY estimate, the probabilistic sensitivity analysis was re-run using this lower response rate for the comparator arm. The mean cost per QALY from the 1000 samples was £25,770 and the cost per QALY had a 28% probability of being under £20,000 per QALY and a 51% probability of being under £30,000 per QALY.

The threshold analysis showed that a response to treatment would need to provide more than 0.054 QALYs per annum to give a cost per QALY of under £20,000 in the basecase analysis. When the utility gain associated with a response to treatment was increased to 0.135 (equivalent to the QALY gain expected for a complete remission of symptoms) the cost per QALY was significantly lower at £8,081

When we assumed there was no fall-off in response up to 52 weeks post-intervention, the cost per QALY was decreased to £6,859. This would be further reduced by any continued response beyond 52 weeks. When we assumed that there was no significant difference between hypnotherapy and usual care from 6 months, then the cost per QALY is increased to £30,601. Whilst these two scenarios represent extreme possibilities for the estimated fall-off in response, they demonstrate that the cost-effectiveness is sensitive to the rate of fall-off in response after the end of intervention.

When we assumed that the reduction in resource use observed in the one year after psychotherapy from the Creed (2003) study could also be expected in patients receiving hypnotherapy, the cost of providing hypnotherapy in additional to usual care was lower than the cost of providing hypnotherapy alone. Under these assumptions hypnotherapy in addition to usual care dominated usual care alone by providing significant health gains, whilst lowering cost.

Table 2: Sensitivity results for hypnotherapy in addition to usual care compared to usual care alone for 100 patients with refractory IBS (all subtypes)

Scenario	**Usual care**		**Behavioural intervention and usual care**		**Incremental**
	Cost	QALY	Cost	QALY	Cost per QALY
Basecase	£0	2.02	£17,092	3.14	£15,300
Lower response rate in comparator arm (9%)	£0	0.72	£17,092	1.38	£25,809
No fall-off in effect for 1 year	£0	2.02	£17,092	4.51	£6,859
Effect falls off over first 6 months	£0	2.02	£17,092	2.58	£30,601
Resource use reduction from	£0	2.02	-£9,026	3.14	-£8,080 Hypnotherapy

Creed (2003) study					dominates
High utility gain of 0.135	£0	3.83	£17,092	5.94	£8,081
Threshold analysis on lowest utility	A cost per QALY of £20,000 is reached when the QALY gain associated with responding to treatment lies between 0.054 and 0.055.				

Further analyses on the cost-effectiveness of hypnotherapy compared to other behavioural interventions are given in section 9.7.

EVIDENCE STATEMENTS

For this review, the evidence was assessed using the GRADE process and tables are shown in Appendix F. The following evidence statements are derived from the GRADE tables.

1. There is moderately good evidence to show a significant global improvement in symptoms after 12 weeks, for hypnotherapy compared with attention control or symptom monitoring or usual management, mainly in patients with refractory IBS, both in primary and secondary care.

2. There is moderately good evidence to show no significant improvement either in global symptoms or in pain after 52 weeks, for hypnotherapy compared with usual management, in patients with refractory IBS in primary care.

3. There is moderately good evidence to show a significant reduction in pain for hypnotherapy compared with attention control or usual management, in patients with refractory IBS, both in primary and secondary care.

4. There is limited evidence to show a significant reduction in bloating for hypnotherapy compared with attention control, in patients with refractory IBS, in secondary care.

5. There is moderately good evidence to show no significant improvement in diarrhoea or constipation or quality of life, after 12 weeks, for hypnotherapy compared with usual management, in patients with refractory IBS in primary care.

6. There is limited evidence to show a significant reduction over 12 months, in the number of prescriptions for other IBS medications, for hypnotherapy compared with usual management, in patients with refractory IBS in primary care.

7. There is limited evidence to show no significant difference between group and individual hypnotherapy, in patients with refractory IBS and psychological problems in secondary care.

HEALTH ECONOMIC STATEMENT

Evidence from a decision analytic model showed that the addition of hypnotherapy to usual care is cost-effective in individual with refractory IBS although the cost-effectiveness was sensitive to uncertainty around the proportion of patients experiencing an improvement in global symptom score with usual care alone.

GDG DISCUSSION

The GDG's view was that hypnotherapy may be considered a developing intervention for IBS and the amount of evidence is limited. Despite this, the judgement and experience of GDG clinicians together with the limited RCT evidence from the review suggest that gut directed hypnotherapy strategies provide people with IBS with benefits in a cost-effective manner. Currently hypnotherapy is used as a second line therapy option, usually for people with unresolved IBS symptoms, who have failed to respond to a combination of management strategies. It features on the patient care pathway as one of the behavioural therapies that primary care clinicians should consider if symptoms persist.

Although there is currently a lack of research in hypnotherapy, the GDG agreed there is potential for long-term benefits to the NHS from this behavioural therapy that need to be investigated further, including its use as a first line therapy. The GDG therefore decided to include hypnotherapy in one of its top five research recommendations, with the potential for this intervention to be considered as a first line therapy option.

EVIDENCE TO RECOMMENDATION

The evidence to recommendation statement for psychotherapy, CBT and hypnotherapy is detailed in section 9.8.

The combined guideline recommendation for psychotherapy, CBT and hypnotherapy is also stated in section 9.8.

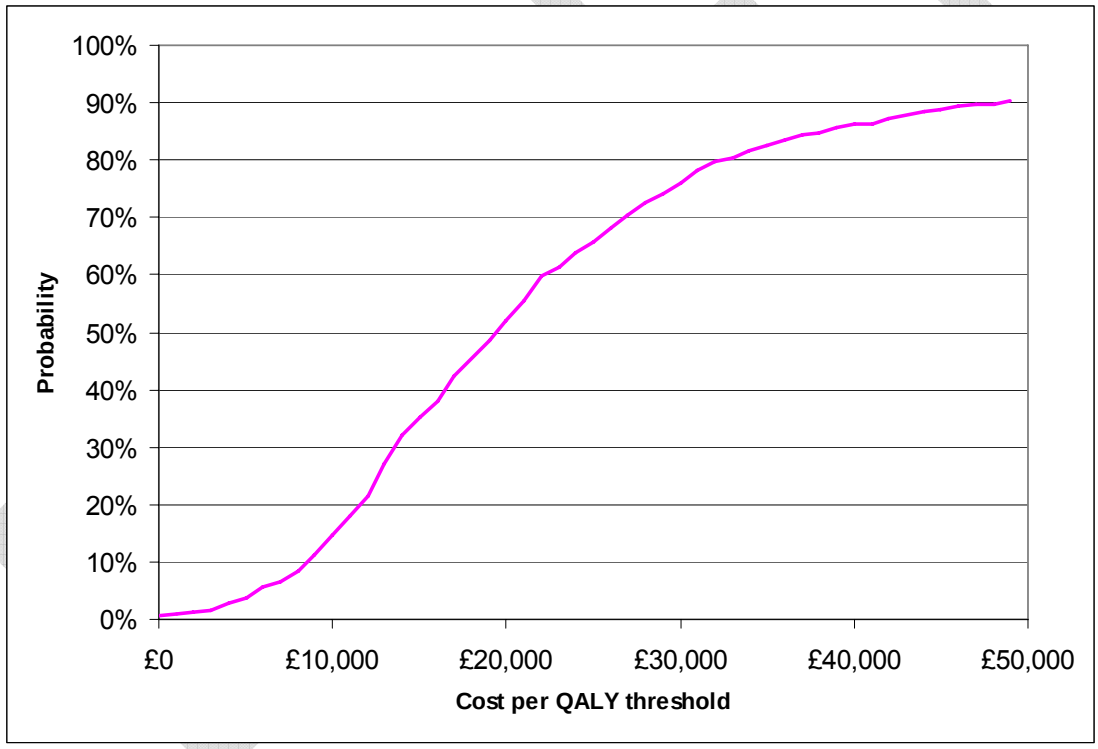
9.7 Indirect comparison of behavioural therapies

We have undertaken an indirect comparison to assess the relative cost-effectiveness of the behavioural therapies (CBT, psychotherapy and hypnotherapy). It is indirect because it is based on the cost-effectiveness of each intervention compared to usual care as no trials were identified which compared behavioural therapies head-to-head. The results are presented for two scenarios. In the first scenario the basecase assumptions are maintained from the analysis of each intervention compared to usual care. In the second scenario the basecase assumptions are maintained except that the resource use reduction from the Creed (2003) study has been excluded from the cost-effectiveness estimate for psychotherapy. This has been done because the GDG felt that there was a lack of similar evidence for CBT and hypnotherapy but that this

was due to a lack of trials reporting economic outcomes for these interventions rather than a true difference in the cost-effectiveness compared to psychotherapy.

Hypnotherapy provided the smallest QALY gain compared to usual care but is likely to be cost-effective compared to usual care as discussed in section 9.6. As CBT provided more QALY gain than hypnotherapy at additional cost, we have considered the incremental cost-effectiveness of CBT compared to hypnotherapy. The CEAC in Figure 1 shows that CBT has a 52% probability of being cost-effective compared to hypnotherapy at a cost per QALY threshold of £20,000 and a 76% probability of at a threshold of £30,000. The mean cost per QALY for CBT compared to hypnotherapy under the basecase assumptions was £18,158 for the deterministic model. There was concern that this comparison had been biased by the use of different unit costs for therapy sessions for CBT and hypnotherapy so we carried out a sensitivity analysis using the unit costs for CBT for both behavioural therapies. This gave a cost per QALY of £15,301.

Figure 1: CEAC for CBT vs hypnotherapy



Under the basecase assumptions, psychotherapy provided additional QALY gain compared to CBT but the mean cost for psychotherapy was less than for CBT. The CEAC in Figure 2 shows the incremental cost-effectiveness of psychotherapy compared to CBT. Psychotherapy has a 68% probability of providing additional QALY gain at no additional cost compared to CBT and a 73% probability of providing additional QALY gain for less than £20,000 per QALY. There was concern that this comparison had been biased by the use of different unit costs for therapy sessions for CBT and psychotherapy so we carried out a sensitivity analysis using the unit costs

for CBT for both behavioural therapies. This raised the intervention cost for psychotherapy, but it still had a lower overall cost than CBT.

The lower cost of psychotherapy is driven by the assumption on lower resource use for psychotherapy compared to usual care. When this factor was excluded from the analysis psychotherapy had a mean cost per QALY of £11,314 compared to hypnotherapy with a 61% probability of a being under £20,000 and a 70% probability of being under £30,000 per QALY. These results suggest that each of the interventions would result in the cost-effective use of NHS resources but it does not address which is the most cost-effective.

Figure 2: CEAC for psychotherapy compared to CBT

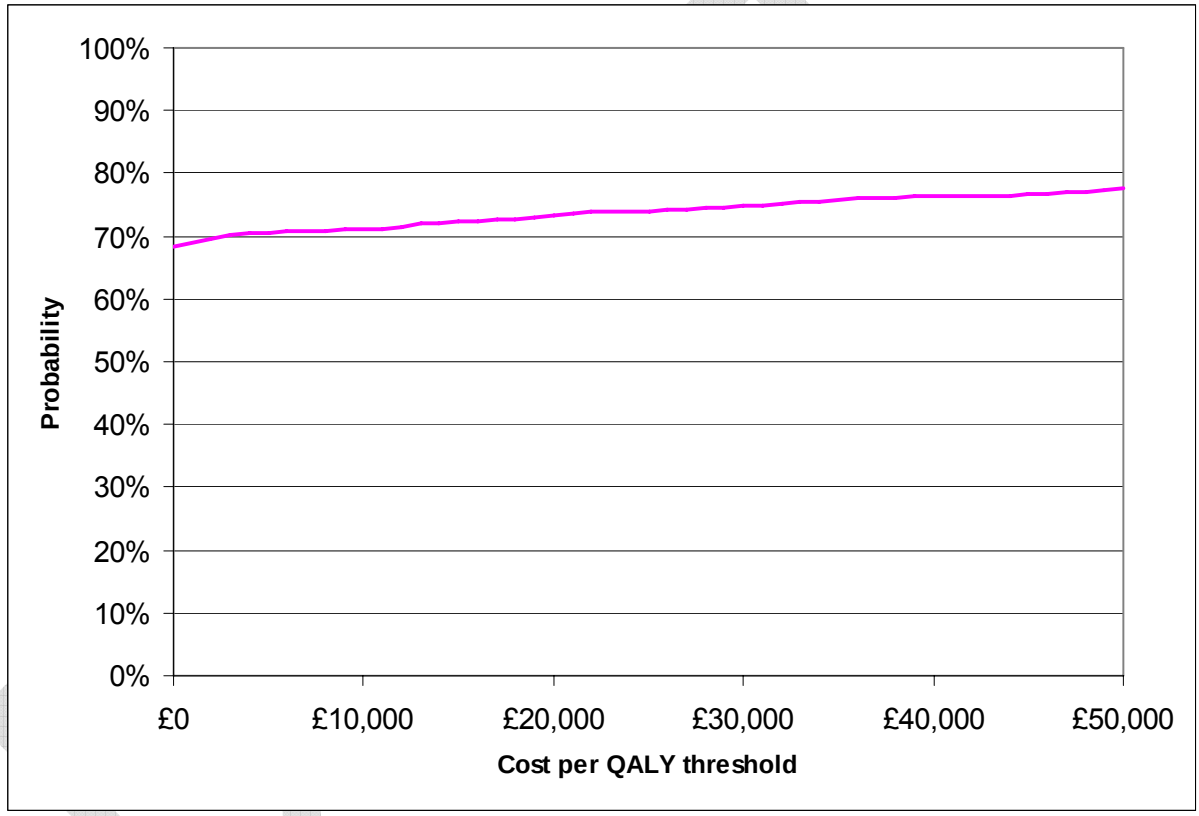


Figure 3 is a multi-way cost-effectiveness acceptability curve which shows the probability that each of the three behavioural therapies is optimal compared to the other two at various cost per QALY thresholds. The optimal intervention is the one that provides the most QALY gain at a cost per QALY under the threshold. This is most easily described by considering the incremental net benefit of each intervention, which is the (monetary) value of a strategy compared with an alternative strategy for a given cost-effectiveness threshold. For example, if society is willing to pay £20,000 for an additional QALY then the incremental NB is:

Net benefit = (Additional QALY gain x £20,000) – additional cost

The strategy with the greatest incremental net benefit compared to usual care, at a given cost per QALY threshold, is the optimal strategy at that threshold. We used the results of the probabilistic sensitivity analysis to estimate the probability that each behavioural therapy is optimal at various cost per QALY thresholds. Figure 3 shows that under the basecase assumptions, psychotherapy has the highest probability of being the optimal strategy at willingness to pay thresholds of £10,000 to £50,000.

Figure 4 shows that when a similar exercise is carried out for the second scenario, in which we assumed that none of the three interventions result in reduced resource use, psychotherapy had a lower probability of being the optimal strategy, but it is still the most likely to be optimal for willingness to pay thresholds of £20,000 to £50,000 per QALY. Hypnotherapy has the highest probability of being the optimal strategy for cost per QALY thresholds under £20,000.

These results suggest that providing psychotherapy for people with refractory IBS is likely to result in more efficient use of NHS resources than providing CBT or hypnotherapy. However, the analysis did not take into account factors that may be important in deciding the optimal treatment for an individual. For example, if the effectiveness of these behavioural interventions is higher in patients who are committed to a particular intervention then choosing to provide the intervention preferred by the patient may result in treatment being more cost-effective. The results of the cost-effectiveness modelling suggest that all three behavioural interventions would result in the cost-effective use of NHS resources at willingness to pay thresholds of £20,000 to £30,000, given the evidence currently available.

Figure 3: Multi-way CEAC for behavioural therapies under the basecase assumptions

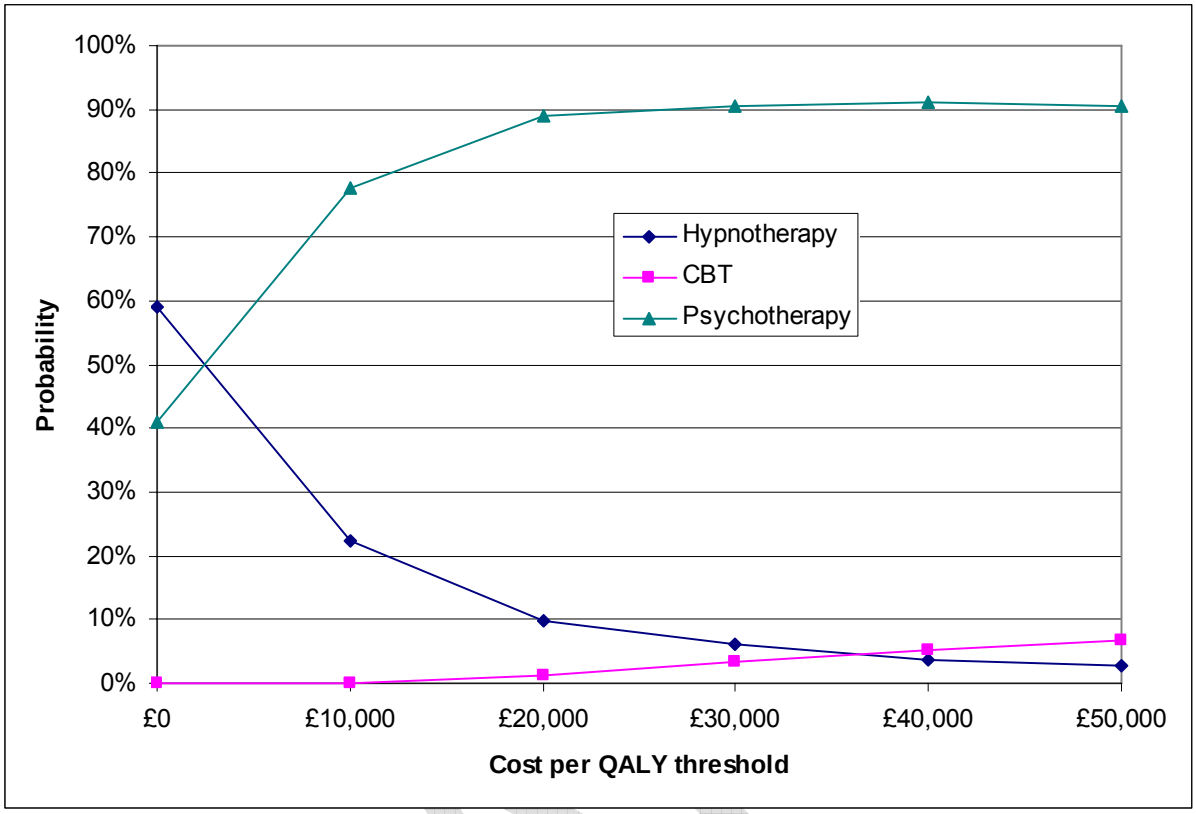
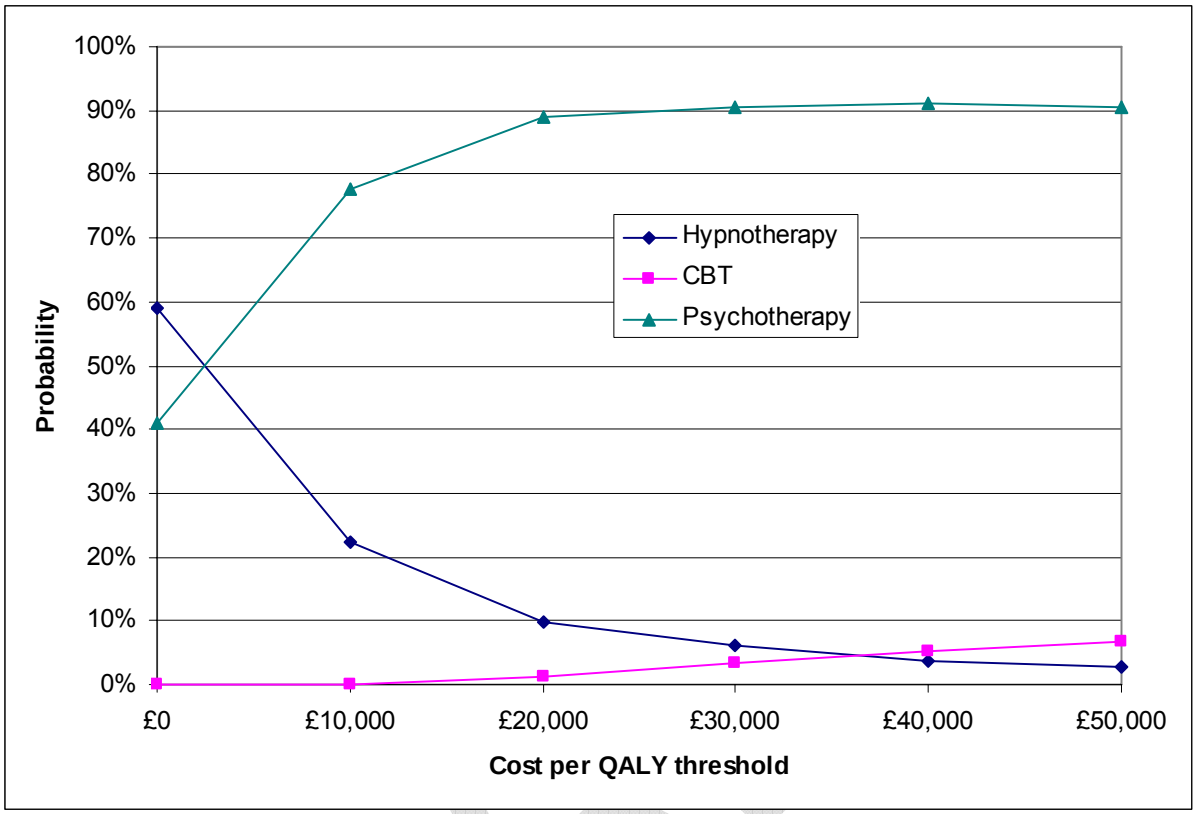


Figure 4: Multi-way CEAC for behavioural therapies when we assumed that there is no resource use reduction associated with any of the therapies



9.8 Evidence to recommendation: psychotherapy, CBT and hypnotherapy

The GDG considered CBT, hypnotherapy and psychotherapy, as a group of similar, but distinct therapies when making recommendations, and took into account several factors:

Firstly, they considered the clinical effectiveness reviews and cost effectiveness modelling that have been carried out mainly for the treatment of people with refractory IBS. The GDG interpreted the cost effectiveness analyses, including the indirect comparisons between the three therapies. The GDG noted that the trials were mainly in people with refractory IBS, and, for this group, the therapies were all cost effective.

Secondly, the GDG highlighted the current national variation relating to where these therapies are accessed, and noted that this is dependent on the commissioning patterns of individual strategic health authorities. Typically, they are more available in secondary care.

Thirdly, the GDG took into consideration the need to give people with IBS and their primary care clinician a choice in which behavioural therapy was most appropriate for them, and what might be available locally.

On balance, the GDG decided not to distinguish between the three therapies, and recommended that any one of them should be considered for people who have had IBS for at least 12 months, and who have not responded to first line therapies and whose symptoms continued. This patient profile has been defined for the purpose of this guideline as refractory IBS.

The GDG discussed whether there was an optimum time for treatment with any of these behavioural therapies: leaving patients too long may have meant the person was no longer able to respond. In addition, the GDG was keen to determine whether these therapies could be used as first line treatments, as they had potential to enable people with IBS to cope with their symptoms by giving initial treatments which would have long term sustainability. This view was supported by evidence in children with IBS, which showed that hypnotherapy is clinically effective as a first line therapy. The GDG therefore proposed a recommendation for research to compare, head-to-head, the three therapies as first line therapies, with follow-up at various time points up to a year.

During GDG discussion relating to behavioural therapies, it was recognised that it would be very useful for clinicians to be able to predict which people would have refractory IBS and which factors put them at risk. Therefore a second research recommendation was proposed to investigate what factors are important. These research recommendations are given in chapter 12.

RECOMMENDATION

Primary care clinicians should consider referring for behavioural therapies (cognitive behavioural therapy, hypnotherapy, psychological therapy) people with IBS who do not respond to first-line therapies after 12 months and who develop a continuing symptom profile (described as refractory IBS).

10 COMPLEMENTARY AND ALTERNATIVE THERAPIES

Clinical Questions

1. Is acupuncture an effective intervention in managing IBS symptoms?

2. Is reflexology an effectives intervention in managing IBS symptoms?

BACKGROUND

Complementary and alternative medicine (CAM) may be defined 'as wide ranging therapies which may be used exclusively i.e. complete healing systems, or in combination with orthodox medical treatment' (House of Lords Select Committee on Science and Technology 2000 p.2). The terms 'Alternative' and 'Complementary' are used to define the use and setting of a therapy in relation to orthodox medicine. 'Alternative' usually refers to treatment modalities that are generally a substitute for orthodox treatment whereas 'complementary' refers to treatments that are used alongside orthodox medical treatments. CAM is usually considered to include the practice of therapies that are not considered integral to the dominant health care model of a country, society or culture.

The House of Lords Select Committee on Science and Technology Sixth Report addressed the future of CAM in relation to research, service delivery, education and training and regulation. The report stated that there is very little evidence about the efficacy of many complementary and alternative treatments but the use of CAM is widespread and is increasing across the developed world. There is a clear need for more effective guidance for the public and health professionals who advise patients as to what does and does not work and what is and is not safe.

In order to begin to establish the effectiveness of CAM it is important to identify specific therapies and particular conditions where the use of CAM may be appropriate. It is not uncommon for those suffering from chronic conditions, for whom conventional medicine has been less than successful in alleviating symptoms, to seek complementary and alternative medicine (CAM). Irritable Bowel Syndrome is an example of such a condition.

The guideline considered commonly used therapies, Acupuncture (Chinese Herbal Medicine) and Reflexology. Hypnotherapy was considered with the psychological interventions.

Acupuncture

Acupuncture is defined as a therapeutic and/or preventive medical procedure used in or adapted from Traditional Chinese Medicine (TCM) performed by the insertion of 1 or more specially manufactured solid metallic needle(s) into specific location(s) on the body. The intent is to stimulate acupuncture points, with or without subsequent manual manipulation. The acupuncture points are situated on fourteen major 'meridians'. The TCM theory is that acupuncture stimulates 'qi' (translated as life force) that circulates through the meridians. In optimum health the flow of 'qi' is unobstructed. Interruption or stagnation of the flow of 'qi' results in diverse symptoms. The theory is that insertion and manipulation of needles at particular points stimulates the energy flow, restoring the balance and thus normalising the function of the organ. An alternative theory is that acupuncture is a specialised sensory stimulation that is analysed through sensory neural pathways.

Reflexology

Reflexology is an ancient form of complementary medicine thought to originate in China, however research has shown that reflexology was also used by some early African tribes, Native American Indians and early Egyptians. Reflexology is a complementary therapy based on the theory that by the application of pressure to specific reflex points on the feet and hands, which correspond to the organs of the body, it is possible to 'normalise' function. In conventional medical terms reflexology could be said to facilitate homeostasis. Reflexology is a widely used therapy; it has been estimated that between 6 and 12% of the population use it and anecdotal evidence suggests that many people find it extremely effective for a range of chronic conditions including functional bowel conditions, although there is little rigorous research to support this view.

People with IBS may be drawn to acupuncture and reflexology's ancient roots and the desire for non-pharmacological treatment. Alterations in pain modulation, motility, and autonomic nervous system function are likely mechanisms of IBS symptoms, which may have physiological responses to acupuncture and reflexology.

People with IBS are interested in CAM and will continue to use these modalities as long as medical therapy fails to relieve their symptoms. To optimise the care of people with IBS there is a need for further evidence of the potential benefits and safety of these treatments. Integration of CAM into Western medical practice will require more than selection of a few isolated acupoints, or yoga positions. A wider understanding of the paradigm specific use of these techniques, mechanisms of action, and potential pitfalls is required.

10.1 Reflexology

SELECTION CRITERIA

The selection criteria described in the general methodology section were used. Interventions were any form of reflexology.

SEARCH STRATEGY FOR IDENTIFICATION OF STUDIES

Searches were performed on the following core databases: MEDLINE, EMBASE, CINAHL, and *The Cochrane Library* (1966 to current day with guidance from the GDG). Additionally, the AMED database was searched for this review. Search strategies are given in Appendix B.

The search strategy identified 560 studies. The titles and abstratcs of these studies were assessed. One was identified to be potentially relevant to this review and this paper was retrieved. The reference lists of these studies were inspected for further potential papers, but none were identified.

DESCRIPTION OF STUDIES

Types of Studies

Only one study was identified: a quasi randomised trial in a UK primary care setting (Tovey 2002).

Types of Participant

Thirty four patients were allocated treatments. The groups were comparable at baseline as regards age; gender; duration, and; severity of condition.

Inclusion criteria were that patients had to have a diagnosis of IBS in line with Rome II criteria, and they should be currently under the care of a primary care physician following referral to a gastroenterologist to exclude organic GI disease. Patients were excluded if they had organic GI disease or had previously used reflexology.

Intervention

Six 30-minute sessions of reflexology delivered in a way that was as close as possible to normal practice conditions, over an eight week period. The control group received six 30-minute sessions of foot massage that excluded pressure on key points of the foot.

METHODOLOGICAL QUALITY

Sequence generation was by alternation, and the allocation concealment was inadequate. A power calculation was carried out and the sample size required was 18 patients per group for

the outcome of abdominal pain. 4/19 (21%) in the reflexology group were lost to follow-up and 2/15 in the control group.

The study reported no significant differences in baseline characteristics (pain; diarrhoea; constipation; bloating).

RESULTS

Individual symptoms of IBS were recorded daily using a 5 point scale, but global symptoms were not reported.

a) Pain

Pain was the primary outcome measure. There was no significant difference between the reflexology and control groups for this outcome, either at assessment 2 weeks after completion of the intervention (p=0.32) or at 3 month follow-up.

Table 1.

a) Reflexology Baseline **b) Pain score (0-4 scale)** f) Median:1.4 g) IQR: 0.6 to 2.1	c) Change from baseline: reflexology post treatment h) End of treatment: Median: i) -0.10 (IQR: -0.80 to 0.10) j) 3 months follow up: Median 0.00	d) Control Baseline k) Median:0.7 l) IQR:0.5 to 1.3	e) Change from baseline: control post treatment m) Median:-0.40 (IQR: -0.90 to 0.00) n) 3 months follow up: Median -0.25

b) Bowel function

There was no significant difference, 2 weeks after completion of the intervention, in bowel function (change in constipation or diarrhoea) (p=0.47) between intervention and control groups.

Table 2.

o) Reflexology Baseline **p) Bowel Function (scale 0-4)** t) Median: 1.9 u) IQR: 1.2 to	q) Change from baseline: reflexology post treatment v) Median: 0.05 w) IQR: -0.53 to	r) Control Baseline x) Median: 1.2 y) IQR: 0.3 to	s) Change from baseline: control post treatment z) Median:-0.30 aa) IQR: -0.80

2.1	0.43	1.7	to 0.20

c) Bloating

There was also no significant difference, 2 weeks after completion of the intervention, in bloating (p=0.0.17) between intervention and control groups.

Table 3.

bb) Reflexology Baseline **cc) Bloating dd) (scale 0-4)**	ee) Change from baseline: reflexology post treatment	ff) Control Baseline	gg) Change from baseline: control post treatment
hh) Median: 2.5	jj) Median: -0.10	ll) Median:2.0	nn) Median: -0.40
ii) IQR: 1.3 to 3.1	kk) IQR: -0.60 to 0.20	mm) IQR: 1.0 to 2.2	oo) IQR: -1.05 to -0.15

HEALTH ECONOMIC EVIDENCE

The cost effectiveness of reflexology was not taken into consideration for this review because reflexology is not prescribed with treatment being purchased independently by people with IBS.

EVIDENCE STATEMENT

There is limited evidence from a single study in people with IBS in Primary Care showing no significant effect on pain, bowel function and bloating compared with the foot massage placebo group.

GDG CONSENSUS

The GDG was concerned that the foot massage group may not have been reliable as a placebo group. The limited evidence from this small, quasi-randomised trial does not lend support to the use of reflexology in the management of IBS in adults. However, there may be a need for further research.

EVIDENCE TO RECOMMENDATION

The review reported limited evidence that showed reflexology is not effective in the management of IBS symptoms. The GDG's clinical view was that the current lack of effectiveness precludes a positive recommendation.

RECOMMENDATION

Primary care clinicians should not encourage the use of reflexology in the treatment of IBS.

10.2 Acupuncture

SELECTION CRITERIA

The selection criteria described in the general methodology section were used, but some were specific to the acupuncture review and are reported below.

Types of studies

Crossover trials could be included, but those with a washout period of less than 2 weeks were to be excluded. All study designs were included for adverse effects. Specific searches for adverse effects were not carried out.

Types of intervention

Studies to be considered for inclusion included the following interventions:

- Single acupuncture needling point
- Combination acupuncture needling points.

Methods of acupuncture that do not involve needle insertion for example laser or acupressure were to be excluded. For the purposes of this review the minimum acceptable dose was to be

two treatments of acupuncture. Studies that included a single acupuncture treatment were to be excluded.

Types of comparisons

The following comparisons were to be included:

- Single acupuncture versus sham acupuncture (placebo)
- Combination acupuncture versus sham acupuncture (placebo)
- Single acupuncture versus another type of treatment
- Combination acupuncture versus another type of treatment
- Acupuncture + treatment 2 versus treatment 2

Subgroup analyses

Subgroup analyses were to be carried out if there is heterogeneity as follows:

- Symptom severity
- Dose
- Type of acupuncture.

SEARCH STRATEGY FOR IDENTIFICATION OF STUDIES

Searches were performed on the following core databases: MEDLINE, EMBASE, CINAHL and *The Cochrane Library* (1966 to current day with guidance from the GDG). Additionally, the AMED database was searched for this review. The search strategies are listed in Appendix B. The search strategy identified 764 studies. The titles and abstracts of these studies were assessed. Of these studies, 20 were identified on the basis of the title and abstract as being potentially relevant to the review and these papers were retrieved in full. All reference lists of these studies were inspected for potential papers for inclusion in the review, but no further potential studies were found in addition to the titles already identified. Nineteen studies and one Cochrane review were identified (Manheimer 2006). Of these, eight were excluded and these are listed in Appendix E, along with reasons for exclusion.

DESCRIPTION OF STUDIES INCLUDED IN THE REVIEW

Twelve studies met the inclusion criteria for the review (Chung 2003; Burford-Mason 2003; White 2001; Ernst and White 1997; Ernst and White 2001; MacPherson 2001; Yamashita 2001; Schneider 2006; Lowe 2000; Forbes 2005; Conboy 2006; Fireman 2001). Five studies (Schneider 2006; Lowe 2000; Forbes 2005; Conboy 2006; Fireman 2001) investigated the effectiveness of acupuncture for the treatment of IBS. One was conducted in the UK (Forbes 2005) and one each in Germany, Canada and Israel. Seven studies investigated adverse effects (Chung 2003; Burford-Mason 2003; White 2001; Ernst and White 1997; Ernst and White 2001; MacPherson 2001; Yamashita 2001).

Study Design

All the studies in the review were parallel studies, with the exception of Fireman (2001) which was a crossover study. The latter had a three week washout period, but first period results were also reported, which were used in preference because of the uncertainty about carry-over effects. One study (Lowe 2000) was only reported as a conference abstract.

All the studies took place in secondary care. The studies investigating adverse effects included medical doctors in primary and secondary care and non-medical acupuncturists.

The Cochrane Review 'Acupuncture for treatment of irritable bowel syndrome' (Manheimer 2006) included six trials. Two were excluded from the guideline review: one used electrical ear acupuncture (Liu 1995) and the other was a study in Chinese (Liao 2000). The Cochrane review authors stated that there was a possibility that Liao (2000) was not an RCT.

Population

All studies included people with a diagnosis of IBS, although the definition varied. Three used the Rome I criteria (Fireman 2001; Forbes 2005; Lowe 2000) and two used the Rome II criteria (Schneider 2006; Conboy 2006). All studies included a combination of IBS types and none of the studies stated that any participants had IBS as result of gastrointestinal infection. All studies included some participants with bloating. One study (Schneider 2006) identified all patients as having bloating, and in another (Fireman 2001) 80% had bloating.

All of the studies described symptom severity as mixed. The age range of participants was 17 to 79 years with the average mean age being approximately 46 years. No study particularly identified elderly participants. All studies had more women than men.

The Forbes (2005) study only included people who were refractory to other treatments; Fireman (2001) had participants who had had clinical symptoms for at least a year.

The numbers of participants ranged from 25 to over 100 (Conboy 2006; Liu 1997).

Interventions

The included studies all used different acupuncture protocols, but all used Chinese style acupuncture. One study used a single acupuncture point (Fireman 2001) and the remainder used a combination of points (Lowe 2000; Forbes 2005; Conboy 2006; Schneider 2006). The number of sessions of acupuncture varied from two (Fireman 2001) to ten (Forbes 2005; Schneider 2006).

Comparisons

The majority of studies compared true acupuncture with sham acupuncture. One study compared acupuncture plus psychotherapy with acupuncture alone and psychotherapy alone (Liu 1997).

The sham acupuncture varied between studies:

- Multiple needling versus sham needling at non acupuncture points (Schneider 2006)
- Single needling versus sham needling at an inappropriate acupuncture point (Fireman 2001)
- Multiple needling versus sham needling at inappropriate acupuncture points (Forbes 2005)
- Multiple needling versus non-needling at the same acupuncture points (Lowe 2000; Conboy 2005).

Two studies used a validated sham needling device (Conboy 2005; Schneider 2006).

Outcomes

The studies measured a range of outcomes using different scales.

1. Global score

a) Number of people with global improvement of symptoms

The Forbes (2005) study reported the number of people who recorded a reduction in symptom score of four points, which constituted an improvement. The Lowe (2001) study recorded a patient-determined success rate, which was based on individual patient expectations stated at baseline.

b) Global improvement of symptoms score

Fireman (2001) used a visual analogue scale (1 to 5), on which 5 equated to significant improvement in global symptoms. Liu (1997) used a three point scale, 1 = cured, 2 = improved, 3 = no effect.

c) Global symptom score

Forbes (2005) used a global symptom score with a scale of 0 to 30 based on symptom diaries plus the Bristol stool chart. A reduction of 4 points was considered clinically significant.

2. Individual symptoms

a) Pain

Three studies reported a pain score (Fireman 2001, Lowe 2000, Scheider 2006). In all cases the highest rating meant worst symptoms, although the scales used were not the same. The Lowe (2000) study only gave p-values for the pre-post comparison for each group and the Scheider (2006) study recorded scores on the pain subscale of SF36.

b) Bloating

One study reported bloating as an individual symptom (Fireman 2001).

c) Bowel habits

No studies reported bowel habit as an individual symptom in all patients, although Fireman (2001) reported diarrhoea scores for 11 patients with diarrhoea and defaecation difficulty scores in 13 people with constipation. We decided that these small subgroups broke the randomisation and were likely to give unreliable results.

3. Mental health

One study (Forbes 2005) assessed participants using the Hospital Anxiety and Depression (HAD) scale and recorded the change score.

4. Quality of Life

One study (Forbes 2005) assessed participants using using the EuroQol quality of life questionnaire.

Schneider (2006) used the FDDQL (scale 0 to 100), which assesses the disease related impact of bowel symptoms on quality of life; and the SF36 health-related quality of life measure. The primary outcome of the study was improvement in the global score of the FDDQL i.e. a reduction in score after 10 sessions. Lowe (2001) used the validated quality of life tool, IBS-36, but only reported p-values for changes from baseline.

METHODOLOGICAL QUALITY

The quality assessment for included trials is shown in Appendix D.

The method of randomisation was reported in three studies, all of which were classified as adequate (computer generated: Forbes 2005; Schneider 2006; Conboy 2006). The other studies did not state the method of randomisation (Fireman 2001; Lowe 2000).

Allocation concealment was reported in two studies (Forbes 2005; Schneider 2006). The Schneider (2006) study had adequate concealment (sequence retained by a central telephone centre) and the Forbes (2005) had partial concealment (sealed envelopes).

Three studies reported that the outcome assessors and the patients were blinded to the interventions (Fireman 2001; Forbes 2005; Schneider 2006). It was unclear whether the patients were blinded in Lowe (2000).

Most studies described the details of the placebo and active intervention giving the location of acupuncture points used. Lowe (2000) was the exception.

Four studies (Lowe 2000; Forbes 2005; Schneider 2006; Conboy 2006) described an *a-priori* power calculation. Two studies used an intention to treat analysis (Schneider 2006; Forbes 2005). Most studies included in the review demonstrated some level of baseline comparability of the groups, but one provided no data regarding baseline characteristics (Lowe 2000). The number of people who withdrew from the studies or were lost to follow-up was minimal. None of the studies were considered to be at high risk of bias.

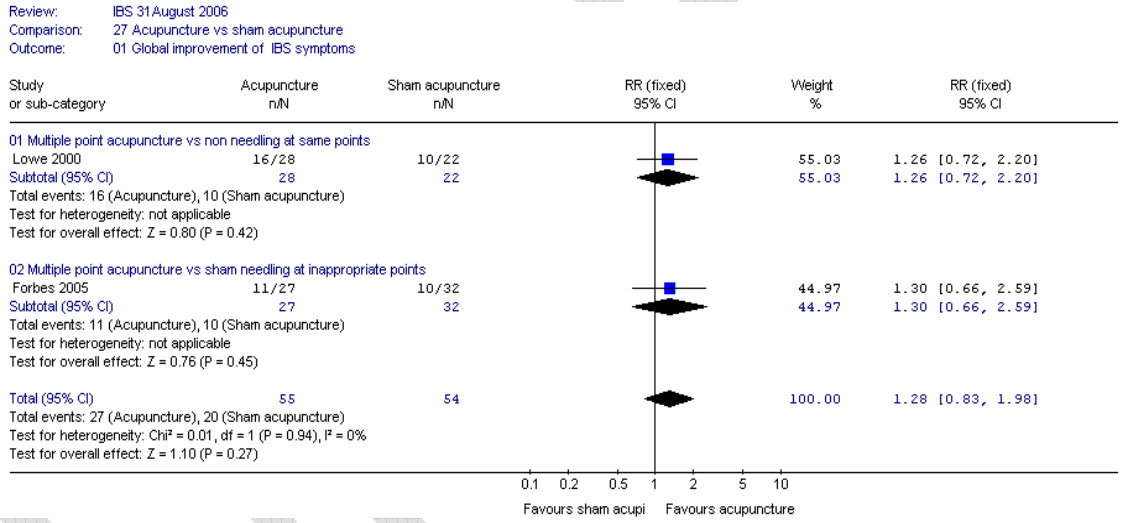
RESULTS

1. Global symptoms

a) Number of people with global improvement of symptoms

Two studies recorded the number of people with an improvement in global symptoms (Lowe 2000, Forbes 2005). These two studies were combined in a meta-analysis of 109 participants, even though the studies used different types of sham acupuncture. There was no statistically significant difference between acupuncture and sham acupuncture.

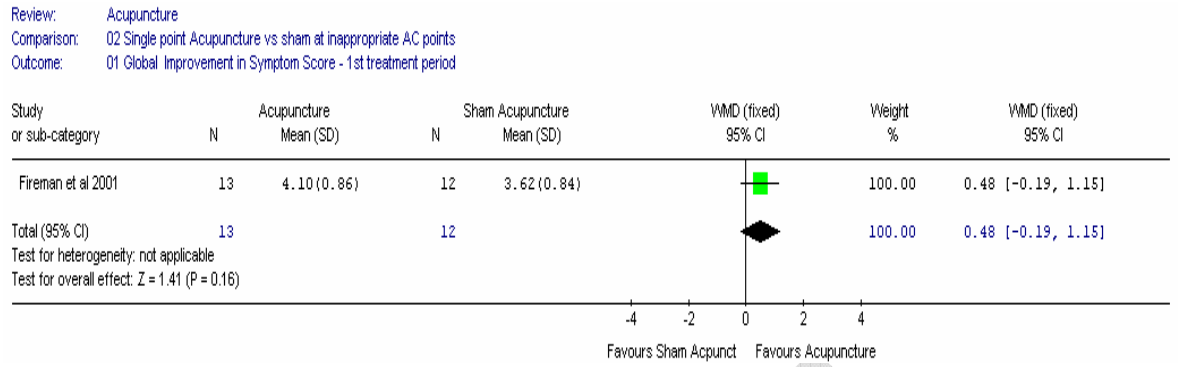
Figure 1: Number of people with global improvement of symptoms



b) Global improvement of symptoms score

Fireman (2001) recorded the global improvement in symptoms score (based on symptoms of pain; defaecation difficulties; diarrhoea; alternating diarrhoea and constipation; bloating; abdominal discomfort relieved by defaecation, and; mucus in stools), in 25 patients, using a visual analogue scale (1 to 5), on which 5 equated to significant improvement in global symptoms. As this study was a crossover design, data were used from the first period only. There was no significant difference between interventions.

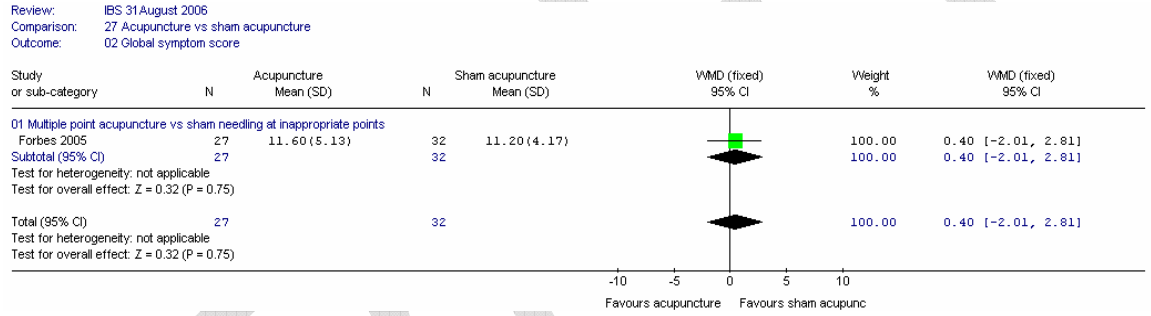
Figure 2: Global improvement of symptoms score



c) Global symptom score

One study (Forbes 2005) recorded the global symptom score on a scale of 0 to 30. There was no significant difference between acupuncture and sham acupuncture.

Figure 3: Global symptom score



2. Individual symptoms

a) Pain

Two studies recorded pain scores, Fireman (2001) and Scheider (2006). The latter used the discomfort subscale of SF36. The studies differed in the type of acupuncture used (single versus multiple point, respectively), and therefore were not combined in a meta-analysis. There was no significant difference between interventions in either study, although the sham acupuncture is favoured in the Fireman (2001) study.

Figure 4: Pain score

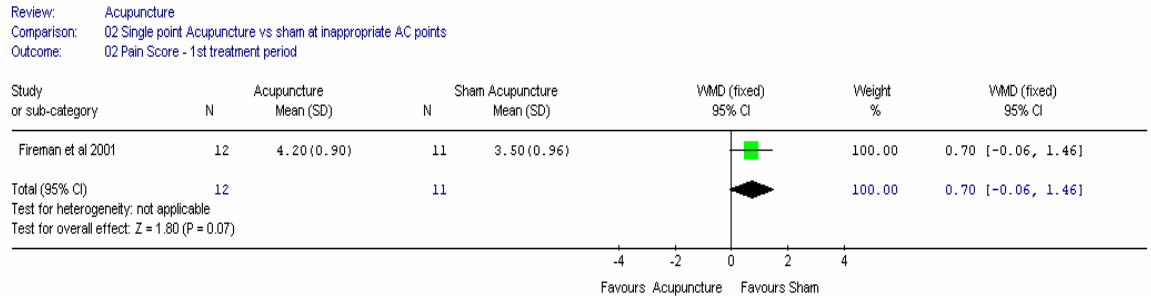
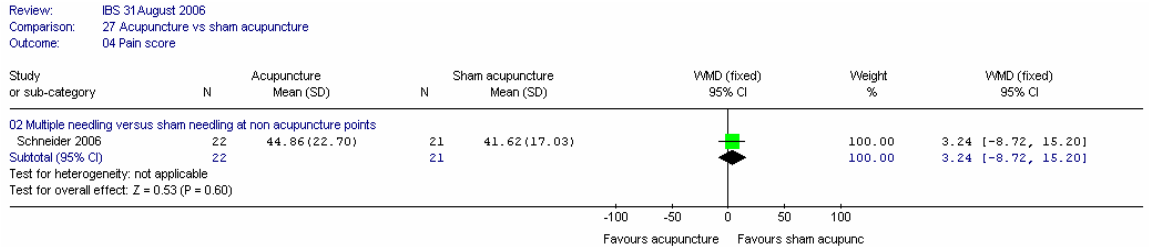


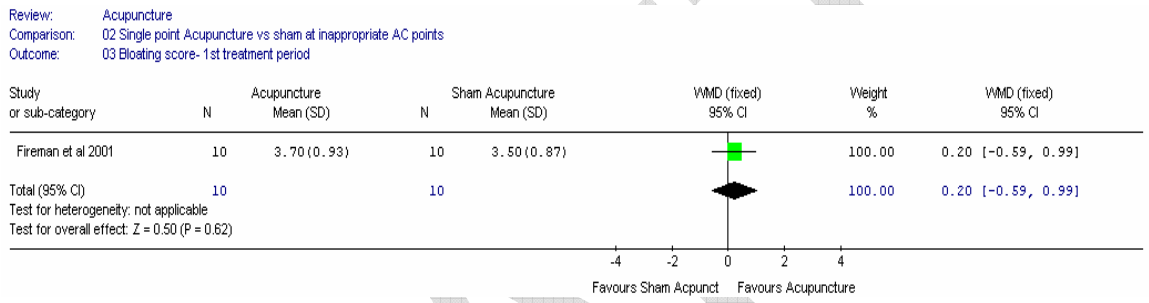
Figure 5: Oain component of SF 36



3. Bloating

Fireman (2001) reported a bloating score on a VAS of 1 to 5 in 20 participants. There was no significant difference between acupuncture and sham acupuncture.

Figure 6: Bloating score



4. Quality of life

Three studies reported quality of life measurements (Forbes 2005, Lowe 2000 and Schneider 2006). Forbes 2005 reported a small improvement in the EuroQol scores over baseline in both the acupuncture (59.4 to 64.6%) and sham acupuncture (64.6 to 65.6%) groups, neither difference was significant. Lowe (2000) reported a marked improvement in the IBS-36 quality of life score in both true and sham groups. There was no significant difference between the two groups. Schneider reported a mean difference of 1.98 (95%CI -3.59, 7.39) in 43 people, at the end of treatment, on a scale of 0 to 100, i.e. no significant difference. After three months follow-up, there was still no significant difference (MD 3.41 (95%CI -3.02, 9.83)

5. Adverse effects

The benefit of acupuncture cannot be evaluated without considering the risks associated with treatment. The incidence of adverse effects is largely unknown. However, for the purposes of this review, we included seven studies investigating adverse effects (Chung 2003; Burford-Mason 2003; White 2001; Ernst and White 1997; Ernst and White 2001; MacPherson 2001;Yamashita 2001). Three of these were systematic reviews (Ernst and White 1997; Ernst and White 2001; Yamashita 2001), two were surveys of acupuncture practice and one a commentary. The systematic reviews identified ten reports which included surveys from Europe and eighty-nine reports from the Far East. The most common adverse events identified in Europe were:

- Pain at the site of needling
- Pain due to aggravation of the presenting condition
- Bleeding – petechia, ecchymosis, haematoma
- Nausea and/or vomiting
- Fainting
- Tiredness.

Potentially serious adverse effects are rare: two cases of pneumothorax and two cases of needle fracture requiring surgical removal of the fragment, and one case of burn injury following moxibustion. There were no reports of infection complications or transmission of disease through needling.

The review from the Far East (Yamashita 2001) synthesised 89 papers that reported 124 cases of adverse events. These were classified into five categories:

- Injuries or foreign bodies (42 cases)
- Infections (32 cases, including 11 cases of Hepatitis B)
- Neurological problems (29 cases, including 18 cases of spinal cord injury, 10 of which were caused by needle breakage)
- Dermatological problems (17 cases)
- Other (4 cases).

The reviewers had previously demonstrated that severe adverse effects seem to be uncommon in standard practice for adequately trained acupuncturists.

The two Ernst and White, European reviews also found that there was no standard definition of adverse effects and estimated that there may be under-reporting of adverse events. It is also possible that there is over reporting of adverse effects so that the true incidence of serious complications may be very low. They emphasise the need to ensure appropriate training standards and appropriate regulatory and surveillance systems to enable more accurate assessment.

HEALTH ECONOMIC EVIDENCE

The cost effectiveness of acupuncture was not taken into consideration for this review because acupuncture is not prescribed, with the majority of acupuncture treatment being purchased independently by people with IBS.

EVIDENCE STATEMENTS

1. There is fair evidence to show no significant effect of acupuncture on IBS global symptoms, pain, and quality of life compared with placebo.

2. There is limited evidence of potentially serious adverse effects associated with acupuncture treatments.

GDG DISCUSSION

The GDG was concerned about the reported adverse effects (some of which were severe), non-registration and the safety of acupuncture. They noted an additional adverse effect that occurs with moxibustion, which can lead to burns. Members of the GDG were not surprised that acupuncture has been shown to have no significant effect in IBS: this might be expected because acupuncture is thought to work by producing endorphins which give pain relief, but they have no effect on visceral pain.It was noted that the patient community widely supports Traditional Chinese Medicine acupuncture.

The GDG's clinical view was that, although people with IBS widely support the use of acupuncture, the current lack of effectiveness and potential harm precludes a positive recommendation.

EVIDENCE TO RECOMMENDATION

The GDG took into consideration the lack of effectiveness of acupuncture, the limited evidence showing harm, and registration and regulation difficulties, and decided they would not recommend the use of acupuncture for IBS.

RECOMMENDATION

Primary care clinicians should not encourage the use of acupuncture in the treatment of IBS.

11 Psychosocial interventions: patient information and support groups

Clinical Questions

1. Do psychosocial interventions have a role in managing IBS symptoms?
2. Do self help/support groups have a role in managing IBS symptoms?
3. Information determines patient experience by facilitating informed choices.
4. What role does patient information play in IBS?

BACKGROUND

Psychosocial factors contribute to the predisposition to IBS; some authors believe it the most important factor in terms of who manifests IBS, how severe it becomes and how people with IBS cope with managing the condition. The multifaceted nature of IBS requires an appreciation and understanding of psychosocial principles that relate to the disorder and the way these may be addressed in treatment strategies. It is important to explore the possible indicators of psychological distress which may affect the ways in which a person with IBS presents their condition and the associated coping behaviours. Physical and sexual abuse is twice more common in people with IBS than in people with organic gastrointestinal disease. Anxiety and other major life stress and/or trauma have been shown to correlate with the development of IBS and the severity of its symptoms (Gunn 2003; Camilleri 2001; Jones 2000). The presence of psychosocial factors is also an indicator for the likelihood that people will seek medical attention for IBS as well as other medical conditions.

Addressing psychosocial factors with an ongoing collaborative multi-disciplinary approach leads to improvement in the clinical outcomes and while psychosocial factors do not cause IBS symptoms, they do influence the patients' response both to the condition and treatment (Gaynes 1999).

Support groups and patient information

People with IBS often experience a sense of frustration, isolation, and a need to identify a niche in the health/sick role continuum. Frustration may arise from their perceived inability to control symptoms, prevent episodes, identify episode triggers, and obtain medical validation of the condition. Many people with IBS consider their condition to be severe and greatly affecting their lives. They feel that some health care professionals do not give credence to IBS as a chronic debilitating condition and that information which may help them understand more about how to live with the condition is often not forthcoming. The

constant anticipation of the next IBS episode, the nature of the bowel symptoms, the requirement for quick and easy access to toilet facilities, often results in embarrassment and withdrawal from social activities with resultant isolation (Bertram 2001). Providing people with IBS appropriate information about their disorder may promote a strong physician-patient interaction and may reduce healthcare use. Most people with IBS feel insufficiently informed, particularly in relation to risk of serious disease and the role of diet (Dancey 1993; O'Sullivan 2000).

The isolation people with IBS experience in many aspects of their lives may also be addressed by the use of support groups. Support groups have been suggested as a way for people to help one another by having the opportunity to discuss coping strategies with others who are experiencing similar issues. However provision and access to IBS support groups may vary throughout the UK.

*"*There is no self help group near to me at the moment, but maybe that will happen in due course. I am sure that to talk with fellow sufferers must be a great help. So many people are striving to get the better of this awful affliction without much luck, but, ever the optimist, I shall continue to look for an answer*."*

This anonymous quote is not atypical of the IBS patient experience, and to address these concerns through effective diagnosis and management interventions is an essential aspect of this clinical guideline. Support group discussion may provide people with an opportunity to share others' difficulties with IBS, which may affirm their own IBS experiences. They may be relieved to finally be able to discuss their problems and symptoms with others who understand the challenges.

People appear to cope better with this chronic illness if they have sufficient information about IBS and appropriate support networks. Within the context of the whole IBS patient journey, evidence suggests that an important feature of effective coping and improved quality of life is for people to take responsibility through shared management with their primary care clinician (Kennedy 2003; Lacy 2007; Rogers 2007). Therefore, due consideration of the information needs of people with IBS is fundamental to the provision of effective management strategies.

Review of the literature for psychosocial interventions, support groups and patient information led to two reviews, one on support groups and self help, and the other on patient information. There was no evidence for other psychosocial interventions. The support groups and patient information reviews are closely linked: a common theme is the investigation of the effectiveness of a guidebook giving patient information. The two reviews are presented in sections 11.1 and 11.2; section 11.3 describes the process of evidence to recommendation for both reviews, leading to a single recommendation.

11.1 Support Groups and Self Help

SELECTION CRITERIA

The selection criteria described in the general methodology section were used, except that crossover studies were excluded as inappropriate due to the carry-over effect of the interventions.

The following comparisons were to be included:

- Support group versus waiting list control
- Support group plus other intervention versus other intervention only
- Support group versus other intervention.

SEARCH STRATEGY FOR IDENTIFICATION OF STUDIES

Searches were performed on the following core databases: MEDLINE, EMBASE, CINAHL, and *The Cochrane Library* (1966 to current day with guidance from the GDG). Additionally, the PSYCINFO database was searched for this review. The search strategies are given in Appendix B.

The titles and abstracts of these studies were assessed. Three studies were identified as being potentially relevant to the review and these papers were retrieved in full. The reference lists for each of the retrieved studies were inspected for further potential papers, but none were identified. The one excluded study is listed in Appendix E, along with reasons for exclusion.

CHARACTERISTICS OF INCLUDED STUDIES

Study Design

Two randomised trials were found (Payne 1995; Robinson 2006). One was carried out in the USA (the setting was not stated) (Payne 1995); the other was carried out in primary care in the UK (Robinson 2006).

Population

The 34 patients (5 men and 29 women) in the Payne (1995) study had IBS satisfying the Rome I criteria; their mean age was around 40 years (range 22 to 70 years); 29/34 had an Axis I disorder.

The 420 patients (50 men and 370 women) in the Robinson (2006) study had IBS, of whom 38% satisfied Rome II criteria (the rest diagnosed by GP or specialist if they had previously been referred); patients were excluded if they were unable to read or understand English; their mean age was 40 years (SD 14.4 years); psychiatric co-morbidities were not stated. They had had bowel symptoms for a mean of 6 years (SD 7.2 years).

Neither of the studies reported the number of participants with bloating or whether the symptoms were post-infective.

Interventions and comparisons

Payne (1995) compared three groups: 1) support group; 2) cognitive behavioural therapy; 3) waiting list control for 8 weeks. The self-help group intervention involved guided discussion on aspects of IBS, for example, stress and diet, for 1 hour 15 minutes per week for 8 weeks.

Robinson (2006) compared three groups: 1) self-help support group plus educational guidebook; 2) guidebook only; 3) usual care. The self-help guidebook included information on: lifestyle; diet; drugs, and; alternative therapies. The self-help meeting was a one-off 2-hour meeting of 8 to 12 people at a time; only 59 of 139 attended. The study carried out some additional qualitative research and noted that some people were unwilling to discuss bowel related symptoms with strangers, which may have been the cause of the poor attendance rate. The control group had usual care at the discretion of the primary care physician. Data were collected at one year.

People in Payne (1995) continued to take their medication unchanged. Participants in Robinson (2006) were informed that they were free to continue to visit their primary care physician without restriction.

Comparisons were:

- Support group versus waiting list control for 8 weeks
- Self-help support group plus educational guidebook versus guidebook only, followed at one year
- Guidebook only versus usual care, followed at one year
- Support group versus cognitive behavioural therapy (this is reported in the CBT review), at 8 weeks.

Outcomes

The outcomes examined were:

1. Global symptoms:
    a) Global improvement in symptoms (number of patients) (Payne 1995)
    b) Global symptom score on a 7-point scale from unbearable to no symptoms (i.e. higher score is better) (Robinson 2006)
    c) Global improvement of IBS symptoms (mean Composite Primary Symptom Reduction [CPSR] score; CPSR represents the proportional reduction in score from baseline); i.e. high = bad (Payne 1995)
    d) Global assessment of treatment on symptoms (Robinson 2006).

2. Mental health outcomes (overall mental health; depression; anxiety)

Overall anxiety and psychological distress (Anxiety, State-Trait Anxiety Inventory [STAI]); Scale range 20 to 80; high = bad (Payne 1995)

Beck depression inventory (scale maximum 63; high=bad) (Payne 1995).

METHODOLOGICAL QUALITY

The quality assessment for included trials is shown in Appendix D.

The method of randomisation was adequate in Robinson (2006), which stated that it used a randomisation system based on minimisation. Allocation concealment was adequate in one study using a central telephone randomisation system (Robinson 2006) and not stated in the other (Payne 1995). The patients were not blinded (because of the type of intervention). Neither study reported an *a priori* power calculation. Payne (1995) demonstrated baseline comparability between the groups; this was not stated in Robinson (2006). All the participants were followed up in Payne (1995), while in Robinson (2006) data were missing for 56 patients overall (13%). Overall, neither study was considered to be at risk of bias.

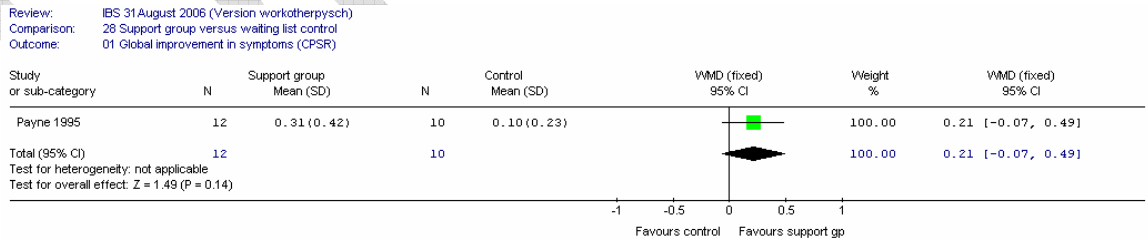
RESULTS

A. Support group versus waiting list control

1) Global symptoms

Global improvement of IBS symptoms was reported by Payne (1995) at 8 weeks, in 22 people, using the mean Composite Primary Symptom Reduction [CPSR] score; CPSR represents the proportional reduction in score from baseline. The study gave individual patient data, allowing calculation of standard deviations. There was no significant difference between interventions, but the confidence interval was fairly wide.

Figure 1:

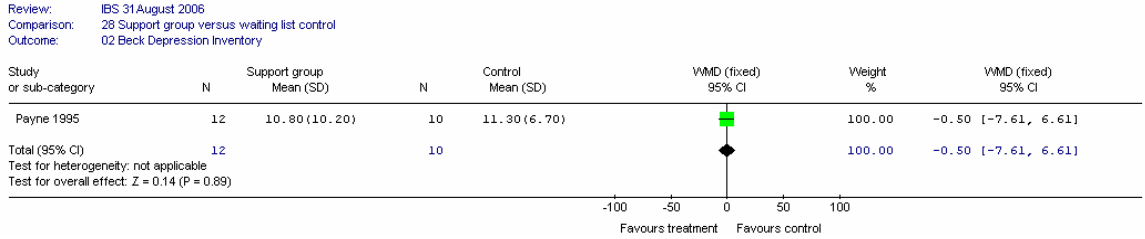


2) Mental health outcomes

a) Beck Depression Inventory

Payne (1995) reported Beck Depression Inventory scores (scale maximum 63; high=bad) at the end of treatment (8 weeks). There was no significant difference between interventions.

Figure 2:



b) Overall anxiety and psychological distress: State-Trait Anxiety Inventory (STAI)

Payne (1995) reported STAI scores (20 to 80; high=bad) at the end of treatment (8 weeks). Again there was no significant difference between interventions.

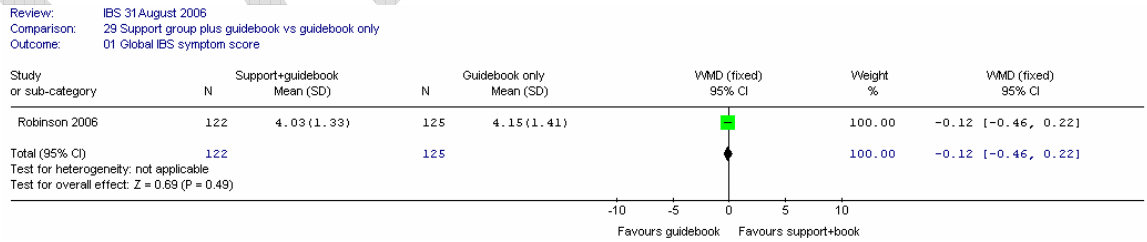
Figure 3:

B. Self-help support group plus educational guidebook versus guidebook only

1. Global symptoms

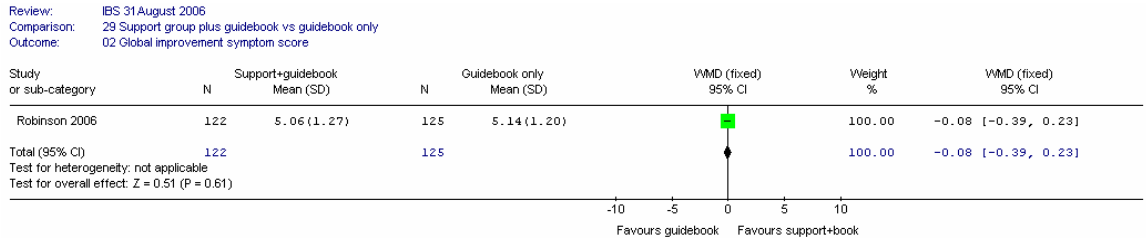
Robinson (2006) reported a global IBS symptom score on a 7-point scale from unbearable to no symptoms (i.e. higher score is better) at the 52-week follow-up in 247 patients. There was no significant difference between interventions. We note, however, that only 59 of the 139 participants attended the support group meeting (although the global symptoms scores were still reported).

Figure 4:



People also reported their assessment of treatment on symptoms (global improvement of symptoms score) on a 7-point scale from very much worse to very much improved (i.e. higher score is better). There was no significant difference between interventions.

Figure 5:



C. Guidebook only versus usual care

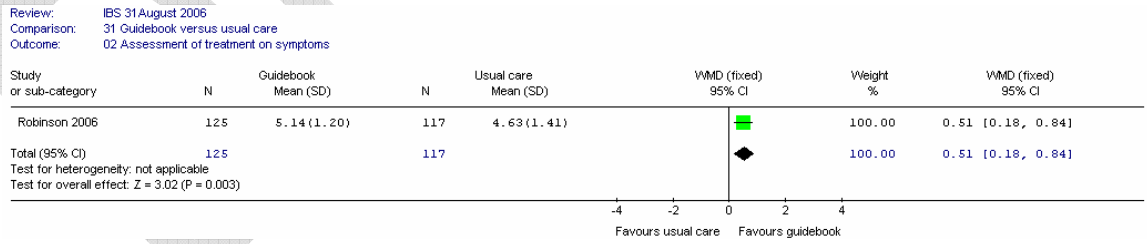
1) Global symptoms

Robinson (2006) reported a global IBS symptom score on a 7-point scale from unbearable to no symptoms (i.e. higher score is better) at the 52-week follow up in 242 patients. There was no significant difference between interventions.

Figure 6:

Patients also reported their assessment of treatment on symptoms (global improvement of symptoms) on a 7-point scale from very much worse to very much improved (i.e. higher score is better). There was a statistically significant difference, in favour of the guidebook.

Figure 7:



The results from Robinson (2006) suggest that the guidebook may have helped patients, with little additional benefit from the support group (a single 2-hour meeting, which only 59 of the 139 patients in this randomisation arm actually attended).

ECONOMIC LITERATURE FOR PSYCHOSOCIAL INTERVENTIONS / SUPPORT GROUPS

One relevant health economic analysis was identified on the cost-effectiveness of psychosocial interventions or support groups in the management of IBS. Robinson (2006) was a trial based economic analysis looking at the impact of two self help interventions (a guidebook and a self-

help group session) on clinical and economic outcomes in primary care patients with IBS. Only the economic outcomes are described here as the clinical effectiveness results have been described in the clinical effectiveness review. The economic outcomes reported were GP visits, hospital consultation rates, prescription costs and overall costs.

This study provided evidence that the provision of a self-help guidebook reduced GP visits (-1.56 visits per annum, P<0.001), hospital visits (-0.22 visits per annum, p=0.038) and prescription costs (£24, p=0.031) but the addition of a self-help group session did not further reduce resource use. Overall costs for GP visits, hospital visits and prescribed drugs were reduced for those who received the guidebook (-£73, 95%CI -£43 to -£103, p<0.001) but there was no significant effect on overall costs from the addition of the self-help session. The guidebook was also associated with a significant increase in the use of self-care activities such as dietary interventions and relaxation therapy.

This study was a partial economic evaluation as it did not assess the incremental cost of any benefit achieved by the provision of a guidebook or self-help group session in the form of a cost-effectiveness ratio. A particular limitation of this study was the failure to include intervention costs for the guidebook or self-help group. This limitation would only affect the conclusions drawn from this study if the cost of providing the guidebook exceeded the cost-savings resulting from reduced resource use in patients provided with a guidebook. The evidence provided by this study was considered relevant to the guideline as it considered both costs and effects for the intervention in an appropriate population and setting. No potential areas of significant bias were identified except for the exclusion of intervention costs. Whilst this study did not provide a full economic analysis of the provision of guidebooks, with or without a self-help group session, this evidence was considered alongside the clinical effectiveness evidence to inform recommendations on the use of self-help groups and self-help information in the management of IBS.

EVIDENCE STATEMENTS

1. There was limited evidence to show no significant difference in global improvement of symptoms or in depression on the Beck inventory for a self help group intervention, involving guided discussion on aspects of IBS, for example, stress and diet, for 1hour 15 minutes per week for eight weeks, compared with waiting list control.

2. There was good evidence to show no significant additional effect on global symptoms of a single two-hour self help meeting of 8 to 12 people at a time, in people already receiving a guidebook. It is noted that less than half the people attended the self help meeting.

3. There was good evidence to show no significant additional effect on the number of primary care consultations and hospital visits of a single two-hour self help meeting of 8 to 12 people

at a time, in people already receiving a guidebook. It is noted that less than half the people attended the self help meeting.

4. There was good evidence to show no significant additional effect of a single two-hour self help meeting of 8 to 12 patients at a time, in patients already receiving a guidebook, on the overall cost of GP visits, hospital visits and prescription drugs. It is noted that less than half the people attended the self help meeting.

5. There was good evidence to show a significant improvement in global symptoms for people receiving a self-help guidebook, which included information on lifestyle, diet, drugs and alternative therapies, in comparison with usual care.

6. There was good evidence to show a significant decrease in the number of primary care consultations and hospital visits for people receiving a self-help guidebook, which included information on lifestyle, diet, drugs and alternative therapies, in comparison with usual care.

7. There was good evidence to show a significant reduction in the overall cost of GP visits, hospital visits and prescription drugs for people receiving a self-help guidebook, which included information on lifestyle, diet, drugs and alternative therapies, in comparison with usual care.

GDG DISCUSSION

The GDG commented that people may not attend support groups because of travel difficulties (due to lack of control of symptoms) and a general reluctance to discuss bowel problems with others. The superior effect of the guidebook compared to usual care was not surprising, and the GDG noted that a simple guide to IBS has proved popular in the past. It was also noted that many people with IBS do make a great effort to attend support groups and those that attend find these beneficial.

11.2 Patient Information

OBJECTIVE

To review the evidence on the information needs of people who have been diagnosed with IBS, assessing the impact that information has in their self management of the syndrome and their ability to maximise quality of life when living with the syndrome.

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

Quantitative (RCTs, prospective studies, survey) and qualitative (eg. focus group) study designs were considered for this review.

SEARCH STRATEGY FOR IDENTIFICATION OF STUDIES

Searches were performed on the following core databases: MEDLINE, EMBASE, CINAHL, and *The Cochrane Library.* Searches were performed from the beginning of each database and updated to June 2007. The search strategies are given in Appendix B:
Following sifting, five studies were included in the review.

CHARACTERISTICS OF CLINICAL STUDIES INCLUDED IN THE REVIEW

Five studies were included in this review: three were prospective studies (Kennedy 2003, Lacy 2007, Bogalo 2006) and two were separate papers from a randomised trial (Robinson 2006, Rogers 2007). One study was excluded and is given in Appendix E.

Prospective non-randomised studies

The Lacy (2007) study used a questionnaire that addressed two main domains:

- Participant knowledge of IBS (epidemiology and natural history; aetiology; symptoms; diagnosis and treatment)
- Participant attitudes towards IBS (relationships of IBS to functional status; concerns and fears about IBS; ability of the medical system to address patients' needs).

People with IBS were identified from a search of the medical records in Lebanon, New Hampshire, USA and the records were examined to ensure that the participants met the Rome II criteria. 261 of 664 contacted (39%) returned the questionnaires.

Bogalo (2006) was a prospective study of 31 people assigned to the treatment group in an RCT. These participants received a self-help treatment manual over six weeks, with one chapter per week. Each chapter was task oriented. Topics covered in each of the six weeks were: IBS

explained; assessing symptoms and self monitoring; managing IBS symptoms; cognitive restructuring, personal expectations and activity patterns; relaxation and stress management; and maintenance. The study investigated the hypothesis that treatment group participants who had a higher level of engagement in the homeworking tasks would experience greater relief from their IBS symptoms.

The Kennedy (2003) study used focus groups of 12 people to explore participants' knowledge and experience of IBS. Participants were recruited from an article in a regional paper asking for volunteers. Focus group meetings were held over a two week period and lasted 1¼ to 1½ hours. Each session was taped and transcribed. Transcripts were read and analysed using a framework developed for the study. Four main areas were outlined (perceptions and expectations; experience of IBS; information needs and sources; managing IBS) and these were divided into 16 subheadings. Each comment in the focus group was allocated to one of the sub-headings. The patients' views and experiences were used in the development of a self-help guidebook.

Randomised studies

The Robinson (2006) study measured the clinical and cost effectiveness of three interventions: the Kennedy self-help guidebook; the guidebook together with a two-hour one-off support group meeting; and usual care. It is noted that less than half of the people in the support group arm attended the support group meeting. This study has been reported and discussed in the Support groups review (section 11.1)

Rogers (2007) is a report of a qualitative study of a purposefully selected group of 12 of the Robinson (2006) trial patients: four of these participants had received the guidebook only; four had received the guidebook and had attended the support group meeting; one who had received the guidebook but did not attend the meeting; and three control group participants. Interviews were carried out with the participants, lasting between 40 and 90 minutes. These were transcribed and transcripts were analysed thematically, against one another by constant comparison. Key themes included: the lived experience of IBS (impact on everyday life; experience of symptoms; and reaction of others); ways of managing; lay epidemiology; experience of medical management and diagnosis; alternative help-seeking views about medication; the guidebook as projected identification with others; use of the guidebook, together with perceived changes; and continuity from being part of the trial.

Quantitative and qualitative narrative review was carried out to assimilate the evidence on the reported benefits of information in enabling people with IBS to better understand their condition and make lifestyle adjustments. A thematic analysis was carried out across included studies.

RESULTS

From the qualitative study data, several distinct themes emerge. These are:

- There is a lack of clear information to support people with IBS, which creates misunderstanding and misconception
- People with IBS are often misinformed at the point of diagnosis, not fully understanding the diagnosis and its potential impact on quality of life
- Medical management is often one-dimensional, with no attention given to lifestyle and other therapeutic interventions
- Developing coping mechanisms are augmented by structured information. Patient experience was improved through exposure to a guidebook which focused on self-management in partnership with the primary care clinician
- Structured information provides an instant source of help, sensitive to the episodic nature of IBS, facilitating the sharing of experience and ongoing IBS management
- Patient information is essential for shared decision-making and partnership between clinicians and people with IBS
- Information should be patient-centered with involvement of the person with IBS
- Primary care clinicians should take responsibility to ensure that their knowledge of IBS enables expressed concerns to be answered, offering support through clear explanation
- People with IBS need information relating to cause, cure and long-term prognosis for IBS
- Appropriate sources of information for people with IBS include magazine articles, leaflets in shops, books, support groups, internet, medical journals and books.

Information needs

The importance of good information is highlighted in this review of published papers relating to the information needs, experiences, and quality of life issues for people with IBS. Given the chronic nature of IBS, information quality will contribute to the development of an effective shared decision making model between primary care clinician and the person with IBS. The primary care clinician is a key resource for the person who presents with IBS, and following positive diagnosis the importance of information sharing and shared decision making relating to their symptom profile and treatment response is a key aspect.

Respondents in the Kennedy study (2003) highlighted that primary care clinicians had little knowledge about IBS, and subsequently were unable to provide much in the way of clear information that encouraged self-help strategies for people with IBS. Magazine articles, leaflets, books, support groups, internet sources and published journal articles were highlighted as useful. The inclusion of patients in producing patient information emerged as a contemporary theme within this study, this is consistent with NICE's approach to developing patient information, and is produced as part of this clinical guideline suite of information. Lacy (2007) supports points raised for discussion from the Kennedy study, highlighting that specific guidance

on diagnosis, treatment, misconceptions about natural history of the disease and subsequent confusion should all feature in prepared information.

Information clearly has an educative role, in correcting inappropriate concerns relating to cancer, and in developing the shared care model that provides clarity in symptom based presentation and subsequent treatment interventions that are appropriate for that particular person with IBS.

The Robinson (2006) study found that use of the self-help guidebook compared with usual care resulted in fewer primary care consultations, and a greater improvement in global symptoms. Well prepared information appears to be at least cost neutral, with a cost per patient reduction reported as £73. This aspect is discussed further in the support groups review (section 11.1)

Understanding the importance of patients as agents of change is a key aspect to effective implementation of evidence, where patients become the drivers for change in healthcare behaviours. The success of the patient self-help booklet reported in the Kennedy study (2003) is a clear example of the importance of patient information, in meeting the needs of people learning to live with IBS or adapting lifestyle for those people who have lived with IBS for a significant period of time.

Quality of life

Chronic illness remains a significant challenge to the individual in terms of effective coping, and to the NHS in identifying the appropriate level of support to that individual. In this review, quality of life issues are raised consistently in studies that ask people with IBS questions relating to the level of impact that IBS has on their daily living activities. People often express the desire for cure and information relating to long term prognosis, reflecting the over-medicalised language relating to effective coping. Living with IBS is the challenge, and symptom based management relating to the quality of life experience is key in the shared care model. In the Lacy (2007) study, nearly all participants (n=261) reported that IBS affected their lives in some way. Clearly this relates to severity and quality of life when considered as a continuum, and one can see the person moving from coping to not coping, reflecting the episodic nature of the syndrome.

The role of information and its added value in addressing misconceptions, diagnosis, providing reliable answers to questions, treatment interventions and indicating when access to a primary care clinician should be considered due to continued worsening of symptoms are all aspects highlighted within this clinical guideline. If addressed, collectively they should provide a foundation for the patient to develop effective coping strategies.

GDG DISCUSSION

Information should be clear, concise and relate to the symptom-based management of the syndrome. It should deal with areas of misconception, embarrassment and quality of life issues.

This should be provided at the earliest opportunity by the primary care clinician following positive diagnosis of IBS.

The role of well prepared information provides the basis for the development of the shared care model between the primary care clinician and the person with IBS. Evidence supports the use of information booklets that encourage self help activity.

EVIDENCE STATEMENTS

1. There is fair evidence indicating that if people with IBS receive directed information and encouragement to be actively involved in the management of their condition that this contributes to:
    - A positive impact on treatment outcomes
    - An improvement in quality of life perception and reduction in symptom severity
    - Reduction in primary care consultations.

2. There is weak evidence indicating that people with IBS lack appropriate information relating to their condition. This can lead to misunderstanding and reduced quality of life experiences.

11.3 Evidence to Recommendation

The GDG took into consideration the evidence in both reviews. This included the clinical and cost effectiveness results from the quantitative studies, and the qualitative analysis in the patient information review, which was supported by the experiences of all members of the GDG. The evidence from the support groups review showed improved clinical outcomes and reduced health care costs for people provided with a self-help guidebook, and indicated that providing self-help information in the management of IBS is likely to be clinically and cost-effective. There did not appear to be an additional effect from a support group meeting, but this may have been confounded by the poor attendance. Some members of the GDG had extensive experience of self-help groups and reported that they are a current voluntary sector patient provision, providing social support, and that people with IBS comment positively on their involvement in self help organisations. The GDG decided not to make a recommendation on the usefulness of support groups.

Based on the qualitative data in the patient information review and their own experience, the GDG recognised the need for clear unambiguous information, and indicated its role and importance in helping people with IBS develop coping strategies in partnership with their primary care clinician. The GDG noted that patient information should be provided early in the patient pathway following a positive diagnosis of IBS, and that self-help information should be wide ranging, covering areas such as general lifestyle, physical activity, diet and symptom-targeted medication.

RECOMMENDATION

People with IBS should be given information that explains the importance of self-help in effectively managing their IBS. This should include information on general lifestyle, physical activity, diet and symptom-targeted medication.

12 RECOMMENDATIONS FOR RESEARCH

1. Tricyclic antidepressants, SSRIs and SNRIs

Are low-dose tricyclic antidepressants (TCAs), SSRIs and SNRIs effective in the treatment of IBS as a first line therapy, and which is the more effective and the safer option?

Why is this important?

Reviews have shown that TCAs and SSRIs have each been compared with placebo, but not at low dose. In practice, TCAs are used at higher doses and concordance with treatment is poor because of side effects. GDG clinicians believe that at low doses (e.g. 5 to 10 mg equivalent of amytriptyline), TCAs could be the treatment of choice, but there is a lack of evidence. Newer antidepressants, SNRIs, maybe useful in the treatment of IBS pain. A large randomised trial is proposed, comparing an SSRI, a TCA, an SNRI and placebo. Participants should be adults with a positive diagnosis of IBS, stratified by type of IBS and randomised to treatments. The primary outcome should be global improvement in IBS symptoms. Health related quality of life should also be measured. Adverse effects should be recorded. Study outcomes should be assessed at 12, 26 and 52 weeks after the start of therapy.

2. Behavioural therapies

Are behavioural therapies (psychological therapy, hypnotherapy and CBT) equally effective in the management of IBS symptoms, either as first line therapies in primary care, or in the treatment of people with IBS that is refractory to other treatments?

Why is this important?

Reviews show some evidence of effect when comparing behavioural therapies with control, mainly in people with refractory IBS. Many trials are small in size. The behavioural therapies of psychological therapy, hypnotherapy and CBT are thought to be useful in helping people with IBS cope with their symptoms, but it is unclear at what stage these should be given, including their use as first line therapies in primary care. A large randomised trial is proposed, comparing CBT, hypnotherapy and psychological therapy (psychodynamic interpersonal

therapy). Participants should be adults with a positive diagnosis of IBS, and they should be stratified into those with and without refractory IBS and then randomised to treatments. The primary outcome should be global improvement in IBS symptoms. Health related quality of life should also be measured. Adverse effects should be recorded. Study outcomes should be assessed at 12, 26 and 52 weeks after the start of therapy.

3. What factors contribute to refractory symptoms in IBS?

Why is this important?

Most individuals with IBS experience symptoms that are relatively short lived or only trouble them on an intermittent basis. Some people, however, develop chronic and severe symptoms that are difficult to treat. There are relatively few prospective studies that have investigated this problem.

A large, prospective, population based cohort study is proposed, which would evaluate people in the community with IBS symptoms, according to measures of bowel symptomatology, physical symptom profile, psychological symptoms, childhood adversity, past history of psychiatric disorder, social supports, quality of life and other relevant potential predictors. Individuals would be re-evaluated 12 and 24 months later using similar measures. Baseline variables would be used to predict chronicity of symptoms, quality of life and healthcare utilisation at 12 months and at 24 months.

4. Relaxation and biofeedback

What is the effect of relaxation and biofeedback therapies on IBS symptoms and patient-related outcomes?

Why is this important?

Reviews of biofeedback and relaxation therapies suggest a positive effect on the control of IBS symptoms, but evidence is limited and not sufficient to make recommendations. Patient representation within the group supports this view, from a personal and anecdotal perspective.

Recent developments in computer-aided biofeedback methods merit investigation. A large randomised trial is proposed to compare relaxation therapy, computer-aided biofeedback therapy and attention control in primary care. Participants should be adults with a positive diagnosis of IBS, and they should be stratified into those with and without refractory IBS, and then randomised to treatments. The primary outcome should be global improvement in IBS symptoms. Health related quality of life should also be measured. Adverse effects should be recorded. Study outcomes should be assessed at 12, 26 and 52 weeks after the start of therapy. Qualitative data should be generated relating to how people with IBS perceive their IBS condition.

5. Physical activity

What is the effect of physical activity on IBS symptoms in adults?

Why is this important?

To date there has been no comparative intervention study examining the effect of physical activity on IBS symptoms in adults independently or in combination with other lifestyle counselling. A large randomised trial is proposed, comparing physical activity with waiting list control or with usual activity. Participants should be adults with a positive IBS diagnosis and should be stratified by IBS type and then randomised to treatments. The physical activity dose should be moderate intensity physical activity (e.g. walking, light group exercises) and could be delivered within a class structure (e.g. as part of an IBS education class) or performed independently.

The primary outcome should be global improvement in IBS symptoms, with symptom scores being recorded using a validated scale. Health related quality of life should also be measured. Data on adverse events should also be recorded. Study outcomes should be assessed at 12, 26 and 52 weeks post intervention.

13 IMPLEMENTATION OF THE GUIDELINE

The Healthcare Commission assesses the performance of NHS organisations in meeting core and developmental standards set by the Department of Health in 'Standards for better health', issued in July 2004. Implementation of clinical guidelines forms part of the developmental standard D2. Core standard C5 says that national agreed guidance should be taken into account when NHS organisations are planning and delivering care.

NICE has developed tools to help organisations implement this guidance (listed below). These are available on our website (www.nice.org.uk/CGXXX). *[NICE to amend list as needed at time of publication]*

- Slides highlighting key messages for local discussion.
- Costing tools:
  - Costing report to estimate the national savings and costs associated with implementation
  - Costing template to estimate the local costs and savings involved.
- Implementation advice on how to put the guidance into practice and national initiatives that support this locally.
- Audit criteria to monitor local practice.

14 RELATED NICE GUIDANCE

Published

Depression: Depression, management of depression in primary and secondary care. NICE clinical guideline 23 (2004). Available from www.nice.org.uk/CGXXX

Referral for Suspected Cancer: Referral Guidelines for Suspected Cancer in Adults and Children. NICE clinical guideline 27 (2005). Available from www.nice.org.uk/CGXXX

Physical Activity. NICE public health intervention guidance PH1002 (2006). Available from www.nice.org.uk/PHIXXX

15 UPDATE OF THE GUIDELINE

NICE clinical guidelines are updated as needed so that recommendations take into account important new information. We check for new evidence 2 and 4 years after publication, to decide whether all or part of the guideline should be updated. If important new evidence is published at other times, we may decide to do a more rapid update of some recommendations.

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