Acupuncture for irritable bowel syndrome
– an exploratory randomised controlled trial

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Abstract

Background The evidence on the effectiveness of acupuncture for irritable bowel syndrome (IBS) is inconclusive. However, many patients with IBS are self referring for acupuncture, therefore it is of interest to know whether acupuncture is effective or not. The aim of this study was to establish variability in the primary outcome measure to enable a sample size to be calculated for a full scale trial, and to explore feasibility and design criteria.

Methods A pragmatic randomised controlled trial compared 10 sessions of acupuncture plus usual GP care with usual GP care alone. Thirty patients were recruited from four GP databases in Birmingham, UK, and randomised one-to-two to acupuncture or usual care alone. The primary outcome was the IBS Symptom Severity Score (SSS) at three months (maximum score 500). Analysis was by intention-to-treat, and multiple imputation was used for missing data.

Results From the databases, 189 patients with IBS were identified, of whom 30 were eligible and consented to randomisation. At three months, a statistically and clinically significant difference between groups of 138 points (SD 90) in favour of acupuncture was observed on the IBS SSS (95% CI: 66 to 210; P=0.001) using multiple imputation. For a full scale trial, we estimate that a sample size of 108 patients per arm is required, based on a minimum clinically significant change of 50 points, drawn from a primary care population of 140 000.

Conclusions We established the feasibility of a full scale trial, successfully recruiting patients and calculating the sample size required. The results of our pilot analysis suggest that more definitive research into acupuncture for IBS is merited. A pragmatic trial design will not be able to distinguish between acupuncture specific effects and placebo effects; however, it is the design of choice to determine cost effectiveness.

Keywords

Acupuncture, irritable bowel syndrome, randomised controlled trial.

Introduction

Irritable bowel syndrome (IBS) is typically a chronic, recurrent disorder, associated with substantial health, social and economic costs.[1,2] As well as the physical symptoms, which can be severe, there is a high incidence of psychiatric disorders amongst IBS sufferers.[3] The prevalence of IBS in the UK population is estimated to lie somewhere between 5% and 22%,[4] and it is the most common functional bowel disorder seen by GPs.[5] Surveys among GPs have found that 'under half of the general practitioners felt that drugs were effective (for IBS)'[6] and IBS was the fourth most common condition cited in a list of 'effectiveness gaps'.[7] Systematic reviews of conventional medications for IBS have found that 'the evidence for efficacy of drug therapies is weak',[8] and that 'no drug is effective in treating all symptoms (of IBS)'.[9]

A recent Cochrane review of acupuncture for IBS was unable to make either a positive or negative recommendation because of the poor quality of studies.[10] Nevertheless, many patients are turning to alternatives: it has been estimated that almost half of those with a functional bowel disorder have used some form of complementary or alternative treatment, one of the most popular being Traditional

Chinese Medicine (TCM).[11] A cross-sectional study found that just under 5% of patients consulting acupuncturist members of the British Acupuncture Council cited digestive disorders as their main complaint.[12]

On the basis of this widespread use, combined with an inadequate evidence base, it is in the public interest to know whether acupuncture is effective for IBS or not. This context has provided the rationale for our aim to conduct an exploratory study for a full scale randomised controlled trial.

Methods

Design

The design for this study was that of a pragmatic randomised controlled trial comparing acupuncture plus usual GP care to usual GP care alone. The rationale for this open design was that it would best answer practical questions regarding the clinical and cost implications of offering an additional treatment as an adjunct to conventional medical care.[13] The aim of this exploratory study was to: pilot procedures and processes; establish the variability in the outcome measure among this population of patients; estimate the sample size for a full scale trial; assess the requirement in terms of the number of GP practices that might be required; identify the key cost drivers for the cost effectiveness analysis (not reported here); and refine additional design features of the full scale trial.

Ethics approval was obtained from the South Birmingham Local Research Ethics Committee (Ref: 06/Q2706/3).

Participants and methods

Patients were identified via the databases of four GP practices in Birmingham. We aimed to recruit 30 patients to our study, which is sufficient to be able to estimate a parameter.[14] We searched for patients who were aged 18-80, with either a diagnosis of IBS from their GP or given medications used to treat IBS symptoms, who had consulted in primary care for IBS within the last two years. Patients were invited to participate by postal questionnaire which included screening questions so we could include those with IBS according to the Rome II diagnostic criteria,[15] but exclude those with a score of less than 100 on the IBS Symptom Severity Score (SSS),[16] a current diagnosis of haemophilia or cancer, major gastrointestinal surgery in the preceding six months or current acupuncture treatment.

Randomisation and blinding

We randomised patients, with stratification based on baseline severity of IBS, to receive either a short course of traditional acupuncture plus usual care or usual care only in the ratio 1:2, as there were limited resources for providing acupuncture treatments. The randomisation sequence was computer generated by an independent researcher and concealed allocation was achieved by remote central telephone contact. Selection of acupuncture practitioner was by availability of appointments and convenience to patients. As this was a pragmatic trial, neither participants nor researchers were blind to treatment assignment.

Intervention

Acupuncture was provided by five generalist acupuncturists who were registered with the British Acupuncture Council, and had at least five years' experience. The acupuncture, which was provided at independent clinics and funded by a University of York research grant, comprised up to 10 treatment sessions over three months. Acupuncturists followed a protocol adapted from one that had been devised by acupuncturists taking part in a previous pilot trial of acupuncture for depression and neck pain.[17;18] The protocol allowed sufficient standardisation to assist replication, yet was flexible enough to allow individualised treatments. Practitioners used logbooks to record details of treatments provided. All patients remained under the care of their general practitioner. Patients in the usual care group received their usual NHS treatment. Both groups could seek care elsewhere according to need. We collected information from patients in both groups at one and three months on all treatments they had received.

Outcomes measures

Our primary outcome measure was the IBS Symptom Severity Score (SSS) at three months.[15] Scored from 0 to 500 (<75 = no IBS, 75-175 = mild case, 175-300 = moderate and 300+ = severe), this measure had been validated for use in IBS patients. The measure was administered at baseline, one and three months. A minimum clinically significant change is considered to be 50 points.[16] Our secondary outcomes

at three months were Global Impact Score (question 4 of the SSS: 'How much does your IBS affect and interfere with your life in general' scored 0-100);[19] Non-Colonic Symptom Score (which includes lethargy & tiredness, 'wind', backache, and other symptoms);[16] Hospital Anxiety and Depression scale;[20] and EQ-5D.[21] We also collected data on medication use, health services use and days lost from work. Follow up was carried out by post; where this failed, the main outcome measure was sought by telephone. An open text question at one and three months gathered qualitative data on outcomes (not reported here) and adverse events. We also collected data on safety and treatment process from logs completed by the acupuncturists. Acceptability was assessed through patient reports on satisfaction and willingness to try acupuncture again and the uptake of acupuncture.

Data analysis

Data were analysed using SPSS version 14 and Stata 8 on an intention-to-treat basis. We estimated the standard deviation of changes in the primary outcome measure in order to calculate the sample size, taking into account loss to follow up. We conducted analyses of covariance on the main outcome measures, using baseline scores as covariates, reporting an adjusted estimated effect with 95% confidence intervals. Sensitivity to missing outcomes data was addressed in three ways: last observation carried forward, assigning the overall mean to missing values, and multiple imputation based on the standard best subset regression method.

Results

Patient characteristics

During May and June 2006, 186 potential participants were identified from the four GP practice databases covering a registered population of 20 301 patients, and were sent screening questionnaires. Forty nine patients responded prior to randomisation (26% response rate) (see Fig 1). After further screening, 30 were recruited to the study. Another two patients responded after randomisation. No patients refused acupuncture. Table 1 shows the baseline characteristics of patients in each group. Both groups had mean IBS symptom severity scores over 300 which is 'severe'. There were some differences at baseline in Non-Colonic Symptom Score, working status, anxiety and depression, differences that can be expected in a sample of this size. By using analysis of covariance we were able to take into account baseline differences in outcomes measures between groups in the analysis.

Table 1 **Baseline patient characteristics**

Characteristic		GP care only (n=20)	Acupuncture (n=10)
Mean (SD) age in years		37.5 (13.5)	34 (7.1)
Number (%) of females		15 (75)	8 (80)
Mean (SD) duration of IBS in months		79.8 (81.8)	44 (25.6)
Mean (SD) baseline IBS Symptom Severity Score (SSS)		343.4 (73.1)	322.1 (79.5)
Mean (SD) Non-Colonic Symptom Score (NCSS)		211.7 (85.2)	291 (74)
Mean (SD) HAD Depression score		4.4 (3.5)	9.5 (4.8)
Mean (SD) HAD Anxiety score		8.4 (5.4)	13.4 (5.4)
EQ-5D (range 0-1) (SD)		0.641 (0.292)	0.543 (0.351)
Working full time		13 (65)	3 (30)
Working part time		4 (20)	2 (20)
Not working – looking after family/home		1 (5)	5 (50)
Not working – retired		1 (5)	0 (0)
Full-time education		1 (5)	0 (0)
Belief in acupuncture:	yes	11 (55)	4 (40)
	don't know	8 (40)	6 (60)
	no	1 (5)	0
Thinks acupuncture will help IBS:	yes	9 (45)	1 (10)
	don't know	11 (55)	9 (90)
	no	0	0
Preference for acupuncture:	yes	12 (60)	6 (60)
	don't mind	8 (40)	4 (40)
	no	0	0

Data shown are numbers (percentages) except where stated otherwise

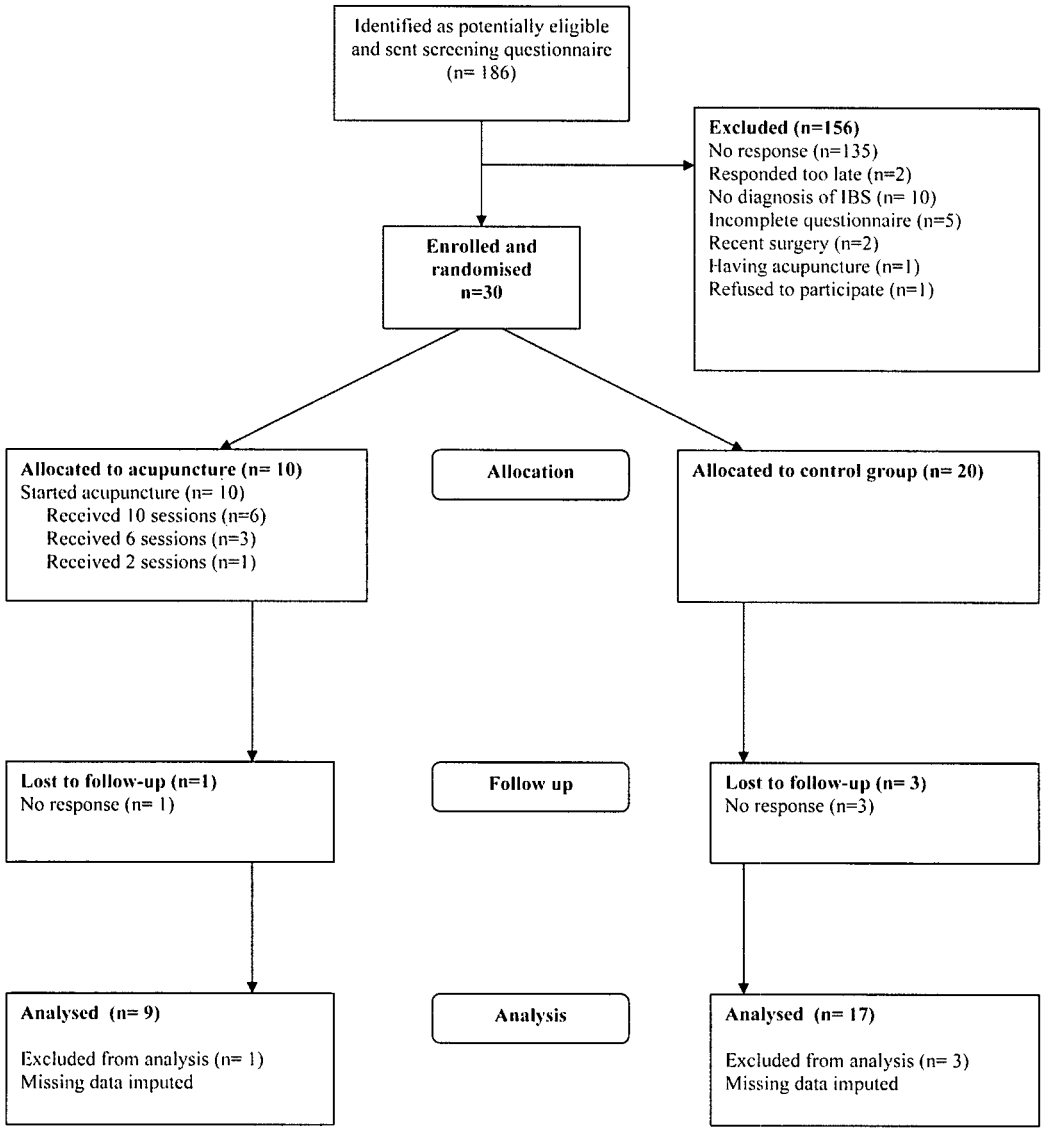

Figure 1 This CONSORT diagram shows the flowchart of the trial.

Treatments provided

Patients allocated to acupuncture received an average of eight treatments, mostly on a weekly basis. Three patients chose to stop attending treatment after six sessions, and one stopped attending after two treatments, when she moved from the area (but all patients were included in the analysis). Four out of five of the acupuncturists primarily practised the Five Element style with a diagnostic focus on individual 'Causative Factors',[22] and one used the Traditional Chinese Medicine (TCM) style with diagnosis primarily based on syndrome patterns.[23] Both styles are rooted in traditional acupuncture theory, and they are the most common traditional approaches used by professional acupuncturists in the UK today.[24] Across styles, there was considerable overlap in the treatments given, the most commonly used point overall was ST36, which was needled in 48% of treatments. Other commonly used points were PC6 (used in 20% of treatments), LI4 (19%), SP6, SP8, KI3 and CV12 (17%), and LR3 and LI11 (16%). The mean number of points needled per session was six. The points were usually needled bilaterally. Stimulation techniques used were 'tonification' and 'evens', and four out of five practitioners sought a *de qi* response (dull, achy

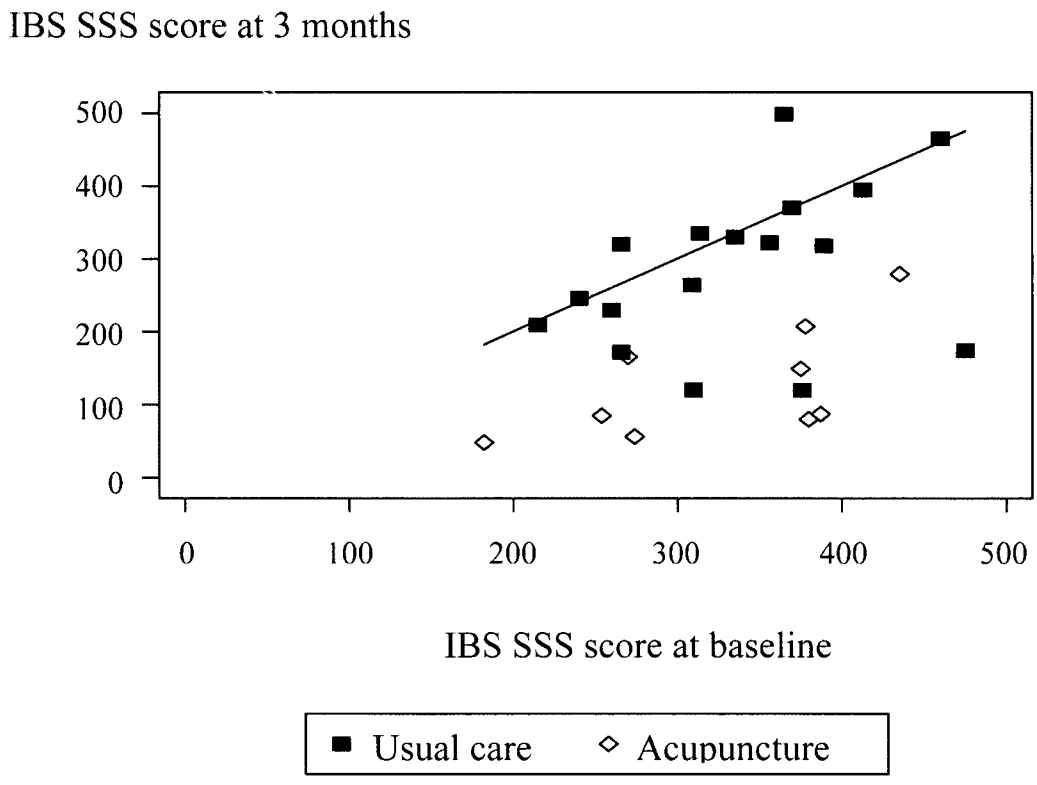

Figure 2 The unadjusted scores on the IBS Symptom Severity Score (SSS) at baseline and three months are shown for individual patients in the acupuncture and usual GP care groups; the line of equivalence is shown.

sensation felt on needling). Needles used were 1 to 1½ inches long, 36 to 40 gauge, and inserted to a depth of between 2-5mm. Needles were withdrawn immediately for tonification, and retained for up to 20 minutes for the evens technique. Direct moxibustion (a warming, stimulating herb) was used in seven of the patients' treatment courses and advice relevant to the diagnosis was given to nine out of ten of the acupuncture patients, most commonly about diet, relaxation and exercise.

Medical record data collected on conventional care revealed that 80% of acupuncture patients (8/10) had made at least one visit to their GP during the three months of the trial compared to 71% (12/17) of the usual care group. In both groups, 80% had been taking prescribed medication for their IBS at baseline. At three months, 44% of the usual care group (7/16) had stopped or reduced their medication, compared to 75% of the acupuncture group (6/8). One acupuncture patient was referred to an NHS counsellor during the trial, one usual care patient was referred to an NHS dietician, and one usual care patient consulted a nutritionist privately.

Main outcomes

The addition of acupuncture to usual GP care for patients with IBS is associated with a decrease in the IBS SSS scores at three months. The unadjusted change in scores for each patient is shown in Fig 2, where the line of equality is the line about which patients will be scattered if there is no change in score over time.

One patient (1/10) was lost to follow up from the acupuncture group: a female with no treatment preference, a moderate severity score at baseline, who had only received two treatments. Three (3/20) were lost to follow up in the usual GP care group, they were all male, had more severe baseline IBS severity scores and a preference for acupuncture.

Unadjusted scores on the IBS SSS dropped from 322 to 287 in the usual care group and from 343 to 128 (215 points) in the acupuncture group. Using

analysis of covariance which adjusted for differences in baseline scores, we found a 153 point difference on the IBS SSS (95% CI: 73 to 233; P=0.001). The three missing value methods discussed above all showed the same level of significance for the difference in the primary outcome at three months (P=0.001), with minor modifications to the size of effect. The most robust of these, the multiple imputation, showed a difference of 138 points on the IBS SSS (95% CI: 66 to 210) and a residual standard deviation of 90.

Acupuncture had a similarly positive effect on IBS Global Impact Score with an adjusted between group difference of 37 (95% CI: 25 to 49; P=<0.001). We also found a significant difference in the Non-Colonic Symptom Score which, when adjusted, favoured the acupuncture group by 106 (95% CI: 44 to 169: P=0.002). We also explored possible interactions between treatment group and belief or preference but found no significant effects.

Sample size calculations

In order to estimate the sample size required for a full scale trial, we have selected a minimal clinical difference on the primary outcome measure that would lead clinicians to change the treatment that they offered. For the IBS Symptom Severity Score, this is 50 points.[16] Given the observed residual standard deviation of 90 points, and taking into account potential sampling bias by using a one sided 90% confidence interval for the variance,[14] we estimate an adjusted standard deviation to be 105 points. Using this estimate, the sample size required to detect a difference at 90% power and 5% significance level is 188 patients in a two-arm trial. To allow for loss to follow up of a similar proportion to what we observed (13%), a trial would require 216 patients. To calculate a list size of GP practices needed for recruitment purposes, we use our finding that 32 eligible patients came from a total registered population of just over 20 300. For 216 patients, a total primary care list size of approximately 140,000 patients is required, equivalent to 28 GP practices with an average of 5000 patients each.

Adverse events

No serious adverse events were reported. The acupuncturists reported some mild adverse effects of the acupuncture treatment (mild dizziness during treatment and temporary worsening of symptoms followed by improvement). Some patients also reported mild adverse effects, but they all continued to attend for treatment. Eight out of nine patients reported that they would have acupuncture again.

Discussion

Main findings

In this study we are the first to report on the use of acupuncture for irritable bowel syndrome in a primary care setting. We have shown a large effect size, with highly significant differences, both clinically and statistically, between the outcomes in the acupuncture group and those receiving usual GP care alone. This was an unexpected finding, one which strongly suggests that acupuncture should be further investigated for IBS, a condition for which treatment is known to be a major challenge in primary care. A secondary benefit was to several non-colonic symptoms of IBS, symptoms for which IBS drugs are not effective.[9] For replication in a large scale trial, we have determined an appropriate sample size (216 patients for a two arm trial), as well as the required list size that will be needed when using database recruitment (140 000 patients).

We found acupuncture treatment to be an acceptable treatment for IBS, with high levels of attendance (an average of 8 out of 10 sessions). Our data reinforce existing evidence that acupuncture is safe in competent hands.[25] There were no serious adverse events, and all but one of the patients said they would have acupuncture again.

Limitations and strengths of study

Whilst there is previous evidence of a physiological effect of needling on the gut,[26] it is also known that the placebo response has been observed to be high in some IBS studies, though not all.[27] Evidence from a trial involving food elimination for patients with IBS showed that the placebo response is much smaller than the size of the effect found in the study we report here.[18] Using the same IBS Symptom Severity Score, with similar levels of severity at baseline, the researchers found that at three months the average score in the sham group had only reduced by 61.5 points, compared to the 215 we observed in our acupuncture treatment group. We accept however that there are obvious differences between these interventions and their associated placebo responses. Our treatment effect of 138 points (95% CI: 66 to

210) on the IBS SSS scale compares favourably with their mean difference of 39 (95% CI: 5-72), as well as a 71 point difference (95% CI: 32 to 109) on the same scale found at three months in a recent trial of cognitive behavioural therapy plus mebeverine versus mebeverine alone for IBS.[28]

To answer questions of whether acupuncture has a specific effect over and above placebo, a different design would be required, one that controlled for non-specific effects.[29] There are several options here, all of which have unique challenges. Sham acupuncture is an obvious choice in theory, but the physiological effects of sham acupuncture are yet to be determined, and it is possible that the large effect sizes observed with sham acupuncture undermine its adequacy as an inert placebo, thereby making comparisons hard to interpret. Alternative strategies might include some sort of time and attention control, such as relaxation or reflexology sessions. While it is accepted that unpicking the specific and non-specific effects of treatment has a useful role in acupuncture research, this study was not designed to do this, but rather evaluate the overall effects of acupuncture care.

In the context of the research question that we asked, we believe that the pragmatic randomised controlled trial is the design of choice. One of the strengths of our study was the use of a primary care population with a varying range of symptoms, and with broad inclusion criteria. We also used five acupuncturists, so the results may be generalised to typical practitioners who practise traditional acupuncture in the UK.

Our results at this stage cannot provide evidence of long term effects of acupuncture treatment for IBS; although it is suggested that the effects of acupuncture can last for up to two years in the case of low back pain.[30] Our use of retrospective recruitment means that we cannot know whether results would be applicable to newly presenting patients if they were referred for acupuncture. Our data cannot provide guidance on which individual contexts and patient characteristics might affect outcomes, so we cannot say how and if these should impact on a referral. The economic data, which we have not reported here, will also require a full analysis in a large scale study.

We have addressed some of the methodological weaknesses noted in the systematic review of acupuncture for IBS:[10] these were mainly potential problems with randomisation and allocation, and use of inappropriate acupuncture techniques and/or controls. None of the trials included in the review used a pragmatic approach, so we have been able to provide new evidence about the use of traditional acupuncture to treat IBS in comparison with usual GP care alone.

Further research

There is a need to conduct a large scale study to replicate our results, assess long term benefits and facilitate a full economic evaluation. Additional questions that are relevant to this area include: how long after the onset of IBS should patients be referred, whether there any contexts or characteristics which predict better or worse outcomes of acupuncture for IBS patients, and whether benefits might differ for new and established consulters.

Conclusion

This exploratory study established the feasibility of conducting a large scale trial, and clarified certain design features, including the variability in the primary outcome measure, which allowed us to calculate the sample size required. In addition, we established the acceptability of acupuncture. Though our pilot analysis showed a large effect size associated with acupuncture for IBS, the study sample was small. Therefore there is a need for more definitive research into acupuncture for IBS, such that the results can be generalised more widely. This pragmatic trial design has not distinguished between specific effects of acupuncture and placebo effects; however, it is the design of choice for determining cost effectiveness and aiding decision making on commissioning services where resources are limited.

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Contributions JR developed the protocol with HM, from an original developed by HM. JR was principal investigator and recruited patients, acupuncturists

and general practices. HM secured funding and was grant holder, and advised at all stages of the study. JMB undertook independent statistical analysis of the primary outcomes. CG advised on economic data collection and findings. All authors commented on the draft paper and contributed to the interpretation of the findings.

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Trial registration number: ISRTCN 32823820.

Conflict of interest

None declared.

Summary points

Irritable bowel syndrome (IBS) is typically a chronic, recurrent disorder, associated with substantial health, social and economic costs

In a pilot study, 30 patients with irritable bowel syndrome were randomised to acupuncture or usual care – at three months, the acupuncture group showed significant symptom relief

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