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ORIGINAL PAPER

Interim results of a randomised controlled trial of homeopathic treatment for irritable bowel syndrome

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Irritable bowel syndrome (IBS) is a chronic condition for which there is no consensus on the optimum treatment. Gastroenterology problems are some of the most common conditions treated by homeopaths, yet few trials have explored the effectiveness of individualised homeopathic treatment for IBS. A three-armed trial was conducted which compared: usual care, homeopathic treatment plus usual care and supportive listening plus usual care. The primary outcome was change in irritable bowel symptom severity score between baseline and 26 weeks, calculated using ANCOVA. An interim ANCOVA adjusted for baseline IBS severity, age and employment status found no statistically significant difference between the three arms. However, a post-hoc test comparing homeopathic treatment plus usual care to usual care alone found a statistically significant difference in favour of homeopathic treatment. In addition, 62.5 percent of patients in the homeopathic treatment arm (compared to 25.0 percent of those in the usual care arm), achieved a clinically relevant change in irritable bowel symptom severity score, which indicates a promising effect for homeopathic treatment, though these results should be interpreted with caution due to the low number of participants in the study. *Homeopathy* (2014) **103**, 172–177.

Keywords: Irritable bowel syndrome; Homeopathy; Randomised controlled trial; Attention control

Background

Irritable bowel syndrome (IBS) is a chronic condition for which, at present, there is no cure.[1] There are an estimated 240,000 primary care consultations per year in the UK of new cases of IBS[2] and the economic costs of IBS in primary care are estimated to be over £200 million.[3] IBS is characterised by recurrent symptoms (i.e., abdominal pain or discomfort, bloating, nausea, vomiting, early satiety, constipation, or diarrhoea) that indicate a dysfunctional gastrointestinal tract despite a lack of organic change or specific diagnosis. There is currently no consensus on optimum treatment, however many sufferers seek complementary and alternative medicine.[4] Homeopathic treatment is one such option, yet there is much debate as to whether or not homeopathic treatment is anything more than a placebo.[5] Gastroenterology problems are the fourth most common referral to NHS homeopathic hospitals[6] and one of the eight most common conditions treated by NHS homeopaths in General Practice.[7] This study therefore aimed to investigate the effectiveness of homeopathic treatment for patients with IBS. The paper presented here reports the interim results of this study.

Methods/design

The rationale for this study was to test whether or not homeopathic treatment plus usual care was any different from

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usual care alone in the treatment of IBS. In addition the study aimed to explore the feasibility of including supportive listening as an attention control arm in a trial of individualised homeopathic treatment. The design was a three armed pragmatic randomised controlled trial which used the novel cohort multiple randomised trial methodology.[8] This involved recruiting patients to an IBS cohort, (Barnsley Irritable Bowel Syndrome Cohort (BIBSC)) from both primary and secondary care. Recruitment was *via* GP databases for primary care and consultants' lists in secondary care. Upon identification potentially eligible participants were mailed a questionnaire to complete and return. Informed consent was sought and given for all participants included in this study.

There were two sets of inclusion criteria for this study: inclusion criteria for the BIBSC and inclusion criteria for the randomised controlled trial (RCT). To meet the inclusion criteria for the RCT participants first had to meet the inclusion criteria for BIBSC. The inclusion criteria for BIBSC were broader due to the potential for BIBSC to be used for future RCTs exploring IBS. The inclusion criteria for both the BIBSC and the RCT are shown in Figure 1.

All patients in the BIBSC who met the inclusion criteria for the RCT were randomly selected to one of the three arms in this trial: usual care alone, the offer of 5 one hour sessions of homeopathic treatment plus usual care or the offer of 5 one hour sessions of supportive listening plus usual care. Full details of the methods and design of this trial are reported elsewhere.[9]

Interventions

The homeopathic treatment provided was classical/individualised homeopathic treatment delivered by two homeopaths registered with the Society of Homeopaths who had been in practice for at least five years. The homeopaths were able to prescribe any remedy from the homeopathic pharmacopeia in a potency and frequency of their choice.

The supportive listening was delivered by two counsellors registered with the British Association for Counselling & Psychotherapy who had been in practice for at least five years. The purpose of including a supportive listening arm in this trial was to assess the feasibility of including a supportive listening arm as an attention control, and to control for the time and attention given to the patient by the homeopath. All consultations were conducted at Barnsley Hospital NHS Foundation Trust.

This study was pragmatic in design and the nature of the interventions, and the study design, did not allow for the blinding of the therapists or the participants. The analysis was carried out blind to treatment allocation.

Outcome measures

Patient outcomes were collected at 26 weeks by postal questionnaire. The primary outcome was the difference in the Irritable Bowel Syndrome Symptom Severity Score (IBS-SSS) between baseline and 26 weeks.[10] Secondary outcome measures were the Hospital Anxiety and Depression Scale (HADS),[11] EQ-5D and Consultation and Relational Empathy (CARE)[12] and expectation of benefit. The expectation of benefit is based on a scale designed by Borkovec and Nau[13] and adapted for IBS by Drossman,[14] to assess a treatment's credibility to patients and how likely patients felt that the treatment would help their symptoms. The number of treatment sessions attended by patients in the homeopathic treatment arm and the supportive listening arm were also recorded.

The primary clinical outcome was the difference between IBS-SSS[10] at baseline and 26 weeks analysed using ANCOVA.

Sample size

It was estimated that to detect a minimal clinical difference of 50 points on the IBS-SSS[10] at 90 percent power and 5 percent significance, a total of 198 people would be

Inclusion criteria for BIBSC	
• Age 18 or over • IBS diagnosis using ROME III criteria • Consent to complete and return postal questionnaires	
RCT	
Inclusion criteria	Exclusion criteria
• Scored ≤ 100 • Fluent in English	• Major gastrointestinal surgery in last 6 months • Pregnant or breast feeding • Current diagnosis of cancer, unstable psychiatric disorder or other serious physical illness

Figure 1 Inclusion and exclusion criteria.

needed to take part in this trial. The study used an uneven randomisation of 4:1:1 of usual care:homeopathic treatment:supportive listening.

Ethical approval for this study was sought and received from Leeds (East) Research Ethics Committee.

Results

Between January 2011 and June 2011, 113 people were recruited to the BIBSC and 94 participants were eligible for the randomised controlled trial. A 4:1:1 ratio was used for randomisation. 60 people were not offered an intervention and made up the usual care arm of the trial, 16 were randomly selected to the offer of homeopathic treatment and 18 to the offer of supportive listening. Return rates of completed questionnaires were lower than expected. A previous study had achieved a 70% response rate to a postal survey of IBS patients,[15] whilst in this study there was a return rate of 26%. Figure 2 shows a CONSORT diagram of the recruitment process and Figure 3 a CONSORT diagram of the randomisation process. All participants lived in the Barnsley area and described themselves as being of white British origin, with the majority of participants being female (83%). The mean age of the participants was 49 (standard deviation 14.70) and most (53%) were employed, the remainder were; not employed (44%), or did not provide

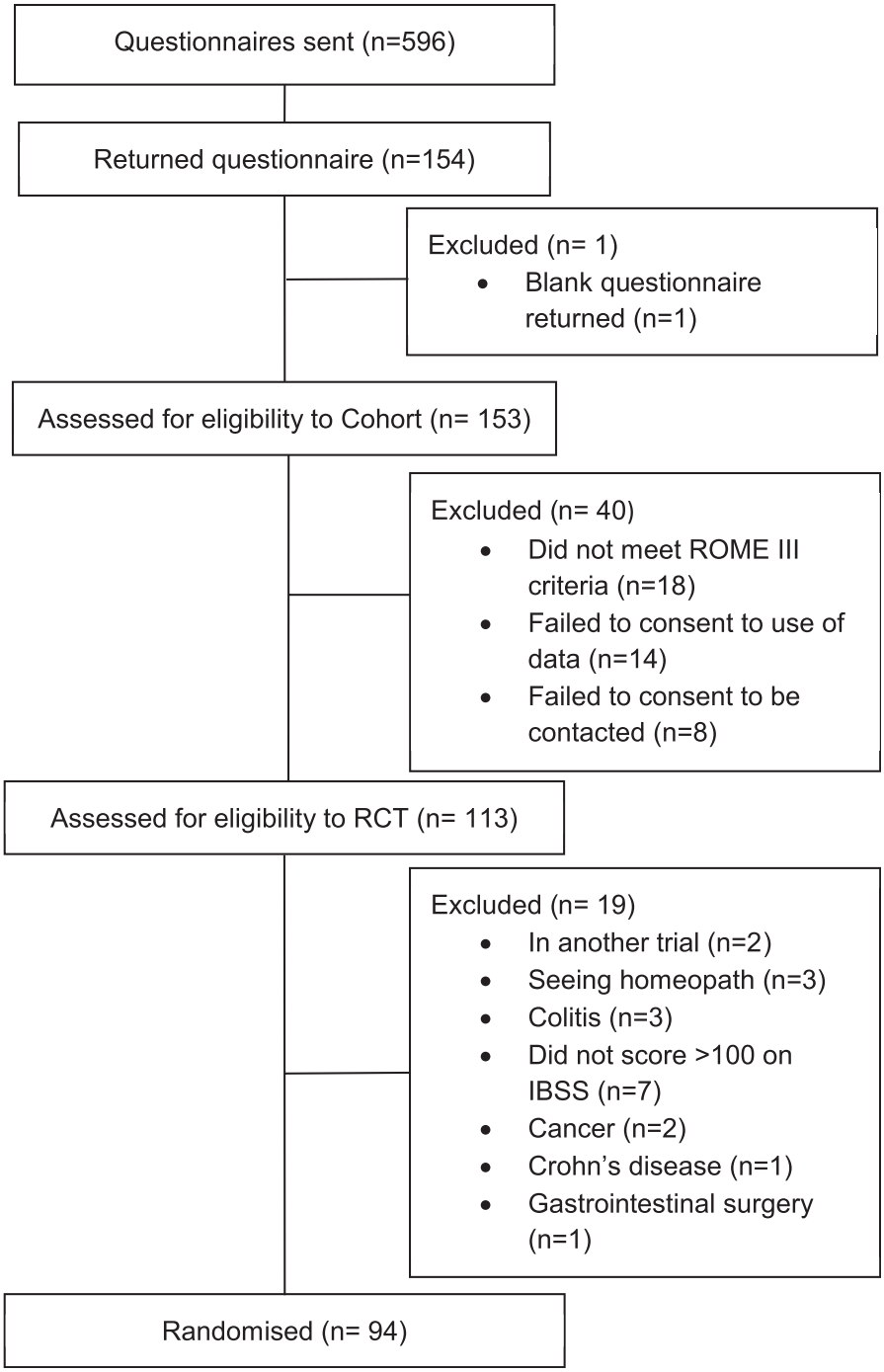

Figure 2 CONSORT diagram of recruitment process.

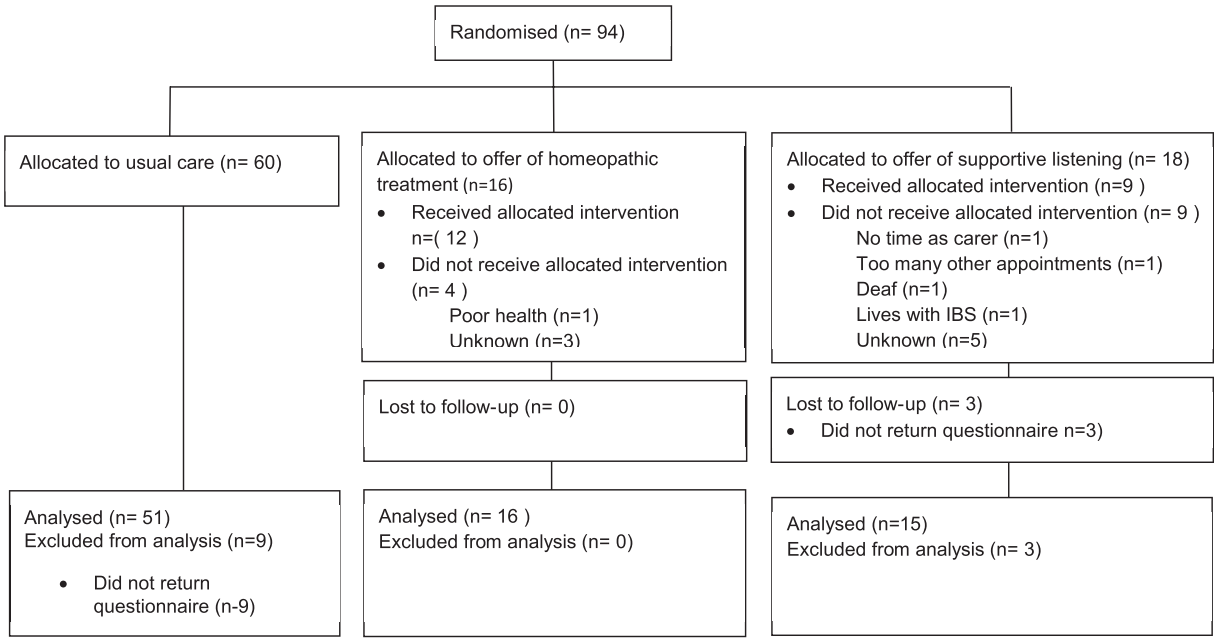

Figure 3 CONSORT diagram of randomisation process.

this information (3%). Baseline characteristics of the patients are given in Table 1.

Outcome data were analysed in PASW version 17 on an intention to treat basis. A comparison of baseline data were made between those who had missing data and those who did not, this indicated that there was a relationship between age, employment status and missing data, hence employment status and age were included in the ANCOVA model for IBS-SSS and HADS. Participant data at 26 weeks are given in Table 2.

Primary outcome

The primary outcome was change in IBS-SSS between baseline and 26 weeks. On inspection of histograms for distribution of change in IBS-SSS the distribution of change appeared to deviate from Normality. Despite this when carrying out the Kolmogorov–Smirnov and Shapiro–Wilk tests for Normality, no significant departure from Normality was found. It was therefore assumed that the change scores were close enough to Normality to carry out parametric tests.

An ANCOVA adjusting for age, employment status and initial IBS-SSS did not detect a statistically significant difference between the three arms $F(2,73) = 1.83$, $p = 0.167$. In addition to the primary outcome of change in IBS-SSS between baseline and 26 weeks the number of people in each arm who achieved a clinically relevant change of 50 points in their IBS-SSS was also calculated.[10] 25% of those in the usual care arm, 63% in the homeopathic treatment arm and 39% in the supportive listening arm achieved a clinically relevant change of 50 points in their IBS-SSS between baseline and 26 weeks. Due to the issues surrounding multiple comparisons and the increased likelihood of a Type I error, or false positive where a difference is found

Table 1 Participants' baseline data

		Usual care	*Offer of homeopathic treatment*	*Offer of supportive listening*
		N = *60*	N = *16*	N = *18*
Gender	Male	12 (20%)	0 (0%)	4 (22%)
	Female	48 (80%)	16 (100%)	14 (78%)
Age	Mean (sd)	51.71 (14.20)	48.19 (13.45)	42.50 (16.17)
	Missing	2	0	2
Employment	Employed	28 (46.7%)	11 (68.8%)	11 (61.1%)
	Unemployed	31 (51.7%)	5 (31.3%)	5 (27.8%)
	Did not say	1	0	2
IBS-SSS	Mean (sd)	250.87 (78.60)	280.38 (79.43)	291.61 (74.38)
	Median (IQR)	243.50 (188.00–324.00)	275.00 (205.00–344.25)	289.50 (224.75–340.00)
	Missing	0	0	0
HADS-D	Mean (sd)	5.82 (3.69)	5.88 (4.54)	6.94 (4.91)
	Median (IQR)	6.00 (2.25–8.00)	3.50 (3.00–9.50)	6.00 (2.75–10.25)
	Missing	0	0	0
HADS-A	Mean (sd)	10.13 (4.74)	11.13 (4.49)	10.11 (4.80)
	Median (IQR)	10.00 (6.25–14.00)	10.50 (7.50–15.25)	11.50 (6.50–14.00)
	Missing	0	0	0
EQ-5D Global	Mean (sd)	58.25 (25.39)	59.00 (15.64)	62.57 (23.46)

Table 2 Results at 26 weeks

		Usual care	*Offer of homeopathic treatment*	*Offer of supportive listening*
		N = *60*	N = *16*	N = *18*
Number who took up the offer of treatment		Not applicable	12	9
Number of appointments	Median (IQR)	Not applicable	5 (1.25–5)	1.5 (0–5)
IBS-SSS 26 weeks	Mean (sd)	237.3 (110.22)	210.44 (112.40)	262.0 (120.72)
	Missing	7	0	3
Change in IBS-SSS 26 weeks	Mean (sd)	−10.5 (78.77)	−69.9 (114.75)	−45.7 (87.56)
	Missing	7	0	3
Number of people who achieved a clinically relevant change	Number (%)	15 (25)	10 (62.5)	7 (38.9)
	Missing	7	0	3
HADS 26 weeks	Mean(sd)	13.9 (7.37)	17.27 (6.28)	15.3 (8.52)
	Missing	9	1	7
Change in HADS 26 weeks	Mean (sd)	−1.78 (4.64)	−0.2 (7.57)	−0.18 (4.75)
	Missing	9	1	7

when no difference is really present,[16] no statistical tests were carried out on the percentages of people in each arm who achieved a clinically relevant change. Rather these results are reported as a narrative.

A post hoc Student's *t*-test to compare the change in IBS-SSS for usual care alone and individualised homeopathic treatment (IHT) plus usual care gave change in IBS-SSS of −10.45 (78.77) and −69.94 (114.75) respectively with a mean difference −59.48 (95% confidence interval (CI) −109.65 to −9.32); $t(67) = -2.37$, ($p = 0.021$). This means that a statistically significant difference between homeopathic treatment and usual care was found, with the change in IBS-SSS being 59.48 points greater in the homeopathic treatment arm than in the usual care arm.

Secondary outcomes

There was no statistically significant difference in change in HADS between baseline and 26 weeks when tested using an ANCOVA adjusted for baseline IBS-SSS, age and employment status, $F(2,67) = 0.53$, $p = 0.591$.

The mean EQ-5D visual analogue score was increased at 26 weeks in all three arms, compared to baseline, indicating that participants in all three arms experienced an improvement in their overall health. EQ-5D results are given in Table 3.

Discussion

This randomised controlled trial has so far recruited 94 participants, half the number indicated in the power calculation. The trial encountered significant difficulties in recruiting sufficient participants. Prior to the commencement of the study GP surgeries who were willing to take part in the study were identified and a calculation carried out to check whether it was likely that these GP surgeries would be able to recruit the required number of participants. However due to changes in personnel between the time that this calculation was carried out and ethical approval being granted, some of the GP surgeries were no longer able to recruit. In addition the number of patients within the GP practices currently suffering with IBS was lower than anticipated. In an effort to increase recruitment, attempts were made to enlist further GP practices to recruit patients. This proved difficult due to financial

Table 3 EQ-5D results

EQ-5D dimension		*Usual care*		*Offer of homeopathic treatment*		*Offer of supportive listening*	
		Before	*After*	*Before*	*After*	*Before*	*After*
Mobility	No problems	45	37	10	12	15	7
	Problems	15	13	5	3	3	3
	Missing	0	8	1	1	0	4
Self care	No problems	50	44	15	15	18	9
	Problems	9	16	0	0	0	1
	Missing	1	8	1	1	1	4
Usual activities	No problems	35	30	11	9	13	7
	Problems	25	20	5	6	5	3
	Missing	0	8	0	1	0	4
Pain/discomfort	No problems	9	6	0	2	5	1
	Problems	50	44	16	12	13	10
	Missing	1	8	0	2	0	3
Anxiety/depression	No problems	24	22	6	4	11	4
	Problems	36	27	10	11	7	6
	Missing	0	9	0	1	0	4
EQ-5D VAS	Mean (sd)	62.57 (23.46)	63.41 (23.31)	59 (15.64)	69.07 (17.35)	58.25 (23.39)	63.09 (24.38)
	Median (IQR)	68.0 (47–82)	69 (46–80)	60 (50–70)	72.5 (61–81)	63.5 (39–80)	70 (40–85)
	Missing	2	7	1	2	7	9

constraints, and in the interests of transparency it was decided to publish these interim results.

In terms of the primary outcome an ANCOVA did not find a statistically significant result in favour of the homeopathic treatment arm, however, due to the trial not meeting its recruitment target, the potential for a Type II error (false negative) cannot be ruled out. In addition, in light of the fact that the inclusion of the supportive listening arm was to explore the feasibility of including a comparator control in a trial of homeopathic treatment, a *t*-test comparing homeopathic treatment plus usual care to usual care alone was carried out post hoc. This test found a statistically significant result in favour of homeopathic treatment arm over the usual care arm. It should be noted that this test was carried out post hoc and the possibility of a Type I error cannot be ruled out.

The percentage of people who achieved a clinically relevant change in their IBS symptoms was also calculated for each of the three arms, the results of which provided a promising indication for homeopathic treatment compared to both supportive listening and usual care, in terms of the percentage of people who achieved a clinically relevant change in IBS-SSS. However these results should be viewed with caution due to the low number of participants in this study.

Whilst it is difficult to know how to view the findings from this study in the context of the overall evidence base of homeopathy, it does provide important information regarding the acceptability of homeopathic treatment to people with IBS. In comparison to supportive listening, 75% of those offered homeopathic treatment took up the offer of homeopathic treatment, compared to 50% of those offered supportive listening. The reasons for this difference are unclear and may be a chance occurrence due to the low number of participants in this study. Yet all those who took up the offer of homeopathic treatment attended all five of the treatment sessions that they were offered. This indicates that homeopathic treatment is an acceptable form of treatment to IBS patients and suggests that those receiving homeopathic treatment for IBS perceived it to offer some degree of benefit. Those in the supportive listening arm were less likely to attend all five of the sessions that they were offered which suggests that supportive listening was less acceptable to IBS patients than homeopathic treatment. It was planned that a statistical analysis of the results of the CARE measure and the expectation of treatment would be carried out. Unfortunately, due to the lower than anticipated recruitment rate and the lower than expected uptake to the offer of supportive listening, there were insufficient numbers to carry out these analyses.

In terms of supportive listening as an attention control for homeopathic treatment the most important factor is whether supportive listening is a credible treatment for the condition being treated.

Further funding is currently being sought to recruit the additional participants required to fully power this study.

Trial Registration: Current Controlled Trials ISRCTN90651143.

Conflict of interest statement

The authors have no conflicts of interest to disclose.

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