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Systematic review, meta-analysis with subgroup analysis of hypnotherapy for irritable bowel syndrome, effect of intervention characteristics

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ABSTRACT

Background: Hypnotherapy has been shown to be effective at relieving global gastrointestinal symptoms (GGS) in irritable bowel syndrome (IBS). This study examines the impact of hypnotherapy delivery and participant characteristics on IBS outcomes.

Methods: This systematic review searched CINAHL, Cochrane Library, Conference Citation Index, Embase, PubMed, PsycARTICLES, PsychINFO, Science Citation index-expanded, Social Science Citation Index. Titles and abstracts, then full-text articles were screened against inclusion criteria: trials with a concurrent comparator of hypnotherapy in adults with IBS diagnosed using Manning or ROME criteria, which provided symptom data. Included studies were extracted and assessed for bias using Cochrane Collaboration 2011 guidance. Random-effects meta-analysis was conducted with sub-group analysis to assess the impact of delivery characteristics on outcomes.

Results: Twelve trials were included, 7 in the meta-analyses. Hypnotherapy reduced the risk of GGS, but this was not statistically significant, (standardised mean difference (SMD) 0.24, [-0.06, 0.54], I^2 66 %). Higher frequency of sessions (≥1/week) reduced GGS (SMD 0.45 [0.23,0.67] I^2 0 %), as did higher volumes of intervention (≥8 sessions with ≥6 h of contact) (SMD 0.51 [0.27,0.76] I^2 0 %) and group interventions (SMD 0.45 [0.03, 0.88] I^2 62 %). Only volume of intervention produced a significant effect between the subgroups.

Conclusion: This review suggests that high volume hypnotherapy is more beneficial than low and should be adopted for GDH. Both high frequency and group interventions are effective in reducing GGS in IBS. However, the sample size is small and more studies are needed to confirm this.

1. Introduction

Irritable bowel syndrome (IBS) is a chronic functional bowel disorder characterised by volatility in bowel movements. It is often accompanied by abdominal pain[1] which significantly impacts quality of life (QoL).[2,3] Hypnotherapy, the use of hypnosis[4] to enhance therapeutic outcomes,[5] has been used for IBS since the 1980s,[6,7] with a specific set of techniques, known as Gut Directed Hypnotherapy (GDH) having developed[6] (see Box 1).

Recent meta-analyses have confirmed hypnotherapy's effectiveness

Abbreviations: GGS, Global gastrointestinal symptoms; IBS, irritable bowel syndrome.

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Box 1
Commonly used content of gut directed hypnotherapy.

Gut Directed hypnotherapy (GDH) typically consists of 6−12 sessions of hypnotherapy which may include:
Suggestions for digestive calm, reduced sensitivity, increased comfort and the establishment of healthy digestive rhythm, possibly coupled with calming imagery such as waves lapping on a shore.[8] align="none"The 'Warm hand visualisation', in which suggestions are used to enable the patient to access the idea of a warm hand, often enhanced by imagining the hand as a warm colour. Patients then learn to transfer this perceived warmth into their gut, mimicking the effect of resting a hot water bottle on their stomach.[9] align="none"The 'River metaphor', in which the patient is encouraged to imagine a river which may be turbulent or blocked as appropriate to their symptoms and to imagine it calming or unblocking.[10] align="none"

for IBS.[11–14] However, individual trials have different delivery characteristics.[1] There are variations in the treatment protocol, such as using the GDH model[15] when other approaches combine hypnotherapy with cognitive behavioural therapy (CBT),[16] and others use hypnotherapy as part of a much wider 'integrated therapy'.[17] Further, there are differences in the amount of therapy, with some protocols having just three[18] sessions of hypnotherapy and others sixteen.[16] Equally, overall contact time varies, with some studies having 150 minutes[19] and others 720 min.[20] An understanding of the effects of delivery characteristics would inform service commissioning and delivery.

The objective of this review is to investigate the effect of patient and delivery characteristics on outcomes of hypnotherapy for IBS. The aim of this is to identify ways to deliver the most efficient approach to provide hypnotherapy for IBS.

2. Methods

2.1. Study registration

This review has been registered on PROSPERO CRD42018065533 and methods reported in detail elsewhere.[21]

2.2. Identifying literature

The following electronic databases were searched: CINAHL, Cochrane Library, Conference Citation Index, Embase, PubMed, PsycARTICLES, PsychINFO, Science Citation index-expanded, Social Science Citation Index.

The search strategies included the Medical Subject Headings (MeSH) "colonic disease" "colonic diseases, functional" "irritable bowel syndrome" and "hypnosis" and text words: irritable bowel, hypnotherapy$ or hypnos$ or auto-hypnos$ or Self-hypnos$ or mesmerism$.[21] Searches were undertaken from inception of the database until 27 April 2020. Two reviewers (MK, AF) independently screened titles and abstracts and subsequently examined full text articles for inclusion. Disagreements were adjudicated by a third reviewer (KJ). Data on trial methods, outcomes, intervention, patient and delivery characteristics were extracted.

2.2.1. Eligibility

Study design - Randomised controlled trials and quasi-randomised studies with a concurrent comparator published in English language journals only.

Type of participant – Adults (≥18 years of age). No limitation was placed on gender, location or ethnicity. Diagnosis of IBS using one of the prevailing diagnostic criteria at the time, namely Manning[22] or Rome I-IV.[23–26]

Type of intervention - had to have an element explicitly identified as hypnotherapy.

Type of comparator – Comparator groups had to be in receipt of an alternative treatment, this could include a different hypnotherapeutic approach, treatment as usual, placebo intervention or waiting list. Waiting list was included on the assumption that participants would receive usual care.[27,28,29]

Outcome measures – could either be clinician or self-assessed.

The outcomes of interest were any continuous measure of global gastrointestinal symptoms (GGS), QoL, anxiety or depression. Follow-up point was defined as the furthest data point from the start of the study at which relevant data were available.

2.3. Assessment of risk of bias in included studies

Studies were assessed independently by two reviewers (MJ, AF) for risk of bias using the 2011 Cochrane Collaboration[30] tool for randomised studies, with differences resolved by a third reviewer (KJ). The overall bias rating was defined by the highest single risk of bias category assessed for the paper. As 'blinding of participants and personnel' is impossible in hypnotherapy trials this category was not assessed.

2.4. Statistical analysis

Inverse variance random effects models were selected due to an anticipated high level of clinical heterogeneity. Studies reported outcomes using different measurement tools and therefore the effect is reported as the standardised mean difference (SMD). Data were analysed using the Cochrane Collaboration's Revman software, version 5.3.[31]

Studies which provided both mean and standard deviation figures, at baseline and follow up or the difference between these two points, were included in the meta-analyses. When the difference between baseline and follow up had not been calculated the standard deviation was calculated using Gaußian error propagation $\sqrt{([SD_1]^2+[SD_2]^2)}$. When trials contained multiple hypnosis arms, for example a group hypnotherapy arm, an individual hypnotherapy arm, and a comparator arm, the hypnotherapy arms were combined using Revman's calculator feature for comparisons where the group or individual element was not a factor of interest.[32]

An initial pooled SMD was calculated with 95 % CI, with all trials included. Statistical significance was defined as having a 95 % CI that did not include zero. Where data were available, we planned to explore the importance of the multiple patient and delivery characteristics on effectiveness of hypnotherapy, using meta-regression if ten or more studies were available and subgroup analysis where fewer were present.

The proposed comparisons were

- Frequency of sessions: <1/week / ≥1 session/week.[33,34]
- Number of sessions: ≤7 sessions / >7 sessions.[35]
- Total contact time: ≤6 h / >6 h.[35]
- Level of hypnotherapy training.[36]
- Hypnotherapist gender[37] and age.[38]
- Population age[39] and education level.[40]
- Duration of symptoms.[41]

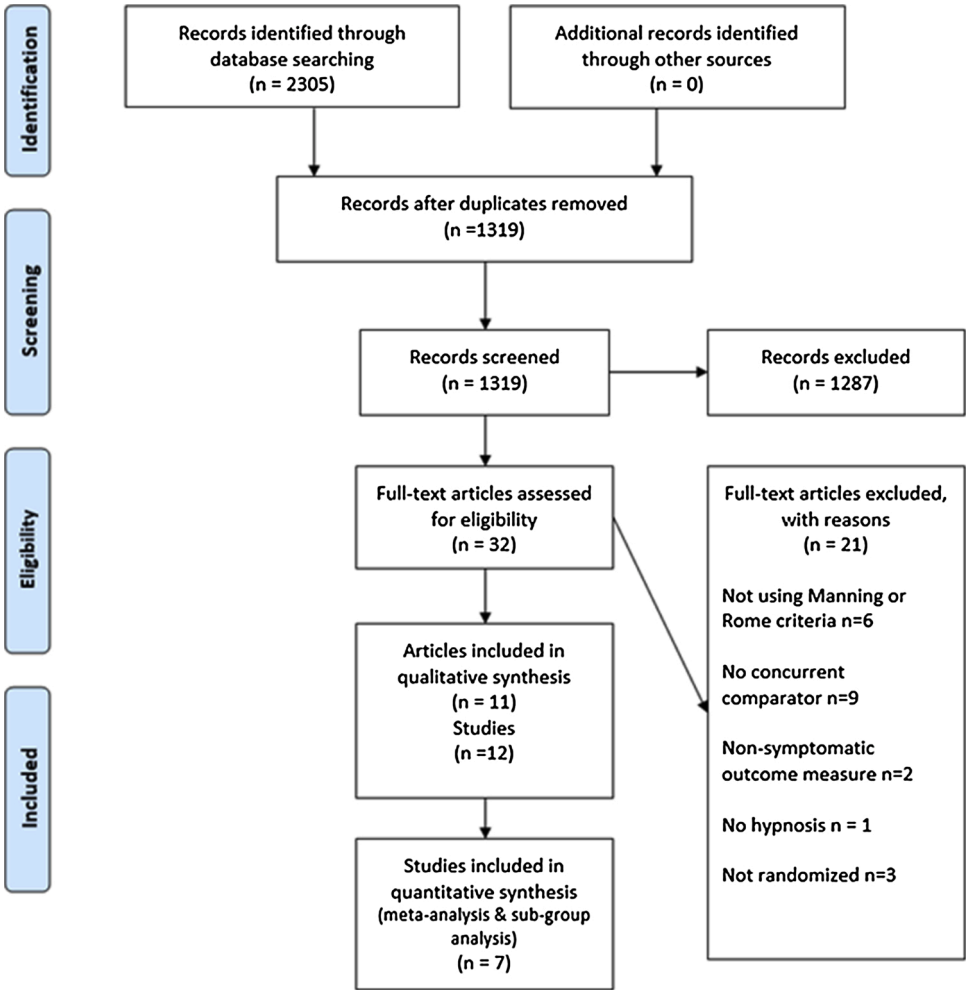

Fig. 1. PRISMA.

- Group / individual hypnotherapy.[35,42]
- GDH compared to 'other' hypnotherapy approaches.[43]
- Recruitment and delivery setting.[44,45]
- IBS by predominant symptom type.[46]

3. Results

3.1. Search results

After the removal of 986 duplicates, 1319 articles were identified, 1287 were excluded on title and abstract, leaving 32 full text articles assessed for eligibility (Fig. 1). Twelve studies[20] in eleven papers[17,18,20,47–54] met the inclusion criteria, seven provided sufficient data for meta-analysis and subgroup analysis.

3.2. Narrative review

3.2.1. Study characteristics

Eight studies were carried out in Europe,[17,18,20,47–50] two in Australia[51,53] and one each in North America[54] and Asia[52] (Table 1). Seven studies provided sufficient detail for subgroup analysis. The twelve studies included 1030 participants, the seven in the meta-analysis included 723 of these. All trials used some variant of GDH, although one used GDH as the core of a wider therapeutic approach,[17] another had a study arm which received both GDH and low FODMAP advice,[53] a third had a GDH arm but also an alternative hypnotherapy approach.[51] Comparators varied substantially and included waiting lists,[20] waiting lists with active medical intervention,[20,52] enhanced medical care,[17] supportive therapy,[47,50] progressive relaxation,[51] low FODMAP diet[53] and biofeedback.[18] Several studies compared different GDH approaches, such as recorded suggestions versus in-person therapy,[48] individual versus group,[47,49] personalised suggestions versus generic[51] and GDH with pain specific suggestion to GDH without pain specific suggestions.[54] All the non-gender specific studies had predominantly female participants (63.3 %[17] - 86.3 %).[51] The number of sessions varied from three[18] to twelve,[17,20] with most of them lasting around an hour, but ranged from thirty[48] to ninety minutes,[17] delivered weekly,[17,20,50,53] approximately every other week,[47–4951,54] or less frequently.[18]

3.2.2. Outcome measures

A wide variety of outcome measures were reported. One study[47] used the binary 'adequate relief question'[55] to measure symptoms, however continuous measures of GGS were most common, such as the IBS severity scoring system (IBS-SSS),[56] used by three studies,[17,18,47] with another using just the visual analogue scale element of it,[53] the Bowel Symptom Scale (BSSI-5) was used by one,[51] and a number of studies used ad hoc measures.[20,48,49] Several studies reported QoL measures, the IBS QoL (IBS-QoL) [57] measure was used by four trials,[20,47,52,53] the SF-36 QoL scale[58] was used by two,[48,50] and the Functional Digestive Disorder QoL questionnaire (FDD-QoL) [59] was used in one.[17] Six studies[18,20,48,53,60] used the Hospital Anxiety and Depression Scale (HADS).[61]

Table 1
Characteristics of trials.

Trial, design	Inclusion	Population	Intervention	Comparator	Outcome Measures and follow-up (FU) point for meta-analysis (FUFM)
Berens et al [17] RCT Germany	18–65 yrs. Rome III. Refractory. Abdominal pain of ≥3 on an 11-point Likert scale. Exclusion criteria: Psych, taking antidepressants, Lang, Psych Dis and substance abuse	N = 34, 5 lost to FU. Int = 15 (52 %) Con = 14 (48 %)	Integrative therapy including psychodynamics, GDH, and education. 12 Sessions of 90 min. All in Group.	Enhanced medical care and online diary.	IBS – SSS FUFM = End of treatment
Dobbin et al 2013 [18] RCT UK	Women. 18–60 yrs. ROME III criteria. Exclusion: Psych Dis, clinical history of cardiovascular, neurological, renal or endocrine disease, or ingestion of prescribed medication known to influence cardio autonomic tone.	N = 97 randomized 36 lost to FU. Int: 30 (49 %) Con: 31 (51 %)	IGDH 3 sessions.	Biofeedback 3 sessions	IBS-SSS HADS FUFM = 12 weeks post treatment
Flik et al 2019 [47] RCT Holland	18–65 yrs. Rome III Exclusion - lang, psych Dis, CCDB, GS, or radiotherapy.	N = 354, 150 GGDH, 150 IGDH, 54 Con.	GGDH: six 60 -minute sessions with 6 patients every two weeks. IGDH was six 45-minute sessions every two weeks.	Six x 60-minute supportive therapy. Group.	AR CF-FBD IBS – Qol IBS-SSS SCL-90 Self-efficacy Scale[62]TiC-P FUFM = 12 months for start of treatment
Forbes et al (2000) [48] RCT UK	Adults. Rome I. Exclusion for current organic disease and upper GI symptoms if they were predominant over lower GI symptoms.	N = 25 IGDH N = 27 audiotape	IGDH, 6 sessions of 30 min at 2-week intervals delivered in a specialist hospital.	30-minute audiotape to be listened to once a day.	GHQ HADS SF-36
Harvey et al (1989) [49] RCT UK	Defined by combined abdominal pain, disordered bowel habit, and abdominal distention. Exclusion, CCBD, abnormality on physical examination by sigmoidoscopy, blood test and barium enema.	N = 36. 3 lost to FU. 17 GGDH, 16 IGDH.	4 × 40 min of IGDH.	4 x 40 min of GGDH.	1-week symptom diary GQH
LIndfors et al (2012) Study 1 [20] RCT Sweden	Adults. ROME II.	N = 90 randomised 45 in each arm.	Treated at private psychological practices. 12 × 60-minute IGDH.	Supportive therapy	GI-SQ HADS IBS-Qol FUFM = 3 months from baseline
Lindfors et al (2012) study 2 [20] RCT Sweden	Rome II criteria and refractory. Exclusion - CCBD	N = 48 3 lost to FU. 22 Int. 23 Con.	12 × 60-minutes IGDH	Waiting list control	GSRS-IBS HADS SF-36. FUFM = 3 months from baseline
Moser et al 2013 [63] Austria RCT	Inclusion – 18-70 rs. Rome III and refractory. Exclusion – taking antidepressants, Psych. Dis, pregnancy, bowel surgery, mental retardation,	N=100. 51 Int. 49 Con.	10 × 45-minute GGDH.	Supportive therapy.	IBS-IS SF-36 HADS FUFM = 12 month post treatment
Palsson et al 2002 study1[54] USA RCT	Eligibility – Rome 1. Exclusion – CCBD, abdominal surgery, psychotropic medication.	N=18 9 Int. 9 Con.	7 x 45 min IGDH with pain specific suggestion.	7 x 45 min IGDH without pain specific suggestion.	14-day symptom diary. Barostat[64] BDL SCL-90
Peters et al 2016 [53] Australia RCT	Eligibility – Adult. Rome III. coeliac disease excluded. Exclusion criteria- CCBD, psych.dis, disorder, excessive alcohol intake, pregnancy. Previous experience with gut directed hypnotherapy or the low FODMAP diet.	N-78 enrolled. 4 lost to FU. 25 received IGDH. 24 received the comparator Low (FODMAP). 25 received combined IGDH and low FODMAP	6 × 60 IGDH. The combined intervention group received the same as both the GDH and the low FODMAP group (see comparator)	A single 1 -h session on the low FODMAP diet. Weekly phone contact.	100-point VAS HADS IBS-Qol FUFM = 6 months from baseline.
Phillips-Moore et al (2015) [51] RCT Australia	Eligibility –meeting Rome II. Refractory. 4 days in the 14 following screening in which they had experienced moderate or worse pain. Exclusion –coeliac disease, CCBD. Eligibility –Rome III.	N-51 17 individualised hypnotherapy. 17 IGDH 17 Con. N = 60.	5 x 30 min. Group 1 received 'individualised' suggestions and standard imagery. Group 2 received standard IGDH. GDH – 5 × 45–60 min.	5 x 30 min of progressive relaxation.	Bowel Symptom Scale 1–5 [65] [66]SCL-90 SF-36 QoL IBS-34

(*continued on next page*)

Table 1 (*continued*)

Trial, design	Inclusion	Population	Intervention	Comparator	Outcome Measures and follow-up (FU) point for meta-analysis (FUFM)
Shahbazi et al 2016 [52] RCT Iran	Exclusion – psychiatric medication taken in the last three months, having had psychological intervention in the last six months.	30 int. 30 Con.		Standard medical treatment	

CCBD: Comorbid Chronic Bowel Disease; CF-FBD – Cognitive Scale for Functional Bowel Disorders [67]; con: control; FUFM : Follow-up used in meta-analysis; GDH – Gut direct hypnotherapy; GHQ – General Health Questionnaire [68]; GI-SQ - GI-symptom questionnaire [20]; GGDH : Group gut direct hypnotherapy; GS: gastrointestinal surgery; GSRS- IBS – Gastrointestinal Symptom Rating Scale IBS version [69]; HADS – hospital anxiety and depression scale [61]; IBS – Qol – IBS Quality of Life [57]; IBS-IS – IBS Impact scale [70]; IBS-SSS – IBS symptom scoring system [56]; IGDH: individual gut directed hypnotherapy; int: intervention; Lang : language skills insufficient for hypnosis work, Psych : recent or on-going psychological intervention; Psych Dis : severe psychiatric disorder ; QoL IBS-34 – Quality of Life IBS – 34 question scale [71]; Rome: meet Rome criteria for IBS; SF-36 – Short Form health survey [58]; SCL-90 – Symptom checklist [72]; TiC-P – Questionnaire for cost associated with psychiatric illness [73] ; VAS : Visual analogue scale; yrs : years of age;

3.2.3. *Risk of bias*

All the trials were randomised; seven studies were assessed to have a high risk of bias, four were unclear and only one was at low risk (see Table 2). Of the seven used for the subgroup calculations four were at high risk, two unclear and one at low risk of bias. The main reason for the high risk of bias was incomplete outcome data, predominantly this was the result of inadequate reporting.

3.2.4. *Effectiveness of hypnotherapy for IBS*

All but one study,[18] found hypnotherapy to be superior to the comparator, three to a statistically significant level.[20,50,52] The exception was a study in which biofeedback was the intervention of interest and hypnotherapy the comparator,[18] the hypnotherapy element of this study was designed to reflect the level of intervention of the biofeedback arm, a level which was lower in frequency and volume than any of the other studies.

Several studies conducted research into group GDH[17,47,49,50]; in those studies which compared group GDH to a non-hypnotherapy group based comparator,[17,47,50] all were superior to the comparator in effect on GGS. However, in one study the comparator was received by the GDH arm in addition to the GDH[17] making it unclear if the intervention or the increased contact time was the active factor, despite this, the results suggest that group GDH is effective. Two studies directly compared group GDH with individual GDH.[47,49] One reported[49] that a higher proportion (70.1 %; 12/17) of the group intervention had fewer or no symptoms at follow-up compared to baseline than individual GDH (50 %; 8/16); however, the differences were non-significant. Another[47] however, found mixed results with individual and group GDH arms being both inferior and superior depending upon the measure, the follow-up period and method of analysis, all to a non-significant level, presenting no overall dominant pattern but suggesting possible equivalence. Overall, from this data, group GDH appears to be beneficial for IBS and as effective as individual GDH.

Three studies compared different approaches to treating IBS with hypnotherapy. One compared recorded suggestions with in-person, reporting in-person therapy to be substantially better,[48] suggesting recordings may be useful as part of the approach but in themselves have limited value. Another examined the effects of GDH with specific suggestions to reduce pain compared to GDH without, concluding this made no difference.[54] The third compared a psychologically holistic hypnotherapy approach to GDH, with a relaxation control, finding the best improvements with the holistic hypnotherapy arm but not significantly different to the others.[51]

As has been seen, several studies reported effects of the intervention characteristics, however only one reported the effect of participant characteristics and this in only one area.[47] A subgroup comparison of the various types of IBS as defined by predominant symptom; diarrhoea, constipation and mixed, found no significant difference between outcomes for these groups.[47]

The narrative overview suggests despite substantial variation with the protocols, hypnotherapy for IBS appears to be consistently effective for IBS, and this holds true when delivered in groups.

3.3. *Meta-analysis and subgroup analysis*

3.3.1. *Overall effectiveness*

Six papers, covering seven studies, provided sufficient information for a meta-analysis.[17,18,20,47,50,53] The SMD for GGS in the hypnotherapy

Table 2
Quality of studies – Cochrane tool for randomised trial.

	Random sequence generation	Allocation conceal-ment	Blinding of outcome assessment	*Incomp-lete outcome data*	Select-ive report-ing	Other bias	Overall – defined by highest pre-sent risk factor.
Berens et al [17]	Low	Low	Unclear	Low	Unclear	Low	Unclear
Dobbin et al 2013 [18]	Unclear	Unclear	Unclear	High	Low	Low	High
Flik et al 2019 [47]	Low	low	Low	Low	Low	Low	Low
Forbes et al (2000) [48]	Low	Unclear	Low	High	Low	Low	High
Harvey et al (1989) [49]	Unclear	Unclear	Unclear	Unclear	Unclear	Low	Unclear
Lindfors et al (2012) study 1 [20]	High	Unclear	Unclear	Low	Low	Low	High
Lindfors et al (2012) study 2 [20]	Low	Unclear	Unclear	Low	Unclear	Low	Unclear
Moser et al 2013 [63]	Low	Low	Unclear	High	Low	Low	High
Palsson et al (2002) study 1 [54]	Unclear	Unclear	Unclear	Low	Low	Low	Unclear
Peters et al. (2016) [53]	Low	Unclear	High	High	Unclear	Low	High
Phillips-Moore et al (2015) [51]	Low	High	Unclear	High	low	Low	High
Shahbazi et al (2016) [52]	Unclear	Unclear	Unclear	High	Low	Low	High

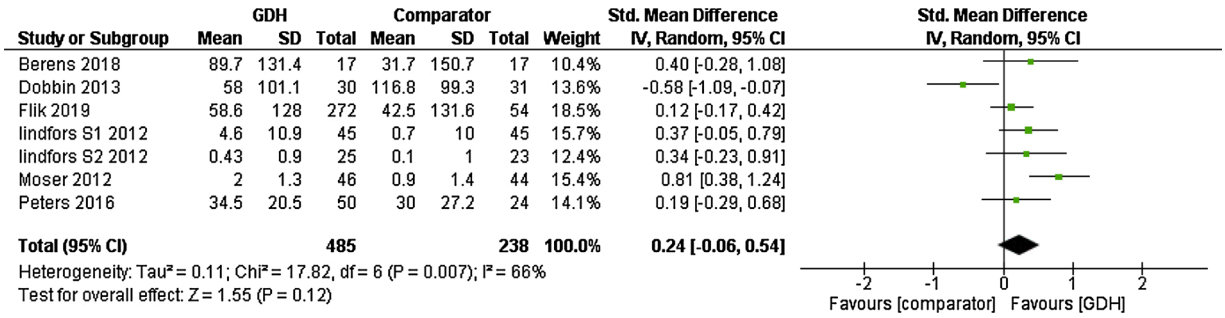

Fig. 2. Standardised mean difference in global gastrointestinal symptoms.

group compared to control was 0.24 (95 % CI -0.06, 0.54), but this was not statistically significant (p = 0.12) and heterogeneity was high (I^2 66 %). (Fig. 2)

One study included in the meta-analysis used an 'integrated therapy' approach which had GDH as a component of a broader approach which took in elements of mindfulness, diet and approaches to stress.[17] Although the study met the inclusion requirements it was judged to be sufficiently different that a sensitivity analysis[30] would be carried out to assess its impact on the overall findings and in any subgroup analysis in which it appeared. The sensitivity analysis found similar results to the full data analysis with an SMD of 0.22 (95 % CI −0.12, 0.55) with the findings remaining non-significant (p = 0.22).

3.3.2. Subgroups

Subgroup analyses were not possible for most of the proposed comparisons described in the protocol paper[21] because the data were not available. The studies with 8 or more sessions were found to be the same ones with more than 6 h contact time so these have been renamed as high-volume interventions (≥8 sessions with ≥6 h total contact time) and compared to low volume interventions (<8 sessions with <6 h contact time).

3.3.2.1. Volume of intervention - global gastrointestinal symptoms. Four studies had higher volumes of intervention, (≥8 sessions with ≥6 h total contact time),[17,20,50] and three lower.[18,47,53] The higher volume produced significant improvements in GGS compared to controls (SMD 0.51 [0.27,0.76] p = 0.0001; I^2 0%) (Fig. 4), whereas low volume interventions did not (SMD −0.06 [−0.49,0.37] p = 0.79; I^2 0%;) (Fig. 4). The difference between the two was significant (p = 0.02). Removing the 'integrated therapy' trial[17] from the high volume group did not alter the pattern of the findings with the high volume group remaining significantly effective (SMD 0.53 [0.22,0.83] p = 0.0007; I^2 23 %).

3.3.2.2. Frequency of sessions – global gastrointestinal symptoms. Five studies delivered weekly sessions[17,20,50,53] two with a lower frequency.[18,47] The SMD in GGS was significantly higher than the comparators (SMD 0.45 [0.23,0.67] p < 0.0001; I^2 0 %) (Fig. 3) for the studies delivering weekly sessions. There was no significant difference in GGS in the interventions delivered less than once weekly (SMD −0.19 [−0.88,0.49] p = 0.58; I^2 82 %) (Fig. 3). Removing the 'integrated therapy' trial[17] from the weekly trials in a sensitivity analysis, did not change the nature of the results which remain significant (SMD 0.45 [0.18, 0.72] p = 0.0001; I^2 25 %) (Fig. 3) and the difference between the frequency groups remained non-significant (p = 0.09).

3.3.2.3. Group vs. Individual therapy – global gastrointestinal symptoms. Three studies used a group hypnotherapy approach[17,50,53] and three individual hypnotherapy,[18,20] another was a three arm trial, including both group and individual GDH arms.[47] No significant effect on GGS was seen for the individual therapy approaches (SMD 0.08 [-0.22, 0.39] I^2 57 %) (Fig. 5) whilst the group intervention did produce significant effects (SMD 0.45 [0.03, 0.88] p = 0.04; I^2 62 %) (Fig. 5). However, sub-group analysis showed that the differences in effectiveness between group and individual delivery were not significant (p = 0.16). On removing the 'integrated therapy' trial[17] from the group trials for the sensitivity analysis, the effects of group GGS became non-significant (SMD 0.48 [-0.13,1.09] P = 0.12) and the relationship between the two groups remained non-significant (p = 0.25).

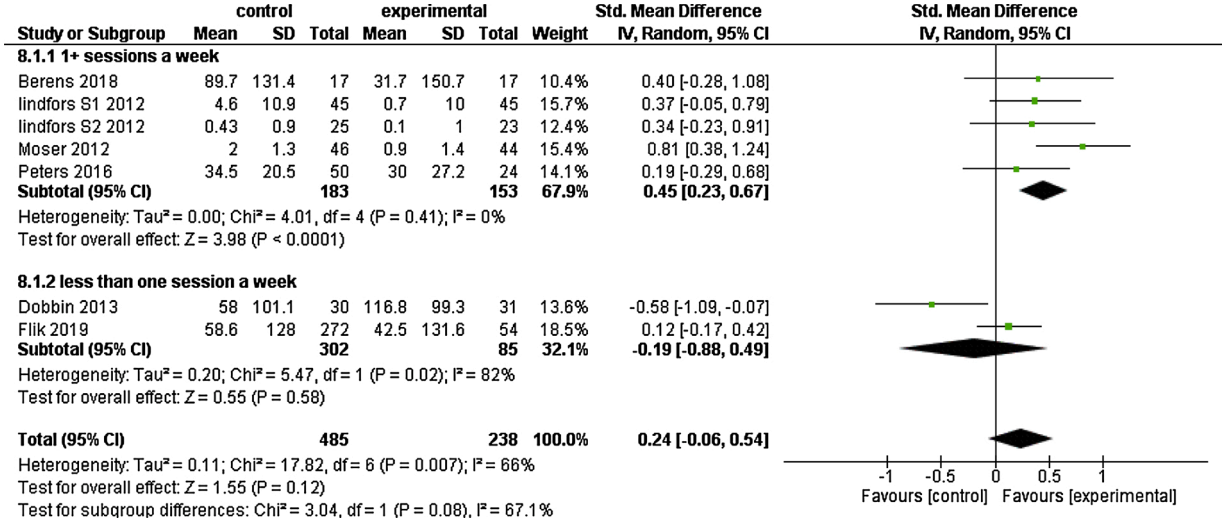

Fig. 3. Standardised mean difference in global gastrointestinal symptoms of high frequency GDH (1+sessions per week) interventions vs. low frequency interventions (less than one session a week).

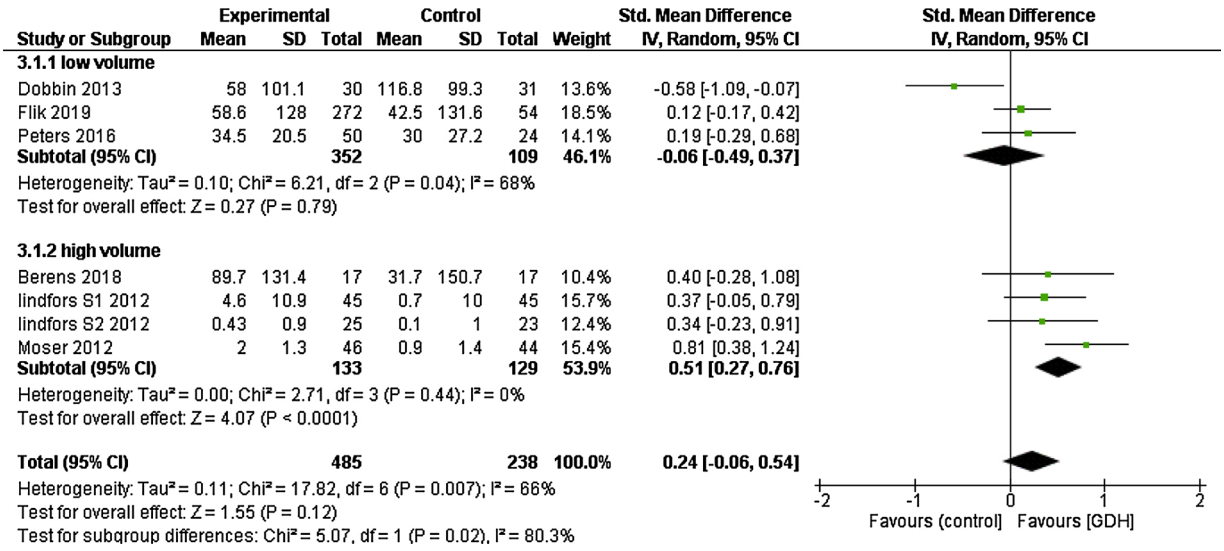

Fig. 4. Standardised mean difference in global gastrointestinal symptoms of high volume GDH interventions vs. low volume interventions.

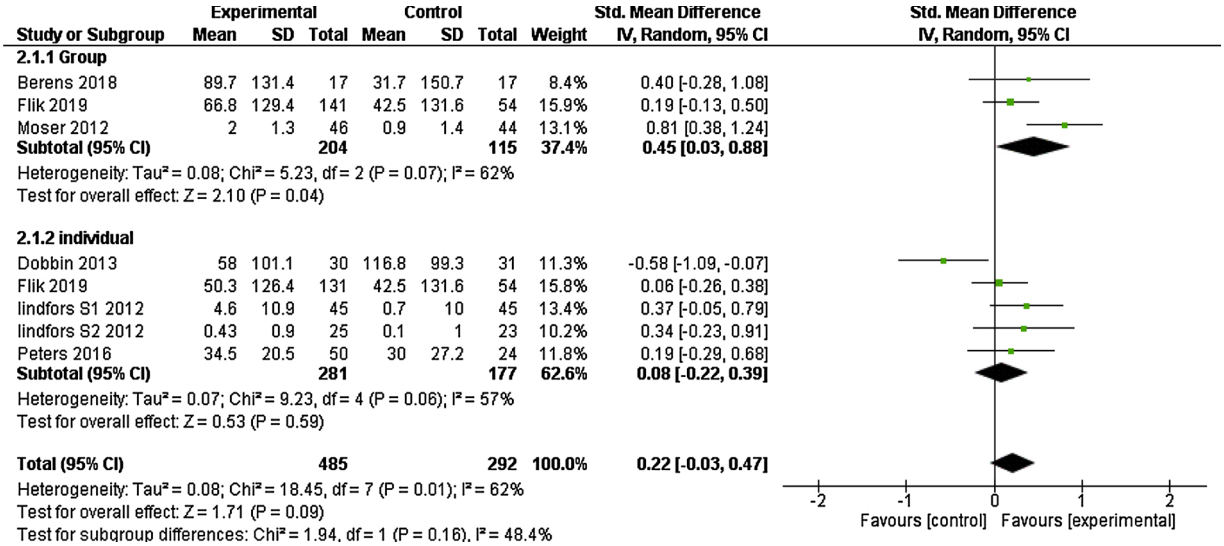

Fig. 5. Standardised mean difference in global gastrointestinal symptoms in group and individual hypnotherapy delivery.

3.3.2.4. Group vs. individual therapy – mental health. Three studies reported usable generic mental health measures[20,63] two were individual therapy trials[20] which produced a non-significant improvement (SMD 0.14 [-0.19, 0.48]) and one group therapy trial[63] which produced a significant improvement (SMD 0.72 [0.29,1.12] $p < 0.001$). Subgroup analysis showed a significant difference between groups ($p = 0.04$).

4. Discussion

The objective of this review was to investigate the effects of patient and delivery characteristics upon outcomes of hypnotherapy for IBS, however, as part of this an all-trials meta-analysis was conducted which found non-significant benefits to hypnotherapy for IBS, which conflicts with the findings of previous meta-analyses.[11,13] This results from the inclusion of a single study, which had the most infrequent sessions and the lowest volume of intervention[18] of the included studies. A post-hoc sensitivity analysis excluding this study shows a significant (0.35 [0.13, 0.57] $p = 0.002$) beneficial effect of hypnotherapy over comparators. This study[18] has not been present in previous meta-analysis conducted since its publication, possibly because it is comparing two psychological interventions[13] or because it published only continuous findings, not dichotomous.[11] The substantial impact upon the meta-analysis of this one trial,[18] reinforces the need for the kind of subgroup work conducted in this paper, which helps highlight where certain delivery characteristics may fall below an effective level.

Three main insights can be drawn from this review. Firstly, that high volume GDH (≥8 sessions with ≥6 h total contact time) are significantly more effective than lower volume interventions. Secondly, that GDH was found to be effective if delivered at least once a week, whilst lower frequency delivery was less effective than comparators, however the difference between high and low frequency delivery was non-significant. This means that, based on these studies, low frequency GDH appears to be as effective as high frequency GDH. The third was that group GDH was found to have a significant effect on patients' GGS whereas individual GDH did not, although this did not hold true once the sensitivity analysis was performed. The difference between group and individual GDH was non-significant in both the main analysis and the sensitivity analysis, this suggests group is comparable to individual GDH. However, the modest sample sizes involved mean these calculations are likely to be underpowered and as such all these findings suggest trends but are not conclusive. Further, as a meta-regression analysis was not possible, potential confounding factors have not been controlled for.

That high volumes of intervention produce better outcomes than low volume interventions is, as would be expected. However, one study, reported as a conference abstract, concluded GDH beyond six sessions provided no additional benefit [74] however, as we lack the details of this study for comparison or pooling with these findings we cannot draw any meaningful conclusions. Disentangling the composite factors of number of sessions and overall contact time may allow for the identification of the active factor. Equally, further subgroup comparisons which examine more specific incremental ranges of intervention may prove insightful. However, larger data sets are required.

As higher frequency interventions had a statistically significant effect on GGS, whilst lower frequency interventions did not, the possibility is raised that high frequency may prove superior to low frequency, even though the difference between the two was non-significant. The small number of studies in the low frequency group, just two,[18,47] suggests caution, especially as one of these studies[18] had only three sessions over twelve weeks. Further studies are needed to investigate the potential superiority of a high frequency approach for hypnotherapy.

Finding group GDH was comparable in its effectiveness to individual GDH is consistent with previous trial findings.[47,49] This may be counter to expectation as the group situation limits adaptation to individuals, which can effect outcomes.[75] It is possible that different populations volunteer for group hypnotherapy trials compared to individual ones, however, this would not have been present in trials comparing group to individual,[47,49] which find better outcomes for group. A possible mechanism by which group hypnotherapy may be more effective than individual is through mutual support and sharing of effective remedies.[76] Whatever the cause, based on this evidence it appears that group hypnotherapy is as valid an approach as individual hypnotherapy and is likely to offer substantial cost savings.

Most of the trials provided insufficient information for all the potential subgroup comparisons originally proposed, either because data was not reported or because subgroups data were not reported separately. The use of the TIDieR reporting checklist[77] would have allowed for more comparisons and as such it is recommended this be used in future trials.

It should be noted that even after subgrouping, heterogeneity remained high for the low frequency (I^2 82 %), low volume (I^2 68 %), group GDH (I^2 62 %) and individual GDH groupings (I^2 57 %). This strongly suggests that additional factors, which this study has not been able to investigate, are influencing results, possibly the patient and hypnotherapist's characteristics currently unavailable from the papers.

4.1. Strengths and limitations

The study has maintained a high degree of rigour through the use of established tools, such as the Cochrane risk of bias assessment,[78] by following established procedures[30] and the use of two independent researchers for screening and data extraction. The PRISMA tool[79] has provided internal consistency and both study registration on Prospero (CRD42018065533) and the publication of a protocol[21] have ensured a high level of fidelity to the original study goals. The use of English only journals may have limited the evidence base available. The pooling of data available for the meta-analyses was small with only 723 participants over seven trials. The ability to conduct subgroup analysis was severely limited by the breadth of information reported in the studies.

Of the twelve trials identified by this systematic review only three overlap with those of the most recently published meta-analysis,[80] which identified four papers (reporting 5 trials).[20,50,81,82] The difference is the result of three factors in this analysis: stricter inclusion criteria, using five more databases and a more recent search. The stricter inclusion criteria resulted in: the inclusion of trials using only identifiable formal diagnostic criteria, which resulted in exclusion of one article,[82] excluding trials which used only non-symptomatic measures resulted in exclusion of another because it measured changes in artificially induced gastric discomfort rather than natural discomfort.[81] The publication of papers since the previous analysis resulted in the inclusion of two additional trials.[17,47]

5. Conclusion

The findings suggest using high frequency, high volume, and group GDH approaches for the treatment of IBS. With high-volume approaches it remains unclear if the number of sessions or total contact time is the active factor. Future studies should provide a greater level of detail regarding the factors of potential effect, such as reporting findings by gender, age and primary symptom type in a way which allows for in-group comparison. Further research is required to assess the possible superiority of group GDH to individual GDH, or high frequency over low, and to establish the relative importance of contact time and number of sessions in the effectiveness of GDH for IBS.

Disclaimer

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References

1 Lacy BE, Mearin F, Chang L, et al. Bowel disorders. *Gastroenterology*. 2016;150(6), 1393-1407. e1395.
2 Penny KI, Smith GD. The use of data-mining to identify indicators of health-related quality of life in patients with irritable bowel syndrome. *J Clin Nurs*. 2012;21(19–20): 2761–2771.
3 Hahn B, Kirchdoerfer L, Fullerton S, Mayer E. Patient-perceived severity of irritable bowel syndrome in relation to symptoms, health resource utilization and quality of life. *Aliment Pharmacol Ther*. 1997;11(3):553–559.
4 Green JP, Barabasz AF, Barrett D, Montgomery GH. Forging ahead: the 2003 APA Division 30 definition of hypnosis. *Int J Clin Exp Hypn*. 2005;53(3):259–264.
5 Hammond D. *Corydon-handbook of hypnotic suggestions and metaphor*. NY: WW Norton & Company; 1990.
6 Whorwell PJ, Prior A, Faragher EB. Controlled trial of hypnotherapy in the treatment of severe refractory irritable-bowel syndrome. *Lancet*. 1984;2(8414):1232–1234.
7 Dotevall G, Svedlund J, Sjödin I. Studies/reviews of hypnotherapy for IBS (Irritablel Bowel Syndrome) and related subjects. *Scand J Gastroenterol Suppl*. 1982;79:16–19.
8 Palsson OS. Standardized hypnosis treatment for irritable bowel syndrome: the North Carolina protocol. *Int J Clin Exp Hypn*. 2006;54(1):51–64.
9 Gonsalkorale WM. Gut-directed hypnotherapy: the Manchester approach for treatment of irritable bowel syndrome. *Int J Clin Exp Hypn*. 2006;54(1):27–50.
10 Zimmerman J. Cleaning up the river: a metaphor for functional digestive disorders. *Am J Clin Hypn*. 2003;45(4):353–359.
11 Ford AC, Quigley EM, Lacy BE, et al. Effect of antidepressants and psychological therapies, including hypnotherapy, in irritable bowel syndrome: systematic review and meta-analysis. *Am J Gastroenterol*. 2014;109(9):1350–1365. quiz 1366.
12 Lee HH, Choi YY, Choi MG. The efficacy of hypnotherapy in the treatment of irritable bowel syndrome: systematic review and meta-analysis. *Am J Gastroenterol*. 2013;108. S566-S566.
13 Schaefert R, Klose P, Moser G, Hauser W. Efficacy, tolerability, and safety of hypnosis in adult irritable bowel syndrome: systematic review and meta-analysis. *Psychosom Med*. 2014;76(5):389–398.
14 Ford AC, Lacy BE, Harris LA, Quigley EM, Moayyedi P. Effect of antidepressants and psychological therapies in irritable bowel syndrome: an updated systematic review and meta-analysis. *Am J Gastroenterol*. 2018:1.
15 Whorwell PJ. Effective management of irritable bowel syndrome - the Manchester model. *Int J Clin Exp Hypn*. 2006;54(1):21–26.
16 Taylor EE, Read NW, Hills HM. Combined group cognitive-behaviour therapy and hypnotherapy in the management of the irritable bowel syndrome: the feasibility of clinical provision. *Behav Cogn Psychother*. 2004;32(1):99–106.
17 Berens S, Stroe-Kunold E, Kraus F, et al. Pilot-RCT of an integrative group therapy for patients with refractory irritable bowel syndrome (ISRCTN02977330). *J Psychosom Res*. 2018;105:72–79.

18 Dobbin A, Dobbin J, Ross SC, Graham C, Ford MJ. Randomised controlled trial of brief intervention with biofeedback and hypnotherapy in patients with refractory irritable bowel syndrome. *J R Coll Physicians Edinb*. 2013;43(1):15–23.
19 Roberts L, Wilson S, Singh S, Roalfe A, Greenfield S. Gut-directed hypnotherapy for irritable bowel syndrome: piloting a primary care-based randomised controlled trial. *Br J Gen Pract*. 2006;56:115–121.
20 Lindfors P, Unge P, Arvidsson P, et al. Effects of gut-directed hypnotherapy on IBS in different clinical settings-results from two randomized, controlled trials. *Am J Gastroenterol*. 2012;107(2):276–285.
21 Krouwel M, Greenfield S, Farley A, Ismail T, Jolly K. Factors which affect the efficacy of hypnotherapy for IBS: protocol for a systematic review and meta-regression. *Eur J Integr Med*. 2018;21:58–62.
22 Manning A, Thompson WG, Heaton K, Morris A. Towards positive diagnosis of the irritable bowel. *Br Med J*. 1978;2(6138):653–654.
23 Vanner S, Depew W, Paterson W, et al. Predictive value of the Rome criteria for diagnosing the irritable bowel syndrome. *Am J Gastroenterol*. 1999;94(10): 2912–2917.
24 Thompson WG, Longstreth G, Drossman D, Heaton K, Irvine E, Müller-Lissner S. Functional bowel disorders and functional abdominal pain. *Gut*. 1999;45(suppl 2): II43–II47.
25 Longstreth GF, Thompson WG, Chey WD, Houghton LA, Mearin F, Spiller RC. Functional bowel disorders. *Gastroenterology*. 2006;130(5):1480–1491.
26 Drossman DA, Hasler WL. Rome IV—functional GI disorders: disorders of gut-brain interaction. *Gastroenterology*. 2016;150(6):1257–1261.
27 Håkanson C. Everyday life, healthcare, and self-care management among people with irritable bowel syndrome: an integrative review of qualitative research. *Gastroenterol Nurs*. 2014;37(3):217–225.
28 Talley NJ, Gabriel SE, Harmsen WS, Zinsmeister AR, Evans RW. Medical costs in community subjects with irritable bowel syndrome. *Gastroenterology*. 1995;109(6): 1736–1741.
29 Hussain Z, Quigley EM. Systematic review: complementary and alternative medicine in the irritable bowel syndrome. *Aliment Pharmacol Ther*. 2006;23(4):465–471.
30 Higgins JP, & Green, S. (Eds.).. Cochrane handbook for systematic reviews of interventions 2011.
31 *Review manager*. 5.3 ed. Copenhagen: The Nordic Cochrane Centre; 2014.
32 Higgins J. Cochrane handbook for systematic reviews of interventions. Version 5.1. 0 [updated March 2011]. *The Cochrane Collaboration*. 2011;5.1.0, 16.15.14 www. cochrane-handbook.org.
33 Palsson OS. Standardized hypnosis treatment for irritable bowel syndrome: the North Carolina protocol. *Int J Clin Exp Hypn*. 2006;54(1):51–64.
34 Miller V, Whorwell PJ. Hypnotherapy for functional gastrointestinal disorders: a review. *Int J Clin Exper Hypnosis*. 2009;57(3):279–292.
35 Peters S, Muir J, Gibson P. Review article: gut-directed hypnotherapy in the management of irritable bowel syndrome and inflammatory bowel disease. *Aliment Pharmacol Ther*. 2015;41(11):1104–1115.
36 Elkins GR, Hammond DC. Standards of training in clinical hypnosis: preparing professionals for the 21st century. *Am J Clin Hypn*. 1998;41(1):55–64.
37 Miller V, Carruthers H, Morris J, Hasan S, Archbold S, Whorwell P. Hypnotherapy for irritable bowel syndrome: an audit of one thousand adult patients. *Aliment Pharmacol Ther*. 2015;41(9):844–855.
38 Fulder S, Munro R. Complementary medicine in the United Kingdom: patients, practitioners, and consultations. *Lancet*. 1985;326(8454):542–545.
39 Andrews EB, Eaton SC, Hollis KA, et al. Prevalence and demographics of irritable bowel syndrome: results from a large web-based survey. *Aliment Pharmacol Ther*. 2005;22(10):935–942.
40 Cutler DM, Lleras-Muney A. *Education and health: Evaluating theories and evidence*. National Bureau of Economic Research; 2006.
41 Webb AN, Kukuruzovic R, Catto-Smith AG, Sawyer SM. *Hypnotherapy for treatment of irritable bowel syndrome*. The Cochrane Library; 2007.
42 Moser G, Tragner S, Gajowniczek EE, et al. Long-term success of GUT-Directed group hypnosis for patients with refractory irritable bowel syndrome: a randomized controlled trial. *Am J Gastroenterol*. 2013;108(4):602–609.
43 Golden WL. Cognitive-behavioral hypnotherapy in the treatment of irritable-bowel-syndrome-induced agoraphobia. *Int J Clin Exp Hypnosis*. 2007;55(2):131–146.
44 Wilson S, Maddison L, Roberts L, Greenfield S, Singh S. *Systematic Review: The effectiveness of hypnotherapy in the management of irritable bowel syndrome*. 2006.
45 Lindfors P, Unge P, Arvidsson P, et al. Effects of gut-directed hypnotherapy on IBS in different clinical settings—results from two randomized, controlled trials. *Am J Gastroenterol*. 2012;107(2):276–285.
46 Rey de Castro NG, Miller V, Carruthers HR, Whorwell PJ. Irritable bowel syndrome: a comparison of subtypes. *J Gastroenterol Hepatol*. 2015;30(2):279–285.
47 Flik CE, Laan W, Zuithoff NPA, et al. Efficacy of individual and group hypnotherapy in irritable bowel syndrome (IMAGINE): a multicentre randomised controlled trial. *Lancet Gastroenterol Hepatol*. 2019;4(1):20–31.
48 Forbes A, MacAuley S, Chiotakakou-Faliakou E. Hypnotherapy and therapeutic audiotape: effective in previously unsuccessfully treated irritable bowel syndrome? *Int J Colorectal Dis*. 2000;15(5–6):328–334.
49 Harvey RF, Gunary RM, Hinton RA, Barry RE. Individual and group hypnotherapy in treatment of refractory irritable bowel syndrome. *Lancet*. 1989;1(8635):424–425.
50 Moser G, Tragner S, Gajowniczek EE, et al. Long-term success of GUT-directed group hypnosis for patients with refractory irritable bowel syndrome: a randomized controlled trial. *Am J Gastroenterol*. 2013;108(4):602–609.
51 Phillips-Moore JS, Talley NJ, Jones MP. The mind-body connection in irritable bowel syndrome: a randomised controlled trial of hypnotherapy as a treatment. *Health Psychol Open*. 2015;2(1), 2055102914564583.
52 Shahbazi K, Solati-Dehkordi K, Dehkordi AH. Comparison of hypnotherapy and standard medical treatment alone on quality of life in patients with irritable bowel syndrome: a randomized control trial. *J Clin Diagn Res*. 2016;10(5):OC01–OC04.
53 Peters SL, Yao CK, Philpott H, Yelland GW, Muir JG, Gibson PR. Randomised clinical trial: the efficacy of gut-directed hypnotherapy is similar to that of the low FODMAP diet for the treatment of irritable bowel syndrome. *Aliment Pharmacol Ther*. 2016;44 (5):447–459.
54 Palsson OS, Turner MJ, Johnson DA, Burnett CK, Whitehead WE. Hypnosis treatment for severe irritable bowel syndrome - investigation of mechanism and effects on symptoms. *Dig Dis Sci*. 2002;47(11):2605–2614.
55 Mangel A, Hahn B, Heath A, et al. Adequate relief as an endpoint in clinical trials in irritable bowel syndrome. *J Int Med Res*. 1998;26(2):76–81.
56 Francis CY, Morris J, Whorwell PJ. The irritable bowel severity scoring system: a simple method of monitoring irritable bowel syndrome and its progress. *Aliment Pharmacol Ther*. 1997;11(2):395–402.
57 Patrick DL, Drossman DA, Frederick IO, Dicesare J, Puder KL. Quality of life in persons with irritable bowel syndrome (development and validation of a new measure). *Dig Dis Sci*. 1998;43(2):400–411.
58 Ware Jr JE, Sherbourne CD. The MOS 36-item short-form health survey (SF-36): I. Conceptual framework and item selection. *Med Care*. 1992:473–483.
59 Chassany O, Marquis P, Scherrer B, et al. Validation of a specific quality of life questionnaire for functional digestive disorders. *Gut*. 1999;44(4):527–533.
60 Moser G, Dejaco C, Fuhrer M, et al. Gut-focused group hypnosis for treatment of irritable bowel syndrome - a randomised controlled trial. *J Psychosom Res*. 2012;72 (6):494–495.
61 Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand*. 1983;67(6):361–370.
62 Bleijenberg G, Bazelmans E, Prins J. Chronisch vermoeidheidssyndroom: self-efficacy schaal (SES). *Praktijkreeks Gedragstherapie deel*. 2001;13(13):102.
63 Moser G, Tragner S, Gajowniczek E, et al. Long-term success of GUT-directed group hypnosis for patients with refractory irritable bowel syndrome: a randomized controlled trial. *Am J Gastroenterol*. 2013;108:602–609.
64 Whitehead W, Delvaux M, Azpiroz F, et al. Standardization of barostat procedures for testing smooth muscle tone and sensory thresholds in the gastrointestinal tract. *Dig Dis Sci*. 1997;42:223–241.
65 Boyce PM, Talley NJ, Balaam B, Koloski NA, Truman G. A randomized controlled trial of cognitive behavior therapy, relaxation training, and routine clinical care for the irritable bowel syndrome. *Am J Gastroenterol*. 2003;98(10):2209–2218.
66 Boyce P, Gilchrist J, Talley NJ, Rose D. Cognitive-behaviour therapy as a treatment for irritable bowel syndrome: a pilot study. *Aust N Z J Psychiatry*. 2000;34(2): 300–309.
67 Toner BB, Stuckless N, Ali A, Downie F, Emmott S, Akman D. The development of a cognitive scale for functional bowel disorders. *Psychosom Med*. 1998;60(4):492–497.
68 Goldberg DP, Hillier VF. A scaled version of the general health questionnaire. *Psychol Med*. 1979;9(1):139–145.
69 Wiklund I, Fullerton S, Hawkey C, et al. An irritable bowel syndrome-specific symptom questionnaire: development and validation. *Scand J Gastroenterol*. 2003;38 (9):947–954.
70 Longstreth GF, Bolus R, Naliboff B, et al. Impact of irritable bowel syndrome on patients' lives: development and psychometric documentation of a disease-specific measure for use in clinical trials. *Eur J Gastroenterol Hepatol*. 2005;17(4):411–420.
71 Kanazawa M, Drossman DA, Shinozaki M, et al. Translation and validation of a Japanese version of the irritable bowel syndrome-quality of life measure (IBS-QOL-J): 912. *Am J Gastroenterol*. 2005;100:S333.
72 Derogatis L. *Symptom Checklist-90-R: Administration. Scoring and procedures manual*. Minneapolis: National Computer Systems; 1994.
73 Hakkaart-van Roijen L, Van Straten A, Donker M, et al. *Trimbos/iMTA questionnaire for costs associated with psychiatric illness (TIC-P)*. 2002.
74 Hasan S, Miller V, Morris J, Boswell V, Whorwell P. Six versus twelve sessions of hypnotherapy for irritable bowel syndrome: a randomised, controlled, single blind non-inferiority trial. *Gastroenterology*. 2015;148:S665–s666.
75 Barabasz A, Barabasz M. Effects of tailored and manualized hypnotic inductions for complicated irritable bowel syndrome patients. *Int J Clin Exp Hypn*. 2006;54(1): 100–112.
76 Krouwel M, Jolly K, Greenfield S. How do people with refractory irritable bowel syndrome perceive Hypnotherapy?: Qualitative study. *Complement Ther Med*. 2019; 45(August):65–70.
77 Hoffmann TC, Glasziou PP, Boutron I, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *Bmj*. 2014;348:g1687.
78 Higgins JP, Altman DG, Gøtzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *Bmj*. 2011;343:d5928.
79 Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev*. 2015;4(1): 1.
80 Ford AC, Lacy BE, Harris LA, Quigley EMM, Moayyedi P. Effect of antidepressants and psychological therapies in irritable bowel syndrome: an updated systematic review and meta-analysis. *Am J Gastroenterol*. 2019;114(1):21–39.
81 Simren M, Ringstrom G, Bjornsson ES, Abrahamsson H. Treatment with hypnotherapy reduces the sensory and motor component of the gastrocolonic response in irritable bowel syndrome. *Psychosom Med*. 2004;66(2):233–238.
82 Galovski TE, Blanchard EB. The treatment of irritable bowel syndrome with hypnotherapy. *Appl Psychophysiol Biofeedback*. 1998;23(4):219–232.