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Psychological treatments for irritable bowel syndrome: a comprehensive systematic review and meta-analysis

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ABSTRACT

A wide range of psychological treatments have been found to reduce the symptoms of irritable bowel syndrome (IBS) but their relative effects are unclear. In this systematic review and meta-analysis, we determined the effects of psychological treatments for IBS, including subtypes of cognitive behavior therapy, versus attention controls. We searched 11 databases (March 2022) for studies of psychological treatments for IBS, reported in journal articles, books, dissertations, and conference abstracts. The resulting database comprised 9 outcome domains from 118 studies published in 1983–2022. Using data from 62 studies and 6496 participants, we estimated the effect of treatment type on improvement in composite IBS severity using random-effects meta-regression. In comparison with the attention controls, there was a significant added effect of exposure therapy ($g = 0.52$, 95% CI = 0.17–0.88) and hypnotherapy ($g = 0.36$, 95% CI = 0.06–0.67) when controlling for the pre- to post-assessment duration. When additional potential confounders were included, exposure therapy but not hypnotherapy retained a significant added effect. Effects were also larger with a longer duration, individual treatment, questionnaire (non-diary) outcomes, and recruitment outside of routine

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care. Heterogeneity was substantial. Tentatively, exposure therapy appears to be a particularly promising treatment for IBS. More direct comparisons in randomized controlled trials are needed. OSF.io identifier: 5yh9a.

Introduction

One-tenth of the world's population suffers from irritable bowel syndrome (IBS), a disorder of gut–brain interaction characterized by recurrent abdominal pain and disordered defecation (Ford et al., 2017; Lovell & Ford, 2012). IBS can be highly distressing, often leads to impairment (Frändemark et al., 2018), and becomes chronic in about two-thirds of cases (Ford et al., 2008). The annual direct cost of IBS has been estimated to be \$1 billion in the United States alone (Everhart & Ruhl, 2009), which underscores the importance of effective management.

Psychological treatments work, but their relative effects are unclear

Behavioral and mental processes are known to interact with gastrointestinal functions (Martin et al., 2018; Mayer & Tillisch, 2011) and influence the way in which individuals with IBS perceive and manage their illness (Melchior et al., 2022; Schwille-Kiuntke et al., 2021). Against this background, a large number of theoretical frameworks have been developed that suggest specific therapeutic targets of psychological treatments for IBS (for a more extensive discussion of theoretical approaches to psychological interventions for IBS, see Burton Murray & Ljótsson, 2022). For patients with IBS, psychological treatments can be efficacious and are probably often cost-effective in reducing gastrointestinal and psychiatric symptoms (Laird et al., 2016; E. D. Shah et al., 2021). However, the fact that psychological treatments for IBS can differ substantially with regard to their focus, components, aims, and theoretical rationale highlights the need to investigate what treatments work best, for whom, and given what circumstances.

The relative efficacy of psychological treatments for IBS has been investigated in four recent meta-analyses (Black et al., 2020; Henrich et al., 2015; Laird et al., 2016; K. Shah et al., 2020). One of these included 48 randomized controlled trials (RCTs) and focused on the procedural aspects of therapy (Henrich et al., 2015). This meta-analysis found no significant incremental treatment effect of cognitive restructuring techniques, emotional control training, pleasant imagery in the context of hypnosis, or stress management (Henrich et al., 2015). Another meta-analysis included 41 RCTs and found that the evaluated treatments—cognitive behavior therapy (CBT), relaxation, and hypnosis—had relatively similar pooled controlled effects (Laird et al., 2016). The third meta-analysis included 53 RCTs and was indicative of larger controlled effects when psychological interventions involved exposure,¹ but not when interventions involved hypnosis, meditation, psychoeducation/CBT techniques, or relaxation/biofeedback (K. Shah et al., 2020). The fourth meta-analysis included 41 RCTs and analyzed the treatment format in relation to effects within a network meta-analytic framework. This study found that although several psychological treatments

were more efficacious than a typical non-active or rudimentary control, there was no significant difference in the effect between these treatments (Black et al., 2020). Considering that results from meta-analyses remain inconclusive, despite over 45 years of research on psychological treatments for IBS (Youell & McCullough, 1975) it is still largely unknown if any specific psychological treatment is preferable over another.

Need for a comprehensive review and further analysis

A limitation of the existing literature is the shortage of RCTs where bona fide psychological treatments have been directly compared. Three of the aforementioned meta-analyses also pooled RCTs that used a mixture of different control groups (e.g. inactive waitlists and attention controls), which may have confounded comparisons of controlled effects of psychological treatments (Henrich et al., 2015; Laird et al., 2016; K. Shah et al., 2020). Furthermore, three of the meta-analyses did not make substantial distinctions between various forms of CBT (except in terms of the delivery format; Black et al., 2020; Henrich et al., 2015; Laird et al., 2016) despite the fact that CBT protocols can be quite different in terms of components and purported mechanisms of action (Burton Murray & Ljótsson, 2022; Keefer et al., 2022). Mainstream CBT protocols can include, for example, cognitive restructuring and relaxation techniques (Lackner et al., 2018), stress management techniques with the promotion of health behaviors (Everitt et al., 2019), or systematic exposure exercises with the addition of mindfulness training (Ljótsson et al., 2014). Thus, concluding that “CBT is effective” says very little about what type of CBT is effective in alleviating IBS symptoms. Another limitation of existing summaries of psychological treatments for IBS is that a considerable number of studies have been published only in the form of “grey literature” such as books, dissertations, and conference abstracts, and have thus not been included in existing meta-analyses. Lack of attention to this grey literature may have increased bias in certain analyses, considering an increased impact of publication bias, i.e. the file drawer problem. Prior to this project, there existed no comprehensive database of psychological treatment studies for IBS that included grey literature and a wide range of clinical outcomes.

Aim of this study

Based on a systematic review, using a more comprehensive database than those available for previous meta-analyses, we aimed to compare categories of psychological treatments for IBS to attention controls, i.e. conditions to control for rudimentary credibility effects, attention from a caregiver, and the expectancy of improvement. Treatments were intended to include various forms of CBT analyzed in more specific terms (subtypes) than in previous meta-analyses (see above), and also other treatments. The primary outcome was improvement in composite IBS symptom severity up to the post-treatment assessment.

Methods

Design and search strategy

We present a systematic review and meta-analysis of psychological treatments for IBS reported in accordance with the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) reporting guidelines (Stroup et al., 2000). We conducted a comprehensive search of scientific databases, including Medline, Embase, Cochrane, Web of Science, and PsycInfo, last updated in March 2022. We also searched the gray literature including dissertations and conference abstracts via the Bielefeld Academic Search Engine, DART Europe, SvePub, ProQuest Dissertations and Theses, OpenGrey, and OAlster, last updated in March 2022. Search strings were phrases and terms for IBS (“irritable bowel syndrome”, “colonic diseases, functional” and so on) combined with phrases and terms for psychological interventions (e.g. “psychotherapy”). See Appendix A for details. The extracted study data are freely available, for example for the purpose of validation or power analyses, via the Open Science Framework (identifier: 5yh9a).²

Selection of studies

We employed a systematic de-duplication strategy using EndNote X9 (Bramer et al., 2016). Two raters then independently assessed all unique publications for eligibility. This was done in three phases: First, based on titles. Second, all publications deemed relevant by at least one rater in phase one were assessed based on abstracts. Third, all publications deemed relevant by at least one rater in phase two were assessed by two raters in full text. Publications that did not have a title were assessed based on their abstract, and those without an abstract were assessed in full text. If necessary, authors were contacted to provide additional information. Whenever rater 1 and 2 disagreed over the inclusion of a publication, this was discussed with a third rater and a final decision was then reached by means of voting. We retrieved and reviewed all forms of scientific publications, including peer-reviewed journal articles, dissertations, books, chapters, and conference abstracts.

Eligibility criteria

We included publications that were (a) written in English and (b) presented at least one study of the efficacy of a psychological intervention (c) for participants with IBS based on a clinical diagnosis, typically the Rome criteria (any version) (Schmulson & Drossman, 2017), and not selected on any particular IBS subtype, or anxiety-, mood-, or somatoform disorder. (d) A majority of included participants were required to be at least 18 years old, and (e) publications had to report aggregate numerical outcomes (f) based on at least one self-rated measure of overall IBS symptom severity, abdominal pain, abdominal distension/bloating, constipation, diarrhea, quality of life, general anxiety, depression, or GI-specific anxiety. Studies were required to (g) have a post-treatment assessment earlier than 3 months after treatment completion, (h) allow for the calculation of within-group effects (i) that pertain to patients with IBS, (j) be based on treatment groups (study arms in controlled trials) of at least 5 participants (≥ 10 for the analysis), and (k) not to have introduced a new and structured pharmacological treatment alongside the psychological intervention. However,

study participants were allowed to have taken part in other treatments, including medical treatment, alongside the study.

Data extraction

We tabulated data in electronic spreadsheets. When several measures were presented for the same outcome (e.g. abdominal pain), we coded the validated measure that was first reported in the publication, or, if no validated measure was reported, the first non-validated measure. If there were measurements at several time points after treatment termination, we tabulated that which occurred first. We also tabulated potential moderator variables. These were related to study design (if the study was an RCT), recruitment strategy, if the composite IBS measure weighed in disability such as the IBS-SSS (Francis et al., 1997), continent where the study was conducted (Asia, Europe, North America, or Oceania), participant characteristics (mean age, gender distribution, proportion of IBS subtypes, pre-treatment severity), and treatment format (delivery medium, the time from pre- to post-treatment assessment). We classified treatments as “individual” if conducted one-to-one with a clinician ≥ 3 hours or >4 sessions. We also tabulated all treatment-as-usual and waiting-list control groups.

Classification of treatment types

We classified treatment types based on expert consensus (BL and EHL). The aim was to create distinct categories that were still wide enough to include more than one specific protocol, preferably from different research groups. This process had two phases. In the first phase, treatments were reviewed and categorized based on available descriptions of the content of components and the theoretical reasoning behind the interventions. Each category was briefly described as it emerged from the data and descriptions were amended as new interventions were included. Any uncertainties about categorization were noted in the first phase. In the second phase, all categories with uncertainties were re-reviewed. Any discrepancies were resolved by either changing the categorization of a specific intervention, revising the category description, or creating new categories. If a specific protocol could not be unequivocally judged to belong to only one category or would be the only member in its own category, it was coded as “other” and not included in the meta-analysis. The final 13 specific treatment categories, presented in detail in [Table 1](#), were as follows: acceptance and commitment therapy (ACT), biofeedback, cognitive behavior therapy (CBT), cognitive therapy (CT), CT with relaxation, exposure therapy, expressive writing, hypnotherapy, mindfulness, patient education, relaxation, relaxation and cognitive stress coping, and self-management. There was also a separate category for attention controls: any active comparison intervention that reasonably controlled for unspecific effects of psychological treatments such as credibility, attention from a caregiver, and the expectancy of improvement. This was coded either if the control was explicitly presented as an attention control group, or if this was indicated by an overall assessment of the title, stated hypotheses, and researcher allegiance.

Assessment of risk of bias

We designed a structured system for assessing the risk of bias in this study. A first draft of this instrument was completed in the early tabulation process, and the final version was

Table 1. Treatment type coding scheme.

| Category | Description of main components |
|---|---|
| Acceptance and commitment therapy ^a | Interventions based on acceptance and commitment therapy. |
| Attention control | Any active comparison intervention that reasonably controls for unspecific effects of psychological treatments such as credibility, attention from a caregiver, and expectancy of improvement. Coded either if explicitly presented as an active control group or if indicated by an overall assessment of title, stated hypotheses, and researcher allegiance (e.g. a relaxation intervention is coded as active control if the researchers have clear allegiance to the experimental intervention). |
| Biofeedback ^a | Using biofeedback devices to reduce arousal. |
| Cognitive behavior therapy | Comprehensive interventions that include multiple cognitive and behavioral components, e.g. cognitive restructuring, relaxation, exposure, behavioral experiments, and stress-coping strategies. The components target different proposed processes beyond stress relief and symptom management, e.g. symptom catastrophizing, avoidance behavior, anxiety, depression, and perfectionism. |
| Cognitive therapy | Comprehensive cognitive therapy interventions that use different cognitive strategies to alter dysfunctional thinking patterns and teach problem-solving skills. |
| Cognitive therapy with relaxation | Comprehensive cognitive therapy interventions that use different cognitive strategies to alter dysfunctional thinking patterns and teach problem-solving skills. Relaxation is included but not emphasized as a main intervention. |
| Exposure therapy | Cognitive behavioral interventions with main focus on exposure exercises that aim to decrease symptom-related anxiety and avoidance behavior. Adjunct interventions with explicit purpose to aid exposure training such as attentional training or mindfulness may be included. |
| Expressive writing ^a | Patients are given a task of writing about their thoughts and feelings, specifically about IBS or stressful life events. The writing is repeated over several sessions. The purpose is to gain understanding of feelings, thought, personal goals in order to increase mental physical health. No feedback on the texts are provided. The only support provided is to encourage patients to complete writing assignments. |
| Hypnotherapy | Using hypnosis to induce a state of relaxation and hypnotic suggestions are used to increase bowel control and in some cases to improve self-confidence and coping strategies. |
| Mindfulness | Mindfulness-based stress reduction or mindfulness-based cognitive therapy. |
| Patient education | Low-intensity interventions that primarily aim to inform patients about their disease and helpful and unhelpful strategies to manage their disease. The approach is pedagogical rather than therapeutic and specific homework tasks are not given or limited. |
| Relaxation | Different types of relaxation training. |
| Relaxation and cognitive stress coping ^a | Relaxation training and cognitive stress coping that aids identification of thoughts related to symptom flare-ups and targets catastrophic thinking. Seemingly equal emphasis on relaxation and cognitive stress training. |
| Self-management | Multi-component interventions that emphasize improved symptom management (e.g. improved eating patterns, dietary advice, physical exercise). Also include interventions that aim to reduce stress and maladaptive thinking patterns (e.g. thought records, cognitive restructuring, and problem-solving training). Relaxation training always included. |
| No or minimal treatment control group ^b | Minimal control for non-specific factors, primarily passage of time. Can include symptom monitoring, treatment as usual without control over intensity or content, basic education about IBS, for example a folder or one or two visits to healthcare practitioner. |
| Designed medical care as usual control group ^b | A control intervention with a limited number of sessions with a physician or other non-psychologist healthcare practitioner, addressing non-psychological aspects of IBS. |
| Other ^b | Intervention that does not fit into any of the categories above. |

IBS, irritable bowel syndrome.

^aNot included in the meta-analysis of composite IBS severity because the number of available groups was less than 4.

^bNot used for this meta-analysis.

Table 2. Risk of bias criteria.

| Threat | Criterion | Focus |
|------------------|---|--|
| Selection bias | 1. Valid diagnostic criteria | Were valid IBS diagnostic criteria used, so as to ensure that participants had IBS? |
| Selection bias | 2. Systematic diagnostic assessment | Was the presence of IBS assessed in a systematic manner, so as to ensure that participants had IBS? |
| Information bias | 3. Sufficient description of main treatment | Was the main treatment described in sufficient detail, so as to allow for the coding of treatment components? |
| Information bias | 4. Therapy not confounded by therapist | Was there more than one therapist, so as to ensure that differences in effect were due to treatment protocols? |
| Information bias | 5. Valid composite outcome | Has the composite IBS measure been demonstrated to be valid, so that the pooling of outcomes is justified? |
| Missing data | 6. Incomplete outcome data | Is missing data, or the method of managing this, likely to have resulted in substantial bias? |
| Reporting bias | 7. Selective reporting of outcome | Was at least one measure relevant for the meta-analysis preregistered but not reported? |

See Table B.1 for the coding scheme. IBS, irritable bowel syndrome.

registered when a majority of the data had been extracted, and we had a reasonable idea of which aspects of bias that could be relevant and assessed based on the information available. Studies were rated as contributing with “high risk of bias”, “moderate risk of bias”, “low risk of bias”, or “unclear” on 7 criteria (Table 2; for detailed criteria, see Table B.1).

Statistical analysis

Study characteristics and study selection concordance

We quantified concordance of the full text eligibility ratings as Cohen’s κ . Values of κ below 0 are usually regarded as poor, 0.2–0.4 as fair, 0.4–0.6 as moderate, 0.6–0.8 as substantial, and 0.8–1.0 as almost perfect (Landis & Koch, 1977). We also report the total proportion of agreement, the positive predictive value (PPV; the proportion of inclusions by one rater that was endorsed by the other rater), and the negative predictive value (NPV; the proportion of exclusions by one rater that was endorsed by the other rater).

Meta-regression framework

We used R 4.2.0 with the metafor package (Viechtbauer, 2010) to analyze standardized within-group effects of psychological interventions for IBS using the bias-corrected raw score standardization formula for Hedges’ g , where the mean change from pre- to post-treatment is divided by the pre-treatment standard deviation, multiplied by the bias-correction factor (Hedges, 1981), and the pre-post correlation is used to determine the sampling variance (Becker, 1988; Morris, 2000):

$$g = \frac{M_{pre} - M_{post}}{SD_{pre}} \times \sqrt{\frac{2}{(n-1)} \left(\frac{\Gamma[(n-1)/2]}{\Gamma[(n-2)/2]} \right)}$$

$$\text{approximate variance}(g) = \frac{2(1 - r_{prepost})}{n} + \frac{g^2}{2 * n}$$

Many publications did not report the pre-post correlation. Therefore, we z -transformed the available correlation coefficients, pooled these, and imputed the back-

transformed point estimate for each publication where the correlation was missing. All meta-analyses of change were based on random-effects meta-regression models fitted with the restricted maximum likelihood estimator, using the inverse variance method. Effect sizes are presented so that larger (positive) values are indicative of more beneficial effects, such as a larger reduction in IBS symptoms or a larger increase in quality of life. For the g , absolute values of 0.2 are usually regarded as small, 0.5 as moderate, and 0.8 as large (Cohen, 1988). We quantified heterogeneity using the τ^2 , which stands for absolute heterogeneity, and the I^2 , which stands for the proportion of variance attributable to true differences rather than sampling error. Usually, 25% is said to be indicative of low heterogeneity, 50% of moderate, and 75% of high, though the I^2 also increases with larger original study sample sizes (Rücker et al., 2008).

Average effect on IBS severity versus attention controls

We analyzed active treatments for which at least 4 cohorts of 10 or more study participants providing data at post-treatment could be pooled. All treatment groups and attention control groups were included in the same analysis. The within-group effect was regressed on treatment type, each being a dichotomous predictor with attention control groups as the comparator. Significance tests of the pooled effect over and above the attention controls were conducted for each treatment category. Three variants of the model were run: first, one model without covariates. Second, one model including the pre-post duration as the only covariate. Third, one further adjusted model that also included the following covariates: RCT, individual as opposed to group or self-help treatment, use of an outcome derived from a diary as opposed to a questionnaire, referrals from routine care, and intention-to-treat estimates. We screened for publication bias by visually inspecting for funnel plot asymmetry, and also by the use of Egger's intercept test (Egger et al., 1997). To ensure that asymmetry did not arise simply due to the mix of different treatment formats and study designs that could correlate with study precision and effect size, the funnel plot was constructed using the residuals of the further adjusted model. Similar to previous meta-analysts (Shields et al., 2020), we repeated the adjusted analysis with missing correlation coefficients instead imputed based on the lower or upper bound of the 95% confidence interval for the pooled correlations. We also conducted a sensitivity analysis with data from peer-reviewed journal articles only. Last, we analyzed secondary efficacy outcomes in terms of abdominal pain, distension/bloating, constipation, diarrhea, quality of life, anxiety, and depression using models analogous to the further adjusted model of composite IBS severity.

Results

Comprehensive database of psychological treatment studies for IBS

As shown in Figure 1, we assessed 755 non-duplicate search hits in full text. Of these, 527 were primary publications, of which 163 were identified as candidates for inclusion by both raters (94% agreement, PPV = 0.89–0.93, NPV = 0.94–0.96, κ = 0.86). The most common reason for disagreement was if publications could be said to present a study of a psychological intervention (n = 10), followed by whether studies focused on individuals with IBS and without focusing on an arbitrary subgroup or comorbidity (n = 6), whether studies had a pre-

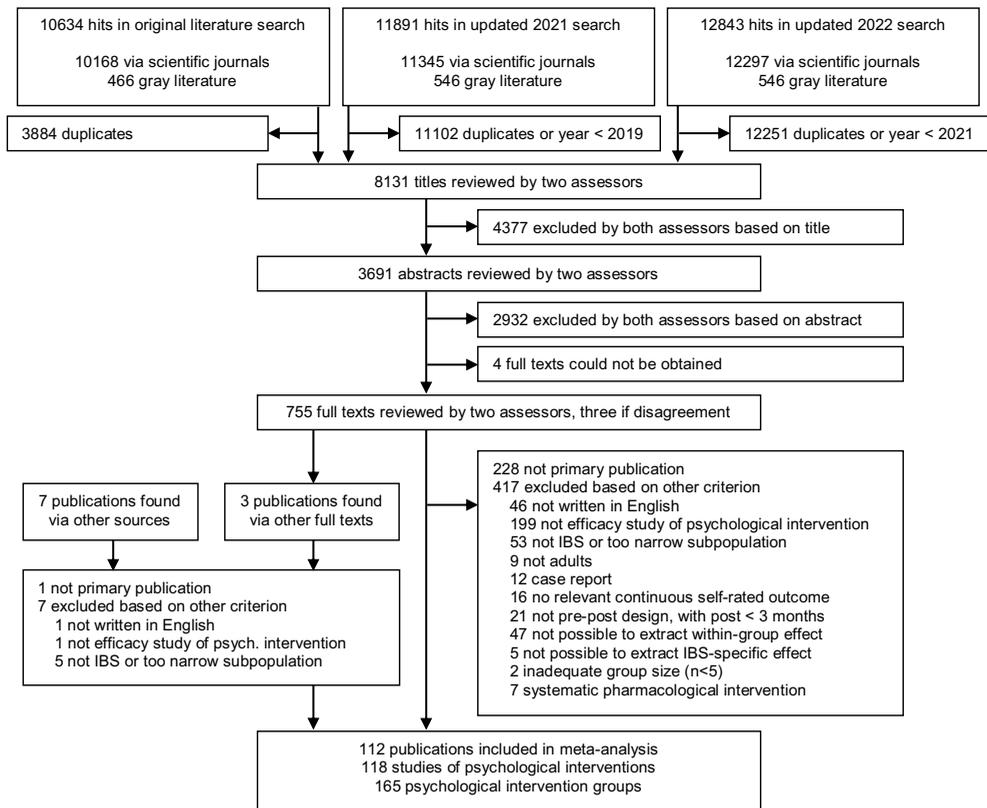


Figure 1. Study selection flowchart. In this systematic review, we included studies of psychological treatments for IBS, reported in English-language journal articles, books, dissertations, and conference abstracts. See Appendix A for a more detailed overview of search terms and search hits. IBS = irritable bowel syndrome.

post design with the endpoint assessment less than 3 months after treatment termination ($n = 6$), if data could be obtained from a group of at least 5 ($n = 3$), if relevant outcome measures had been administered ($n = 1$), and if publications were case reports only ($n = 1$). Fifty-two publications were excluded merely because the data necessary for analysis was missing and could not be retrieved (not possible to extract IBS-specific within-group effects, for example because only medians were reported). Finally, we included 112 publications (Table B.2), of which 94 (84%) were peer-reviewed journal articles, 9 (8%) conference works, and 9 (8%) theses or dissertations. These publications reported on 118 psychological treatment studies, of which 73 (62%; $n = 7073$) were RCTs and 45 (38%; $n = 3343$) other designs.

Studies and data used for this meta-analysis versus attention controls

In this study, we analyzed change in composite IBS severity using data from 6496 participants of which 5858 were enrolled in bona fide psychological treatments and 638 in attention controls. In these treatment groups, the mean age was 39 years, the mean proportion of female participants was 80%, and 43% of the treatment groups (38/

88) were recruited via routine care. Treatments were the following: hypnotherapy ($k = 21$), attention controls ($k = 11$), exposure therapy ($k = 11$), patient education ($k = 11$), self-management ($k = 9$), CBT ($k = 7$), CT with relaxation ($k = 6$), CT ($k = 4$), mindfulness ($k = 4$), and relaxation ($k = 4$). All hypnotherapies analyzed here were “gut-focused”, meaning that the treatment involved some element of suggestions or metaphors expected to help the patient in maintaining control over gastrointestinal functions (Peters et al., 2015). Treatment characteristics are listed per study condition in Table C.1.

Primary outcome: pooled effects on composite IBS severity

Without the inclusion of covariates, versus the attention controls, exposure therapy ($g = 0.57$, 95% CI = 0.21–0.93) and hypnotherapy ($g = 0.42$, 95% CI = 0.11–0.73) were predictive of a significantly larger reduction in IBS severity. There was no significant added effect of CBT, CT, CT with relaxation, mindfulness, patient education, relaxation, or self-management versus the attention controls. We did not test the effect of ACT, biofeedback, expressive writing, or relaxation and cognitive stress coping therapies because the number of treatment groups with data was less than 4. Heterogeneity was significant and substantial ($Q_{78} = 716$, $p < .0001$; $\tau^2 = 0.15$; $I^2 = 90\%$).

Using only the pre-post duration as covariate, the outcome was similar, with a significantly larger reduction in IBS symptom severity in exposure therapy ($g = 0.52$, 95% CI = 0.17–0.88) and hypnotherapy ($g = 0.36$, 95% CI = 0.06–0.67) as compared to the attention controls. There was no significantly larger effect of CBT, CT, CT with relaxation, education, mindfulness, relaxation, or self-management (Figure 2). Heterogeneity was significant and substantial ($Q_{77} = 657$, $p < .0001$; $\tau^2 = 0.14$; $I^2 = 89\%$).

In the further adjusted model—which also included RCT status, individual treatment, diary outcome, referral path, and intention-to-treat analysis as covariates—only exposure therapy had a significant effect versus the attention controls ($g = 0.54$, 95% CI = 0.20–0.88). Notably, CT had a similar effect size but this was not statistically significant ($g = 0.58$, 95% CI = –0.01–1.16, $p = .054$). As for the covariates, effects were significantly larger with a longer pre-post duration, with the individual format as opposed to the group format or self-help, when the outcome measure was a questionnaire and not a diary, and when participants were recruited outside of routine care (see Table 3). Again, heterogeneity was significant and substantial ($Q_{72} = 444$, $p < .0001$; $\tau^2 = 0.12$; $I^2 = 87\%$). The imputation of alternative pre-post correlations and the analysis of peer-reviewed journal articles only resulted in almost identical estimates (Table B.3).

Publication bias

We fitted the residuals of the further adjusted model versus the standard error in a funnel plot. Upon visual inspection, there appeared to be a slight overrepresentation of large effects in small studies (Figure C.1). However, despite the relatively large number of data points (88), Egger’s test of funnel plot asymmetry did not reach significance ($z = 1.43$, $p = .152$).

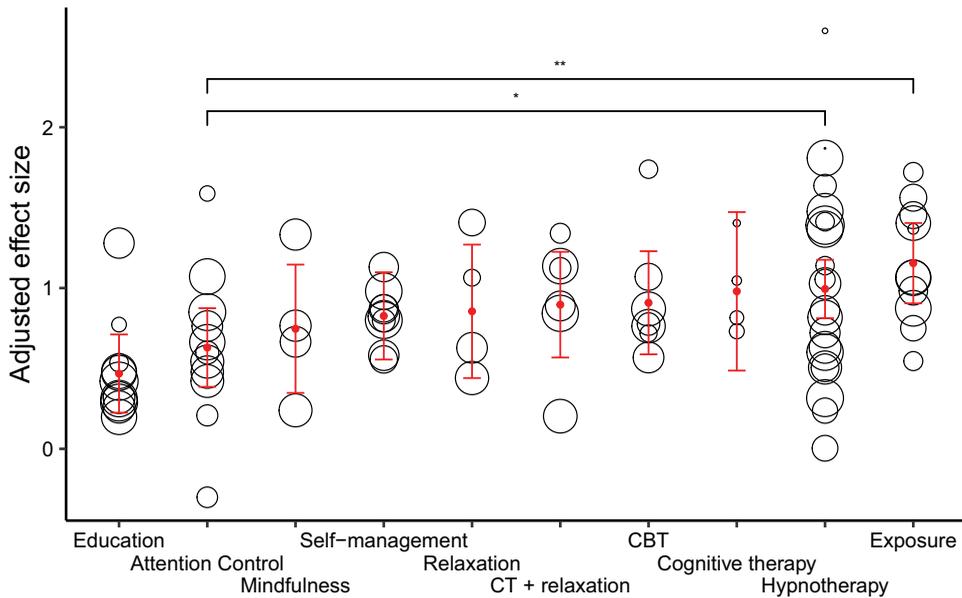


Figure 2. Pooled within-group effect on composite IBS severity by treatment category, adjusted for the pre-post duration. Pooled effects adjusted for the pre-post duration are shown in red. For individual studies, circle sizes are proportional to weights in the meta-analysis. CT = cognitive therapy, CBT = cognitive behavior therapy. Asterisks denote significant differences versus the attention controls, $p < .05$ (*) and $p < .01$ (**).

Original study risk of bias and additional effect moderators

All studies of the database were assessed for the risk of bias, focusing on the primary outcome of composite IBS severity (Table 2, Table B.1). As can be seen in Figure 3, three criteria stood out as threats to validity: First, many treatments were delivered by one therapist only, which is a threat to generalizability. Second, the use of non-validated outcome measures increases uncertainty about outcomes. Third, there was widespread missing data and use of inadequate modeling techniques. In statistical tests, we found that a poor description of the treatment protocol was associated with a larger effect on IBS symptom severity ($g = 0.29$; Table 3). As is further detailed in Table 3, though none of the other risk of bias criteria were significant predictors, larger effects were also predicted by study site being North America (vs. Oceania).

Pooled effects on secondary outcome domains

Adjusted effects of treatment category versus attention controls on other outcomes than overall IBS severity are tabulated in Table 4. Exposure therapy was associated with larger effects than the attention controls in all symptom domains except depression. Self-management was a predictor of larger effects on constipation, CT was associated with larger effects on diarrhea, and CBT and hypnotherapy were associated with larger effects on quality of life. Patient education was associated with worse effects than the attention controls in terms of diarrhea and depression.

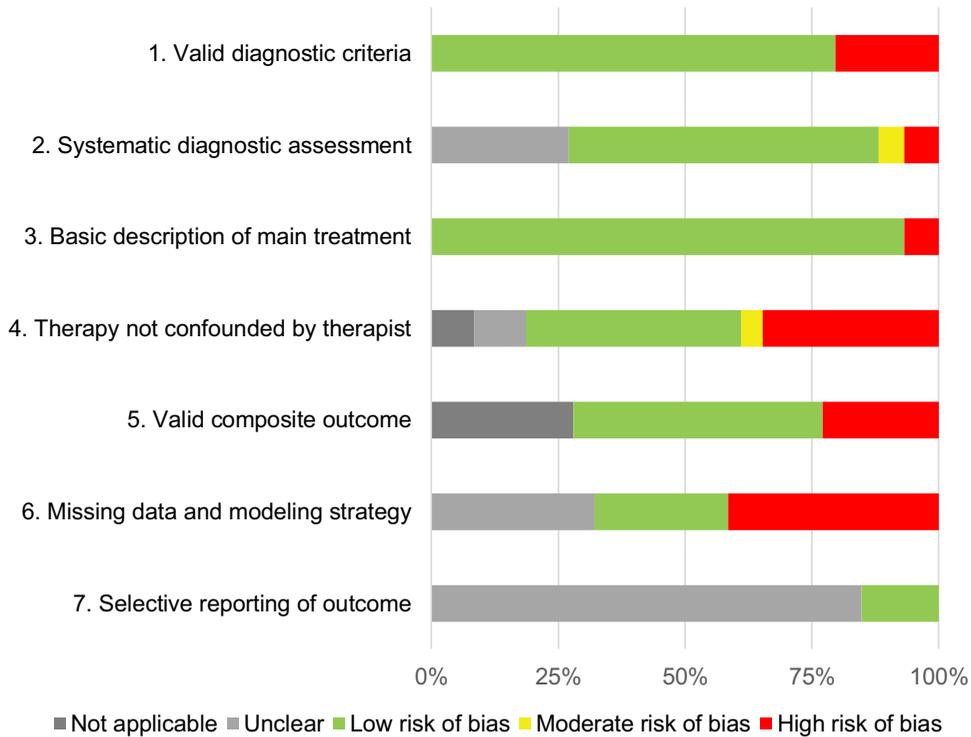


Figure 3. Distribution of risk of bias ratings. Study risk of bias criteria are listed in Table B.1.

Discussion

This article presents a comprehensive systematic search of the existing evidence base pertaining to psychological treatments for IBS. Based on the output of 11 scientific databases, we tabulated a broad set of outcomes and potential effect moderators from 118 studies reported in peer-reviewed journal articles and gray literature over four decades spanning from 1983 to 2022. Based on these data we conducted a meta-analysis of within-group effects to estimate the added effect of psychological treatments over attention controls; the idea being that such added effects are indicative of treatment benefits beyond those of credibility and expectancy effects as well as basic attention from a caregiver. Focusing on the primary outcome of composite IBS severity, in the unconditional models and when only the pre-post duration was included as a covariate in the statistical model, exposure therapy and hypnotherapy showed significant effects versus attention controls. In a further adjusted model that also included other key putative effect moderators, exposure therapy but not hypnotherapy remained significantly superior compared to attention controls. These incremental effects were moderate in size and remained similar in sensitivity analyses using alternative values for the pre-post correlation. The other treatment categories tested—CBT, CT, CT with relaxation, mindfulness, patient education, relaxation, and self-management—were not significantly different from attention controls on improvement in overall IBS symptom severity. Strengths of this study include the comprehensive literature survey, the structured regimen for assessing publications and categorizing treatments, and the coding of risk of bias criteria.

Table 3. Putative moderators of change in IBS symptom severity in psychological interventions for irritable bowel syndrome.

| Putative moderator | <i>p</i> | Reference category | <i>k</i> | Coefficient | 95% CI | <i>I</i> ² |
|---|----------|----------------------------|----------|-------------|--------------|-----------------------|
| Patient characteristics | | | | | | |
| Age, mean years | .225 | | 87 | 0.011 | −0.007–0.029 | 86 |
| Female, proportion | .704 | | 88 | −0.154 | −0.947–0.639 | 87 |
| IBS symptom severity: Severe | .457 | Mild or moderate | 55 | 0.098 | −0.160–0.356 | 86 |
| Constipation subtype, proportion | .888 | | 54 | −0.102 | −1.515–1.311 | 90 |
| Diarrhea subtype, proportion | .095 | | 54 | −0.897 | −1.951–0.157 | 90 |
| Study design | | | | | | |
| Randomized controlled trial (RCT) ^a | .094 | Not an RCT | 88 | −0.181 | −0.393–0.031 | 87 |
| Study site | | | 88 | | | 86 |
| Asia | .742 | North America | | −0.056 | −0.389–0.277 | |
| Europe | .436 | North America | | −0.103 | −0.364–0.157 | |
| Oceania | .017 | North America | | −0.417 | −0.760–0.075 | |
| Recruitment path: Referral or routine ^a | .014 | Convenience/ads or mixed | 88 | −0.264 | −0.475–0.053 | 87 |
| Outcome weighs in function: Yes | .164 | No | 83 | 0.163 | −0.067–0.392 | 87 |
| Outcome is based on a diary: Yes ^a | .024 | No | 88 | −0.381 | −0.711–0.051 | 87 |
| Outcome is intention-to-treat: Yes ^a | .337 | No | 88 | 0.092 | −0.095–0.279 | 87 |
| Weeks from pre to post assessment ^a | .035 | | 88 | 0.022 | 0.002–0.043 | 87 |
| Intervention characteristics | | | | | | |
| Mode of communication | | | 88 | | | 86 |
| Remote (e.g. online) | .630 | Face-to-face | | 0.061 | −0.185–0.306 | |
| Mixed or other | .159 | Face-to-face | | 0.267 | −0.105–0.639 | |
| Individual therapy ^a | .017 | Group therapy or self-help | 88 | 0.254 | 0.046–0.462 | 87 |
| Risk of bias on a scale from 0–2^b | | | | | | |
| 1. Diagnostic criteria | .265 | | 88 | 0.104 | −0.079–0.286 | 87 |
| 2. Diagnostic assessment | .413 | | 88 | −0.073 | −0.248–0.102 | 87 |
| 3. Description of treatment | .015 | | 88 | 0.289 | 0.057–0.521 | 86 |
| 4. Therapy confounded by therapist | .751 | | 88 | 0.019 | −0.098–0.136 | 87 |
| 5. Valid composite outcome | .172 | | 88 | −0.087 | −0.212–0.038 | 86 |
| 6. Missing data, modeling strategy | .269 | | 88 | −0.066 | −0.182–0.051 | 87 |
| 7. Selective reporting | .780 | | 88 | −0.029 | −0.232–0.174 | 87 |

Positive coefficients are indicative of larger standardized effects (Hedges' *g*) in terms of reduction in composite IBS severity.

^aEstimates pertaining these potential moderators were derived from the adjusted model of treatment types. All other potential moderators were added to this model one at a time.

^b"High risk" scored as 2, "moderate risk" or "unclear" as 1, and "low risk" or "not applicable" as 0.

Focusing on the primary outcome of composite IBS severity, the apparent beneficial effects of hypnotherapy seen in the first statistical model are in support of its widespread use, previous meta-analytic findings (Krouwel et al., 2021), and UK guidelines promoting the use of hypnotherapy in routine practice (National Institute for Health and Clinical Excellence, 2017). The finding that exposure therapy could be associated with larger effects than the attention controls is in line with some previous meta-analytic evidence (Black et al., 2020; K. Shah et al., 2020; Vugts et al., 2018). In contrast, on the surface, our finding that CBT was not associated with effects beyond those of the attention controls is seemingly inconsistent with previous meta-analyses (Black et al., 2020; Laird et al., 2017). There are, however, several potential explanations for this discrepancy. Notably, several treatments under the broad "CBT" umbrella were here instead categorized in more specific terms such as acceptance and commitment therapy, cognitive therapy, cognitive therapy with relaxation, and exposure therapy. In other words, CBT as defined narrowly in the present review refers to a smaller and more specific subtype of treatments (seven studies) characterized by the use of both cognitive and behavioral components (see Table B1). The small number of studies in this category may have limited power to



Table 4. Pooled change per treatment type (Hedges' g) versus the attention controls in secondary outcome domains.

| Predictor | Gastrointestinal outcomes | | | | | | Quality of life and psychiatric outcomes | | | | | | | | | | | | | | | | | |
|--------------------|---|-------------|--|-------------|---|-------------|--|-------------|--------------------------------------|-------------|---|-------------|-------------------------------------|--------------|--|-------------|-------------|-------------|-------------|-------------|--------------|--------------|--------------|--|
| | Composite (primary) ($k = 88, I^2 = 87\%$) | | Abdominal pain ($k = 67, I^2 = 73\%$) | | Distension/bloating ($k = 47, I^2 = 64\%$) | | Constipation ($k = 38, I^2 = 0\%$) | | Diarrhea ($k = 38, I^2 = 27\%$) | | Quality of life ($k = 73, I^2 = 91\%$) | | Anxiety ($k = 34, I^2 = 41\%$) | | Depression ($k = 44, I^2 = 77\%$) | | | | | | | | | |
| | <i>B</i> | 95% CI | <i>B</i> | 95% CI | <i>B</i> | 95% CI | <i>B</i> | 95% CI | <i>B</i> | 95% CI | <i>B</i> | 95% CI | <i>B</i> | 95% CI | <i>B</i> | 95% CI | | | | | | | | |
| Active controls | 0.54 | 0.29 | 0.78 | 0.76 | 0.42 | 0.25 | 0.60 | 0.32 | 0.21 | 0.43 | 0.39 | 0.24 | 0.54 | 0.39 | 0.17 | 0.61 | 0.38 | 0.16 | 0.60 | 0.31 | 0.15 | 0.48 | | |
| Added effect of... | | | | | | | | | | | | | | | | | | | | | | | | |
| CBT | 0.33 | -0.06 | 0.71 | 0.35 | -0.06 | 0.76 | | | | | | | | | | | | | | | | | | |
| CT | 0.58 | -0.01 | 1.16 | 0.21 | -0.15 | 0.57 | 0.09 | -0.24 | 0.41 | 0.07 | -0.13 | 0.26 | 0.00 | 0.53 | 0.11 | -0.20 | 0.43 | | | | 0.26 | -0.04 | 0.55 | |
| CT w relaxation | 0.07 | -0.32 | 0.46 | -0.26 | -0.59 | 0.07 | -0.26 | -0.52 | 0.01 | | | | | | | | | | | | | | | |
| Exposure | 0.54 | 0.20 | 0.88 | 0.46 | 0.14 | 0.79 | 0.69 | 0.42 | 0.95 | 0.22 | 0.08 | 0.35 | 0.34 | 0.12 | 0.63 | 0.32 | 0.94 | -0.03 | -0.30 | 0.24 | 0.06 | -0.17 | 0.29 | |
| Hypnotherapy | 0.27 | -0.05 | 0.59 | 0.16 | -0.14 | 0.45 | 0.16 | -0.11 | 0.43 | -0.14 | -0.39 | 0.12 | 0.01 | -0.33 | 0.30 | 0.00 | 0.60 | 0.02 | -0.26 | 0.31 | -0.02 | -0.26 | 0.22 | |
| Mindfulness | 0.02 | -0.43 | 0.47 | | | | | | | | | | | | 0.06 | -0.32 | 0.44 | | | | | | | |
| Patient education | -0.02 | -0.39 | 0.35 | -0.40 | -0.81 | 0.02 | -0.41 | -0.83 | 0.01 | -0.29 | -0.60 | 0.03 | -0.43 | -0.84 | 0.26 | -0.11 | 0.64 | -0.22 | -0.53 | 0.10 | -0.37 | -0.64 | -0.10 | |
| Relaxation | 0.36 | -0.11 | 0.83 | 0.05 | -0.38 | 0.49 | | | | -0.04 | -0.30 | 0.22 | 0.29 | -0.02 | 0.61 | | | | | | | | | |
| Relaxation w CSC | | | | 0.10 | -0.35 | 0.56 | | | | 0.30 | 0.08 | 0.52 | 0.13 | -0.16 | 0.41 | 0.09 | -0.29 | 0.48 | | | | | | |
| Self-management | 0.21 | -0.14 | 0.55 | 0.16 | -0.21 | 0.54 | 0.18 | -0.18 | 0.53 | | | | | | | | | | | | | | | |

Coefficients derived from meta-regression models where each treatment type was required to be represented by at least 4 studies. Positive coefficients are indicative of larger standardized beneficial effects (i.e., a more beneficial Hedges' g) in comparison with the attention controls, and negative coefficients are indicative of smaller beneficial effects. The following covariates were used: randomized controlled trial, individual as opposed to group or self-help treatment, use of an outcome derived from a diary as opposed to a questionnaire, referrals from routine care, and intention-to-treat estimates. Bold text is indicative of significant effects at 5% alpha. *Abbreviations.* CBT, cognitive behavior therapy; CSC, cognitive stress coping; CT, cognitive therapy.

detect superiority over the active control comparators. Also, potentially, some especially effective interventions that commonly fall under the “CBT” umbrella may not have been classified as CBT in the present study. Patient education stood out as being least promising, considering that the effect size on composite IBS severity was small. The secondary analyses were also indicative of a worse course of patient education on diarrhea and depression as compared to the attention controls. This suggests that interventions that focus solely on patient education should not be regarded as best practice psychological treatments, which should be considered for patients who do not improve from education.

Except for treatment category, arguably the most informative effect moderators found in this study were convenience sampling or recruitment via ads, individual therapist contact (as opposed to group treatment or self-help), and a longer duration between the pre- and post-treatment assessment (Table 3). The significant effect of recruitment strategy may mean that when patients self-select to treatment rather than being directed to a specific intervention by a clinician, better effects are seen. The effect of individual therapist contact (either face-to-face or remotely) indicates that it is important for treatment outcome that a therapist has an active role in the patient’s treatment, and dovetails with the finding by Henrich et al. (2015) that personalized feedback on patient behavior is associated with improved outcome. We note that in the meta-analysis by Black et al. (2020), although the authors found no significant differences in effect between treatment formats, pooled point effect sizes were larger for group and telephone “CBT” than face-to-face individual “CBT” which can be said to contrast with our finding that individual therapy, in either face-to-face or remote format, may be particularly beneficial. Several methodological differences are likely to have contributed to this apparent inconsistency. The only two therapies to be classified as group “CBT” in the study by Black et al. were categorized as CT and CT with relaxation here (Tkachuk et al., 2003; Vollmer & Blanchard, 1998), and the only therapy to be classified as telephone “CBT” in the study by Black et al. was categorized as stress management here (Everitt et al., 2019). Another key difference is that whereas Black et al.’s categories conflated the delivery method (e.g. face-to-face, telephone, online), interaction format (e.g. individual, group, guided self-help), and components of treatment (e.g. cognitive, hypnotherapy, relaxation), we tabulated these separately. To some degree, our finding that individual therapy may be especially effective poses a challenge to the wider dissemination of effective IBS treatment, considering that other formats where the therapist devotes less than 3 hours or five sessions per patient constitute a less credible option.

This meta-analysis had limitations. First, the analysis of within-group change is susceptible to confounding by design and sample characteristics. Another threat is allegiance effects, or the fact that many treatment categories have only been evaluated by a limited number of research groups. This highlights the need for further experimental work, and it should be pointed out that few RCTs have so far directly compared active psychological treatments for IBS to each other. Second, because the premise of this meta-analysis was to classify treatments based on their category, therapies that showed little resemblance to other protocols had to be excluded from the analysis. Furthermore, our categorization scheme may have obscured individual protocols that are more efficacious than other protocols that were categorized as belonging to the same category. For example,

the cognitive behavioral treatment evaluated by Lackner et al. (2018), which we categorized as cognitive therapy with relaxation, showed superiority over an attention control in a recent large-scale randomized trial (Lackner et al., 2018). This is an inherent problem in a meta-analytic approach that necessitates lumping of different studies. Thus, our results should not be interpreted as showing that specific protocols are not superior to attention controls, but rather as identifying broad treatment categories that show promising evidence of effects that are not attributable to unspecific factors. Third, there were indications of original study bias for example in that many publications provided little or no information about missing data, or had a high proportion of missing data and did not manage this in a convincing manner. Fourth, certain original studies, despite investigating the effect of a psychological treatment on IBS severity, could not be tabulated because these did not report a composite IBS severity outcome or did not report the relevant statistics. Similarly, the primary outcome of some original studies was disregarded in favor of secondary outcomes that were more relevant for this project. Fifth, in this meta-analysis, the dependency between conditions evaluated in the same clinical trial was not modelled explicitly. This said, considering that the further adjusted meta-regression model included several key study characteristics as moderators we believe that our estimates are likely to be a fair representation of the true effects. Last, upon visual inspection of the funnel plot, there appeared to be a slight overrepresentation of large effects in small studies in this systematic review. Though this may have led to a slight overestimation of treatment effects, this was probably a subtle bias. Despite the relatively large number of data points, Egger's formal test of funnel plot asymmetry did not reach significance.

Conclusion

Tentatively, exposure therapy appears to be a particularly promising treatment for IBS. For more firm conclusions, there is a need for head-to-head comparisons of bona fide psychological treatments in randomized controlled trials. Further analyses of the existing evidence base, for example for the estimation of statistical power, can also be based on the dataset from this project which is freely available via the Open Science Framework (5yh9a).

Notes

1. Though the text on page 6 reads “the mixed effect analyses (Table 4) show no significant differences for specific treatment components of exposure [...]”, Table 4 which states that p was $< .05$ was confirmed to be correct by the author via e-mail on 16 April 2020.
2. This study originally focused on treatment components instead of treatment categories, but the peer review process raised conceptual problems related to the component classification scheme. In the interest of transparency, and in line with the original study registration, the results from the original analysis are reported on the Open Science Framework (identifier: 5yh9a) where this systematic search and meta-analysis was pre-registered.

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Disclosure statement

EHL and BL are founders and shareholders of Hedman-Lagerlöf och Ljótsson Psykologi Inc., a company that licenses exposure-based online treatment for IBS. EHL, PL, HH, EAn, OO, MB, ML, and BL have made previous contributions to the developed and/or evaluation of exposure-based treatment for IBS. EAx, DK, EHL, HH, EAn, OO, MB, ML, and BL have made previous contributions to the developed and/or evaluation of exposure-based treatment for other somatic conditions, functional somatic syndromes, or somatic symptom and related disorders. PL and BL have made previous contributions to the evaluation of hypnotherapy for IBS. EAx, PL, and BL have made previous contributions to the evaluation of patient education for IBS. The authors have no additional personal or financial conflicts to disclose.

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References

- Becker, B. J. (1988, November). Synthesizing standardized mean-change measures. *British Journal of Mathematical and Statistical Psychology*, 41(2), 257–278. <https://doi.org/10.1111/j.2044-8317.1988.tb00901.x>
- Black, C. J., Thakur, E. R., Houghton, L. A., Quigley, E. M. M., Moayyedi, P., & Ford, A. C. (2020, August). Efficacy of psychological therapies for irritable bowel syndrome: Systematic review and network meta-analysis. *Gut*, 69(8), 1441–1451. <https://doi.org/10.1136/gutjnl-2020-321191>
- Bramer, W. M., Giustini, D., de Jonge, G. B., Holland, L., & Bekhuis, T. (2016, July). De-duplication of database search results for systematic reviews in EndNote. *Journal of the Medical Library Association: JMLA*, 104(3), 240–243. <https://doi.org/10.3163/1536-5050.104.3.014>
- Burton Murray, H., & Ljótsson, B. (2022, December). Future of brain-gut behavior therapies: Mediators and moderators. *Gastroenterology Clinics of North America*, 51(4), 723–739. <https://doi.org/10.1016/j.gtc.2022.06.011>
- Cohen, J. (1988). 2.2.3 “Small,” “medium”, and “large” d values. In J. Cohen (Ed.), *Statistical power analysis for the behavioral sciences* (2nd ed., pp. 24–27). Lawrence Erlbaum Associates.
- Egger, M., Smith, G. D., Schneider, M., & Minder, C. (1997, September 13). Bias in meta-analysis detected by a simple, graphical test. *BMJ*, 315(7109), 629–634. <https://doi.org/10.1136/bmj.315.7109.629>
- Everhart, J. E., & Ruhl, C. E. (2009). Burden of digestive diseases in the United States Part I: Overall and upper gastrointestinal diseases. *Gastroenterology*, 136(2), 376–386. <https://doi.org/10.1053/j.gastro.2008.12.015>
- Everitt, H. A., Landau, S., O’Reilly, G., Sibelli, A., Hughes, S., Windgassen, S., Holland, R., Little, P., McCrone, P., Bishop, F., Goldsmith, K., Coleman, N., Logan, R., Chalder, T., Moss-Morris, R., & Grp, A. T. (2019, September). Assessing telephone-delivered cognitive-behavioural therapy (CBT) and web-delivered CBT versus treatment as usual in irritable bowel syndrome (ACTIB): A multicentre randomised trial. *Gut*, 68(9), 1613–1623. <https://doi.org/10.1136/gutjnl-2018-317805>
- Ford, A. C., Forman, D., Bailey, A. G., Axon, A. T., & Moayyedi, P. (2008, May). Irritable bowel syndrome: A 10-yr natural history of symptoms and factors that influence consultation behavior. *The American Journal of Gastroenterology*, 103(5), 1229–1239. quiz 1240. <https://doi.org/10.1111/j.1572-0241.2007.01740.x>
- Ford, A. C., Lacy, B. E., Talley, N. J., & Longo, D. L. (2017, June). Irritable bowel syndrome. *New England Journal of Medicine*, 376(26), 2566–2578. <https://doi.org/10.1056/NEJMra1607547>
- Francis, C. Y., Morris, J., & Whorwell, P. J. (1997, April). The irritable bowel severity scoring system: A simple method of monitoring irritable bowel syndrome and its progress. *Alimentary Pharmacology & Therapeutics*, 11(2), 395–402. <https://doi.org/10.1046/j.1365-2036.1997.142318000.x>
- Frändemark, A., Törnblom, H., Jakobsson, S., & Simrén, M. (2018, October). Work productivity and activity impairment in irritable bowel syndrome (IBS): A multifaceted problem. *American Journal of Gastroenterology*, 113(10), 1540–1549. <https://doi.org/10.1038/s41395-018-0262-x>
- Hedges, L. V. (1981). Distribution theory for Glass’s estimator of effect size and related estimators. *Journal of Educational and Behavioral Statistics: A Quarterly Publication Sponsored by the American Educational Research Association and the American Statistical Association*, 6(2), 107–128. <https://doi.org/10.3102/10769986006002107>
- Henrich, J. F., Knittle, K., De Gucht, V., Warren, S., Dombrowski, S. U., & Maes, S. (2015, March). Identifying effective techniques within psychological treatments for irritable bowel syndrome: A meta-analysis. *Journal of Psychosomatic Research*, 78(3), 205–222. <https://doi.org/10.1016/j.jpsychores.2014.12.009>
- Keefe, L., Ballou, S. K., Drossman, D. A., Ringstrom, G., Elsenbruch, S., & Ljótsson, B. (2022, January). A rome working team report on brain-gut behavior therapies for disorders of gut-brain interaction. *Gastroenterology*, 162(1), 300–315. <https://doi.org/10.1053/j.gastro.2021.09.015>

- Krouwel, M., Farley, A., Greenfield, S., Ismail, T., & Jolly, K. (2021, January 27). Systematic review, meta-analysis with subgroup analysis of hypnotherapy for irritable bowel syndrome, effect of intervention characteristics. *Complementary Therapies in Medicine*, 57, 102672. <https://doi.org/10.1016/j.ctim.2021.102672>
- Lackner, J. M., Jaccard, J., Keefer, L., Brenner, D. M., Firth, R. S., Gudleski, G. D., Hamilton, F. A., Katz, L. A., Krasner, S. S., Ma, C. X., Radziwon, C. D., & Sitrin, M. D. (2018, July). Improvement in gastrointestinal symptoms after cognitive behavior therapy for refractory irritable bowel syndrome. *Gastroenterology*, 155(1), 47–57. <https://doi.org/10.1053/j.gastro.2018.03.063>
- Laird, K. T., Tanner-Smith, E. E., Russell, A. C., Hollon, S. D., & Walker, L. S. (2016, July). Short-term and long-term efficacy of psychological therapies for irritable bowel syndrome: A systematic review and meta-analysis. *Clinical Gastroenterology and Hepatology*, 14(7), 937–947 e934. <https://doi.org/10.1016/j.cgh.2015.11.020>
- Laird, K. T., Tanner-Smith, E. E., Russell, A. C., Hollon, S. D., & Walker, L. S. (2017, February). Comparative efficacy of psychological therapies for improving mental health and daily functioning in irritable bowel syndrome: A systematic review and meta-analysis. *Clinical Psychology Review*, 51, 142–152. <https://doi.org/10.1016/j.cpr.2016.11.001>
- Landis, J. R., & Koch, G. G. (1977, March). The measurement of observer agreement for categorical data. *Biometrics*, 33(1), 159–174. <https://doi.org/10.2307/2529310>
- Ljótsson, B., Hesser, H., Andersson, E., Lackner, J. M., El Alaoui, S., Falk, L., Aspvall, K., Fransson, J., Hammarlund, K., Ljöfström, A., Nowinski, S., Lindfors, P., & Hedman, E. (2014, April). Provoking symptoms to relieve symptoms: A randomized controlled dismantling study of exposure therapy in irritable bowel syndrome. *Behaviour Research and Therapy*, 55, 27–39. <https://doi.org/10.1016/j.brat.2014.01.007>
- Lovell, R. M., & Ford, A. C. (2012, July). Global prevalence of and risk factors for irritable bowel syndrome: A meta-analysis. *Clinical Gastroenterology and Hepatology*, 10(7), 712–721 e714. <https://doi.org/10.1016/j.cgh.2012.02.029>
- Martin, C. R., Osadchiy, V., Kalani, A., & Mayer, E. A. (2018). The brain-gut-microbiome axis. *Cellular and Molecular Gastroenterology and Hepatology*, 6(2), 133–148. <https://doi.org/10.1016/j.jcmgh.2018.04.003>
- Mayer, E. A., & Tillisch, K. (2011). The brain-gut axis in abdominal pain syndromes. *Annual Review of Medicine*, 62(1), 381–396. <https://doi.org/10.1146/annurev-med-012309-103958>
- Melchior, C., Colomier, E., Trindade, I. A., Khadija, M., Hreinsson, J. P., Tornblom, H., & Simren, M. (2022, September). Irritable bowel syndrome: Factors of importance for disease-specific quality of life. *United European Gastroenterology Journal*, 10(7), 754–764. <https://doi.org/10.1002/ueg2.12277>
- Morris, S. B. (2000, May). Distribution of the standardized mean change effect size for meta-analysis on repeated measures. *British Journal of Mathematical and Statistical Psychology*, 53(Pt 1), 17–29. <https://doi.org/10.1348/000711000159150>
- National Institute for Health and Clinical Excellence. (2017). *Irritable bowel syndrome in adults: diagnosis and management*. Retrieved June 18, 2020, from <https://www.nice.org.uk/guidance/cg61/chapter/1-Recommendations#psychological-interventions>
- Peters, S. L., Muir, J. G., & Gibson, P. R. (2015, June). Review article: Gut-directed hypnotherapy in the management of irritable bowel syndrome and inflammatory bowel disease. *Alimentary Pharmacology and Therapeutics*, 41(11), 1104–1115. <https://doi.org/10.1111/apt.13202>
- Rücker, G., Schwarzer, G., Carpenter, J. R., & Schumacher, M. (2008, November 27). Undue reliance on I(2) in assessing heterogeneity may mislead. *BMC Medical Research Methodology*, 8(79). <https://doi.org/10.1186/1471-2288-8-79>
- Schmulson, M. J., & Drossman, D. A. (2017, April 30). What is new in Rome IV. *Journal of Neurogastroenterology and Motility*, 23(2), 151–163. <https://doi.org/10.5056/jnm16214>
- Schwille-Kiuntke, J., Rudlin, S. L., Junne, F., Enck, P., Brenk-Franz, K., Zipfel, S., & Rieger, M. A. (2021, July 19). Illness perception and health care use in individuals with irritable bowel syndrome: Results from an online survey. *BMC Family Practice*, 22(1), 154. <https://doi.org/10.1186/s12875-021-01499-5>

- Shah, K., Ramos-Garcia, M., Bhavsar, J., & Lehrer, P. (2020, May). Mind-body treatments of irritable bowel syndrome symptoms: An updated meta-analysis. *Behaviour Research and Therapy*, 128, 103462. <https://doi.org/10.1016/j.brat.2019.103462>
- Shah, E. D., Salwen Deremer, J. K., Gibson, P. R., Muir, J. G., Eswaran, S., & Chey, W. D. (2021, January-June). Pharmacologic, dietary, and psychological treatments for irritable bowel syndrome with constipation: Cost utility analysis. *MDM Policy and Practice*, 6(1), 2381468320978417. <https://doi.org/10.1177/2381468320978417>
- Shields, G. S., Spahr, C. M., & Slavich, G. M. (2020, June). Psychosocial interventions and immune system function: A systematic review and meta-analysis of randomized clinical trials. *JAMA Psychiatry*, 77(10), 1031. <https://doi.org/10.1001/jamapsychiatry.2020.0431>
- Stroup, D. F., Berlin, J. A., Morton, S. C., Olkin, I., Williamson, G. D., Rennie, D., Moher, D., Becker, B. J., Sipe, T. A., & Thacker, S. B. (2000, April). Meta-analysis of observational studies in epidemiology: A proposal for reporting. Meta-analysis of observational studies in epidemiology (MOOSE) group. *JAMA*, 283(15), 2008–2012. <https://doi.org/10.1001/jama.283.15.2008>
- Tkachuk, G. A., Graff, L. A., Martin, G. L., & Bernstein, C. N. (2003, March). Randomized controlled trial of cognitive-behavioral group therapy for irritable bowel syndrome in a medical setting. *Journal of Clinical Psychology in Medical Settings*, 10(1), 57–69. <https://doi.org/10.1023/A:1022809914863>
- Viechtbauer, W. (2010). Conducting meta-analyses in R with the metafor package. *Journal of Statistical Software*, 36(3), 1–48. <https://doi.org/10.18637/jss.v036.i03>
- Vollmer, A., & Blanchard, E. B. (1998). Controlled comparison of individual versus group cognitive therapy for irritable bowel syndrome. *Behavior Therapy*, 29(1), 19–33. <https://doi.org/10.1016/S0005-7894-98-80016-6>
- Vugts, M. A. P., Joosen, M. C. W., van der Geer, J. E., Zedlitz, A., Vrijhoef, H. J. M., & Yang, J. (2018). The effectiveness of various computer-based interventions for patients with chronic pain or functional somatic syndromes: A systematic review and meta-analysis. *PloS One*, 13(5), e0196467. <https://doi.org/10.1371/journal.pone.0196467>
- Youell, K. J., & McCullough, J. P. (1975). Behavioral treatment of mucous colitis. *Journal of Consulting and Clinical Psychology*, 43(5), 740–745. <https://doi.org/10.1037/0022-006x.43.5.740>