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Document Version
Peer reviewed version

Citation for published version (Harvard):
krouwel, M, Greenfield, S, Farley, A, Ismail, T & Jolly, K 2018, 'Factors which affect the efficacy of hypnotherapy for IBS: Protocol for a systematic review and meta-regression', *European Journal of Integrative Medicine*.

Link to publication on Research at Birmingham portal

Publisher Rights Statement:
Published as above, final version of record available at: [add DOI].

Checked 20/06/2018.

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Factors which affect the efficacy of hypnotherapy for IBS: Protocol for a systematic review and meta-regression

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Word count – Abstract 248
Body 2420

Abstract

Introduction – Hypnotherapy for the treatment of Irritable Bowel Syndrome (IBS) has accumulated a broad evidence base, resulting in its inclusion in the UK National Institute of Health and Care Excellence (NICE) Guidelines in 2008. Although several high quality systematic reviews and meta-analyses of hypnotherapy's efficacy have been conducted, subgroup analysis of factors which contribute to this are absent. The goal of this systematic review is to evaluate the current literature to identify factors which contribute to its effectiveness.

Methods and analysis –We will conduct searches in CINAHL, Cochrane library, Conference Citation Index (science & social science), Embase (excerpta medica), Medline, PubMed, PsycARTICLES, PsychINFO, Science Citation Index-expanded and Social Science Citation Index. Data will be included from randomised (RCTs) and non-randomised controlled trials with a concurrent comparator of hypnotherapy interventions for IBS, reported in English. Two authors will independently review studies for inclusion, with arbitration by a third reviewer if needed. We will assess for risk of bias using the Cochrane Collaboration's risk of bias tool for RCTs and the Robins-I tool for non-RCTs.

Where appropriate a meta-regression analysis of pre-defined subgroups will be conducted using a random effects model. Where quantitative analysis is not possible a narrative description will be given.

Discussion – These will be disseminated via peer review journals and at appropriate conferences. The results may be of use in establishing the most efficient formulation of services delivering hypnotherapy for IBS.

Study registration number: PROSPERO CRD42018065533

Keywords – Hypnotherapy, irritable bowel syndrome, hypnosis, meta-regression analysis, systematic review, protocol

1.Introduction

Irritable Bowel Syndrome (IBS) is a chronic functional bowel disorder characterised by a high degree of variability in bowel movement frequency and composition accompanied by recurrent abdominal pain (1). The disorder affects large numbers of people worldwide with prevalence figures around 11% often cited (2-5), however due to substantial variation between studies brought about by differences in who identifies the IBS, (6) and the diagnostic criteria used (7) no universal prevalence rate can currently be agreed upon (8).

IBS consumes a substantial amount of primary (9, 10) and secondary care time (10, 11) and money, with an estimated £70 million being spent by the UK's National Health Service (NHS) on antispasmodics and laxatives specifically for the treatment of IBS (12). In addition to physical symptoms, sufferers experience negative impacts on quality of life (13), frequently experience anxiety and depression (14) and express higher than average levels of suicidal ideation and behaviour (15).

Historically IBS has had a reputation as difficult to both diagnose (16, 17) and treat (18), with traditional pharmacological approaches such as antispasmodics, anti-motility agents and bulking agents (19) being focused upon symptom control rather than cure. Sufferers sometimes have a low opinion of traditional medicines (20) and commonly turn to complementary and alternative therapies (CAM) for help (21). The last few decades have seen the exploration of a raft of potential novel treatments, with some proving efficacious, albeit to varying degrees; these include peppermint oil (22), probiotics (23, 24) and 5-HT antagonists (25). Some of these treatments have sufficient evidence of efficacy to warrant inclusion in National Institute for Health and Care Excellence (NICE) guidelines (19), such as exercise (26), antidepressants (27), and the FODMAP diet (28). One of these novel NICE approved approaches is hypnotherapy, which is specifically recommended for IBS sufferers 'who do not respond to pharmacological treatments after 12 months and who develop a continuing symptom profile', known as 'refractory' (19). There is evidence that general practitioners may be open to hypnotherapy for IBS (29), although IBS sufferers themselves appear cautious,

with one study finding that 36.3% of sufferers consider it an unacceptable treatment option (30).

Hypnotherapy is hypnosis (31) used with the intention of generating a beneficial outcome. The earliest trials of hypnotherapy for the treatment of IBS date back to the early 1980s (32, 33) using a package of broadly similar techniques, the most well-known of which are the Manchester Model (18) and the North Carolina Protocol (34) which have been termed gut-directed hypnotherapy (GDH) (35); these models were quickly adopted as the norm (36, 37).

GDH is a multisession approach which combines general relaxation with gut specific suggestions and imagery to promote digestive calm, control and strength (38). The mechanisms by which GDH improves outcomes are unclear (39, 40). There is evidence that suggests it may normalise rectal sensitivity (41), but this is not a universal finding (42). Equally, there is evidence to suggest it may have an effect on digestive motility (43), but recent work has failed to confirm this (44). Other factors which have been implicated as possible mechanisms of action of GDH include changes to bowel distention perception (45), cognitive alteration (46) and moderation of activity in the posterior insula region of the brain (47), an area associated with processing sensations from inside the body, which suggests that hypnotherapy may moderate the signals from the body in some way, although exactly how remains unclear.

Hypnotherapy for IBS has a demonstrable record of effectiveness (48, 49), however older reviews lacked sufficient data to conduct meaningful subgroup analysis, (4, 39), and those more recent reviews which have carried out subgroup analysis have focused upon symptoms such as pain and constipation (48-50).One review did examine the difference between refractory sufferers' and non-refractory sufferers' responsiveness (48), however due to substantial heterogeneity in sample populations and symptom measures these findings cannot be considered conclusive. Heterogeneity is a consistent problem as studies do not use consistent interventions or outcome measures; to date two systematic reviews have attempted to address the heterogeneity of outcome measures by reporting a standardised mean difference (SMD) (48, 49). Beyond this, concerns exist that outcomes may be subject to a degree of variability

dependent upon as yet unexamined factors (51). Factors that might affect the outcome of hypnotherapy for IBS include the hypnotherapist's skill, training and experience (10, 52); patient demographics (51), with evidence suggesting that gender may be a factor (53, 54), but no meta-analysis has assessed the validity of these findings over different populations. The clinical setting may be a factor (48, 52) as may the nature of the hypnotherapeutic approach itself (51).

Hypnotherapy for IBS is notably time intensive, currently delivered for up to 12 hours contact time per patient on a one-to-one basis (40). Any findings which help to increase this treatment's efficacy, be that by identifying the most responsive populations, efficient dose, effective type of practitioner or clinical setting, are likely to reduce the costs of this NICE approved therapy.(19)

1.1. Objectives

The review aims to assess the impact of different variables within and around the hypnotherapeutic treatment of IBS. Specifically, the review will address the following questions:

Are the outcomes of hypnotherapy for IBS affected by:

1. recruitment location: primary and community, secondary and tertiary care
2. delivery location: primary and community, secondary and tertiary care
3. hypnotherapist's characteristics such as gender, age and duration of training
4. number of sessions delivered
5. total therapy time
6. time between sessions
7. mode of delivery: individual or group treatment
8. population variables, such as gender, age, educational status
9. duration of symptoms

10. type of hypnotherapy: GDH approaches versus hypnotherapy with a distinctly different underlying philosophy such as hypnotherapeutically enhanced Cognitive Behavioural Therapy (CBT) (55)
11. Type of IBS: There are three main types of IBS as defined by the main symptom experienced, IBS-D where the person predominantly experiences diarrhoea, IBS-C where constipation is predominant, and IBS-A, the alternating type where both diarrhoea and constipation are frequent.(56)

2. Methods

2.1. Study registration

This protocol review has been registered on PROSPERO CRD42018065533

2.2. Eligibility criteria

2.2.1 Type of study – Eligible studies include randomised, quasi-randomised or non-randomised studies comparing an intervention with a definable element of hypnotherapy to an explicit concurrent comparator, such as another treatment, or placebo such as sham therapy. Due to financial constraints only English language journals will be used No limits will be placed on publication date.

2.2.2 Type of participant –No exclusion will be made on grounds of gender, ethnicity, duration of symptoms or socio-economic status. Studies of children (≤17 years of age) will be excluded.

Participants will have received a diagnosis of IBS in line with one of the major criteria, Manning(57), Rome I(58), II(59), III(60) or IV(61). Although these criteria have been superseded by each other, i.e. Rome I replaced Manning, Rome II replaced Rome I and so on, they were the definable criteria of their time and represent a recognised diagnosis, as such they will be accepted as a valid definition of IBS status which is consistent with previous reviews' practice (50, 62).

2.2.3 Type of intervention

The intervention will contain some degree of hypnotherapy for the treatment of IBS. The work will be conducted by an individual identified as possessing hypnotherapeutic skill. To this end, therapy identified as guided imagery, relaxation or any other treatment which is not explicitly defined as hypnosis will be excluded.

2.2.4 Type of comparator

This group will be in receipt of an alternative treatment, which may include another hypnotherapeutic approach, treatment as usual or a placebo intervention.

2.2.5 Type of outcome measure

2.2.5.1 Primary – Any continuous measure of global gastrointestinal symptoms. Several of these exist, some of the most commonly used are presented below in preferential order for use if more than one is present in a single study.

1) IBS Symptom Severity Scoring System (IBS-SSS) (63).

2) The gastrointestinal symptoms rating scale (GRS-IBS)(64).

3) Functional Bowel Disorder Severity Index(65)

4) IBS Symptom Questionnaire (65)

5) Visceral Sensitivity Index (VSI) (66, 67).

6) Other continuous measure of global gastrointestinal symptoms

- **2.2.5.2 Secondary** – These are for specific symptoms, for example physical, mental or quality of life which cannot be combined within the study, as it is

unlikely that studies will use more than one measure for these outcomes no preferential order has been specified; Mental health, such as the Hospital Anxiety and Depression Scale (HADS) (68, 69)

- Quality of life, such as: The IBS quality of life scale (IBS-QOL) (70) and the SF-36 generic health-related quality of life measure.(71)
- Single symptom specific measures of: improvement in abdominal pain, discomfort or distention; stool frequency; bowel transit times and stool consistency
- Adverse events
- Dropout rates
- Failure to respond to referral (DNA rates)

Any of the primary or secondary measures may be clinician or self-assessed.

2.3 Search methods for identification of studies

2.3.1. Electronic searching

The following databases will be searched:

CINAHL, Cochrane library, Conference Citation Index (science & social science), Embase (excerpta medica), Medline, PubMed, PsycARTICLES, PsychINFO, Science Citation index-expanded, Social Science Citation Index.

Using the Medical Subject Headings (MeSH) search terms “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$

2.3.2. Reference search

A hand search will be conducted of the reference lists of included studies to identify any possible studies that may not have otherwise been captured.

2.3.3. Unpublished trials

Contact with lead authors from studies which have been included will be undertaken where possible to see if they are aware of any unpublished trials.

2.4 Data collection and analysis

2.4.1 Selection of studies

Two parties will independently assess titles and abstracts resulting from searches for inclusion and exclusion; their lists will be compared and any disagreements will either be resolved at this stage by the two reviewers or the article will be moved forward to the next stage of selection. The remaining articles will be obtained in full and eligibility assessed independently by both reviewers. Any disagreements will be resolved through consensus between the two parties, should this prove insufficient then adjudication will be made by a third party.

2.4.2 Data extraction

Data extraction will be by two parties working independently, with a third to adjudicate on any disagreements.

Data extraction is intended to identify the nature of the intervention, the comparator used, and the outcome measures employed in the study i.e. GSRS (64), VSI (66) and any evidence of variables of interest to the review questions; i.e. number of sessions, therapist contact time, therapist characteristics, training and experience, setting and format of delivery (individual/group).

The corresponding authors of included studies will be contacted to ask further details about the setting of their intervention (primary/secondary/tertiary) and for details about the demographic characteristics, training and experience of the hypnotherapist. In addition, authors will be contacted for missing data. A data extraction form will be used to both assess quality and capture key information in a standardised way.

2.5 Assessment of risk of bias

All articles included at this point will be independently assessed by two parties for risk of bias, any unresolvable disagreements will again be adjudicated by a third party. There is a growing body of evidence and opinion to suggest that quantitative approaches to risk of bias assessment are unsupported and possibly misleading (72); therefore a more nuanced model, based on the model used in the 2011 Cochrane collaboration (72) will be used for randomised and semi-randomised studies and the ROBINS-I (73) tool will be used for the non-randomised studies. Specifically, the following markers, in line with Cochrane risk of bias tool (74) will be recorded in a bespoke extraction sheet, covering the presence of random sequence generation, allocation concealment, blinding and the recording and explanation of exclusions, withdrawals and drop outs. In addition, the recently developed ROBINS-I (73) tool will be used for the non-randomised and quasi-randomised studies. ROBINS-I assesses seven key domains; confounding, selection, classification of intervention, measurements, departures from interventions, missing data and reported results.

2.6 Statistical analysis

If possible, data will be quantitatively synthesised using a random effects meta-analysis. Random effects has been chosen as it is anticipated that there will be a high level of clinical heterogeneity (i.e. differences in the population, intervention, comparator) between studies. Differences in effect size by study characteristics will be investigated using sub group analyses, unless head to head comparisons are available. If sufficient data is available (10 or more studies per comparison) meta-regression analysis will be performed to investigate subgroup differences whilst holding other study characteristics constant. This will be conducted for all identified studies and

where possible separately for the RCTs alone. If there is insufficient data for quantitative synthesis, then a narrative review approach will be taken. The following comparisons are proposed, these are based on divisions observed during scoping activities and examination of previous reviews. Where continuous measures are being used dichotomously the average of the measure will be used as the defining point, for example a patient population may have an age range of 18-51, but if the average is 39 they will be treated in the 40 and under age group.

- Frequency of sessions: <1 per week compared to ≥1 session in a week. (34, 75)
- Number of sessions: ≤7 sessions compared to >7 sessions. (51)
- Total contact time: ≤6 hours compared to >6 hours. (51)
- Level of hypnotherapy training: short course (≤40 hours training) compared to long course (>40 hours training). (76)
- Hypnotherapist characteristics: Female compared to male. (53) Up to and including 40 years of age and 41 or older. (77)
- Population characteristics: Up to and including 40 years of age and 41 or older. (78) Graduate/college education or higher compared to non-graduate/college education. (79) A population will be classified within a group if it consists of ≥80% or more of the intended population.
- Duration of symptoms: ≤1 year since first medical identification of symptoms compared to >1. (50)
- Group hypnotherapy compared to individual hypnotherapy. (51, 80)
- GDH compared to ‘other’ hypnotherapy approaches. (55)
- Recruitment and delivery setting: primary and community compared to secondary and tertiary care. (4, 52)
- IBS by predominant symptom type– Diarrhoea predominant compared to constipation predominant type, diarrhoea predominant type compared to alternating type, alternating type compared to constipation type.

If there are not enough studies for meta-analysis, the results will be described narratively. Version 5.3 of RevMan will be used for the data analysis.

3. Conclusion

This review of factors affecting the effectiveness of hypnotherapy for IBS will provide valuable insights which may allow for a greater cost effectiveness in hypnotherapy for IBS services by guiding such services to the most efficient type of hypnotherapy, location of recruitment or intervention, population, level of hypnotherapist's training and amount and frequency of contact time required. For an expensive treatment such as hypnotherapy any factor identified which can be reduced without affecting outcomes will save money for healthcare budgets. Equally, any factors which are vital to sustained beneficial outcomes, and need to be retained need to be identified to reduce future relapse of symptoms.

Conflict of interest & funding

MK is a hypnotherapist and is not receiving any funding and is unaware of any commercial interest in the findings. SG and KJ are part funded by the National Institute for Health Research (NIHR) Collaboration for Leadership in Applied Health Research and Care West Midlands. The views expressed in this article are those of the authors and not necessarily those of the NIHR, the NHS or the Department of Health and Social Care.

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