

**Introduction** Hypermobile Ehlers-Danlos syndrome (hEDS), characterized by skin hyperextensibility, tissue fragility and joint hypermobility, is associated with features consistent with irritable bowel syndrome (IBS) (Nelson et al 2015, Zeitoun et al, 2013). In IBS, abdominal pain is associated with increased colonic sensitivity and increased density of nerve fibres (Akbar et al 2008) and mast cells (Barbara et al 2004). Tenascin X knockout mice, that are phenotypically similar to hEDS, also have increased afferent sensitivity and expression of nociceptive calcitonin gene related peptide (CGRP) nerve fibres in the colonic mucosa (Aktar et al 2018). Therefore, we hypothesize that nerve and mast cell profile are also altered in hEDS patients with IBS features; similar to findings in previous IBS studies and in animal models of hypermobility.

**Methods** Immunofluorescence-immunohistochemistry (IF-IHC) was used to evaluate expression of mast cell tryptase (AA1 Dako, M7052, 1:400) and the neural markers CGRP (Thermo Scientific ABS 0260502, 1:200) and Protein Gene Product (PGP9.5, Dako, Z5116, 1:400) in the colonic mucosa of: IBS patients (N=4), and IBS patients with comorbid hEDS (N=4). To determine the presence of positive fibres a threshold of 20% above background (0% = black image) was used. The positive areas were highlighted to give a 'region of interest;' thereafter the number of pixels in the region of interest were measured. Mast cells were counted on Image J using the multipoint tool. Results were analysed using an unpaired *t*-test for each marker; with significance set at *p*<0.05.

**Results** The comorbid IBS/hEDS group demonstrated a 2-fold proliferation in PGP 9.5 immunoreactive fibers (41476 ± 6196) compared to those with IBS alone (22245 ± 3404, *p* = 0.003). However, CGRP positive fibers and mast cells were significantly reduced in hEDS/IBS overlap compared to IBS alone (CGRP: comorbid IBS/hEDS: 329 ± 165 vs IBS alone 1557 ± 559, *p* = 0.015), (Mast cell tryptase:

comorbid IBS/hEDS: 25 ± 3 vs IBS alone 44 ± 5, *p* = 0.001). (Figure 1).

**Conclusion** This difference in colonic neuronal innervation and mast cell expression in IBS patients with hEDS suggests that different inflammatory/nociceptive pathways are involved in comorbid IBS/hEDS. The overlap group may form its own subgroup within a wider IBS cohort; however, this requires further investigation in larger number of patients. Ultimately, this data may enable more targeted treatment of IBS symptoms in hEDS versus IBS alone in the future.

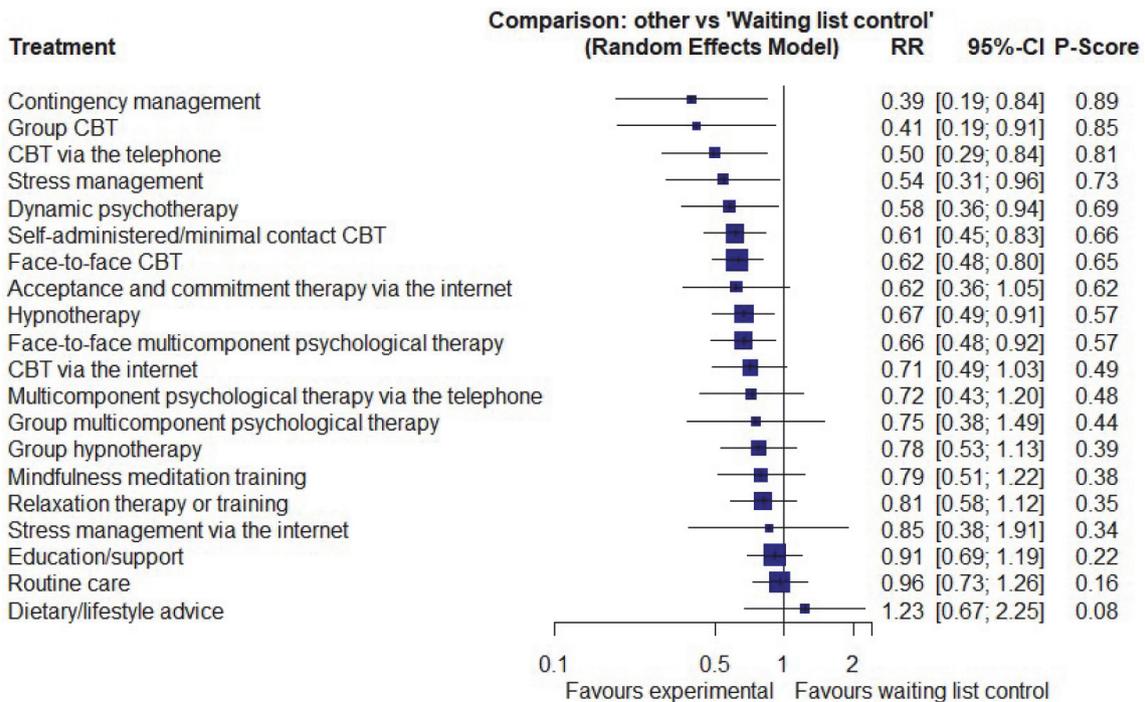
**061 EFFICACY OF PSYCHOLOGICAL THERAPIES FOR IRRITABLE BOWEL SYNDROME: SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS**

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**Introduction** National guidelines for the management of irritable bowel syndrome (IBS) recommend that psychological therapies should be considered, but their relative efficacy is unknown, because there have been few head-to-head trials. We conducted a network meta-analysis to resolve this uncertainty.

**Methods** We searched MEDLINE, EMBASE, EMBASE Classic, PsychINFO, and the Cochrane central register of controlled trials through January 2020 to identify randomised controlled



**Abstract O61 Figure 1** Forest Plot for Failure to Achieve an Improvement in IBS Symptoms at First Point of Follow-up Post-treatment

trials (RCTs) assessing the efficacy of psychological therapies for adults with IBS. Trials included in the analysis reported a dichotomous assessment of symptom status after completion of therapy ( $\geq 4$  weeks), and data were pooled using a random effects model. We examined 6 and 12-month outcomes, where reported. Efficacy was reported as a pooled relative risk (RR) of remaining symptomatic, with a 95% confidence interval (CI) to summarise efficacy of each comparison tested. Treatments were ranked by therapy according to P-score.

**Results** We identified 41 eligible RCTs, containing 4072 participants. At the first point of follow-up, after completion of the therapy, contingency management was ranked first, but 95% CIs were wide (RR of remaining symptomatic = 0.39; 95% CI 0.19 to 0.84, P-score 0.89), and this was based on only one small RCT (figure 1). The psychological interventions with the largest numbers of trials, and patients recruited, included self-administered or minimal contact CBT (RR = 0.61; 95% CI 0.45 to 0.83, P-score 0.66), face-to-face CBT (RR = 0.62; 95% CI 0.48 to 0.80, P score 0.65), and gut-directed hypnotherapy (RR = 0.67; 95% CI 0.49 to 0.91, P-score 0.57). CBT-based interventions and gut-directed hypnotherapy were the most efficacious long-term. Risk of bias of individual trials was high, meaning that the efficacy of all psychological therapies studied is likely to have been overestimated.

**Conclusions** Several psychological therapies are efficacious for IBS, although none were superior to another. CBT-based interventions and gut-directed hypnotherapy had the largest evidence base. Future RCTs should examine the effect of psychological therapy earlier in the disease course, before patients are refractory to medical management.

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### PSYLLIUM REDUCES COLONIC HYDROGEN PRODUCTION FOLLOWING INGESTION OF INULIN IN IRRITABLE BOWEL SYNDROME

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**Introduction** Patients with irritable bowel syndrome (IBS) often develop symptoms of gas and flatulence after intake of the prebiotic inulin, leading to dietary avoidance that may have deleterious effects on gut microbiota. Our aim was to determine if co-administering inulin with psyllium, a viscous virtually non-fermentable fibre, known to improve symptoms in IBS, would increase viscosity in the ascending colon and slow fermentation, therefore reducing gas production.

**Methods** A randomised, four-period, four-treatment, placebo-controlled, crossover trial of 19 patients with IBS (meeting Rome IV criteria, 10 diarrhoea- and 9 constipation-predominant). Patients followed a standardised low-fibre diet on the day preceding each visit then fasted overnight prior to MRI investigations. Interventions were ingested as 500 ml drinks

containing either inulin 20 g, psyllium 20 g, inulin 20 g + psyllium 20 g or placebo (dextrose) 20 g. A 446 kcal meal was consumed after 3 hours. Breath hydrogen and GI symptoms were recorded every 30 minutes and MRI scanning was performed hourly for 6 hours.

**Results** Breath hydrogen rose significantly from 120 minutes after inulin; the addition of psyllium strikingly reduced this rise (51 [95% CI 33–69] ppm versus 18 [95% CI 6/30] ppm at 360 minutes,  $p=0.0004$ ). Psyllium alone or dextrose produced no significant rise. At the end of the study, patients reported significantly less flatulence with inulin + psyllium than inulin alone ( $p=0.008$ ). The rise in small bowel water content was highest after psyllium ingestion, peaking at 3 hours. Co-administration of inulin with psyllium significantly reduced SBWC AUC (mean difference -15.8(95% CI 1.5–30.1) l.min,  $p=0.028$ ). Colonic volumes rose steadily through the study day, peaking at 6 hours. Inulin + psyllium had the fastest rate of rise from fasting, which was significantly greater than psyllium (0.89 [95%CI 0.68 to 1.1] ml/min versus 0.39 [95% CI 0.22 to 0.55] ml/min,  $p=0.0004$ ) but not inulin.

**Conclusions** Psyllium significantly slows the fermentation of inulin, reducing the production of hydrogen and the symptoms of flatulence. This was likely due to its high viscosity reducing the access of the microbiota to inulin. Whether co-administration with psyllium increases the tolerability of prebiotics in IBS warrants a large-scale randomised controlled trial.

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### GASTROINTESTINAL SYMPTOM-SPECIFIC ANXIETY AND SYMPTOM SEVERITY IN IRRITABLE BOWEL SYNDROME: NEW INSIGHTS FROM FACTOR ANALYSIS

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**Introduction** Gastrointestinal symptom-specific anxiety and somatisation have both been associated with higher symptom severity in patients with irritable bowel syndrome (IBS). However, the relationship between these two factors and IBS symptom severity has not been explored fully. In addition, the performance of the instrument that measures gastrointestinal symptom-specific anxiety, the visceral sensitivity index (VSI), has not been examined in a UK population. We conducted a cross-sectional survey to examine these issues.

**Methods** We measured levels of gastrointestinal symptom-specific anxiety, using the VSI, somatisation via the patient health questionnaire-12 (PHQ-12), as well as symptom severity in adult subjects from the UK community with Rome IV-defined IBS. We carried out exploratory factor analysis on the VSI, prior to subsequent analyses, to establish its factor structure. We carried out multiple regression analysis to determine the relationship between demographic features, different factors of the VSI, somatisation, and IBS symptom severity.

**Results** 811 individuals with IBS provided complete data. The mean age was 47.4 years, and 85.9% were female. Factor analysis of the VSI revealed a three-factor structure, accounting for 47% of the variance. Three VSI items that loaded onto factor one were concerned with awareness of abdominal