Digestive Diseases and Sciences (2022) 67:5593–5601
https://doi.org/10.1007/s10620-022-07464-1

ORIGINAL ARTICLE

Evaluation of a Multidisciplinary Integrated Treatment Approach Versus Standard Model of Care for Functional Gastrointestinal Disorders (FGIDS): A Matched Cohort Study

Nicola A. Bray[1] · Natasha A. Koloski[2,3] · Michael P. Jones[4] · Anh Do[2] · Siong Pang[2] · Jeff S. Coombes[1] · Sarah McAllister[2] · Jane Campos[2] · Leela Arthur[2] · Paul Stanley[2] · Katherine DeMaria[2] · Che-yung Chao[2] · Rachel Catague[2] · Amanda Whaley[2] · Nicholas J. Talley[3] · Gerald J. Holtmann[1,2]

Received: 5 July 2021 / Accepted: 14 February 2022 / Published online: 1 April 2022

Abstract

Background Functional gastrointestinal disorders (FGID) are linked to a variety of potential causes, and treatments include reassurance, life-style (including diet), psychological, or pharmacologic interventions.

Aims To assess whether a multidisciplinary integrated treatment approach delivered in a dedicated integrated care clinic (ICC) was superior to the standard model of care in relation to the gastrointestinal symptom burden.

Methods A matched cohort of 52 consecutive patients with severe manifestation of FGID were matched with 104 control patients based upon diagnosis, gender, age, and symptom severity. Patients in the ICC received structured assessment and 12-weeks integrated treatment sessions provided as required by a gastroenterologist and allied health team. Control patients received standard medical care at the same tertiary center with access to allied health services as required but no standardized interprofessional team approach. Primary outcome was reduction in gastrointestinal symptom burden as measured by the Structured Assessment of Gastrointestinal Symptoms Scale (SAGIS). Secondary outcome was reduction in anxiety and depressive symptoms as measured by the Hospital Anxiety and Depression Scale (HADS).

Results Mixed models estimated the within ICC change in SAGIS total as −9.7 (95% CI −13.6, −5.8; $p<0.0001$), compared with −1.7 (95% CI −4.0, 0.6; $p=0.15$) for controls. The difference between groups reached statistical significance, −7.6 (95% CI −11.4, −3.8; $p<0.0001$). Total HADS scores in ICC patients were 3.4 points lower post-intervention and reached statistical significance ($p=0.001$).

Conclusion This matched cohort study demonstrates superior short-term outcomes of FGID patients in a structured multidisciplinary care setting as compared to standard care.

Keywords Irritable bowel syndrome · Functional gastrointestinal disorders · Multidisciplinary treatment approach · Biopsychosocial model of health

Introduction

Functional gastrointestinal disorders (FGIDS) are chronic, heterogeneous disorders of the intestinal tract defined by a combination of gastrointestinal (GI) symptoms that are not explained by structural abnormalities [1], with irritable bowel syndrome and functional dyspepsia among the most common [2, 3] and often overlap [4, 5]. As proposed by the Rome Foundation, these gastrointestinal symptoms arise from perturbed gut-brain interactions, and they share a combination of physiological features such as visceral hypersensitivity, dysmotility, mucosal and immune dysfunction, altered gut microbiota, and central nervous system (CNS) dysregulation [1]. A biopsychosocial conceptualization of FGIDs has been proposed as a model for understanding FGIDs [1], implicating interactions between early life factors, psychosocial factors, physiological functioning, and the brain-gut axis influence the patient's subjective experience of the illness. Although FGIDs are not life-threatening, and have no long-term impact on mortality [6, 7], the personal, economic, and societal costs associated with FGIDs are

✉ Gerald J. Holtmann
g.holtmann@uq.edu.au

Extended author information available on the last page of the article

significant including high rates of health care seeking and utilization [8], high rates of absenteeism and lower levels of productivity in the workplace [9, 10], lower quality of life [11], and high rates of depression and anxiety [12–15]. Indeed, about 50% to 90% of IBS patients have associated psychiatric disorders; namely, anxiety, depression, somatoform disorders [12, 13], and psychological symptoms may precede gastrointestinal symptoms and alter gut physiology function [1].

However, in the absence of structural or biochemical abnormalities, routine clinical treatment focuses on the patient's predominant GI symptom, with management mainly based on pharmacological or diet treatment [16]. Treatment follows a trial-and-error approach [17], with response to treatment measured by symptom improvement [18]. Yet, routine medical treatment is largely met with limited success. Overall, only a 50–60% efficacy gain is reported in IBS patients [19], which suggests that treatment is only benefitting a subset of patients whose symptoms are specifically targeted by the relevant drugs [18]. In particular, many FGID patients report they remain symptomatic despite receiving all the available medical care treatments [20]. Furthermore, the placebo rate is high in FGIDs, with a meta-analysis showing a pooled response rate in IBS of nearly 40% [21], and a similar rate of 36% in FD [22]; clinical trials show pharmacological treatment only has 7–15% therapeutic gain over placebo [23].

Therefore, due to treatment challenges and insufficient patient response to existing routine management of FGIDs, there is a need for a novel, more efficacious approach to management that considers the heterogeneity of FGIDs and offers customized personalized care. There is a general consensus that a multidisciplinary integrated intervention including pharmacologic and behavioral interventions is potentially a strategy for treatment [11, 18, 24–26]. However, such an approach is rarely delivered in clinical practice [27]. The few studies that have evaluated the efficacy of a multi-disciplinary treatment for FGID in a gastroenterology outpatient setting have highlighted the benefits of such an approach [28–31]; however, none included statistics on participants with IBS/FD overlay sub-type.

Our primary aim was to examine whether a structured 12-week integrated care clinic (ICC) approach with a multidisciplinary integrated treatment program for patients who had failed to respond to standard medical reduced the overall symptom burden in FGID patients compared to standard treatment in the setting of a busy gastroenterology department. We hypothesized that in line with the biopsychosocial model of FGIDs, a 12-week multidisciplinary integrated treatment approach would reduce gastrointestinal symptom burden in patients with severe manifestation of FGID post-intervention compared to a standard medical treatment approach. Our secondary aim was to examine whether anxiety and depression symptoms were reduced in patients receiving ICC post-intervention.

Methods

Study Design

This study is a mix of a matched cohort design (measuring the intervention group pre-and-post intervention and applying the same time frame to the matched control group) to assess gastrointestinal symptom burden, and a longitudinal design (measuring the intervention group pre-and post-intervention) to assess anxiety and depression symptoms.

Ethical approval was obtained from Metro South Human Research Ethics Committee (clearance number HREC/17/QPAH/557 & HREC/14/QPAH/677) and from The University of Queensland Human Ethics Research Office (clearance number 2019000291).

We compared a cohort of patients who received a novel multidisciplinary integrated treatment approach to a historical cohort that was treated by the standard care treatment approach at the Princess Alexandra Hospital, Brisbane, Australia. A digital database was searched to identify consecutive patients who had been clinically diagnosed with functional dyspepsia (FD), irritable bowel syndrome (IBS) or FD/IBS overlap who had received a multidisciplinary treatment approach through the integrated care clinic (ICC) between November 2017 and February 2019. The study included ICC patients ($N=52$) who were matched to historical controls patients ($N=104$) who had been clinically diagnosed with FD, IBS, or FD/IBS overlap, and had received standard care (standard assessment and routine management) within the Gastroenterology OPD between 2016 and 2017. Matching was done by means of 1:2 pairwise matching according to diagnosis, sex, age, duration of intervention, and GI symptom severity as measured by the validated Structured Assessment of Gastrointestinal Symptoms (SAGIS) Scale [32]. As the matched cohorts were closely matched on influential variables, this addressed potential selection and information bias.

In addition, ICC patients self-rated symptoms of anxiety and depression before ($N=44$), and after the intervention ($N=44$) using the Hospital Anxiety and Depression Scale (HADS) [33]. No psychological data were available for historical controls.

Participants

Patients in the ICC group were referred from primary and tertiary care, and following assessment by a specialist medical consultant to confirm eligibility patients were invited to participate in an individualized integrated care model

(psychology, diet, and exercise). The number of allied health consultations varied, and participants received concurrently any combination of psychological, dietary, or exercise care as determined by the health professionals in consultation with the patient, and this care continued for a maximum of 12 weeks. Eligibility criteria included patients over 18-years old, English speaking, with a clinician diagnosis of FGID, gastrointestinal symptoms for greater than three years, and no sufficient response to standard treatment. Written consent was obtained in the form of the Participant Information Sheet and Consent Form (PICF). Patients completed questionnaires at baseline and at 12-weeks (post-intervention).

Intervention – Multidisciplinary Integrated Care Treatment

The multidisciplinary team was led by a gastroenterologist who also chaired the multidisciplinary team meetings that were used to tailor treatment toward the patient needs. The gastroenterologist specialist was the responsible consultant for all patients treated. Besides the gastroenterologists, a GI fellow and a primary care physician were other physicians involved in the treatment. The primary care physician's responsibility was primarily to develop ongoing management plans for patients utilizing health care services routinely available in the primary care setting. All patients were initially assessed by all health professionals involved in the treatment and subsequently an individualized treatment plan developed.

Psychology

Psychological care was provided by experienced registered psychologists. Patients received psychological therapy based on their individualized needs. This included cognitive-behavioral therapy (CBT), Acceptance and Commitment Therapy (ACT), relaxation techniques, or Mindfulness. All patients were provided with psychoeducation regarding IBS, including an explanation of the relationships that exist between psychological factors and the gut and the rationale for psychological treatment.

Diet

First line therapy was provided by experienced dieticians and included basic dietary advice such as including regular meals, achieving a healthy diet, and restricting dietary triggers (e.g. caffeine, alcohol). Second line therapy was implemented if patients were already achieving a healthy diet and incorporated low FODMAP dietary advice. If the low FODMAP diet has previously been attempted without success, patients were advised to trial probiotic therapy.

Exercise Physiology

Patients received individualized and supervised cardiorespiratory, resistance, flexibility, balance, and/or neuromotor training by experienced exercise physiologists. Exercise programs were tailored based on the disease, co-morbidities, exercise history, preferences and barriers to maximize patient outcomes.

In terms of medication, there were no specific restrictions. All medications approved by the Therapeutic Goods Administration (TGA) and listed on the Australian Medical Benefit Scheme were used when clinically indicated.

At the conclusion of the integrated care clinic, the Specialist assessed the patient in relation to the need for ongoing management (e.g., discharge to primary care physician).

Standard Treatment

The standard treatment of the historical cohort included a standardized assessment and routine management by a Gastroenterologist over a 12-week period. Each visit was approximately 30 min in duration. Patients completed SAGIS at each visit as part of routine clinical care. Dietary advice and referral to psychological treatment followed routine clinical guidelines for patients who required this.

Assessment and Outcome Measures

The Structured Assessment of Gastrointestinal Symptoms Scale (SAGIS)

This validated self-report scale was used to measure the intensity of 22 upper and lower gastrointestinal symptoms (0 = no problem to 4 = very severe problems). Primary outcome was change in the number of items scored moderate or above (indicating problems which cannot be ignored) on the SAGIS between pre-and post-intervention. Secondary outcome was change in total symptom burden score (range from 0 to 88) on the SAGIS pre-and post-intervention Minimally clinically important change is considered a 8 points reduction on the SAGIS post-intervention which corresponds to a Cohen's d value of 0.5, a moderate effect size.

The Hospital Anxiety and Depression Scale (HADS)

This clinical scale is a validated 14-item self-reported scale divided into two 7-item subscales of anxiety and depression. HADS-anxiety scores (HADS-A) ≥ 8 points indicate possible anxiety and HADS-depression scores (HADS-D) ≥ 8 points indicate possible depression. Minimally clinically important change is considered 1.5 points reduction on the HADS-A or HADS-D post-intervention. The HADS was only available for cases.

Statistical Approach

Descriptive statistics were shown as the mean and standard deviation for continuous variables and percentages for categorical variables. Due to the 2:1 control to case matching which may induce some within-cluster correlation, mixed linear models estimated via maximum likelihood have been employed. This approach also allows all available data to be used, including for patients who did not complete therapy. The inclusion of all available data and treating all patients as belonging to whichever study group they were assigned is consistent with the intention-to-treat approach to statistical analysis. The model included case–control status, time and the interaction between these factors, with the interaction term being used to determine whether the change from pre- to post-therapy was greater for cases than controls. Patient diagnosis group was included in the model. Due to the non-normal distribution of outcome measures, formal statistical inference was via the nonparametric bootstrap with 2000 bootstrap replications.

The total score for the Hospital Anxiety and Depression Scale (HADS) as well as the HADS sub scores for anxiety and depression were analyzed with a paired sample t test. In addition, a McNemar's test for change in percentage above the clinical thresholds for HADS-A and HADS-D was conducted.

Results

Eighty patients started the 12-week ICC treatment, and 28 patients did not continue the intervention after at least 1 consultation. Data for participant attrition are not available; however typical reasons include family and work commitments, time and scheduling conflicts, and long-distance travelling. Patients who dropped out before the end of treatment had a slightly higher baseline SAGIS score (mean 29.3, SD 16.1) than those who completed treatment (mean 25.5, SD 13.6) and this difference reached statistical significance ($p < 0.001$).

Thus, data from 52 patients who had completed the ICC and pairwise matching created a final cohort of 52 intervention patients and 104 controls. The patients were well matched (Table 1); mean age for the intervention group and matched control was 42 years (range 19–71) and 41 years (range 19–71), respectively, with 81% female (Table 1). Primary diagnosis was either irritable bowel syndrome (52%), functional dyspepsia (10%), or overlap of both (38%). The mean length of treatment for the intervention group and matched control was 3.45 months (range 1.64–6.5) and 4.13 months (range 0.72–9.0), $P = 0.007$, respectively. The mean total number of allied health consultations over the 12-wk intervention was 24 (range 3 to 27), the mean number of psychological consultations was 5 (range 0–12), the mean number of dietician consultations was 2 (range 0–6), and the mean number of exercise physiologist consultations was 5 (range 0–13).

Table 1 Participant characteristics

	ICC ($N = 52$)	Control ($N = 104$)
Age (M,SD) (years)	42 (14.77)	41 (14.58)
Gender (%)		
Female	81	81
Male	19	19
Diagnosis (%)		
Irritable bowel syndrome (IBS)	52	52
Functional dyspepsia (FD)	10	10
IBS/FD	38	38
Duration of intervention (months)	3.45 (1.20)	4.13 (1.40)

Mixed models estimated the within ICC change in SAGIS total as −9.7 (95% CI −13.6, −5.8; $p < 0.0001$), compared with −1.7 (95% CI −4.0, 0.6; $p = 0.15$) for controls (Fig. 1). The difference between groups was estimated as −7.6 (95% CI −11.4, −3.8; $p < 0.0001$), indicating the greater improvement in the ICC group was unlikely to due to random chance (Fig. 2). The same analysis for number of moderate or above items yielded −3.8 (95% CI −5.4, −2.2; $p < 0.0001$) for the ICC group compared with −0.4 (95% CI −1.4, 0.6; $p = 0.45$) for controls (Fig. 3). This difference also reached statistical significance, −3.4 (95% CI −5.0, −1.8; $p < 0.0001$) (Fig. 4).

For the HADS analyses in ICC patients, total HADS scores in ICC patients were 3.4 points lower (HADS score = 13.5 ± 8.14 vs 16.91 ± 7.81, 95%CI[1.54, 5.28], $p = 0.001$ (Fig. 5). This difference was clinically and statistically significant. For the sub scales, post-intervention, HADS-D scores were 1.6 points lower (5.4 ± 4.44 vs 7.0 ± 4.39, 95%CI[0.58, 2.64],$p = 0.003$) and total HADS-A scores were 1.8 points lower (8.1 ± 4.36 vs 9.9 ± 3.91, 95%CI[0.70, 2.89], $p = 0.002$). Furthermore, the percentage of HAD-D ≥ 8 was lower post intervention than pre-intervention (30% vs 48%). A McNemar test indicated the difference in the proportion of HADS-D ≥ 8 pre- and post-intervention was significant, $p = 0.039$. The percentage of HADS-A ≥ 8 was lower post-intervention than pre intervention (50% vs 71%). A McNemar test indicated the difference in the proportion of HADS-A ≥ 8 pre- and post-intervention was significant, $p = 0.035$.

Discussion

This study assessed the efficacy of an integrated multidisciplinary treatment approach compared to a standard care treatment approach in the management of FGIDs in a

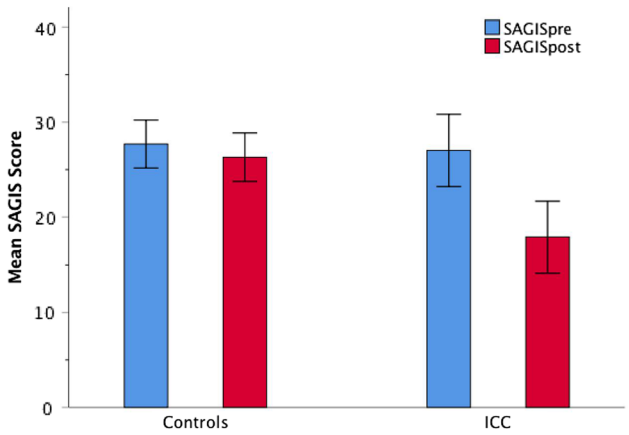

Fig. 1 Change in total mean SAGIS score pre and post intervention in ICC patients vs control

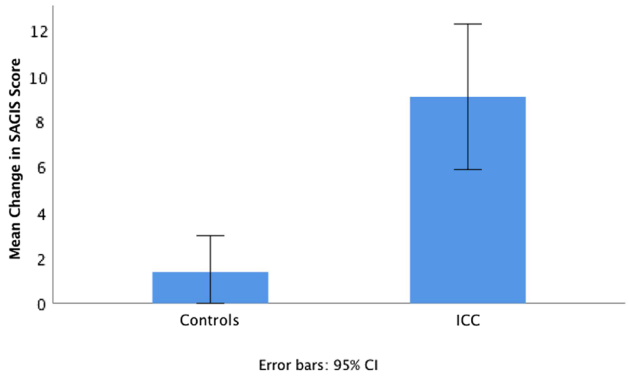

Fig. 2 Mean change in reduction of SAGIS score post-intervention in ICC patients vs control

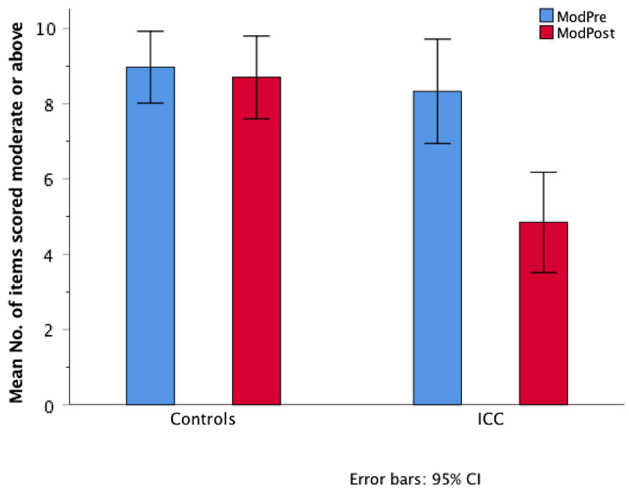

Fig. 3 Change in total SAGIS mean number of items scored moderate or above for pre- and post-treatment in ICC patients vs controls

gastroenterology outpatient setting. Based on the theoretical framework of a biopsychosocial model of FGIDs, the multidisciplinary treatment incorporated sessions with a gastroenterologist, general practitioner, psychologist, dietician, and exercise physiologist. In line with the proposed hypothesis, a multidisciplinary treatment approach significantly reduced GI symptoms compared to standard treatment. In particular, the numbers of items scored moderate or above on the SAGIS, and the total GI symptom burden significantly reduced post intervention.

These results support the findings of previous studies proposing the benefits of a multi-disciplinary treatment approach for reducing gastrointestinal symptoms in FGID patients [28–31]. Berens, Stroe-Kunold [28] and McDonald, Teets [30], also found symptom severity in IBS patients improved significantly post a 12-week integrative intervention. However, due to a small sample in the study by Berens and Stroe-Kunold [28], the difference was not statistically significant; yet, a strength of the current study is a priori power analysis indicated that for a Cohen's d effect size of 0.5, we would achieve statistical power 0.8 at the 0.05 level of statistical significance, if $N = 50$ for the intervention and $N = 100$ for the controls; therefore, our power was sufficient with pairwise matching analyses on a 2:1 ratio. While Kruimel, Leue [29] also found improvements in symptom severity in FGID patients post a 6-month integrative approach, the current study showed improvements in a shorter time frame of 12-weeks. Unlike previous studies, the current study included patients with overlay of IBS/FD symptoms. The results suggested that a multidisciplinary approach is effective for patients with IBS, FD and IBS/FD overlay. In addition, the current study included a number of psychosocial components namely; lifestyle changes including increasing physical activity to national guidelines, strengthening and conditioning exercises, and stress-reduction, as well as dietary education (low FODMAP advice) and modification, and psychological therapy (psychoeducation, cognitive-behavioral therapy (CBT), mindfulness and acceptance and commitment therapy (ACT). These components were individually tailored to the patient thus recognized the heterogeneous nature of FGIDs by treating patients particular presenting symptoms.

Furthermore, we observed both anxiety and depression symptoms in ICC patients were significantly reduced post intervention. This is consistent with a study of gastroenterology outpatients with FGIDs, where significant reductions on the HADS were reported 6-months after a similar multidisciplinary approach [29]. Of note, in the present study these reductions in anxiety and depression symptoms were present within 3 months of intervention.

It is encouraging that the results suggest a shorter treatment period produces beneficial results considering multidisciplinary treatment approaches are not readily available

to most gastroenterology patients largely due to the financial constraints of establishing such a treatment approach [27]. However, another potential barrier to multidisciplinary treatment is the dearth of appropriately trained health professionals with expertise in GI psychology [34, 35]. Nevertheless, the clinical implications of this study are that the inclusion of behavioral interventions in routine management is a potential strategy to enhance the limited effectiveness of pharmacological treatment, and should be considered as a model of care in FGID treatment.

This study has several strengths. The matched cohorts were closely matched on influential variables; thus, the examination of two different treatment approaches and the GI symptom burden outcomes in the same setting could be examined while controlling for individual differences, namely primary diagnosis. Furthermore, the use of historical matched controls addressed the ethical issue as discussed in a previous study of including patients with psychological morbidity in a prospective case–control study when psychological therapy is available [29]. Another strength is the use of a valid measure of GI symptom severity that has excellent psychometric properties [32]. The SAGIS measures the severity of a range of gastrointestinal symptoms and was available for both cohorts. Furthermore, the SAGIS in addition to measuring total symptom burden also measures symptoms scored moderate or above (problems which cannot be ignored), therefore capturing pertinent data of the impact severity of symptoms.

There are limitations in this study. Although, careful consideration was taken in matching on influential variables, some potential confounders could not be controlled for such as duration of consultation and intervention time. The study was conducted in a tertiary setting where patients are referred due to severe manifestations of FGIDs, with all patients reporting very severe symptoms on the SAGIS and insufficient response to long-term treatment; therefore, while the patient demographics were typical of an outpatient setting, the results may not be extended to the general FGID population. Although given the potential for individuals with higher baseline scores to reduce more than those with lower scores, this baseline imbalance would tend to bias the contrast toward the null hypothesis rather than the reverse. However, these patients who have a higher GI symptom burden have been shown to report higher costly emergency department visits [36] and thus alternative approaches such as the integrated care clinic would be beneficial from a health care system cost perspective. Furthermore, as the majority of patients presented with co-morbid psychological distress, they may have been better suited to a multidisciplinary approach which included a psychotherapy component as compared to patients with FGIDs managed in a GP setting. Participants had substantial psychological co-morbidities; thus, the samples might be more complex than those generally recruited for RCTs. While the present study looked at pre-post psychological outcomes no psychological data was available for historical controls. However, due to the limited research on multidisciplinary approaches in FGID patients, the psychological outcome results support recommendations that psychological therapy should be considered in patients with refractory FGID symptoms that have shown no improvements with standard treatments alone, and who present with psychological distress [20, 37]. In addition, due to the non-randomization of treatment arms, the relative contribution of each intervention component (psychology, diet, exercise) is unknown. While the dropout rate was relatively high, the majority of patients who dropped out pointed towards the time required and subsequent travel requirements. Some of the patients travelled more than 200 km for every appointment. While this project started before the Covid pandemic, remote modes of service delivery have since been developed that are currently being tested in relation to efficacy. The interventions are suitable to be delivered in the community setting provided that specialized expertise is available. Future prospective randomized controlled trials (RCTs) are clearly warranted to examine the causal relationship between intervention type and outcome [38], and to determine the relative contributions of intervention components. It would also be of interest for future research to explore the underlying mechanisms of action of a multidisciplinary approach, and the long-term effects on both patient outcomes and health care utilization.

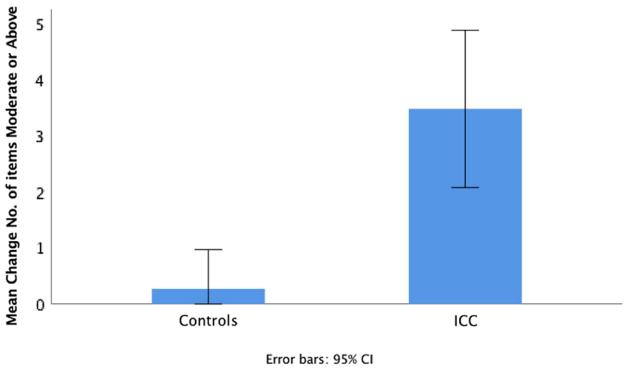

Fig. 4 Mean change in reduction of SAGIS number of items scored moderate or above post-intervention in ICC patients vs control

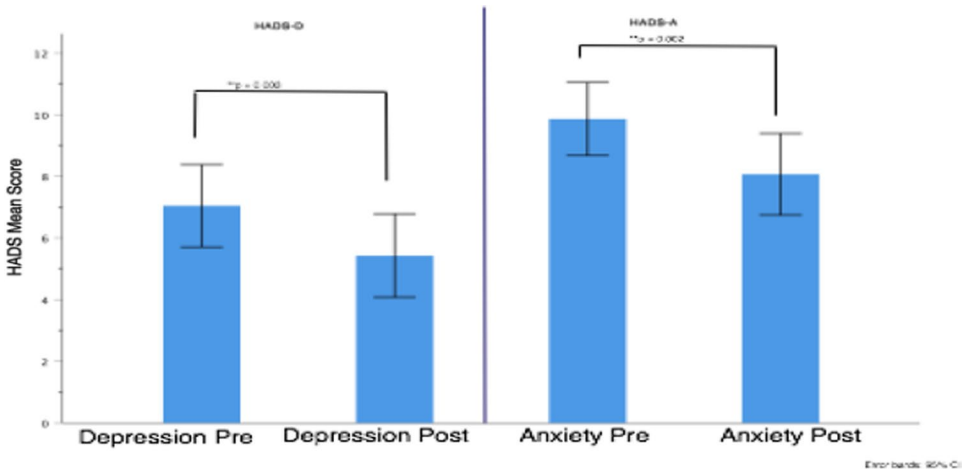

Fig. 5 Change in HADS-D scores and HADS-A scores pre- and post-intervention.

Conclusion

Although strategies have been proposed to incorporate pharmacologic and behavioural interventions in the management of FGIDs [11, 18, 24–26], behavioural interventions are seldom included in clinical practice or evaluated. This study found in patients with severe FGID manifestations; a personalized, integrated multidisciplinary approach including gastroenterologists, general practitioners, psychologists, dieticians and exercise physiologists results in superior GI symptom improvements and reduction of anxiety and depression symptoms. Thus, this study has shown the potential of an integrated personalized multidisciplinary model of care in contrast to standard care FGID treatments, but randomized controlled trials are warranted to determine the relative contributions of the individual components of treatment and the economic health cost benefit.

Acknowledgments NJT: reports personal fees from Allakos, from Aviro Health, from Antara Life Sciences, from Arlyx from Bayer, from Danone, from Planet Innovation, from Takeda, from Viscera Labs, from twoXAR, from Viscera Labs, from Dr Falk Pharma, from Censa, from Cadila Pharmaceuticals, from Progenity Inc, from Sanofi-aventis, from Glutagen, from ARENA Pharmaceuticals, from IsoThrive, from BluMaiden, from HVN National Science Challenge, non-financial support from HVN National Science Challenge NZ, outside the submitted work; In addition, NJT has a patent Biomarkers of IBS licensed (#12735358.9 -1405/2710383 and (#12735358.9 -1405/2710384), a patent Licensing Questionnaires Talley Bowel Disease Questionnaire licensed to Mayo/Talley, a patent Nestec European Patent licensed, and a patent Singapore Provisional Patent NTU Ref: TD/129/17 "Microbiota Modulation Of BDNF Tissue Repair Pathway" issued and copyright Nepean Dyspepsia Index (NDI) 1998 and Editorial: Medical Journal of Australia (Editor in Chief), Up to Date (Section Editor), Precision and Future Medicine, Sungkyunkwan University School of Medicine, South Korea, Med (Journal of Cell Press). NJT participates Committees: Australian Medical Council (AMC) Council Member (2016-2019), MBS Review Taskforce (2016-2020), NHMRC Principal Committee, Research Committee (2016-2021), Asia Pacific Association of Medical Journal Editors (APAME) (current), GESA Board Member (2017-2019). NJT Misc: Avant Foundation (judging of research grants) (2019). NJT community and patient advocacy groups: Advisory Board, IFFGD (International Foundation for Functional GI Disorders). NJT acknowledges funding from the National Health and Medical Research Council (NHMRC) for the Centre for Research Excellence in Digestive Health. NJT holds an NHMRC Investigator grant. GH: Gerald Holtmann has received unrestricted educational support from Bayer and the Falk Foundation; research support via the Princess Alexandra Hospital, Brisbane, from GI Therapies, Takeda Development Center Asia, Eli Lilly Australia, F. Hoffmann–La Roche, MedImmune, Celgene, Celgene International II Sarl, Gilead Sciences, Quintiles, Vital Food Processors, Datapharm Australia, Commonwealth Laboratories, Prometheus Laboratories, Falk, Nestlé, and Mylan. He is a patent holder on a device for aseptic biopsies (US 20150320407 A1).

Author's contribution All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by BN, KN, JM, DA, MS, PS, AL, CJ, SP, DK, CJ, CR, WA, TNJ, HG. The first draft of the manuscript was written by Nicola Bray and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Funding Open Access funding enabled and organized by CAUL and its Member Institutions. This study was supported by a grant from Department of QLD Health, NHMRC Centre of Research Excellence in Digestive Health, 2020 Metro South Health Research Support Scheme (MSH RSS) Project Grant.

Declarations

Conflict of interest The authors declare that they do not have any conflict of interest to declare.

Ethical approval This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Metro South Human Research Ethics Committee (Clearance Number HREC/17/QPAH/557 & HREC/14/QPAH/677) and from The University of Queensland Human Ethics Research Office (Clearance Number 2019000291).

References

1. Drossman DA. Functional gastrointestinal disorders: history, pathophysiology. *Clin. Features Rome IV. Gastroenterol.* 2016;150:1269–1272.
2. Lacy BE, Patel NK. Rome criteria and a diagnostic approach to irritable bowel syndrome. *J. Clin. Med.* 2017;6:99.
3. Aziz I, Palsson OS, Törnblom H, Sperber AD, Whitehead WE, Simrén M. The prevalence and impact of overlapping Rome IV-diagnosed functional gastrointestinal disorders on somatization, quality of life, and healthcare utilization: a cross-sectional general population study in three countries. *Am. J. Gastroenterol.* 2018;113:86–96.
4. von Wulffen M, Talley NJ, Hammer J et al. Overlap of irritable bowel syndrome and functional dyspepsia in the clinical setting: prevalence and risk factors. *Dig. Dis. Sci.*2019;64:480–486.
5. Choi YJ, Kim N, Yoon H et al. Overlap between irritable bowel syndrome and functional dyspepsia including subtype analyses. *J. Gastroenterol. Hepatol.* 2017;32:1553–1561.
6. Mahadeva S, Goh KL. Epidemiology of functional dyspepsia: a global perspective. *World J. Gastroenterol.* 2006;12:2661–2666.
7. Canavan C, West J, Card T. Review article: the economic impact of the irritable bowel syndrome. *Aliment. Pharmacol. Ther.* 2014;40:1023–1034.
8. Buono JL, Mathur K, Averitt AJ, Andrae DA. Economic burden of inadequate symptom control among US commercially insured patients with irritable bowel syndrome with diarrhea. *J. Med. Econ.* 2017;20:353–362.
9. Brook RA, Kleinman NL, Melkonian AK, Smeeding JE, Talley NJ. Functional dyspepsia impacts absenteeism and direct and indirect costs. *Clin. Gastroenterol. Hepatol.* 2010;8:498–503.
10. Ballou S, Bedell A, Keefer L. Psychosocial impact of irritable bowel syndrome: A brief review. *World J. Gastrointest. Pathophysiol.* 2015;6:120–123.
11. Ballou SK. *Living with Irritable Bowel Syndrome physical, emotional, and cognitive factors associated with impairment in daily functioning*. 2016, ProQuest Information & Learning: US. p. No Pagination Specified-No Pagination Specified.
12. Whitehead WE, Palsson O, Jones KR. Systematic review of the comorbidity of irritable bowel syndrome with other disorders: What are the causes and implications? *Gastroenterology* 2002;122:1140–1156.
13. Levy RL, Olden KW, Naliboff BD et al. Psychosocial aspects of the functional gastrointestinal disorders. *Gastroenterology* 2006;130:1447–1458.
14. Fond G, Loundou A, Hamdani N et al. Anxiety and depression comorbidities in irritable bowel syndrome (IBS): a systematic review and meta-analysis. *Eur. Arch. Psychiatry Clin. Neurosci.* 2014;264:651–660.
15. Koloski NA, Jones M, Talley NJ. Evidence that independent gut-to-brain and brain-to-gut pathways operate in the irritable bowel syndrome and functional dyspepsia: a 1-year population-based prospective study. *Aliment. Pharmacol. Ther.* 2016;44:592–600.
16. Simren M, Tack J. New treatments and therapeutic targets for IBS and other functional bowel disorders. *Nature Rev. Gastroenterol. Hepatol.* 2018;15:589–605.
17. Moayyedi PM, Lacy BE, Andrews CN, Enns RA, Howden CW, Vakil N. ACG and CAG clinical guideline: management of dyspepsia. *Am. J. Gastroenterol.* 2017;112:988–1013.
18. Chang L, Di Lorenzo C, Farrugia G et al. Functional bowel disorders: a roadmap to guide the next generation of research. *Gastroenterology* 2018;154:723–735.
19. Chey WD. SYMPOSIUM REPORT: An Evidence-Based Approach to IBS and CIC: Applying New Advances to Daily Practice: A Review of an Adjunct Clinical Symposium of the American College of Gastroenterology Meeting October 16, 2016 * Las Vegas. *Nevada. Gastroenterol. Hepatol. (N Y)* 2017;13:1–16.
20. Palsson OS, Whitehead WE. Psychological treatments in functional gastrointestinal disorders: a primer for the gastroenterologist. *Clin. Gastroenterol. Hepatol.* 2013;11:208–16.
21. Ford AC, Moayyedi P. Meta-analysis: factors affecting placebo response rate in the irritable bowel syndrome. *Aliment. Pharmacol. Ther.* 2010;32:144–158.
22. Patel N, Kusema E, Crowell MD, Lacy BE. The placebo response in complementary and alternative medicine trials for functional dyspepsia. *Am. J. Gastroenterol.* 2017;112:S249–S250.
23. Chey WD, Maneerattaporn M, Saad R. Pharmacologic and complementary and alternative medicine therapies for irritable bowel syndrome. *Gut Liver* 2011;5:253–266.
24. Van Oudenhove L, Crowell MD, Drossman DA et al. Biopsychosocial aspects of functional gastrointestinal disorders. *Gastroenterology* 2016;150:1355–1367.
25. Ford AC, Lacy BE, Talley NJ. Irritable bowel syndrome. *New England J. Med.* 2017;376:2566–2578.
26. Berens S, Kraus F, Gauss A et al. A specialty clinic for functional gastrointestinal disorders in tertiary care: concept and patient population. *Clin. Gastroenterol. Hepatol.* 2017;15:1127–1129.
27. Basnayake C, Kamm MA, Salzberg M et al. Outcome of hospital outpatient treatment of functional gastrointestinal disorders. *Intern. Med. J.* 2019;49:225–231.
28. 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.
29. Kruimel J, Leue C, Winkens B et al. Integrated medical-psychiatric outpatient care in functional gastrointestinal disorders improves outcome: a pilot study. *Eur. J. Gastroenterol. Hepatol.* 2015;27:721–727.
30. McDonald E, Teets R, Ortiz C et al. A randomized trial of a group-based integrative medicine approach compared to waitlist control on irritable bowel syndrome symptoms in adults. *Explore (NY)* 2018;14:406–413.
31. Beinvogl B, Burch E, Snyder J et al. Multidisciplinary treatment reduces pain and increases function in children with functional gastrointestinal disorders. *Clin. Gastroenterol. Hepatol.* 2019;17:994–996.
32. Koloski NA, Jones M, Hammer J et al. The validity of a new structured assessment of gastrointestinal symptoms scale (SAGIS) for evaluating symptoms in the clinical setting. *Dig. Dis. Sci.* 2017;62:1913–1922.
33. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr. Scand.* 1983;67:361–370
34. Ballou S, Keefer L. Psychological interventions for irritable bowel syndrome and inflammatory bowel diseases. *Clinical and Translational Gastroenterology* 2017;8:e214.
35. Kinsinger SW. Cognitive-behavioral therapy for patients with irritable bowel syndrome: Current insights. *Psychol. Res. Behav. Manag.* 2017;10:231–237.

36. Koloski N, Santosh B, Shah A et al. IBS-symptoms and healthcare utilisations of patients seen in a hospital outpatient setting. *United Euro. Gastroenterol. J.* 2019;7:PO5233.
37. Talley NJ, Ford AC. Functional dyspepsia. *N. Engl. J. Med.* 2015;373:1853–1863.
38. Hariton E, Locascio JJ. Randomised controlled trials - the gold standard for effectiveness research: Study design: randomised controlled trials. *BJOG: An Int. J. Obstet. Gynaecol.* 2018;125:1716–1716.

Authors and Affiliations

Nicola A. Bray[1] · Natasha A. Koloski[2,3] · Michael P. Jones[4] · Anh Do[2] · Siong Pang[2] · Jeff S. Coombes[1] · Sarah McAllister[2] · Jane Campos[2] · Leela Arthur[2] · Paul Stanley[2] · Katherine DeMaria[2] · Che-yung Chao[2] · Rachel Catague[2] · Amanda Whaley[2] · Nicholas J. Talley[3] · Gerald J. Holtmann[1,2]

Nicola A. Bray
nicola.bray@uq.edu.au

Natasha A. Koloski
natasha.koloski@newcastle.edu.au

Michael P. Jones
mike.jones@mq.edu.au

Anh Do
a.do@uq.edu.au

Siong Pang
siong.pang@health.qld.gov.au

Jeff S. Coombes
jcoombes@uq.edu.au

Sarah McAllister
sarah.mcallister@health.qld.gov.au

Jane Campos
jane.campos@health.qld.gov.au

Leela Arthur
leela.arthur@health.qld.gov.au

Paul Stanley
paul.Stanley@health.qld.gov.au

Katherine DeMaria
katherine.DeMaria@health.qld.gov.au

Che-yung Chao
che-yung.chao@health.qld.gov.au

Rachel Catague
rachel.catague@health.qld.gov.au

Amanda Whaley
amanda.whaley@health.qld.gov.au

Nicholas J. Talley
nicholas.talley@newcastle.edu.au

[1] Faculties of Medicine and Health and Behavioural Sciences, University of Queensland/TRI, Brisbane, QLD, Australia

[2] Gastroenterology and Hepatology, Princess Alexandra Hospital, Brisbane, QLD, Australia

[3] College of Health Medicine and Wellbeing, University of Newcastle/AGIRA, Callaghan, NSW, Australia

[4] School of Psychological Sciences, Macquarie University, Ryde, NSW, Australia