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The Irritable Bowel Syndrome Outcome Study (IBSOS): Rationale and design of a randomized, placebo-controlled trial with 12 month follow up of self- versus clinician-administered CBT for moderate to severe irritable bowel syndrome ☆

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ABSTRACT

Irritable bowel syndrome is a common, oftentimes disabling, gastrointestinal disorder whose full range of symptoms has no satisfactory medical or dietary treatment. One of the few empirically validated treatments includes a specific psychological therapy called cognitive behavior therapy which, if available, is typically administered over several months by trained practitioners in tertiary care settings. There is an urgent need to develop more efficient versions of CBT that require minimal professional assistance but retain the efficacy profile of clinic based CBT. The Irritable Bowel Syndrome Outcome Study (IBSOS) is a multicenter, placebo-controlled randomized trial to evaluate whether a self-administered version of CBT is, at least as efficacious as standard CBT and more efficacious than an attention control in reducing core GI symptoms of IBS and its burden (e.g. distress, quality of life impairment, etc.) in moderately to severely affected IBS patients. Additional goals are to assess, at quarterly intervals, the durability of treatment response over a 12 month period; to identify clinically useful patient characteristics associated with outcome as a way of gaining an understanding of subgroups of participants for whom CBT is most beneficial; to identify theory-based change mechanisms (active ingredients) that explain how and why CBT works; and evaluate the economic costs and benefits of CBT. Between August 2010 when IBSOS began recruiting subjects and February 2012, the IBSOS randomized 171 of 480 patients. Findings have the potential to improve the health of IBS patients, reduce its social and economic costs, conserve scarce health care resources, and inform evidence-based practice guidelines.

Abbreviations: CBT, Cognitive behavior therapy; MC-CBT, Minimal contact CBT; S-CBT, Standard-CBT; GI, gastrointestinal; QALY, Quality Adjusted Life Years; IBSOS, Irritable Bowel Syndrome Outcome Study; IBS, irritable bowel syndrome; DSMB, data safety monitoring board; SEM, structural equation modeling; DCC, Data Coordinating Center; NIDDK, National Institutes of Diabetes and Digestive and Kidney Diseases; SLT, social learning theory; AC, attention control; NIH, National Institutes of Health; SC, Steering Committee; EC, Executive Committee; 12 W, 2 week post treatment follow up; FU3, FU6, FU9, FU12, 3, 6, 9 and 12 month post treatment follow up periods, respectively.

☆ Trial registration: ClinicalTrials.gov # NCT00738920.

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1. Introduction

Irritable bowel syndrome (IBS) is a common, oftentimes disabling functional GI disorder whose symptoms include abdominal pain/discomfort associated with diarrhea, constipation or both in an alternating manner. As one of the most common diagnoses seen by gastroenterologists and primary care physicians [1], IBS exacts substantial economic (e.g., [2,3]) and social (e.g., [4,5]) costs. Making matters worse, there is no satisfactory treatment for the full range of IBS symptoms [6]. With one exception, the few efficacious medications developed for IBS have either been withdrawn or severely restricted in response to concerns about safety, creating an urgent need to train patients to adopt effective self-management strategies for relieving unresolved symptoms. The broader disease management literature [7] indicates that effectively managing the day to day burden of chronic medical conditions involves learning specific behavioral skills (e.g., self-monitoring, goal setting and problem solving). These skills form the basis of a psychological treatment called cognitive behavior therapy (CBT).

A number of clinical trials support the efficacy of CBT for IBS when administered over multiple (weekly) sessions by trained therapists in tertiary care settings [8–10] . Treatment gains associated with CBT include improvements in key GI symptoms (pain, bowel dysfunction) [10], quality of life [4,11], and psychological distress [10,11]. In its standard form, however, CBT has practical limitations (high cost, shortage of adequately trained therapists, long waiting lists, time requirements) that hamper its clinical utility. As the "second generation" of IBS treatments undergoes development, it is increasingly clear that efficacy demonstration is a necessary but not sufficient condition of treatment viability. An unmet need exists for a brief form of CBT that is less costly, less time intensive and more transportable, yet one that retains the clinical efficacy of the "gold standard" CBT delivered in routine office settings.

One strategy for economizing CBT is to decrease therapist contact time through the use of primarily self-administered or "home based" treatments. In a self-administered or minimal-contact (MC) treatment (e.g. [12,13]), self-management skills are introduced in periodic clinic sessions but most of what is learned occurs at home using self-study materials with minimal professional assistance. As a result, MC-CBT requires only 4 clinic sessions rather than the 10–20 weekly sessions of standard CBT (S-CBT). Potential advantages of MC-CBT include greater patient involvement, a reduction in patient costs (e.g., time and travel costs for session attendance), expanded availability of services, lower stigma, easier scheduling and penetration into underserved areas, and easier integration into routine clinical settings. Empirical support for a MC-CBT treatment comes from a pilot study funded through the NIDDK to test the efficacy of MC-CBT [12]. After treatment, 62% of participants receiving MC-CBT described IBS symptoms as much or very much improved compared to 58% of patients receiving S-CBT and 7% on a wait list. Improvement was accompanied by significant reduction in IBS symptom severity and quality of life impairment. These data lend preliminary support for the clinical efficacy of a self-administered version of CBT and laid the empirical foundation for the Irritable Bowel Syndrome Outcome Study (IBSOS).

2. Methods/design

2.1. Study administration

2.1.1. Organizational structure

The IBSOS is an NIH-funded, multi-center, placebo-controlled randomized clinical trial with two clinical centers (University at Buffalo [UB], Northwestern University [NU]), an Administrative Core (UB), a health economics center (Research Triangle Institute [RTI]), a Data Coordinating Center (Frontier Science and Technology Research Foundation [FS]), and the NIDDK Project Office acting together to implement a common protocol and administer the trial. The organizational structure of the IBSOS is diagrammatically represented below in Fig. 1

2.1.1.1. Administrative Core. The Administrative Core at the University at Buffalo (UB) has primary responsibility for developing and implementing mechanisms to ensure quality control and to coordinate the execution of the scientific goals of the study by the Administrative Core, clinical centers, Data Coordinating Center, health economics center, and consultants as dictated by the research plan.

Additional responsibilities of the Administrative Core include:

- Preparing (with the aid of the Steering Committee and NIH staff) the protocol, forms, manuals, and intervention materials
- Developing the experimental statistical design of the trial
- Working with the investigators in the development and pre-testing of forms and procedures, and assuming responsibility for the content of forms and their scheduling
- Collaborating in designing and monitoring the implementation of the trial interventions
- Training clinicians, data coordinators and other clinical center personnel, and monitoring clinic performance
- Developing with the UB Office of Medical Computing software for electronic daily symptom diaries (iDiaries)
- Coordinating central resources among sites and consultants
- Managing quality control aspects associated with the day to day collection and management of raw participant data
- Summarizing clinical center performance at regular intervals for the Steering Committee
- Preparing, in collaboration with the clinical investigators, various manuscripts of trial results

2.1.1.2. Clinical centers. Each of the participating clinical centers, at the University at Buffalo and Northwestern University, has agreed to implement the IBSOS Protocol. The clinical centers will follow participants according to protocol; assume responsibility for the completion of the protocol for each participant enrolled in the study; record participant data related to the above; review and enter information from data forms using a centralized data entry and management system; and respond to edit queries from the Administrative Core. Each clinical center has a Principal Investigator, a Research Coordinator, and additional administrative and clinical staff to carry out the protocol.

2.1.1.3. Data Coordinating Center (DCC). The DCC for the project is Frontier Science and Technology Research Foundation (FS; Amherst, NY). FS works with study statisticians, project