The IRB Protocol

A. Study purpose and rationale

Irritable bowel syndrome (IBS) is a chronic gastrointestinal disorder affecting 7 – 20% of the adult population in the US.[1,2] IBS has an adverse affect on quality of life and has been estimated to cost at least $8 billion annually in U.S. health care costs. Despite a range of dietary, pharmacologic, and nonpharmacologic interventions proposed, treatments so far have been unsatisfactory. A number of factors have been suggested to play a role in the pathogenesis of IBS including alterations in the brain-gut axis. This theory has led to research in psychological treatments for individuals with IBS, with the aim of reducing the impact of CNS activity on gut function. Current guidelines for the treatment of IBS suggest that behavioral treatments may be considered for motivated patients who associate symptoms with stressors, although their benefits remain controversial. This study aims to measure the impact of cognitive behavioral therapy in the reduction of symptoms in IBS.

B. Study Design and Statistical Analysis

• Research subjects will be recruited from Columbia / NewYork-Presbyterian Hospital GI clinic and will be randomly assigned to each treatment arm (CBT + standard of care vs standard of care alone)

• For randomization, a series of security envelopes will be prepared containing a card with the text "CBT + standard of care" or "standard of care alone". On entry to the study, each participant will be allocated a randomly assigned identification number corresponding to an envelope containing the participant's intervention. At the time of enrollment, a secretary will open the envelope and direct the subject to their intervention.

• 80 subjects will be enrolled. While only 10 subjects (5 for each treatment arm) would be needed according to an unpaired T test using a standard deviation of 50 and an effect size of 100 (on symptom severity visual analog scale for patients with IBS), this study oversamples the treatment arms to have minimum of 40 patients in each arm. Calculations were determined based on a power of 80%. Using estimated midpoints for mild, moderate and severe disease, I determined that 100 is the SCDI (smallest difference of clinical interest), as it is roughly the scale needed to move categories (ie, from severe to moderate or moderate to mild). A standard deviation was based on the validation study for the visual analog scale in which the standard deviation for people with moderate and severe disease was roughly 50.

• Subjects will not be crossed over from one group into the other

C. Study Procedure.

• The subjects randomized to CBT + standard of care had monthly 30 minute routine appointments with a Gastroenterologist plus weekly 1-h sessions of CBT conducted by a clinical psychologist for a total of 12 weeks. CBT would follow the

classic Beck's model for behavioral therapy, participants are trained to identify anxiety-provoking dysfunctional thoughts, expectations and assumptions, as they related to bowel symptoms. Participants were then taught to challenge and modify their thinking to produce more rational and helpful thoughts.

• Subjects assigned to standard of care received only monthly 30 minute sessions with a board-certified Gastroenterologist for routine medical management of their IBS in which they were able to discuss their symptoms and to receive standard dietary advice regarding fiber intake.

• Duration of interventions will last three months. Symptom severity scores will be administered to both treatment groups at time of randomization, at 3, 6 and 12 month follow up periods.

D. Study drugs
None

E. Medical device
None

F. Study Questionnaires
See attached forms for the Irritable Bowel Symptom Severity Scoring System

G. Study Subjects
Inclusion criteria are men and woman subjects aged 21 – 65 from CUMC gastroenterology outpatient clinics who fit the Rome III diagnostic criteria for IBS (recurrent abdominal pain or discomfort for at least 3 days per month in the last 3 months associated with two or more of the following: improvement with defecation, onset associated with a change in frequency of stool, or onset associated with a change in form of stool), and have scores of at least moderate severity on the IBS symptom severity scoring system.

Exclusion Criteria would be patients that have prior psychiatric diagnoses, are currently seeing a psychiatric health professional, or are currently taking any type of medication that can affect bowel function.

H. Recruitment of subjects
Subjects will be recruited in gastroenterology outpatient clinics at CUMC by their gastroenterologist if he/she feels they may qualify for the study.

I. Confidentiality of Study Data
All study data will be coded (Hospital Unit numbers, Social Security numbers, subject initials, phone numbers and addresses are all considered to be personal identifiers, and should not be used as coding mechanisms. A unique code number will be used for all study subjects.)
Data will be stored in a secure location, accessible only to the investigators.

J. Potential Conflict of interest
None

K. Location of Study
CUMC outpatient gastroenterology clinics and CUMC clinical psychology outpatient clinic

L. Potential risks
Both the treatment and control arms of the study confer minimal risk to research subjects

M. Potential benefits
While subjects may or may not benefit from the treatment studied, potential benefits of treatment include reduced morbidity and increased quality of life

N. Alternative therapies
There are alternative psychotherapies, pharmacologic and dietary treatments being tried for IBS. The control arm in this study is receiving what is accepted as "standard of care."

O. Compensation to subjects
None

P. Cost to subjects
Subjects are responsible for transportation costs and cost of time spend in treatment and control arm

Q. Minors as Research Subjects
None

R . Radiation or Radioactive Substances
None

References

1. Chey WD, Olden K, Carter E, Boyle J, Drossman D, Chang L. Utility of the Rome I and Rome II criteria for irritable bowel syndrome in U.S. women. *Am J Gastroenterol.* Nov 2002;97(11):2803-2811. bowel disorders. *Gastroenterology.* Apr 2006;130(5):1480-1491.

2. Longstreth GF, Thompson WG, Chey WD, Houghton LA, Mearin F, Spiller RC. Functional