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Meditation and Yoga for Irritable Bowel Syndrome:

Study Protocol for a Randomized Clinical Trial (MY-IBS Study)

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MEDITATION AND YOGA FOR IBS

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Abstract

Introduction: When delivered in person, yoga has been shown to be effective in managing Irritable Bowel Syndrome (IBS) symptoms. Research is needed to test the feasibility and effectiveness of yoga as a therapeutic option when delivered virtually. The primary aim of the MY-IBS randomized controlled trial is to determine the effects of an eight-week virtual meditation and yoga intervention on IBS symptom severity compared with an advice-only active control group.

Methods and analysis: Adults diagnosed with IBS will be randomized to receive either a Hatha yoga intervention or an advice-only control group. The intervention will consist of weekly online classes for eight weeks delivered by a facilitator using Microsoft Office Teams and daily home practice. Feasibility will be evaluated by examining recruitment and attrition rates, adherence, participant satisfaction with the program, and safety. The primary outcome is IBS symptom severity, and key secondary outcomes include (but not limited to) quality of life, anxiety and depression symptoms, COVID-19 related stress and anxiety, and fatigue. Outcomes will be assessed at baseline, four weeks, and eight weeks. An embedded design experimental model sub-study will be conducted post-intervention using qualitative research methods to identify participants' experiences in the yoga program.

Ethics and dissemination: This study has been approved by the Conjoint Health Research Ethics Board (REB ID 20-0084). Findings will be disseminated through peer-reviewed publication, conference presentation, and social media.

Trial registration number: NCT04302623

Introduction

Stress is a physical, mental, or emotional response that causes tension in the mind or the body[1]. Altered stress response from psychological and physiological mechanisms may contribute to altered brain-gut signaling patterns and IBS symptoms. Psychological stressors, such as depression and anxiety, may influence gut function (e.g., reduced motility). Physiological stressors (e.g., infection) in the gut may affect the brain[2]. Therapies focusing on mind-body interactions and stress reduction may be adjunctive treatments for IBS. Stress management techniques that include both mind and body interventions such as yoga[3] have been effective in improving IBS symptom severity and mental health outcomes[3 4]. Mind-body interventions may modulate the brain-gut axis directly by reducing sympathetic activity and increasing parasympathetic activity and the hypothalamus-pituitary-adrenal axis[5].

Yoga is a traditional *mind-body-breath* discipline that includes a triad of postures, structured breathing, and meditation[6]. Our recent review[7] identified four randomized controlled trials that examined traditional yoga practice as therapy for IBS patients[8-11]. These trials demonstrated yoga was more effective compared to pharmacological treatment and equally effective as dietary interventions or moderate-intensity walking. Physical and mental health improvements included IBS symptom severity, gastric motility, and depression.

Research is needed to determine the feasibility and effectiveness of virtual yoga programming as a therapeutic option for patients with IBS. The rationale for virtually delivered interventions to manage IBS is increasing due to rising demand, limited healthcare resources, and cost-effectiveness[12 13]. A recent review found virtual care tools may be effective in managing disease activity and improving outcomes in patients with digestive diseases[14]. This review also highlighted the high acceptability and satisfaction with virtual care among patients with IBS[15-19].

The primary objective of the MY-IBS (Meditation and Yoga for Irritable Bowel Syndrome) study is to explore the feasibility and effectiveness of a virtual yoga program for patients with IBS. MY-IBS is a mixed-methods study including a randomized controlled trial and semi-structured interviews. The primary aim of this randomized controlled trial is to determine the effects of an eight-week virtual yoga intervention on IBS symptom severity, measured with the IBS Symptoms Severity Scale, compared to an advice-only control group. Secondary aims are to determine whether a) a yoga program delivered virtually is feasible for adults with IBS, b) improves health outcomes including quality of life, stress, and fatigue, and c) improves mental health outcomes including depression and anxiety symptoms. An embedded design experimental model qualitative sub-study using semi-structured interviews will explore and describe participants' experiences in the yoga program, and its impact. We hypothesize that the program will be feasible and effective in improving outcomes in the intervention group compared to the control group.

Methods and Analysis

Study design overview

The quantitative study is a superiority randomized non-blinded two-group controlled trial. The qualitative study will use semi-structured interviews and thematic analysis to explore and describe intervention participant experiences and views of the yoga program.

Patient involvement

Patients with lived experience were involved in the conduct of this study. During the development stage, patient partners were invited to participate in a series of discussions with the research team to define the study research question, study design, choice of outcome measures, and methods of recruitment. Following the completion of the trial, the patient partners will be involved in the dissemination of this research.

Sample and selection

The MY-IBS stud will be conducted at the University of Calgary in Alberta, Canada. To be eligible in this study, participants must be diagnosed with IBS based on Rome IV criteria by a health care professional (e.g., physician, nurse, dietician), be 18-70 years old, have an adequate understanding of English, have an ability to provide written informed consent, score at least 75 out 500 points on the IBS Symptoms Severity Scale indicating mild IBS symptoms, and be on stable doses of medications for IBS (including anti-depressants) without major changes to diet or physical activity levels for at least eight weeks prior to starting the intervention. Individuals across Canada are eligible to participate. Exclusion criteria include a major physical impairment that would prevent the individual from doing yoga determined by either the patient or the study coordinator, and diagnosis of any major cognitive, psychological, or psychiatric disorder (e.g., major depression, schizophrenia) as identified by the treating physician or healthcare practitioner or screened by the study coordinator using the Patient Health Questionnaire-9.

Participants will be identified through (a) gastroenterology clinics across Calgary, Alberta; (b) gastroenterologists across Canada who indicated interest in this study for their IBS patients in a previous survey conducted by our team (not published); (c) participants from the previous survey who indicated interest in this study and have given consent to be contacted; (d) through social media; (e) self-referrals through the study website and the University of Calgary

participate in research portal; (f) Canadian Association of Gastroenterologists monthly newsletter; and (g) participants with IBS who are enrolled in the IMAGINE (Inflammation, Microbiome and Alimentation Gastro-intestinal and Neuropsychiatric Effects) cohort study at the University of Calgary and have given their consent to be contacted for future studies.

Participant screening will use the Patient Health Questionnaire-9 (PHQ-9). Individuals who score 20 points or higher on the PHQ-9 indicating severe depression will not be eligible to participate. Reasons for exclusion are lack of compliance in interventional studies among these individuals, potential heterogeneity in the small sample size of participants, and skewed results if patients seek treatment for their depression during the trial.

Interventions

Yoga intervention group

Before their first class, the intervention group will receive an introductory video. The video will consist of information on IBS, information on the style of yoga they will be learning, and rationale for yoga as a treatment for IBS. The intervention will be delivered online by a certified yoga facilitator in class sizes of less than ten participants using the Microsoft Office Teams platform. Classes will be held once per week for the eight-week duration. The first session will be approximately 90 minutes and subsequent sessions up to 60 minutes. The introductory session will include the class setup, introductions, teaching poses, corrections, and a question and answers period. The yoga facilitator will provide participants with modifications for common challenges to support best practices and ensure safety. Subsequent classes will include a review from the previous week, a question and answer period, individual corrections and modifications, and introduce new practices. In addition to the online class component, study staff will ask participants to practice the yoga program at home every day. They will also have

access to the yoga videos, written program instructions, and frequently answered questions accessible through the study website to help support their home practice (https://cumming.ucalgary.ca/research/ascend/resources/patient-resources/my-ibs).

Upa Yoga, developed by the Isha Foundation of Inner Sciences (https://isha.sadhguru.org/us/en), will be promoted. Upa Yoga maintains the ancient principles of Hatha Yoga and will be delivered by a certified yoga facilitator from the Isha Foundation. The Upa Yoga program will consist of (a) directional movements and neck rotations, (b) hatha yoga-based Yoga Namaskar, (c) breathing practices or alternate nostril breathing, (d) mantra meditation consisting of AUM chanting (OM), and e) breath watching. Table 1 shows a description of the program and rationale. Our published prospective study examining the effectiveness of Upa Yoga in patients with Inflammatory Bowel Disease[20] shows improvements in mental health scores after an eight-week yoga program.

Advice-only control group

Control participants will receive a video including general education on IBS, the mind-gut connection in IBS, and the role of mind-body therapies in the management of IBS. These participants will also receive a list of IBS-related resources from the Canadian Digestive Health Foundation, a link to an IBS patient support group (www.ibspatient.org), and information about physical activity guidelines from the World Health Organization. Control participants will be eligible to attend a two-week yoga program and receive the yoga videos eight weeks from the time of enrolment. Data on these participants will not be collected as this participation option is for participants who desire to receive the yoga sessions outside of the study.

Outcome measures

Feasibility outcomes

Recruitment, attendance, and attrition rates. Recruitment will be calculated by the percentage of participants who complete the eligibility and enrollment phases of the study. Attrition will be calculated by the percentage of participants who complete all study measures at baseline and eight weeks. A feasible intervention will be defined as class attendance of at least 75 percent (i.e., attendance in six out of eight classes)[9] and attrition rate of less than 30 percent.

Adherence. Adherence will be defined as practicing daily yoga for at least 80% of days for eight weeks (or 45 out of 56 days minimum). Each week a practice log will be provided to monitor frequency and length of yoga. The yoga facilitator will take attendance during each online class. To increase program adherence, the study coordinator will email intervention participants weekly. Six months following the completion of the intervention, participants will be asked to report the average frequency (i.e., days per month) and duration (i.e., minutes) of their yoga practices over the last seven days to evaluate long-term maintenance.

Program satisfaction. Intervention participants will complete a survey regarding overall satisfaction with their program, including satisfaction with videos and online class instruction. Videos and online classes will be deemed acceptable if at least 70% of participants are at least satisfied (i.e., rank classes as either good, great, or excellent). Participants will also indicate whether they would recommend the program to others on a scale from 1 (strongly disagree) to 7 (strongly agree) and provide feedback on how the program could be improved.

Assessment of harms. The study coordinator will screen potential participants and exclude those with any physical problems that may limit participation with yoga postures. Participants will be asked to report any adverse events experienced during the study period. Participants with adverse events (e.g., injury resulting from the program) will be advised to consult their physician to provide care as appropriate.

Effectiveness outcomes

The primary outcome, IBS symptoms, will be measured using the *IBS-Symptom Severity Scale (IBS-SSS).* The IBS-SSS is a five-question survey that asks the severity of abdominal pain, frequency of abdominal pain, severity of abdominal distention, dissatisfaction with bowel habits, and interference with QOL over the past 10 days. Scores on the IBS-SSS range from 0 to 500 with higher scores indicating more severe symptoms. Participants can be categorized as having mild (75-175), moderate (175-300), or severe (>300) IBS. Symptom reduction of at least 50 points is considered clinically meaningful.

Secondary outcomes (*and their measures*) include quality of life (*IBS-Quality of life*), anxiety (*Generalized Anxiety Disorder-7*), depression (*Patient Health Questionnaire-9*), stress (*Perceived Stress Scale*), COVID-19 stress (*COVID-19 Stress Scale*), fatigue (*Modified Fatigue Impact Scale-21*), somatic Symptoms (*Patient Health Questionnaire-15*), and self-compassion (*Self Compassion Scale-Short Form*) (Supplementary Table 1). Intention to practice yoga will also be assessed. The intervention and control groups will be assessed on effectiveness outcomes at baseline, four, and eight weeks. The intervention group will complete measures of effectiveness outcomes six months after the intervention.

Sample size

We will recruit twenty-five participants per group. However, assuming 30% attrition rate, we will aim to recruit 33 participants per group. Symptom reduction of at least 50 points is considered clinically meaningful, however a group difference has been shown to represent a considerable self-reported improvement [21].We calculated the sample size using a mean difference of at least 83 points on the IBS-SSS (α=0.05, β=0.80, standard deviation of 103.8)[9].

Randomization, treatment allocation, and blinding

Study flow is shown in Figure 1. The study coordinator will obtain consent from participants who will then be enrolled in the study. Participants will be randomized after baseline assessment to either the yoga intervention or the advice-only control group. A statistician blinded to the randomization key will create a computer-generated REDCap randomized sequence to allocate participants. Participants will be aware of the group to which they are allocated, however, the principal investigator and data analyst will remain blinded to the randomization process.

Data management

All quantitative data will be entered into a secure REDCap database at the University of Calgary. After the study, data will be downloaded, and patient identifiers will be removed from the data file. Data will be stored in a password-protected file on a University of Calgary password protected computer. The interviews will be transcribed, deidentified, and uploaded to the University of Calgary's secure SharePoint site. Only the research team will have access to the data.

Statistical analysis

Descriptive analysis will summarize participant characteristics and feasibility outcomes. Univariate analysis of variance (ANOVA) will examine baseline differences between groups for

variables with continuous data. Chi-square tests will examine baseline differences between groups for categorical variables. Unadjusted ANOVA and adjusted analysis of covariance (ANCOVA) models will compare differences in scores from baseline and post-intervention data within and between groups using intent to treat and per protocol analysis. A logistic regression – model examining determinants of responders (a minimum improvement of at least 50 points on the IBS-SSS scale) versus non-responders will be developed to predict a response to the intervention. This model will consider practice in minutes, baseline depression, anxiety, and IBS symptom severity scores. An α of 0.05 will be the threshold for determining statistical significance. If the frequency of missing data is >5%, we will perform additional analyses using imputation methods. Analysis will be conducted using SPSS version 26.

Post-intervention interviews

Participants who were randomized to the intervention and did not withdraw from the study will be invited by email to participate in an interview. We aim to recruit men and women and have equal representation of those who benefited from the program (i.e., experienced improvements in their IBS symptom severity) as well as individuals who did not. We anticipate needing to interview between 10 and 15 participants to reach both code and meaning saturation [22] aiming for a maximum variation sample.

Semi-structured interviews will capture participants' experiences, program satisfaction, facilitators and barriers to participation, perceptions of social support and supervised learning, perceived impact on IBS symptoms and overall physical and mental health, and input on improving future programming (Table 2). Interviews will happen virtually using Microsoft Office Teams and be approximately 30 to 45 minutes in length. The study coordinator will interview the participants, take notes during the interview, and reflect following each interview.

Interview recordings will be transcribed verbatim without identifying information. Data will be coded and analyzed in duplicate using NVivo 12. Thematic analysis inductively reveals patterns and themes providing an understanding of participant experiences, with the program and their perspectives on its impact. Thematic analysis is a method for systematically identifying, organizing, and offering insight into patterns of meaning (themes) across a data set [23]. This method makes sense of shared meanings and experiences that allows the researcher to identify what data is important to the research question [24].

Discussion

The MY-IBS study aims to determine the feasibility and effectiveness of an eight-week virtual yoga and meditation program combined with home-based practice for patients with IBS. Determining feasibility will be based on study recruitment, adherence, safety, and program satisfaction. Improved IBS symptom management (the primary outcome) will determine intervention effectiveness. Secondary outcomes include quality of life, stress, fatigue, depression, anxiety, COVID-19-related stress and anxiety, and self-compassion. These findings will inform potential predictors of responders versus non-responders. Predictors may be considered in clinical practice to target the IBS patients most likely to benefit from the yoga intervention. Interview themes and patterns will refine and inform the development of future virtual yoga programming designed for IBS patients.

To our knowledge, there are no studies of virtual yoga and meditation in the IBS population. The findings from this study may have implications for the management of IBS. The virtual delivery of yoga represents an opportunity to increase access to effective management therapies for patients with IBS. The COVID-19 pandemic has called for the reorganization of

health care including utilization of virtual care. Nearly 90% of care in the United States has been delivered virtually since the pandemic[25]. Due to the COVID-19 pandemic, there is increased psychological distress and gastrointestinal symptoms among individuals with IBS[26 27] compared to individuals without IBS[28]. The present study offers a unique opportunity to examine prospectively the feasibility and effectiveness of a yoga and meditation program delivered virtually to individuals living with IBS with the COVID-19 pandemic restrictions taken into consideration. Study findings may aid in developing interventions and services tailored to patients with IBS. New insight into outcomes will be beneficial for healthcare leaders in planning how to allocate existing resources to support these services and potentially lessen the burden of IBS on both the individual and the health care system.

Ethics and dissemination

Ethics

The study protocol, informed consent form, and other study documents were reviewed and approved by the University of Calgary's ethics board. All protocol modifications will be submitted for review and approval by the ethics board. The trial participants will be informed of any modifications, and re-consented by the study coordinator, if required. Further, the trial registry for this study will be updated.

Participation is voluntary and will not influence standard clinical care. All participants will provide informed written consent and have the right to withdraw from the study at any time. Pending consent from the participant, all data collected up to the time of withdrawal will be used in the final data analyses as advised by the CONSORT guidelines [29].

Dissemination

Our targeted knowledge users and audiences will include researchers, healthcare professionals and service providers, persons with lived experiences, community groups, and professional organizations (e.g., Canadian Association of Gastroenterology). Our goal will be to increase topic area knowledge among these groups and inform future research. Our strategies will include conference presentations, publication in a peer reviewed journal, social media campaigns, development of virtually delivered tools such as mobile applications to increase accessibility and affordability and educational material distributed through the Digestive Health Foundation, IMAGINE SPOR Chronic Disease Network, and Primary Care Networks across Alberta.

Table 1. Overview of the Upa Yoga program.

Program Component	Description	Rationale
Directional Movement of the Arms	This practice involves extending the arms in four directions (sideways, front, up and down) by rotating the wrists, while consciously focusing on the inhalation and exhalation of breath with each movement.	Studies show that fibromyalgia is common among patients living with IBS [30]. This could lead to pain of the muscles and joints, fatigue, and sleep concerns. The principle behind this practice is to lubricate the fluids in the joints, increase circulation and activate the energy nodes in these joints. Doing these practices everyday can relieve muscle and joint stiffness and reduce pain over time. This practice is recommended by the Isha Foundation to increase strengths and flexibility in preparation for Yoga Namaskar.
Neck Practices	There are five sets of neck practices, each stretching the neck and final one working on the shoulder area.	The main cause of neck pain is usually muscle tension. Perceived stress can increase muscle tension. These neck exercises help relieve stress that can aggravate IBS symptoms. This practice is recommended by the Isha Foundation to increase strengths and flexibility in preparation for Yoga Namaskar.
Yoga Namaskar	This practice involves a series of seven consecutive steps of upper body stretching and squatting, aligned with breath.	This practice activates the lumbar region of the spine and strengthens the spinal muscles[31].While Yoga Namaskar has not been specifically studied in patients with IBS, yoga squatting postures have been associated with significant decrease in depression among nine individuals with IBD [20] and anxiety in a randomized self as control study in 30 healthy subjects[32].
Alternate Nostril	The participant sits cross-legged with the spine comfortably erect and eyes closed. Closing the right nostril with the thumb,	Alternate nostril breathing is traditionally considered to alleviate mental unrest and

Breathing (Nadi Shuddhi)	inhaling and exhaling through the left nostril. This is repeated on the right nostril by closing the left nostril with the ring finger.	promote physical and mental balance.[33 34] It has been demonstrated to decrease perceived stress and improve autonomic function in a randomized control trial compared to control subjects in healthy male volunteers, and decreased state anxiety in a prospective study.[35 36]
Mantra Meditation (AUM chanting)	The participants sit cross-legged, and with eyes closed, uttering each of these 3 sounds 7 times. The important aspect to this utterance is the awareness of the reverberations each of the sounds produces in the corresponding parts of the body: a - below the navel, o - mid-point of the chest, m - pit of the throat.	This mantra is thought to facilitate energy flow, and through vibratory mechanisms, creates peace and harmony leading to increased mental alertness and may improve symptoms of depression.[37 38]
Breath watching	The participants sit cross-legged with eyes closed and hold a hand gesture called the Yoga Mudra (the tips of the thumb and index finger come together forming a circle). They are instructed to maintain a gentle focus on the mid-point between both eyebrows (at the level of the pineal gland), while being conscious of the gentle movement of breath happening in their body.	Breathing in a focused manner can be used as a tool to promote positive changes to the mind, body and emotions.[39] Significant reduction in the level of state anxiety was found in a group of healthy male volunteers when they practiced breath awareness.[16]

Table 2. Semi-structured interview questions and probes.

1. **What have you done in the past to manage your IBS?**
    a. Have you tried yoga or mediation?
    b. Have you tried exercise?

2. **I would like to start by asking you what you were hoping for or expecting from the program?**
    a. Why did you join this study?
    b. Did anyone influence your decision to join?
    c. Did that meet your expectations?

3. **Next, I would like to discuss your overall experience in the MY-IBS yoga program in which you participated. Could you describe for me what participating in this program was like for you?**
    a. What did you like most about it?
    b. What didn't you like?
    c. Did this change over the course of the program?

    Sub-questions: *yoga facilitator/supervision, the timing of sessions/scheduling, length of sessions, attending with other members, online experience versus in-person, social support/other participants.*
    d. What was that like?
    e. What stood out for you?
    f. What emotions were you aware of at the time?
    g. What else do you remember about that experience?

4. **How has participating in this program affected how you manage or live with your IBS?**

    Sub-questions: *change in IBS symptoms; physical health, fatigue; mental health - stress, anxiety, depression; feeling better about myself; ability to live with my IBS.*
    a. Tell me more about that.
    b. Can you give me an example of what you mean?
    c. How has that affected you?

5. **What, if anything, has helped you to do your practices at home?**

    Sub-questions*: social support, family support, convenience*
    a. Tell me more about that.
    b. Can you give me an example of what you mean?
    c. How has that affected you?

6. **What challenges did you have, if any, doing your practices at home?**

    Sub-questions*: family, supervision/safety, schedule/time*
    a. Are you satisfied with how you did?
    b. Tell me more about that.

c. Can you give me an example of what you mean?
d. How has that affected you?

7. **What, if anything, has helped you to attend the weekly online class?**
   Sub-questions: *social support, family support, HCP support, yoga facilitator, supervision/safety, online classes, schedule/length*
   a. Tell me more about that.
   b. Can you give me an example of what you mean?
   c. How has that affected you?

8. **What challenges did you have, if any, to attend the weekly online class?**
   Sub-questions: *social support, family, yoga facilitator, supervision/safety, online classes, schedule, technical difficulties*
   a. Are you satisfied with how you did?
   b. Tell me more about that.
   c. Can you give me an example of what you mean?
   d. How has that affected you?

9. **We are interested in any ideas you have about how we might make this program better. What could we do differently?**
   Sub-questions: *content, timing, facilitator, videos, website, delivery, other supports*
   a. Would you explain that further?
   b. Can you give me an example of what you mean?

10. **Based on your experience with yoga, would you incorporate yoga to help manage your IBS? If so, how?**

11. **Before we conclude, is this anything else you would like to say about your experience with this program, that we haven't had a chance to talk about yet?**

Strengths and limitations of this study:

- Mixed methods study composed of a trial and interviews
- First virtual yoga intervention in Irritable Bowel Syndrome
- Canada-wide recruitment
- Self-reported outcome measures
- Lack of data capture on frequency of yoga practice in the control group

Authors' contributions: State how each author was involved in writing the protocol.

AD is involved in all aspects of protocol design and lead author of the manuscript. DM, JKV, YN, VR, and GM assisted with design of the protocol respective to their expertise. DM and GM assisted with the qualitative aspects of the protocol. JKV lead the statistical aspects of the protocol. YN provided their clinical expertise and patient recruitment thought the clinic. VR provided their expertise in yoga therapy. MR is the senior author on the protocol and has guided the work of this research to support AD with their training. All authors reviewed the manuscript for study design and provided critical insight into manuscript content and approved the final version for submission.

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Competing interests statement: None declared.

Data availability: Deidentified participant data will be made available upon reasonable request from the study principal investigator.

Figure 1. Participant flowchart based on the CONSORT guidelines.

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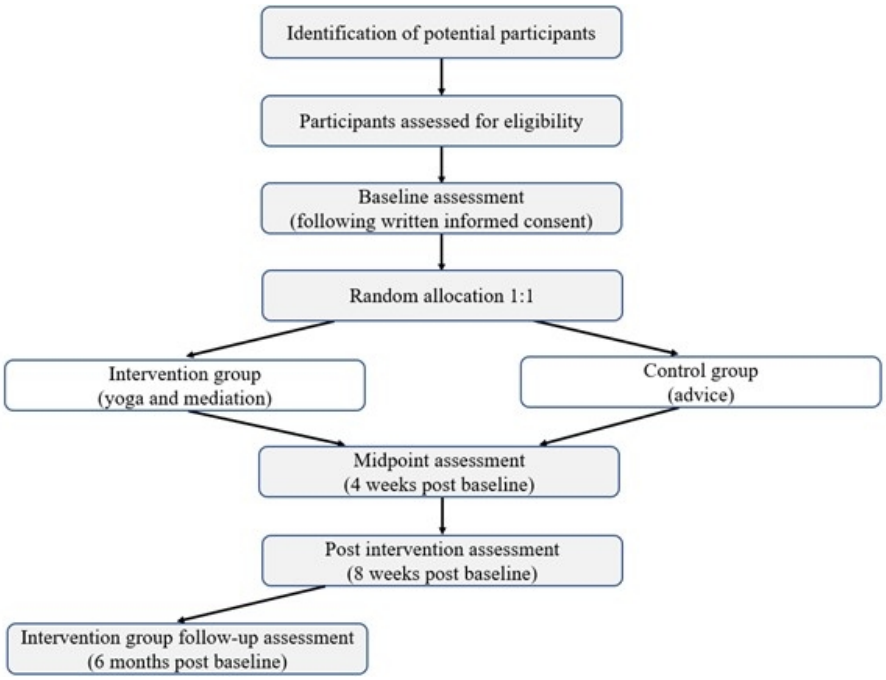
MEDITATION AND YOGA FOR IBS



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Supplementary Table 1. Effectiveness outcomes measures.

Measure	Description	Scoring	Assessments		
Primary outcome			**Baseline**	**4 weeks**	**8 weeks**
IBS-Symptom Severity Scale (IBS-SSS)	The IBS-SSS is a five-question survey that asks the severity of abdominal pain, frequency of abdominal pain, severity of abdominal distention, dissatisfaction with bowel habits, and interference with QOL over the past 10 days. Subjects respond to each question on a 100-point visual analogue scale[22]. The IBS-SSS scale is the most frequently used severity measure for evaluating IBS severity and is commonly used as an outcome measure in clinical trials because it is highly responsive to change with treatment[22].	Scores on the IBS-SSS range from 0 to 500 with higher scores indicating more severe symptoms. Participants can be categorized as having mild (75-175), moderate (175-300), or severe (>300) IBS. Symptom reduction of at least 50 points is considered clinically meaningful; however, the primary endpoint will be the proportion of participants in each group who demonstrate a symptom reduction of 83 points or more, based on the variables used in the sample size calculation[22].	✓	✓	✓
Secondary outcomes					
IBS-Quality of life (IBS-QOL)	The IBS-QOL is a 34-item questionnaire that assesses the degree to which IBS interfered with QOL over the past 30 days. Each item is rated on a 1 to 5 Likert scale, with higher values indicating a lower QOL[25]. The IBS-QOL is currently the most validated and highly responsive self-reported QOL measure specific to IBS that can be used to assess the impact of IBS and its treatment[25].	The individual responses to the 34 items are summed and averaged for a total score and then transformed to a 0-100 scale for ease of interpretation with higher scores indicating better IBS specific QOL[25]. An increment of at least 14 points on the IBS-QOL scale from baseline will demonstrate efficacy.	✓	✓	✓
Generalized Anxiety Disorder (GAD-7)	GAD-7 is seven items, score from 0 (not all at) to 3 (nearly every day), providing a severity score between 0-21. Scores of 5, 10, and 15 represent cut points for	A 5-point change on the GAD-7 is considered clinically significant.	✓	✓	✓

	mild, moderate, and severe anxiety. The GAD-7 also is effective at identifying the presence of other anxiety disorders including panic disorder, social anxiety disorder, and post-traumatic stress disorder[26].				
Physical Health Questionnaire (PHQ-9)	The PHQ-9 is a 9-item survey with each item scored from 0 (not at all) to 3 (nearly every day) totalling from 0 to 27 points. Scores of 5, 10, 15, and 20 represent cut points for mild, moderate, moderately severe and severe depression. The PHQ assesses major depressive disorder, panic disorder, and anxiety disorder[27].	A 5-point change is considered clinically significant.	✓	✓	✓
Perceived Stress Scale (PSS)	The PSS is a 14-item survey that measures perceived stress, or the degree to which situations in one's life are appraised as stressful, on a four-point scale (0=never, 4=very often) over the last 30 days. The PSS is the most widely used psychological instrument for measuring the perception of stress[29].	An 11-point change is considered clinically significant [28].	✓	✓	✓
COVID-19 Stress Scales (CSS)	COVID-19 related stress and anxiety will be measured using the 36-item CSS survey on five scales: (1) COVID danger and contamination fears, (2) COVID fears about economic consequences, (3) COVID xenophobia, (4) COVID compulsive checking and reassurance seeking, and (5) COVID traumatic stress symptoms[33].	Not reported.	✓	✓	✓
Modified Fatigue Impact Scale-21.	This is a self-reported questionnaire consisting of 21 statements that reflect the perceived impact of fatigue on cognitive, physical, and psychosocial	A 16-point change is considered clinically significant[30].	✓	✓	✓

	functioning. Participants are asked to rate the extent to which fatigue has caused problems for them during the last four weeks. Each item is rated on a 5-point scale reflecting how often the person is limited in activities by fatigue, ranging from 0 (never) to 4 (almost always)[31].				
Patient Health Questionnaire-15 (PHQ-15)	The PHQ-15 measures the severity of 15 somatic symptoms (e.g., fatigue, energy, sleeping trouble, and pain) during the past 4 weeks for a score of 0 to 30. Items can be scored as 0 (not at all), 1 (bothered a little), or 2 (bothered a lot). PHQ-15 scores of 5, 10, and 15 represent cut points for low, medium, and high somatic symptom severity, respectively[32].	A 5-point change on the PHQ-15 is considered clinically significant.	✓	✓	✓
Self-Compassion Scale – Short Form (SCS-SF)	Participants will be asked to complete a 12-item self-reported scale measuring their self-compassion, including self-kindness, self-judgement, humanity, isolation, and mindfulness subscales. To encourage their practice and feelings of self-compassion, participants will receive self-compassion messages weekly by email.	Subscale scores are computed by calculating the mean of subscale items responses. Participants will indicate how often they behave in the stated manner, using a scale from 1 (almost never) to 5 (almost always) for a total of 60 points with lower scores indicating more self-compassion[34].	✓	✓	✓

SPIRIT

STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description
Administrative information		
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym **(PG 1)**
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry **(PG 3)**
	2b	All items from the World Health Organization Trial Registration Data Set **(N/A)**
Protocol version	3	Date and version identifier **(N/A)**
Funding	4	Sources and types of financial, material, and other support **(PG 20)**
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors **(PG 1, 2, 20)**
	5b	Name and contact information for the trial sponsor **(N/A)**
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities **(N/A)**
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee) **(N/A)**
Introduction		
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention **(PG 4, 5)**
	6b	Explanation for choice of comparators **(PG 7, 8)**
Objectives	7	Specific objectives or hypotheses **(PG 5)**
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory) **(PG 5)**

Methods: Participants, interventions, and outcomes

Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained **(PG 6)**
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists) **(PG 6)**
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered **(PG 7, 8)**
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease) **(PG 7)**
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests) **(PG 7, 8)**
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial **(N/A)**
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended **(PG 8, 9, 10)**
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure) **(PG 7, 8, 9. Please see supplementary material Table 1.)**
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations **(PG 10)**
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size **(PG 6, 7)**

Methods: Assignment of interventions (for controlled trials)

Allocation:

Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions **(PG 11)**
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned **(PG 11)**
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions **(PG 11)**
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how **(PG 11)**
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial **(N/A)**
Methods: Data collection, management, and analysis		
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol **(PG 8, 9. Please see supplementary material Table 1.)**
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols **(Please see supplementary material Table 1.)**
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol **(PG 11)**
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol **(PG 11, 12)**
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses) **(PG 11, 12)**

	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation) **(PG 12)**
Methods: Monitoring		
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed **(N/A)**
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial **(N/A)**
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct **(N/A)**
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor **(N/A)**
Ethics and dissemination		
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval **(PG 14)**
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators) **(PG 14)**
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) **(PG 14)**
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable **(N/A)**
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial **(PG 11)**
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site **(PG 20)**
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators **(PG 20)**

Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation **(Please see the study consent form.)**
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions **(pg 14, 15)**
	31b	Authorship eligibility guidelines and any intended use of professional writers **(N/A)**
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code **(N/A)**
Appendices		
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates **(Please see the study consent form.)**
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable **(N/A)**

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

BMJ Open

Meditation and Yoga for Irritable Bowel Syndrome: Study Protocol for a Randomized Clinical Trial (MY-IBS Study)

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Meditation and Yoga for Irritable Bowel Syndrome:

Study Protocol for a Randomized Clinical Trial (MY-IBS Study)

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MEDITATION AND YOGA FOR IBS

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MEDITATION AND YOGA FOR IBS

Abstract

Introduction: When delivered in person, yoga has been shown to be effective in managing Irritable Bowel Syndrome (IBS) symptoms. Research is needed to test the feasibility and effectiveness of yoga as a therapeutic option when delivered virtually. The primary aim of the Mind and Yoga for IBS (MY-IBS) randomized controlled trial is to determine the effects of an eight-week virtual meditation and yoga intervention on IBS symptom severity compared with an advice-only active control group.

Methods and analysis: Adults diagnosed with IBS will be randomized to receive either a Upa yoga intervention or an advice-only control group. The intervention will consist of weekly online classes for eight weeks delivered by a facilitator using Microsoft Office Teams and daily home practice. Feasibility will be evaluated by examining recruitment and attrition rates, adherence, participant satisfaction with the program, and safety. The primary outcome is IBS symptom severity, and key secondary outcomes include (but not limited to) quality of life, anxiety and depression symptoms, COVID-19 related stress and anxiety, and fatigue. Outcomes will be assessed at baseline, four weeks, and eight weeks. An embedded design experimental model sub-study will be conducted post-intervention using qualitative research methods to identify participants' experiences in the yoga program.

Ethics and dissemination: This study has been approved by the Conjoint Health Research Ethics Board (REB ID 20-0084). Findings will be disseminated through peer-reviewed publication, conference presentation, and social media.

Trial registration number: NCT04302623

Strengths and limitations:

- Mixed methods study composed of a RCT and interviews
- First virtual yoga interventions in irritable bowel syndrome
- Canada-wide recruitment
- Self-reported outcome measures
- Lack of data capture on the frequency of yoga practice in the control group

Introduction

Stress is a physical, mental, or emotional response that causes tension in the mind or the body[1]. Altered stress response from psychological and physiological mechanisms may contribute to altered brain-gut signaling patterns and IBS symptoms. Psychological stressors, such as depression and anxiety, may influence gut function (e.g., reduced motility). Physiological stressors (e.g., infection) in the gut may affect the brain[2]. Therapies focusing on mind-body interactions and stress reduction may be adjunctive treatments for IBS. Stress management techniques that include both mind and body interventions such as yoga[3] have been effective in improving IBS symptom severity and mental health outcomes[3 4]. Mind-body interventions may modulate the brain-gut axis directly by reducing sympathetic activity and increasing parasympathetic activity and the hypothalamus-pituitary-adrenal axis[5].

Yoga is a traditional *mind-body-breath* discipline that includes a triad of postures, structured breathing, and meditation[6]. Our recent review[7] identified four randomized controlled trials that examined traditional yoga practice as therapy for IBS patients[8-11]. These trials demonstrated yoga was more effective compared to pharmacological treatment and equally effective as dietary interventions or moderate-intensity walking. Physical and mental health improvements included IBS symptom severity, gastric motility, and depression.

Research is needed to determine the feasibility and effectiveness of virtual yoga programming as a therapeutic option for patients with IBS. The rationale for virtually delivered interventions to manage IBS is increasing due to rising demand, limited healthcare resources, and cost-effectiveness[12 13]. A recent review found virtual care tools may be effective in managing disease activity and improving outcomes in patients with digestive diseases[14]. This review also highlighted the high acceptability and satisfaction with virtual care among patients with IBS[15-19].

The primary objective of the MY-IBS (Meditation and Yoga for Irritable Bowel Syndrome) study is to explore the feasibility and effectiveness of a virtual yoga program for patients with IBS. MY-IBS is a mixed-methods study including a randomized controlled trial and semi-structured interviews. The primary aim of this randomized controlled trial is to determine the effects of an eight-week virtual yoga intervention on IBS symptom severity, measured with the IBS Symptoms Severity Scale, compared to an advice-only control group. Secondary aims are to determine whether a) a yoga program delivered virtually is feasible for adults with IBS, b) improves health outcomes including quality of life, stress, and fatigue, and c) improves mental health outcomes including depression and anxiety symptoms. An embedded design experimental model qualitative sub-study using semi-structured interviews will explore and describe participants' experiences in the yoga program, and its impact. We hypothesize that the program will be feasible and effective in improving outcomes in the intervention group compared to the control group.

Methods and Analysis

Study design overview

The quantitative study is a superiority randomized non-blinded two-group controlled trial. The qualitative study will use semi-structured interviews and thematic analysis to explore and describe intervention participant experiences and views of the yoga program.

Patient involvement

Patients with lived experience were involved in the conduct of this study. During the development stage, patient partners were invited to participate in a series of discussions with the research team to define the study research question, study design, choice of outcome measures, and methods of recruitment. Following the completion of the trial, the patient partners will be involved in the dissemination of this research.

Sample and selection

The MY-IBS stud will be conducted at the University of Calgary in Alberta, Canada starting March 2021 and ending early 2022. To be eligible in this study, participants must be diagnosed with IBS based on Rome IV criteria by a health care professional (e.g., physician, nurse, dietician), be 18-70 years old, have an adequate understanding of English, have an ability to provide written informed consent, score at least 75 out 500 points on the IBS Symptoms Severity Scale indicating mild IBS symptoms, and be on stable doses of medications for IBS (including anti-depressants) without major changes to diet or physical activity levels for at least eight weeks prior to starting the intervention. Individuals across Canada are eligible to participate. Exclusion criteria include a major physical impairment that would prevent the individual from doing yoga determined by either the patient or the study coordinator, and diagnosis of any major cognitive, psychological, or psychiatric disorder (e.g., major depression, schizophrenia) as identified by the treating physician or healthcare practitioner or screened by the study coordinator using the Patient Health Questionnaire-9.

Participants will be identified through (a) gastroenterology clinics across Calgary, Alberta; (b) gastroenterologists across Canada who indicated interest in this study for their IBS patients in a previous survey conducted by our team (not published); (c) participants from the previous survey who indicated interest in this study and have given consent to be contacted; (d)

through social media; (e) self-referrals through the study website and the University of Calgary participate in research portal; (f) Canadian Association of Gastroenterologists monthly newsletter; and (g) participants with IBS who are enrolled in the IMAGINE (Inflammation, Microbiome and Alimentation Gastro-intestinal and Neuropsychiatric Effects) cohort study at the University of Calgary and have given their consent to be contacted for future studies.

Participant screening will use the Patient Health Questionnaire-9 (PHQ-9). Individuals who score 20 points or higher on the PHQ-9 indicating severe depression will not be eligible to participate. Reasons for exclusion are lack of compliance in interventional studies among these individuals, potential heterogeneity in the small sample size of participants, and skewed results if patients seek treatment for their depression during the trial.

Interventions

Yoga intervention group

Before their first class, the intervention group will receive an introductory video. The video will consist of information on IBS, information on the style of yoga they will be learning, and rationale for yoga as a treatment for IBS. The intervention will be delivered online by a certified yoga facilitator in class sizes of less than ten participants using the Microsoft Office Teams platform. Classes will be held once per week for the eight-week duration. The first session will be approximately 90 minutes and subsequent sessions up to 60 minutes. The introductory session will include the class setup, introductions, teaching poses, corrections, and a question and answers period. The yoga facilitator will provide participants with modifications for common challenges to support best practices and ensure safety. Subsequent classes will include a review from the previous week, a question and answer period, individual corrections and modifications, and introduce new practices. In addition to the online class component, study

staff will ask participants to practice the yoga program at home every day. They will also have access to the yoga videos, written program instructions, and frequently answered questions accessible through the study website to help support their home practice (https://cumming.ucalgary.ca/research/ascend/resources/patient-resources/my-ibs).

Upa Yoga, developed by the Isha Foundation of Inner Sciences (https://isha.sadhguru.org/us/en), will be promoted. Upa Yoga maintains the ancient principles of Hatha Yoga and will be delivered by a certified yoga facilitator from the Isha Foundation. The Upa Yoga program will consist of (a) directional movements and neck rotations, (b) hatha yoga-based Yoga Namaskar, (c) breathing practices or alternate nostril breathing, (d) mantra meditation consisting of AUM chanting (OM), and e) breath watching. Table 1 shows a description of the program and rationale. Our published prospective study examining the effectiveness of Upa Yoga in patients with Inflammatory Bowel Disease[20] shows improvements in mental health scores after an eight-week yoga program.

Advice-only control group

Control participants will receive a video including general education on IBS, the mind-gut connection in IBS, and the role of mind-body therapies in the management of IBS. These participants will also receive a list of IBS-related resources from the Canadian Digestive Health Foundation, a link to an IBS patient support group (www.ibspatient.org), and information about physical activity guidelines from the World Health Organization. Control participants will be eligible to attend a two-week yoga program and receive the yoga videos eight weeks from the time of enrolment. Data on these participants will not be collected as this participation option is for participants who desire to receive the yoga sessions outside of the study.

Outcome measures

Feasibility outcomes

Recruitment, attendance, and attrition rates. Recruitment will be calculated by the percentage of participants who complete the eligibility and enrollment phases of the study. Attrition will be calculated by the percentage of participants who complete all study measures at baseline and eight weeks. A feasible intervention will be defined as class attendance of at least 75 percent (i.e., attendance in six out of eight classes)[9] and attrition rate of less than 30 percent.

Adherence. Adherence will be defined as practicing daily yoga for at least 80% of days for eight weeks (or 45 out of 56 days minimum). Each week a practice log will be provided to monitor frequency and length of yoga. The yoga facilitator will take attendance during each online class. To increase program adherence, the study coordinator will email intervention participants weekly. Six months following the completion of the intervention, participants will be asked to report the average frequency (i.e., days per month) and duration (i.e., minutes) of their yoga practices over the last seven days to evaluate long-term maintenance.

Program satisfaction. Intervention participants will complete a survey regarding overall satisfaction with their program, including satisfaction with videos and online class instruction. Videos and online classes will be deemed acceptable if at least 70% of participants are at least satisfied (i.e., rank classes as either good, great, or excellent). Participants will also indicate whether they would recommend the program to others on a scale from 1 (strongly disagree) to 7 (strongly agree) and provide feedback on how the program could be improved.

Assessment of harms. The study coordinator will screen potential participants and exclude those with any physical problems that may limit participation with yoga postures. Participants will be asked to report any adverse events experienced during the study period.

Participants with adverse events (e.g., injury resulting from the program) will be advised to consult their physician to provide care as appropriate.

Effectiveness outcomes

The primary outcome, IBS symptoms, will be measured using the *IBS-Symptom Severity Scale (IBS-SSS).* The IBS-SSS is a five-question survey that asks the severity of abdominal pain, frequency of abdominal pain, severity of abdominal distention, dissatisfaction with bowel habits, and interference with QOL over the past 10 days. Scores on the IBS-SSS range from 0 to 500 with higher scores indicating more severe symptoms. Participants can be categorized as having mild (75-175), moderate (175-300), or severe (>300) IBS. Symptom reduction of at least 50 points is considered clinically meaningful.

Secondary outcomes (*and their measures*) include quality of life (*IBS-Quality of life*), anxiety (*Generalized Anxiety Disorder-7*), depression (*Patient Health Questionnaire-9*), stress (*Perceived Stress Scale*), COVID-19 stress (*COVID-19 Stress Scale*), fatigue (*Modified Fatigue Impact Scale-21*), somatic Symptoms (*Patient Health Questionnaire-15*), and self-compassion (*Self Compassion Scale-Short Form*) (Supplementary Table 1). Intention to practice yoga will also be assessed. The intervention and control groups will be assessed on effectiveness outcomes

at baseline, four, and eight weeks. The intervention group will complete measures of effectiveness outcomes six months after the intervention.

Sample size

We will recruit twenty-five participants per group. However, assuming 30% attrition rate, we will aim to recruit 33 participants per group. Symptom reduction of at least 50 points is considered clinically meaningful, however a group difference has been shown to represent a considerable self-reported improvement [21].We calculated the sample size using a mean difference of at least 83 points on the IBS-SSS (α=0.05, β=0.80, standard deviation of 103.8)[9].

Randomization, treatment allocation, and blinding

Study flow is shown in Figure 1. The study coordinator will obtain consent from participants who will then be enrolled in the study. Participants will be randomized after baseline assessment to either the yoga intervention or the advice-only control group. A statistician blinded to the randomization key will create a computer-generated REDCap randomized sequence to allocate participants based on gender (1:1:1 male:female:other) and depression (1:1 depression:no depression). Participants will be aware of the group to which they are allocated, however, the principal investigator and data analyst will remain blinded to the randomization process.

Data management

All quantitative data will be entered into a secure REDCap database at the University of Calgary. Effectiveness outcome measures, program satisfaction, attendance, and adherence will be entered by the participants. Recruitment, attrition, and safety will be recorded by the study coordinator who is not blinded to the randomization. After the study, data will be downloaded, and patient identifiers will be removed from the data file. Data will be stored in a password-

protected file on a University of Calgary password protected computer. The interviews will be transcribed, deidentified, and uploaded to the University of Calgary's secure SharePoint site. Only the research team will have access to the data.

Statistical analysis

Descriptive analysis will summarize participant characteristics and feasibility outcomes. Univariate analysis of variance (ANOVA) will examine baseline differences between groups for variables with continuous data. Chi-square tests will examine baseline differences between groups for categorical variables. Unadjusted ANOVA and adjusted analysis of covariance (ANCOVA) models will compare differences in scores from baseline and post-intervention data within and between groups using intent to treat and per protocol analysis. A logistic regression – model examining determinants of responders (a minimum improvement of at least 50 points on the IBS-SSS scale) versus non-responders will be developed to predict a response to the intervention. This model will consider practice in minutes, baseline depression, anxiety, and IBS symptom severity scores. An α of 0.05 will be the threshold for determining statistical significance. If the frequency of missing data is >5%, we will perform additional analyses using imputation methods. Analysis will be conducted using SPSS version 26.

Post-intervention interviews

Participants who were randomized to the intervention and did not withdraw from the study will be invited by email to participate in an interview. We aim to recruit men and women and have equal representation of those who benefited from the program (i.e., experienced improvements in their IBS symptom severity) as well as individuals who did not. We anticipate needing to interview between 10 and 15 participants to reach both code and meaning saturation [22] aiming for a maximum variation sample.

Semi-structured interviews will capture participants' experiences, program satisfaction, facilitators and barriers to participation, perceptions of social support and supervised learning, perceived impact on IBS symptoms and overall physical and mental health, and input on improving future programming (Table 2). Interviews will happen virtually using Microsoft Office Teams and be approximately 30 to 45 minutes in length. The study coordinator will interview the participants, take notes during the interview, and reflect following each interview. Interview recordings will be transcribed verbatim without identifying information. Data will be coded and analyzed in duplicate using NVivo 12. Thematic analysis inductively reveals patterns and themes providing an understanding of participant experiences, with the program and their perspectives on its impact. Thematic analysis is a method for systematically identifying, organizing, and offering insight into patterns of meaning (themes) across a data set [23]. This method makes sense of shared meanings and experiences that allows the researcher to identify what data is important to the research question [24].

Discussion

The MY-IBS study aims to determine the feasibility and effectiveness of an eight-week virtual yoga and meditation program combined with home-based practice for patients with IBS. Determining feasibility will be based on study recruitment, adherence, safety, and program satisfaction. Improved IBS symptom management (the primary outcome) will determine intervention effectiveness. Secondary outcomes include quality of life, stress, fatigue, depression, anxiety, COVID-19-related stress and anxiety, and self-compassion. These findings will inform potential predictors of responders versus non-responders. Predictors may be considered in clinical practice to target the IBS patients most likely to benefit from the yoga

intervention. Interview themes and patterns will refine and inform the development of future virtual yoga programming designed for IBS patients.

To our knowledge, there are no studies of virtual yoga and meditation in the IBS population. The findings from this study may have implications for the management of IBS. The virtual delivery of yoga represents an opportunity to increase access to effective management therapies for patients with IBS. The COVID-19 pandemic has called for the reorganization of health care including utilization of virtual care. Nearly 90% of care in the United States has been delivered virtually since the pandemic[25]. Due to the COVID-19 pandemic, there is increased psychological distress and gastrointestinal symptoms among individuals with IBS[26 27] compared to individuals without IBS[28]. The present study offers a unique opportunity to examine prospectively the feasibility and effectiveness of a yoga and meditation program delivered virtually to individuals living with IBS with the COVID-19 pandemic restrictions taken into consideration. Study findings may aid in developing interventions and services tailored to patients with IBS. New insight into outcomes will be beneficial for healthcare leaders in planning how to allocate existing resources to support these services and potentially lessen the burden of IBS on both the individual and the health care system.

Ethics and dissemination

Ethics

The study protocol, informed consent form, and other study documents were reviewed and approved by the University of Calgary's ethics board. All protocol modifications will be submitted for review and approval by the ethics board. The trial participants will be informed of any modifications, and re-consented by the study coordinator, if required. Further, the trial registry for this study will be updated.

Participation is voluntary and will not influence standard clinical care. All participants will provide informed written consent and have the right to withdraw from the study at any time. Pending consent from the participant, all data collected up to the time of withdrawal will be used in the final data analyses as advised by the CONSORT guidelines [29].

Dissemination

Our targeted knowledge users and audiences will include researchers, healthcare professionals and service providers, persons with lived experiences, community groups, and professional organizations (e.g., Canadian Association of Gastroenterology). Our goal will be to increase topic area knowledge among these groups and inform future research. Our strategies will include conference presentations, publication in a peer reviewed journal, social media campaigns, development of virtually delivered tools such as mobile applications to increase accessibility and affordability and educational material distributed through the Digestive Health Foundation, IMAGINE SPOR Chronic Disease Network, and Primary Care Networks across Alberta.

Table 1. Overview of the Upa Yoga program.

Program Component	Description	Rationale
Directional Movement of the Arms	This practice involves extending the arms in four directions (sideways, front, up and down) by rotating the wrists, while consciously focusing on the inhalation and exhalation of breath with each movement.	Studies show that fibromyalgia is common among patients living with IBS [30]. This could lead to pain of the muscles and joints, fatigue, and sleep concerns. The principle behind this practice is to lubricate the fluids in the joints, increase circulation and activate the energy nodes in these joints. Doing these practices everyday can relieve muscle and joint stiffness and reduce pain over time. This practice is recommended by the Isha Foundation to increase strengths and flexibility in preparation for Yoga Namaskar.
Neck Practices	There are five sets of neck practices, each stretching the neck and final one working on the shoulder area.	The main cause of neck pain is usually muscle tension. Perceived stress can increase muscle tension. These neck exercises help relieve stress that can aggravate IBS symptoms. This practice is recommended by the Isha Foundation to increase strengths and flexibility in preparation for Yoga Namaskar.
Yoga Namaskar	This practice involves a series of seven consecutive steps of upper body stretching and squatting, aligned with breath.	This practice activates the lumbar region of the spine and strengthens the spinal muscles[31].While Yoga Namaskar has not been specifically studied in patients with IBS, yoga squatting postures have been associated with significant decrease in depression among nine individuals with IBD [20] and anxiety in a randomized self as control study in 30 healthy subjects[32].
Alternate Nostril	The participant sits cross-legged with the spine comfortably erect and eyes closed. Closing the right nostril with the thumb,	Alternate nostril breathing is traditionally considered to alleviate mental unrest and

Breathing (Nadi Shuddhi)	inhaling and exhaling through the left nostril. This is repeated on the right nostril by closing the left nostril with the ring finger.	promote physical and mental balance.[33 34] It has been demonstrated to decrease perceived stress and improve autonomic function in a randomized control trial compared to control subjects in healthy male volunteers, and decreased state anxiety in a prospective study.[35 36]
Mantra Meditation (AUM chanting)	The participants sit cross-legged, and with eyes closed, uttering each of these 3 sounds 7 times. The important aspect to this utterance is the awareness of the reverberations each of the sounds produces in the corresponding parts of the body: a - below the navel, o - mid-point of the chest, m - pit of the throat.	This mantra is thought to facilitate energy flow, and through vibratory mechanisms, creates peace and harmony leading to increased mental alertness and may improve symptoms of depression.[37 38]
Breath watching	The participants sit cross-legged with eyes closed and hold a hand gesture called the Yoga Mudra (the tips of the thumb and index finger come together forming a circle). They are instructed to maintain a gentle focus on the mid-point between both eyebrows (at the level of the pineal gland), while being conscious of the gentle movement of breath happening in their body.	Breathing in a focused manner can be used as a tool to promote positive changes to the mind, body and emotions.[39] Significant reduction in the level of state anxiety was found in a group of healthy male volunteers when they practiced breath awareness.[16]

Table 2. Semi-structured interview questions and probes.

1. **What have you done in the past to manage your IBS?**
    a. Have you tried yoga or mediation?
    b. Have you tried exercise?

2. **I would like to start by asking you what you were hoping for or expecting from the program?**
    a. Why did you join this study?
    b. Did anyone influence your decision to join?
    c. Did that meet your expectations?

3. **Next, I would like to discuss your overall experience in the MY-IBS yoga program in which you participated. Could you describe for me what participating in this program was like for you?**
    a. What did you like most about it?
    b. What didn't you like?
    c. Did this change over the course of the program?

    Sub-questions: *yoga facilitator/supervision, the timing of sessions/scheduling, length of sessions, attending with other members, online experience versus in-person, social support/other participants.*
    d. What was that like?
    e. What stood out for you?
    f. What emotions were you aware of at the time?
    g. What else do you remember about that experience?

4. **How has participating in this program affected how you manage or live with your IBS?**

    Sub-questions: *change in IBS symptoms; physical health, fatigue; mental health - stress, anxiety, depression; feeling better about myself; ability to live with my IBS.*
    a. Tell me more about that.
    b. Can you give me an example of what you mean?
    c. How has that affected you?

5. **What, if anything, has helped you to do your practices at home?**

    Sub-questions*: social support, family support, convenience*
    a. Tell me more about that.
    b. Can you give me an example of what you mean?
    c. How has that affected you?

6. **What challenges did you have, if any, doing your practices at home?**

    Sub-questions*: family, supervision/safety, schedule/time*
    a. Are you satisfied with how you did?
    b. Tell me more about that.

c. Can you give me an example of what you mean?
d. How has that affected you?

7. **What, if anything, has helped you to attend the weekly online class?**
   Sub-questions: *social support, family support, HCP support, yoga facilitator, supervision/safety, online classes, schedule/length*
   a. Tell me more about that.
   b. Can you give me an example of what you mean?
   c. How has that affected you?

8. **What challenges did you have, if any, to attend the weekly online class?**
   Sub-questions: *social support, family, yoga facilitator, supervision/safety, online classes, schedule, technical difficulties*
   a. Are you satisfied with how you did?
   b. Tell me more about that.
   c. Can you give me an example of what you mean?
   d. How has that affected you?

9. **We are interested in any ideas you have about how we might make this program better. What could we do differently?**
   Sub-questions: *content, timing, facilitator, videos, website, delivery, other supports*
   a. Would you explain that further?
   b. Can you give me an example of what you mean?

10. **Based on your experience with yoga, would you incorporate yoga to help manage your IBS? If so, how?**

11. **Before we conclude, is this anything else you would like to say about your experience with this program, that we haven't had a chance to talk about yet?**

Strengths and limitations of this study:

- Mixed methods study composed of a trial and interviews
- First virtual yoga intervention in Irritable Bowel Syndrome
- Canada-wide recruitment
- Self-reported outcome measures
- Lack of data capture on frequency of yoga practice in the control group

Authors' contributions: State how each author was involved in writing the protocol.

AD is involved in all aspects of protocol design and lead author of the manuscript. DM, JKV, YN, VR, and GM assisted with design of the protocol respective to their expertise. DM and GM assisted with the qualitative aspects of the protocol. JKV lead the statistical aspects of the protocol. YN provided their clinical expertise and patient recruitment thought the clinic. VR provided their expertise in yoga therapy. MR is the senior author on the protocol and has guided the work of this research to support AD with their training. All authors reviewed the manuscript for study design and provided critical insight into manuscript content and approved the final version for submission.

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Competing interests statement: None declared.

Data availability: Deidentified participant data will be made available upon reasonable request from the study principal investigator.

Figure 1. Participant flowchart based on the CONSORT guidelines.

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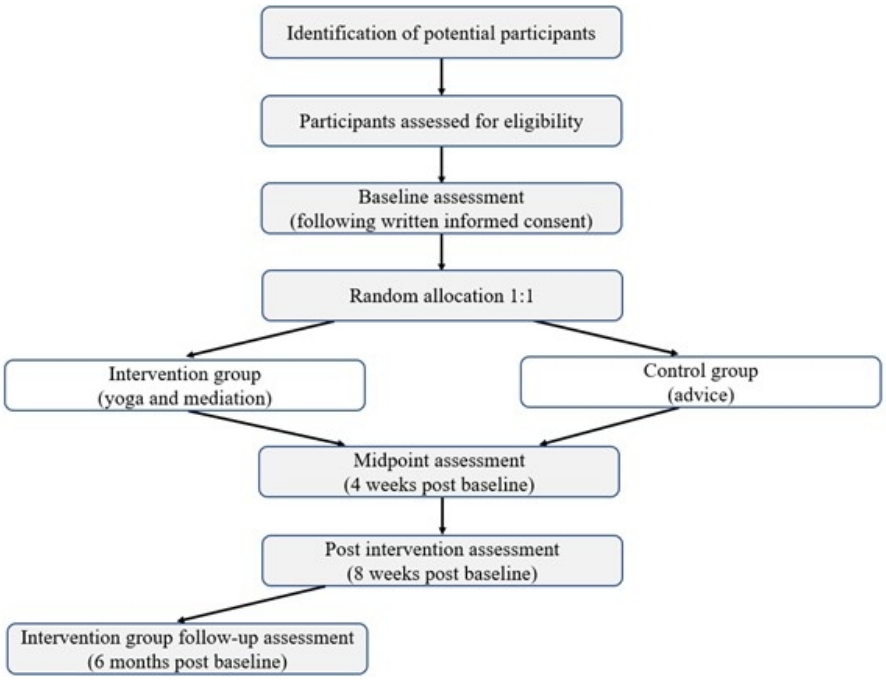

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Supplementary Table 1. Effectiveness outcomes measures.

Measure	Description	Scoring	Assessments		
Primary outcome			**Baseline**	**4 weeks**	**8 weeks**
IBS-Symptom Severity Scale (IBS-SSS)	The IBS-SSS is a five-question survey that asks the severity of abdominal pain, frequency of abdominal pain, severity of abdominal distention, dissatisfaction with bowel habits, and interference with QOL over the past 10 days. Subjects respond to each question on a 100-point visual analogue scale[22]. The IBS-SSS scale is the most frequently used severity measure for evaluating IBS severity and is commonly used as an outcome measure in clinical trials because it is highly responsive to change with treatment[22].	Scores on the IBS-SSS range from 0 to 500 with higher scores indicating more severe symptoms. Participants can be categorized as having mild (75-175), moderate (175-300), or severe (>300) IBS. Symptom reduction of at least 50 points is considered clinically meaningful; however, the primary endpoint will be the proportion of participants in each group who demonstrate a symptom reduction of 83 points or more, based on the variables used in the sample size calculation[22].	✓	✓	✓
Secondary outcomes					
IBS-Quality of life (IBS-QOL)	The IBS-QOL is a 34-item questionnaire that assesses the degree to which IBS interfered with QOL over the past 30 days. Each item is rated on a 1 to 5 Likert scale, with higher values indicating a lower QOL[25]. The IBS-QOL is currently the most validated and highly responsive self-reported QOL measure specific to IBS that can be used to assess the impact of IBS and its treatment[25].	The individual responses to the 34 items are summed and averaged for a total score and then transformed to a 0-100 scale for ease of interpretation with higher scores indicating better IBS specific QOL[25]. An increment of at least 14 points on the IBS-QOL scale from baseline will demonstrate efficacy.	✓	✓	✓
Generalized Anxiety Disorder (GAD-7)	GAD-7 is seven items, score from 0 (not all at) to 3 (nearly every day), providing a severity score between 0-21. Scores of 5, 10, and 15 represent cut points for	A 5-point change on the GAD-7 is considered clinically significant.	✓	✓	✓

	mild, moderate, and severe anxiety. The GAD-7 also is effective at identifying the presence of other anxiety disorders including panic disorder, social anxiety disorder, and post-traumatic stress disorder[26].				
Physical Health Questionnaire (PHQ-9)	The PHQ-9 is a 9-item survey with each item scored from 0 (not at all) to 3 (nearly every day) totalling from 0 to 27 points. Scores of 5, 10, 15, and 20 represent cut points for mild, moderate, moderately severe and severe depression. The PHQ assesses major depressive disorder, panic disorder, and anxiety disorder[27].	A 5-point change is considered clinically significant.	✓	✓	✓
Perceived Stress Scale (PSS)	The PSS is a 14-item survey that measures perceived stress, or the degree to which situations in one's life are appraised as stressful, on a four-point scale (0=never, 4=very often) over the last 30 days. The PSS is the most widely used psychological instrument for measuring the perception of stress[29].	An 11-point change is considered clinically significant [28].	✓	✓	✓
COVID-19 Stress Scales (CSS)	COVID-19 related stress and anxiety will be measured using the 36-item CSS survey on five scales: (1) COVID danger and contamination fears, (2) COVID fears about economic consequences, (3) COVID xenophobia, (4) COVID compulsive checking and reassurance seeking, and (5) COVID traumatic stress symptoms[33].	Not reported.	✓	✓	✓
Modified Fatigue Impact Scale-21.	This is a self-reported questionnaire consisting of 21 statements that reflect the perceived impact of fatigue on cognitive, physical, and psychosocial	A 16-point change is considered clinically significant[30].	✓	✓	✓

	functioning. Participants are asked to rate the extent to which fatigue has caused problems for them during the last four weeks. Each item is rated on a 5-point scale reflecting how often the person is limited in activities by fatigue, ranging from 0 (never) to 4 (almost always)[31].				
Patient Health Questionnaire-15 (PHQ-15)	The PHQ-15 measures the severity of 15 somatic symptoms (e.g., fatigue, energy, sleeping trouble, and pain) during the past 4 weeks for a score of 0 to 30. Items can be scored as 0 (not at all), 1 (bothered a little), or 2 (bothered a lot). PHQ-15 scores of 5, 10, and 15 represent cut points for low, medium, and high somatic symptom severity, respectively[32].	A 5-point change on the PHQ-15 is considered clinically significant.	✓	✓	✓
Self-Compassion Scale – Short Form (SCS-SF)	Participants will be asked to complete a 12-item self-reported scale measuring their self-compassion, including self-kindness, self-judgement, humanity, isolation, and mindfulness subscales. To encourage their practice and feelings of self-compassion, participants will receive self-compassion messages weekly by email.	Subscale scores are computed by calculating the mean of subscale items responses. Participants will indicate how often they behave in the stated manner, using a scale from 1 (almost never) to 5 (almost always) for a total of 60 points with lower scores indicating more self-compassion[34].	✓	✓	✓

SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description
Administrative information		
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym **(PG 1)**
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry **(PG 3)**
	2b	All items from the World Health Organization Trial Registration Data Set **(N/A)**
Protocol version	3	Date and version identifier **(N/A)**
Funding	4	Sources and types of financial, material, and other support **(PG 20)**
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors **(PG 1, 2, 20)**
	5b	Name and contact information for the trial sponsor **(N/A)**
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities **(N/A)**
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee) **(N/A)**
Introduction		
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention **(PG 4, 5)**
	6b	Explanation for choice of comparators **(PG 7, 8)**
Objectives	7	Specific objectives or hypotheses **(PG 5)**
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory) **(PG 5)**

Methods: Participants, interventions, and outcomes

Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained **(PG 6)**
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists) **(PG 6)**
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered **(PG 7, 8)**
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease) **(PG 7)**
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests) **(PG 7, 8)**
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial **(N/A)**
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended **(PG 8, 9, 10)**
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure) **(PG 7, 8, 9. Please see supplementary material Table 1.)**
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations **(PG 10)**
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size **(PG 6, 7)**

Methods: Assignment of interventions (for controlled trials)

Allocation:

Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions **(PG 11)**
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned **(PG 11)**
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions **(PG 11)**
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how **(PG 11)**
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial **(N/A)**
Methods: Data collection, management, and analysis		
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol **(PG 8, 9. Please see supplementary material Table 1.)**
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols **(Please see supplementary material Table 1.)**
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol **(PG 11)**
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol **(PG 11, 12)**
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses) **(PG 11, 12)**

	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation) **(PG 12)**
Methods: Monitoring		
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed **(N/A)**
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial **(N/A)**
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct **(N/A)**
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor **(N/A)**
Ethics and dissemination		
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval **(PG 14)**
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators) **(PG 14)**
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) **(PG 14)**
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable **(N/A)**
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial **(PG 11)**
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site **(PG 20)**
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators **(PG 20)**

Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation **(Please see the study consent form.)**
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions **(pg 14, 15)**
	31b	Authorship eligibility guidelines and any intended use of professional writers **(N/A)**
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code **(N/A)**
Appendices		
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates **(Please see the study consent form.)**
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable **(N/A)**

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

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Meditation and Yoga for Irritable Bowel Syndrome: Study Protocol for a Randomized Clinical Trial (MY-IBS Study)

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Meditation and Yoga for Irritable Bowel Syndrome:

Study Protocol for a Randomized Clinical Trial (MY-IBS Study)

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MEDITATION AND YOGA FOR IBS

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MEDITATION AND YOGA FOR IBS

Abstract

Introduction: When delivered in person, yoga has been shown to be effective in managing Irritable Bowel Syndrome (IBS) symptoms. Research is needed to test the feasibility and effectiveness of yoga as a therapeutic option when delivered virtually. The primary aim of the Mind and Yoga for IBS (MY-IBS) randomized controlled trial is to determine the effects of an eight-week virtual meditation and yoga intervention on IBS symptom severity compared with an advice-only active control group.

Methods and analysis: Adults diagnosed with IBS will be randomized to receive either a Upa yoga intervention or an advice-only control group. The intervention will consist of weekly online classes for eight weeks delivered by a facilitator using Microsoft Office Teams and daily home practice. Feasibility will be evaluated by examining recruitment and attrition rates, adherence, participant satisfaction with the program, and safety. The primary outcome is IBS symptom severity, and key secondary outcomes include (but not limited to) quality of life, anxiety and depression symptoms, COVID-19 related stress and anxiety, and fatigue. Outcomes will be assessed at baseline, four weeks, and eight weeks. An embedded design experimental model sub-study will be conducted post-intervention using qualitative research methods to identify participants' experiences in the yoga program.

Ethics and dissemination: This study has been approved by the Conjoint Health Research Ethics Board (REB ID 20-0084). Findings will be disseminated through peer-reviewed publication, conference presentation, and social media.

Trial registration number: NCT04302623

Strengths and limitations:

- Mixed methods study composed of a RCT and interviews
- First virtual yoga interventions in irritable bowel syndrome
- Canada-wide recruitment
- Self-reported outcome measures
- Lack of data capture on the frequency of yoga practice in the control group

Introduction

Stress is a physical, mental, or emotional response that causes tension in the mind or the body[1]. Altered stress response from psychological and physiological mechanisms may contribute to altered brain-gut signaling patterns and IBS symptoms. Psychological stressors, such as depression and anxiety, may influence gut function (e.g., reduced motility). Physiological stressors (e.g., infection) in the gut may affect the brain[2]. Therapies focusing on mind-body interactions and stress reduction may be adjunctive treatments for IBS. Stress management techniques that include both mind and body interventions such as yoga[3] have been effective in improving IBS symptom severity and mental health outcomes[3 4]. Mind-body interventions may modulate the brain-gut axis directly by reducing sympathetic activity and increasing parasympathetic activity and the hypothalamus-pituitary-adrenal axis[5].

Yoga is a traditional *mind-body-breath* discipline that includes a triad of postures, structured breathing, and meditation[6]. Our recent review[7] identified four randomized controlled trials that examined traditional yoga practice as therapy for IBS patients[8-11]. These trials demonstrated yoga was more effective compared to pharmacological treatment and equally effective as dietary interventions or moderate-intensity walking. Physical and mental health improvements included IBS symptom severity, gastric motility, and depression.

Research is needed to determine the feasibility and effectiveness of virtual yoga programming as a therapeutic option for patients with IBS. The rationale for virtually delivered interventions to manage IBS is increasing due to rising demand, limited healthcare resources, and cost-effectiveness[12 13]. A recent review found virtual care tools may be effective in managing disease activity and improving outcomes in patients with digestive diseases[14]. This review also highlighted the high acceptability and satisfaction with virtual care among patients with IBS[15-19].

The primary objective of the MY-IBS (Meditation and Yoga for Irritable Bowel Syndrome) study is to explore the feasibility and effectiveness of a virtual yoga program for patients with IBS. MY-IBS is a mixed-methods study including a randomized controlled trial and semi-structured interviews. The primary aim of this randomized controlled trial is to determine the effects of an eight-week virtual yoga intervention on IBS symptom severity, measured with the IBS Symptoms Severity Scale, compared to an advice-only control group. Secondary aims are to determine whether a) a yoga program delivered virtually is feasible for adults with IBS, b) improves health outcomes including quality of life, stress, and fatigue, and c) improves mental health outcomes including depression and anxiety symptoms. An embedded design experimental model qualitative sub-study using semi-structured interviews will explore and describe participants' experiences in the yoga program, and its impact. We hypothesize that the program will be feasible and effective in improving outcomes in the intervention group compared to the control group.

Methods and Analysis

Study design overview

The quantitative study is a superiority randomized non-blinded two-group controlled trial. The qualitative study will use semi-structured interviews and thematic analysis to explore and describe intervention participant experiences and views of the yoga program.

Patient involvement

Patients with lived experience were involved in the conduct of this study. During the development stage, patient partners were invited to participate in a series of discussions with the research team to define the study research question, study design, choice of outcome measures, and methods of recruitment. Following the completion of the trial, the patient partners will be involved in the dissemination of this research.

Sample and selection

The MY-IBS stud will be conducted at the University of Calgary in Alberta, Canada starting March 2021 and ending early 2022. To be eligible in this study, participants must be diagnosed with IBS based on Rome IV criteria by a health care professional (e.g., physician, nurse, dietician), be 18-70 years old, have an adequate understanding of English, have an ability to provide written informed consent, score at least 75 out 500 points on the IBS Symptoms Severity Scale indicating mild IBS symptoms, and be on stable doses of medications for IBS (including anti-depressants) without major changes to diet or physical activity levels for at least eight weeks prior to starting the intervention. Individuals across Canada are eligible to participate. Exclusion criteria include a major physical impairment that would prevent the individual from doing yoga determined by either the patient or the study coordinator, and diagnosis of any major cognitive, psychological, or psychiatric disorder (e.g., major depression, schizophrenia) as identified by the treating physician or healthcare practitioner or screened by the study coordinator using the Patient Health Questionnaire-9.

Participants will be identified through (a) gastroenterology clinics across Calgary, Alberta; (b) gastroenterologists across Canada who indicated interest in this study for their IBS patients in a previous survey conducted by our team (not published); (c) participants from the previous survey who indicated interest in this study and have given consent to be contacted; (d)

through social media; (e) self-referrals through the study website and the University of Calgary participate in research portal; (f) Canadian Association of Gastroenterologists monthly newsletter; and (g) participants with IBS who are enrolled in the IMAGINE (Inflammation, Microbiome and Alimentation Gastro-intestinal and Neuropsychiatric Effects) cohort study at the University of Calgary and have given their consent to be contacted for future studies.

Participant screening will use the Patient Health Questionnaire-9 (PHQ-9). Individuals who score 20 points or higher on the PHQ-9 indicating severe depression will not be eligible to participate. Reasons for exclusion are lack of compliance in interventional studies among these individuals, potential heterogeneity in the small sample size of participants, and skewed results if patients seek treatment for their depression during the trial.

Interventions

Yoga intervention group

Before their first class, the intervention group will receive an introductory video. The video will consist of information on IBS, information on the style of yoga they will be learning, and rationale for yoga as a treatment for IBS. The intervention will be delivered online by a certified yoga facilitator in class sizes of less than ten participants using the Microsoft Office Teams platform. Classes will be held once per week for the eight-week duration. The first session will be approximately 90 minutes and subsequent sessions up to 60 minutes. The introductory session will include the class setup, introductions, teaching poses, corrections, and a question and answers period. The yoga facilitator will provide participants with modifications for common challenges to support best practices and ensure safety. Subsequent classes will include a review from the previous week, a question and answer period, individual corrections and modifications, and introduce new practices. In addition to the online class component, study

staff will ask participants to practice the yoga program at home every day. They will also have access to the yoga videos, written program instructions, and frequently answered questions accessible through the study website to help support their home practice (https://cumming.ucalgary.ca/research/ascend/resources/patient-resources/my-ibs).

Upa Yoga, developed by the Isha Foundation of Inner Sciences (https://isha.sadhguru.org/us/en), will be promoted. Upa Yoga maintains the ancient principles of Hatha Yoga and will be delivered by a certified yoga facilitator from the Isha Foundation. The Upa Yoga program will consist of (a) directional movements and neck rotations, (b) hatha yoga-based Yoga Namaskar, (c) breathing practices or alternate nostril breathing, (d) mantra meditation consisting of AUM chanting (OM), and e) breath watching. Table 1 shows a description of the program and rationale. Our published prospective study examining the effectiveness of Upa Yoga in patients with Inflammatory Bowel Disease[20] shows improvements in mental health scores after an eight-week yoga program.

Advice-only control group

Control participants will receive a video including general education on IBS, the mind-gut connection in IBS, and the role of mind-body therapies in the management of IBS. These participants will also receive a list of IBS-related resources from the Canadian Digestive Health Foundation, a link to an IBS patient support group (www.ibspatient.org), and information about physical activity guidelines from the World Health Organization. Control participants will be eligible to attend a two-week yoga program and receive the yoga videos eight weeks from the time of enrolment. Data on these participants will not be collected as this participation option is for participants who desire to receive the yoga sessions outside of the study.

Outcome measures

Feasibility outcomes

Recruitment, attendance, and attrition rates. Recruitment will be calculated by the percentage of participants who complete the eligibility and enrollment phases of the study. Attrition will be calculated by the percentage of participants who complete all study measures at baseline and eight weeks. A feasible intervention will be defined as class attendance of at least 75 percent (i.e., attendance in six out of eight classes)[9] and attrition rate of less than 30 percent.

Adherence. Adherence will be defined as practicing daily yoga for at least 80% of days for eight weeks (or 45 out of 56 days minimum). Each week a practice log will be provided to monitor frequency and length of yoga. The yoga facilitator will take attendance during each online class. To increase program adherence, the study coordinator will email intervention participants weekly. Six months following the completion of the intervention, participants will be asked to report the average frequency (i.e., days per month) and duration (i.e., minutes) of their yoga practices over the last seven days to evaluate long-term maintenance.

Program satisfaction. Intervention participants will complete a survey regarding overall satisfaction with their program, including satisfaction with videos and online class instruction. Videos and online classes will be deemed acceptable if at least 70% of participants are at least satisfied (i.e., rank classes as either good, great, or excellent). Participants will also indicate whether they would recommend the program to others on a scale from 1 (strongly disagree) to 7 (strongly agree) and provide feedback on how the program could be improved.

Assessment of harms. The study coordinator will screen potential participants and exclude those with any physical problems that may limit participation with yoga postures. Participants will be asked to report any adverse events experienced during the study period.

Participants with adverse events (e.g., injury resulting from the program) will be advised to consult their physician to provide care as appropriate.

Effectiveness outcomes

The primary outcome, IBS symptoms, will be measured using the *IBS-Symptom Severity Scale (IBS-SSS).* The IBS-SSS is a five-question survey that asks the severity of abdominal pain, frequency of abdominal pain, severity of abdominal distention, dissatisfaction with bowel habits, and interference with QOL over the past 10 days. Scores on the IBS-SSS range from 0 to 500 with higher scores indicating more severe symptoms. Participants can be categorized as having mild (75-175), moderate (175-300), or severe (>300) IBS. Symptom reduction of at least 50 points is considered clinically meaningful.

Secondary outcomes (*and their measures*) include quality of life (*IBS-Quality of life*), anxiety (*Generalized Anxiety Disorder-7*), depression (*Patient Health Questionnaire-9*), stress (*Perceived Stress Scale*), COVID-19 stress (*COVID-19 Stress Scale*), fatigue (*Modified Fatigue Impact Scale-21*), somatic Symptoms (*Patient Health Questionnaire-15*), and self-compassion (*Self Compassion Scale-Short Form*) (Supplementary Table 1). Intention to practice yoga will also be assessed. The intervention and control groups will be assessed on effectiveness outcomes

at baseline, four, and eight weeks. The intervention group will complete measures of effectiveness outcomes six months after the intervention.

Sample size

We will recruit twenty-five participants per group. However, assuming 30% attrition rate, we will aim to recruit 33 participants per group. Symptom reduction of at least 50 points is considered clinically meaningful, however a group difference has been shown to represent a considerable self-reported improvement [21].We calculated the sample size using a mean difference of at least 83 points on the IBS-SSS (α=0.05, β=0.80, standard deviation of 103.8)[9].

Randomization, treatment allocation, and blinding

Study flow is shown in Figure 1. The study coordinator will obtain consent from participants who will then be enrolled in the study. Participants will be randomized after baseline assessment to either the yoga intervention or the advice-only control group. A statistician blinded to the randomization key will create a computer-generated REDCap randomized sequence to allocate participants based on gender (1:1:1 male:female:other) and depression (1:1 depression:no depression). Participants will be aware of the group to which they are allocated, however, the principal investigator and data analyst will remain blinded to the randomization process.

Data management

All quantitative data will be entered into a secure REDCap database at the University of Calgary. Effectiveness outcome measures, program satisfaction, attendance, and adherence will be entered by the participants. Recruitment, attrition, and safety will be recorded by the study coordinator who is not blinded to the randomization. After the study, data will be downloaded, and patient identifiers will be removed from the data file. Data will be stored in a password-

protected file on a University of Calgary password protected computer. The interviews will be transcribed, deidentified, and uploaded to the University of Calgary's secure SharePoint site. Only the research team will have access to the data.

Statistical analysis

Descriptive analysis will summarize participant characteristics and feasibility outcomes. Univariate analysis of variance (ANOVA) will examine baseline differences between groups for variables with continuous data. Chi-square tests will examine baseline differences between groups for categorical variables. Unadjusted ANOVA and adjusted analysis of covariance (ANCOVA) models will compare differences in scores from baseline and post-intervention data within and between groups using intent to treat and per protocol analysis. A logistic regression – model examining determinants of responders (a minimum improvement of at least 50 points on the IBS-SSS scale) versus non-responders will be developed to predict a response to the intervention. This model will consider practice in minutes, baseline depression, anxiety, and IBS symptom severity scores. An α of 0.05 will be the threshold for determining statistical significance. If the frequency of missing data is >5%, we will perform additional analyses using imputation methods. Analysis will be conducted using SPSS version 26.

Post-intervention interviews

Participants who were randomized to the intervention and did not withdraw from the study will be invited by email to participate in an interview. We aim to recruit men and women and have equal representation of those who benefited from the program (i.e., experienced improvements in their IBS symptom severity) as well as individuals who did not. We anticipate needing to interview between 10 and 15 participants to reach both code and meaning saturation [22] aiming for a maximum variation sample.

Semi-structured interviews will capture participants' experiences, program satisfaction, facilitators and barriers to participation, perceptions of social support and supervised learning, perceived impact on IBS symptoms and overall physical and mental health, and input on improving future programming (Table 2). Interviews will happen virtually using Microsoft Office Teams and be approximately 30 to 45 minutes in length. The study coordinator will interview the participants, take notes during the interview, and reflect following each interview. Interview recordings will be transcribed verbatim without identifying information. Data will be coded and analyzed in duplicate using NVivo 12. Thematic analysis inductively reveals patterns and themes providing an understanding of participant experiences, with the program and their perspectives on its impact. Thematic analysis is a method for systematically identifying, organizing, and offering insight into patterns of meaning (themes) across a data set [23]. This method makes sense of shared meanings and experiences that allows the researcher to identify what data is important to the research question [24].

Discussion

The MY-IBS study aims to determine the feasibility and effectiveness of an eight-week virtual yoga and meditation program combined with home-based practice for patients with IBS. Determining feasibility will be based on study recruitment, adherence, safety, and program satisfaction. Improved IBS symptom management (the primary outcome) will determine intervention effectiveness. Secondary outcomes include quality of life, stress, fatigue, depression, anxiety, COVID-19-related stress and anxiety, and self-compassion. These findings will inform potential predictors of responders versus non-responders. Predictors may be considered in clinical practice to target the IBS patients most likely to benefit from the yoga

intervention. Interview themes and patterns will refine and inform the development of future virtual yoga programming designed for IBS patients.

To our knowledge, there are no studies of virtual yoga and meditation in the IBS population. The findings from this study may have implications for the management of IBS. The virtual delivery of yoga represents an opportunity to increase access to effective management therapies for patients with IBS. The COVID-19 pandemic has called for the reorganization of health care including utilization of virtual care. Nearly 90% of care in the United States has been delivered virtually since the pandemic[25]. Due to the COVID-19 pandemic, there is increased psychological distress and gastrointestinal symptoms among individuals with IBS[26 27] compared to individuals without IBS[28]. The present study offers a unique opportunity to examine prospectively the feasibility and effectiveness of a yoga and meditation program delivered virtually to individuals living with IBS with the COVID-19 pandemic restrictions taken into consideration. Study findings may aid in developing interventions and services tailored to patients with IBS. New insight into outcomes will be beneficial for healthcare leaders in planning how to allocate existing resources to support these services and potentially lessen the burden of IBS on both the individual and the health care system.

Ethics and dissemination

Ethics

The study protocol, informed consent form, and other study documents were reviewed and approved by the University of Calgary's ethics board. All protocol modifications will be submitted for review and approval by the ethics board. The trial participants will be informed of any modifications, and re-consented by the study coordinator, if required. Further, the trial registry for this study will be updated.

Participation is voluntary and will not influence standard clinical care. All participants will provide informed written consent and have the right to withdraw from the study at any time. Pending consent from the participant, all data collected up to the time of withdrawal will be used in the final data analyses as advised by the CONSORT guidelines [29].

Dissemination

Our targeted knowledge users and audiences will include researchers, healthcare professionals and service providers, persons with lived experiences, community groups, and professional organizations (e.g., Canadian Association of Gastroenterology). Our goal will be to increase topic area knowledge among these groups and inform future research. Our strategies will include conference presentations, publication in a peer reviewed journal, social media campaigns, development of virtually delivered tools such as mobile applications to increase accessibility and affordability and educational material distributed through the Digestive Health Foundation, IMAGINE SPOR Chronic Disease Network, and Primary Care Networks across Alberta.

Table 1. Overview of the Upa Yoga program.

Program Component	Description	Rationale
Directional Movement of the Arms	This practice involves extending the arms in four directions (sideways, front, up and down) by rotating the wrists, while consciously focusing on the inhalation and exhalation of breath with each movement.	Studies show that fibromyalgia is common among patients living with IBS [30]. This could lead to pain of the muscles and joints, fatigue, and sleep concerns. The principle behind this practice is to lubricate the fluids in the joints, increase circulation and activate the energy nodes in these joints. Doing these practices everyday can relieve muscle and joint stiffness and reduce pain over time. This practice is recommended by the Isha Foundation to increase strengths and flexibility in preparation for Yoga Namaskar.
Neck Practices	There are five sets of neck practices, each stretching the neck and final one working on the shoulder area.	The main cause of neck pain is usually muscle tension. Perceived stress can increase muscle tension. These neck exercises help relieve stress that can aggravate IBS symptoms. This practice is recommended by the Isha Foundation to increase strengths and flexibility in preparation for Yoga Namaskar.
Yoga Namaskar	This practice involves a series of seven consecutive steps of upper body stretching and squatting, aligned with breath.	This practice activates the lumbar region of the spine and strengthens the spinal muscles[31].While Yoga Namaskar has not been specifically studied in patients with IBS, yoga squatting postures have been associated with significant decrease in depression among nine individuals with IBD [20] and anxiety in a randomized self as control study in 30 healthy subjects[32].
Alternate Nostril	The participant sits cross-legged with the spine comfortably erect and eyes closed. Closing the right nostril with the thumb,	Alternate nostril breathing is traditionally considered to alleviate mental unrest and

Breathing (Nadi Shuddhi)	inhaling and exhaling through the left nostril. This is repeated on the right nostril by closing the left nostril with the ring finger.	promote physical and mental balance.[33 34] It has been demonstrated to decrease perceived stress and improve autonomic function in a randomized control trial compared to control subjects in healthy male volunteers, and decreased state anxiety in a prospective study.[35 36]
Mantra Meditation (AUM chanting)	The participants sit cross-legged, and with eyes closed, uttering each of these 3 sounds 7 times. The important aspect to this utterance is the awareness of the reverberations each of the sounds produces in the corresponding parts of the body: a - below the navel, o - mid-point of the chest, m - pit of the throat.	This mantra is thought to facilitate energy flow, and through vibratory mechanisms, creates peace and harmony leading to increased mental alertness and may improve symptoms of depression.[37 38]
Breath watching	The participants sit cross-legged with eyes closed and hold a hand gesture called the Yoga Mudra (the tips of the thumb and index finger come together forming a circle). They are instructed to maintain a gentle focus on the mid-point between both eyebrows (at the level of the pineal gland), while being conscious of the gentle movement of breath happening in their body.	Breathing in a focused manner can be used as a tool to promote positive changes to the mind, body and emotions.[39] Significant reduction in the level of state anxiety was found in a group of healthy male volunteers when they practiced breath awareness.[16]

Table 2. Semi-structured interview questions and probes.

1. **What have you done in the past to manage your IBS?**
    a. Have you tried yoga or mediation?
    b. Have you tried exercise?

2. **I would like to start by asking you what you were hoping for or expecting from the program?**
    a. Why did you join this study?
    b. Did anyone influence your decision to join?
    c. Did that meet your expectations?

3. **Next, I would like to discuss your overall experience in the MY-IBS yoga program in which you participated. Could you describe for me what participating in this program was like for you?**
    a. What did you like most about it?
    b. What didn't you like?
    c. Did this change over the course of the program?

    Sub-questions: *yoga facilitator/supervision, the timing of sessions/scheduling, length of sessions, attending with other members, online experience versus in-person, social support/other participants.*
    d. What was that like?
    e. What stood out for you?
    f. What emotions were you aware of at the time?
    g. What else do you remember about that experience?

4. **How has participating in this program affected how you manage or live with your IBS?**

    Sub-questions: *change in IBS symptoms; physical health, fatigue; mental health - stress, anxiety, depression; feeling better about myself; ability to live with my IBS.*
    a. Tell me more about that.
    b. Can you give me an example of what you mean?
    c. How has that affected you?

5. **What, if anything, has helped you to do your practices at home?**

    Sub-questions*: social support, family support, convenience*
    a. Tell me more about that.
    b. Can you give me an example of what you mean?
    c. How has that affected you?

6. **What challenges did you have, if any, doing your practices at home?**

    Sub-questions*: family, supervision/safety, schedule/time*
    a. Are you satisfied with how you did?
    b. Tell me more about that.

c. Can you give me an example of what you mean?
d. How has that affected you?

7. **What, if anything, has helped you to attend the weekly online class?**
   Sub-questions: *social support, family support, HCP support, yoga facilitator, supervision/safety, online classes, schedule/length*
   a. Tell me more about that.
   b. Can you give me an example of what you mean?
   c. How has that affected you?

8. **What challenges did you have, if any, to attend the weekly online class?**
   Sub-questions: *social support, family, yoga facilitator, supervision/safety, online classes, schedule, technical difficulties*
   a. Are you satisfied with how you did?
   b. Tell me more about that.
   c. Can you give me an example of what you mean?
   d. How has that affected you?

9. **We are interested in any ideas you have about how we might make this program better. What could we do differently?**
   Sub-questions: *content, timing, facilitator, videos, website, delivery, other supports*
   a. Would you explain that further?
   b. Can you give me an example of what you mean?

10. **Based on your experience with yoga, would you incorporate yoga to help manage your IBS? If so, how?**

11. **Before we conclude, is this anything else you would like to say about your experience with this program, that we haven't had a chance to talk about yet?**

Strengths and limitations of this study:

- Mixed methods study composed of a trial and interviews
- First virtual yoga intervention in Irritable Bowel Syndrome
- Canada-wide recruitment
- Self-reported outcome measures
- Lack of data capture on frequency of yoga practice in the control group

Authors' contributions: State how each author was involved in writing the protocol.

AD is involved in all aspects of protocol design and lead author of the manuscript. DM, JKV, YN, VR, and GM assisted with design of the protocol respective to their expertise. DM and GM assisted with the qualitative aspects of the protocol. JKV lead the statistical aspects of the protocol. YN provided their clinical expertise and patient recruitment thought the clinic. VR provided their expertise in yoga therapy. MR is the senior author on the protocol and has guided the work of this research to support AD with their training. All authors reviewed the manuscript for study design and provided critical insight into manuscript content and approved the final version for submission.

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Competing interests statement: None declared.

Data availability: Deidentified participant data will be made available upon reasonable request from the study principal investigator.

Figure 1. Participant flowchart based on the CONSORT guidelines.

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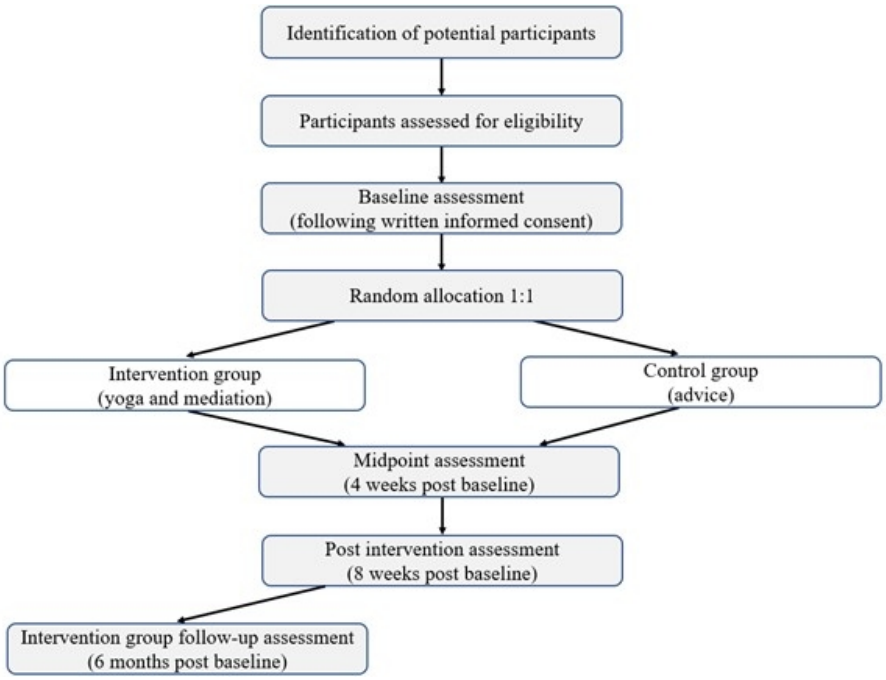

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Supplementary Table 1. Effectiveness outcomes measures.

Measure	Description	Scoring	Assessments		
Primary outcome			**Baseline**	**4 weeks**	**8 weeks**
IBS-Symptom Severity Scale (IBS-SSS)	The IBS-SSS is a five-question survey that asks the severity of abdominal pain, frequency of abdominal pain, severity of abdominal distention, dissatisfaction with bowel habits, and interference with QOL over the past 10 days. Subjects respond to each question on a 100-point visual analogue scale[22]. The IBS-SSS scale is the most frequently used severity measure for evaluating IBS severity and is commonly used as an outcome measure in clinical trials because it is highly responsive to change with treatment[22].	Scores on the IBS-SSS range from 0 to 500 with higher scores indicating more severe symptoms. Participants can be categorized as having mild (75-175), moderate (175-300), or severe (>300) IBS. Symptom reduction of at least 50 points is considered clinically meaningful; however, the primary endpoint will be the proportion of participants in each group who demonstrate a symptom reduction of 83 points or more, based on the variables used in the sample size calculation[22].	✓	✓	✓
Secondary outcomes					
IBS-Quality of life (IBS-QOL)	The IBS-QOL is a 34-item questionnaire that assesses the degree to which IBS interfered with QOL over the past 30 days. Each item is rated on a 1 to 5 Likert scale, with higher values indicating a lower QOL[25]. The IBS-QOL is currently the most validated and highly responsive self-reported QOL measure specific to IBS that can be used to assess the impact of IBS and its treatment[25].	The individual responses to the 34 items are summed and averaged for a total score and then transformed to a 0-100 scale for ease of interpretation with higher scores indicating better IBS specific QOL[25]. An increment of at least 14 points on the IBS-QOL scale from baseline will demonstrate efficacy.	✓	✓	✓
Generalized Anxiety Disorder (GAD-7)	GAD-7 is seven items, score from 0 (not all at) to 3 (nearly every day), providing a severity score between 0-21. Scores of 5, 10, and 15 represent cut points for	A 5-point change on the GAD-7 is considered clinically significant.	✓	✓	✓

	mild, moderate, and severe anxiety. The GAD-7 also is effective at identifying the presence of other anxiety disorders including panic disorder, social anxiety disorder, and post-traumatic stress disorder[26].				
Physical Health Questionnaire (PHQ-9)	The PHQ-9 is a 9-item survey with each item scored from 0 (not at all) to 3 (nearly every day) totalling from 0 to 27 points. Scores of 5, 10, 15, and 20 represent cut points for mild, moderate, moderately severe and severe depression. The PHQ assesses major depressive disorder, panic disorder, and anxiety disorder[27].	A 5-point change is considered clinically significant.	✓	✓	✓
Perceived Stress Scale (PSS)	The PSS is a 14-item survey that measures perceived stress, or the degree to which situations in one's life are appraised as stressful, on a four-point scale (0=never, 4=very often) over the last 30 days. The PSS is the most widely used psychological instrument for measuring the perception of stress[29].	An 11-point change is considered clinically significant [28].	✓	✓	✓
COVID-19 Stress Scales (CSS)	COVID-19 related stress and anxiety will be measured using the 36-item CSS survey on five scales: (1) COVID danger and contamination fears, (2) COVID fears about economic consequences, (3) COVID xenophobia, (4) COVID compulsive checking and reassurance seeking, and (5) COVID traumatic stress symptoms[33].	Not reported.	✓	✓	✓
Modified Fatigue Impact Scale-21.	This is a self-reported questionnaire consisting of 21 statements that reflect the perceived impact of fatigue on cognitive, physical, and psychosocial	A 16-point change is considered clinically significant[30].	✓	✓	✓

	functioning. Participants are asked to rate the extent to which fatigue has caused problems for them during the last four weeks. Each item is rated on a 5-point scale reflecting how often the person is limited in activities by fatigue, ranging from 0 (never) to 4 (almost always)[31].				
Patient Health Questionnaire-15 (PHQ-15)	The PHQ-15 measures the severity of 15 somatic symptoms (e.g., fatigue, energy, sleeping trouble, and pain) during the past 4 weeks for a score of 0 to 30. Items can be scored as 0 (not at all), 1 (bothered a little), or 2 (bothered a lot). PHQ-15 scores of 5, 10, and 15 represent cut points for low, medium, and high somatic symptom severity, respectively[32].	A 5-point change on the PHQ-15 is considered clinically significant.	✓	✓	✓
Self-Compassion Scale – Short Form (SCS-SF)	Participants will be asked to complete a 12-item self-reported scale measuring their self-compassion, including self-kindness, self-judgement, humanity, isolation, and mindfulness subscales. To encourage their practice and feelings of self-compassion, participants will receive self-compassion messages weekly by email.	Subscale scores are computed by calculating the mean of subscale items responses. Participants will indicate how often they behave in the stated manner, using a scale from 1 (almost never) to 5 (almost always) for a total of 60 points with lower scores indicating more self-compassion[34].	✓	✓	✓

SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description
Administrative information		
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym **(PG 1)**
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry **(PG 3)**
	2b	All items from the World Health Organization Trial Registration Data Set **(N/A)**
Protocol version	3	Date and version identifier **(N/A)**
Funding	4	Sources and types of financial, material, and other support **(PG 20)**
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors **(PG 1, 2, 20)**
	5b	Name and contact information for the trial sponsor **(N/A)**
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities **(N/A)**
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee) **(N/A)**
Introduction		
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention **(PG 4, 5)**
	6b	Explanation for choice of comparators **(PG 7, 8)**
Objectives	7	Specific objectives or hypotheses **(PG 5)**
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory) **(PG 5)**

Methods: Participants, interventions, and outcomes

Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained **(PG 6)**
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists) **(PG 6)**
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered **(PG 7, 8)**
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease) **(PG 7)**
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests) **(PG 7, 8)**
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial **(N/A)**
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended **(PG 8, 9, 10)**
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure) **(PG 7, 8, 9. Please see supplementary material Table 1.)**
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations **(PG 10)**
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size **(PG 6, 7)**

Methods: Assignment of interventions (for controlled trials)

Allocation:

Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions **(PG 11)**
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned **(PG 11)**
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions **(PG 11)**
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how **(PG 11)**
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial **(N/A)**
Methods: Data collection, management, and analysis		
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol **(PG 8, 9. Please see supplementary material Table 1.)**
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols **(Please see supplementary material Table 1.)**
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol **(PG 11)**
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol **(PG 11, 12)**
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses) **(PG 11, 12)**

	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation) **(PG 12)**
Methods: Monitoring		
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed **(N/A)**
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial **(N/A)**
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct **(N/A)**
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor **(N/A)**
Ethics and dissemination		
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval **(PG 14)**
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators) **(PG 14)**
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) **(PG 14)**
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable **(N/A)**
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial **(PG 11)**
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site **(PG 20)**
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators **(PG 20)**

Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation **(Please see the study consent form.)**
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions **(pg 14, 15)**
	31b	Authorship eligibility guidelines and any intended use of professional writers **(N/A)**
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code **(N/A)**
Appendices		
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates **(Please see the study consent form.)**
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable **(N/A)**

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

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Meditation and Yoga for Irritable Bowel Syndrome: Study Protocol for a Randomized Clinical Trial (MY-IBS Study)

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Meditation and Yoga for Irritable Bowel Syndrome:

Study Protocol for a Randomized Clinical Trial (MY-IBS Study)

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MEDITATION AND YOGA FOR IBS

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MEDITATION AND YOGA FOR IBS

Abstract

Introduction: When delivered in person, yoga has been shown to be effective in managing Irritable Bowel Syndrome (IBS) symptoms. Research is needed to test the feasibility and effectiveness of yoga as a therapeutic option when delivered virtually. The primary aim of the Mind and Yoga for IBS (MY-IBS) randomized controlled trial is to determine the effects of an eight-week virtual meditation and yoga intervention on IBS symptom severity compared with an advice-only active control group.

Methods and analysis: Adults diagnosed with IBS will be randomized to receive either a Upa yoga intervention or an advice-only control group. The intervention will consist of weekly online classes for eight weeks delivered by a facilitator using Microsoft Office Teams and daily home practice. Feasibility will be evaluated by examining recruitment and attrition rates, adherence, participant satisfaction with the program, and safety. The primary outcome is IBS symptom severity, and key secondary outcomes include (but not limited to) quality of life, anxiety and depression symptoms, COVID-19 related stress and anxiety, and fatigue. Outcomes will be assessed at baseline, four weeks, and eight weeks. An embedded design experimental model sub-study will be conducted post-intervention using qualitative research methods to identify participants' experiences in the yoga program.

Ethics and dissemination: This study has been approved by the Conjoint Health Research Ethics Board (REB ID 20-0084). Findings will be disseminated through peer-reviewed publication, conference presentation, and social media.

Trial registration number: NCT04302623

Strengths and limitations:

- Mixed methods study composed of a RCT and interviews
- First virtual yoga interventions in irritable bowel syndrome
- Canada-wide recruitment
- Self-reported outcome measures
- Lack of data capture on the frequency of yoga practice in the control group

Introduction

Stress is a physical, mental, or emotional response that causes tension in the mind or the body[1]. Altered stress response from psychological and physiological mechanisms may contribute to altered brain-gut signaling patterns and IBS symptoms. Psychological stressors, such as depression and anxiety, may influence gut function (e.g., reduced motility). Physiological stressors (e.g., infection) in the gut may affect the brain[2]. Therapies focusing on mind-body interactions and stress reduction may be adjunctive treatments for IBS. Stress management techniques that include both mind and body interventions such as yoga[3] have been effective in improving IBS symptom severity and mental health outcomes[3 4]. Mind-body interventions may modulate the brain-gut axis directly by reducing sympathetic activity and increasing parasympathetic activity and the hypothalamus-pituitary-adrenal axis[5].

Yoga is a traditional *mind-body-breath* discipline that includes a triad of postures, structured breathing, and meditation[6]. Our recent review[7] identified four randomized controlled trials that examined traditional yoga practice as therapy for IBS patients[8-11]. These trials demonstrated yoga was more effective compared to pharmacological treatment and equally effective as dietary interventions or moderate-intensity walking. Physical and mental health improvements included IBS symptom severity, gastric motility, and depression.

Research is needed to determine the feasibility and effectiveness of virtual yoga programming as a therapeutic option for patients with IBS. The rationale for virtually delivered interventions to manage IBS is increasing due to rising demand, limited healthcare resources, and cost-effectiveness[12 13]. A recent review found virtual care tools may be effective in managing disease activity and improving outcomes in patients with digestive diseases[14]. This review also highlighted the high acceptability and satisfaction with virtual care among patients with IBS[15-19].

The primary objective of the MY-IBS (Meditation and Yoga for Irritable Bowel Syndrome) study is to explore the feasibility and effectiveness of a virtual yoga program for patients with IBS. MY-IBS is a mixed-methods study including a randomized controlled trial and semi-structured interviews. The primary aim of this randomized controlled trial is to determine the effects of an eight-week virtual yoga intervention on IBS symptom severity, measured with the IBS Symptoms Severity Scale, compared to an advice-only control group. Secondary aims are to determine whether a) a yoga program delivered virtually is feasible for adults with IBS, b) improves health outcomes including quality of life, stress, and fatigue, and c) improves mental health outcomes including depression and anxiety symptoms. An embedded design experimental model qualitative sub-study using semi-structured interviews will explore and describe participants' experiences in the yoga program, and its impact. We hypothesize that the program will be feasible and effective in improving outcomes in the intervention group compared to the control group.

Methods and Analysis

Study design overview

The quantitative study is a superiority randomized non-blinded two-group controlled trial. The qualitative study will use semi-structured interviews and thematic analysis to explore and describe intervention participant experiences and views of the yoga program.

Patient involvement

Patients with lived experience were involved in the conduct of this study. During the development stage, patient partners were invited to participate in a series of discussions with the research team to define the study research question, study design, choice of outcome measures, and methods of recruitment. Following the completion of the trial, the patient partners will be involved in the dissemination of this research.

Sample and selection

The MY-IBS stud will be conducted at the University of Calgary in Alberta, Canada starting March 2021 and ending early 2022. To be eligible in this study, participants must be diagnosed with IBS based on Rome IV criteria by a health care professional (e.g., physician, nurse, dietician), be 18-70 years old, have an adequate understanding of English, have an ability to provide written informed consent, score at least 75 out 500 points on the IBS Symptoms Severity Scale indicating mild IBS symptoms, and be on stable doses of medications for IBS (including anti-depressants) without major changes to diet or physical activity levels for at least eight weeks prior to starting the intervention. Individuals across Canada are eligible to participate. Exclusion criteria include a major physical impairment that would prevent the individual from doing yoga determined by either the patient or the study coordinator, and diagnosis of any major cognitive, psychological, or psychiatric disorder (e.g., major depression, schizophrenia) as identified by the treating physician or healthcare practitioner or screened by the study coordinator using the Patient Health Questionnaire-9.

Participants will be identified through (a) gastroenterology clinics across Calgary, Alberta; (b) gastroenterologists across Canada who indicated interest in this study for their IBS patients in a previous survey conducted by our team (not published); (c) participants from the previous survey who indicated interest in this study and have given consent to be contacted; (d)

through social media; (e) self-referrals through the study website and the University of Calgary participate in research portal; (f) Canadian Association of Gastroenterologists monthly newsletter; and (g) participants with IBS who are enrolled in the IMAGINE (Inflammation, Microbiome and Alimentation Gastro-intestinal and Neuropsychiatric Effects) cohort study at the University of Calgary and have given their consent to be contacted for future studies.

Participant screening will use the Patient Health Questionnaire-9 (PHQ-9). Individuals who score 20 points or higher on the PHQ-9 indicating severe depression will not be eligible to participate. Reasons for exclusion are lack of compliance in interventional studies among these individuals, potential heterogeneity in the small sample size of participants, and skewed results if patients seek treatment for their depression during the trial.

Interventions

Yoga intervention group

Before their first class, the intervention group will receive an introductory video. The video will consist of information on IBS, information on the style of yoga they will be learning, and rationale for yoga as a treatment for IBS. The intervention will be delivered online by a certified yoga facilitator in class sizes of less than ten participants using the Microsoft Office Teams platform. Classes will be held once per week for the eight-week duration. The first session will be approximately 90 minutes and subsequent sessions up to 60 minutes. The introductory session will include the class setup, introductions, teaching poses, corrections, and a question and answers period. The yoga facilitator will provide participants with modifications for common challenges to support best practices and ensure safety. Subsequent classes will include a review from the previous week, a question and answer period, individual corrections and modifications, and introduce new practices. In addition to the online class component, study

staff will ask participants to practice the yoga program at home every day. They will also have access to the yoga videos, written program instructions, and frequently answered questions accessible through the study website to help support their home practice (https://cumming.ucalgary.ca/research/ascend/resources/patient-resources/my-ibs).

Upa Yoga, developed by the Isha Foundation of Inner Sciences (https://isha.sadhguru.org/us/en), will be promoted. Upa Yoga maintains the ancient principles of Hatha Yoga and will be delivered by a certified yoga facilitator from the Isha Foundation. The Upa Yoga program will consist of (a) directional movements and neck rotations, (b) hatha yoga-based Yoga Namaskar, (c) breathing practices or alternate nostril breathing, (d) mantra meditation consisting of AUM chanting (OM), and e) breath watching. Table 1 shows a description of the program and rationale. Our published prospective study examining the effectiveness of Upa Yoga in patients with Inflammatory Bowel Disease[20] shows improvements in mental health scores after an eight-week yoga program.

Advice-only control group

Control participants will receive a video including general education on IBS, the mind-gut connection in IBS, and the role of mind-body therapies in the management of IBS. These participants will also receive a list of IBS-related resources from the Canadian Digestive Health Foundation, a link to an IBS patient support group (www.ibspatient.org), and information about physical activity guidelines from the World Health Organization. Control participants will be eligible to attend a two-week yoga program and receive the yoga videos eight weeks from the time of enrolment. Data on these participants will not be collected as this participation option is for participants who desire to receive the yoga sessions outside of the study.

Outcome measures

Feasibility outcomes

Recruitment, attendance, and attrition rates. Recruitment will be calculated by the percentage of participants who complete the eligibility and enrollment phases of the study. Attrition will be calculated by the percentage of participants who complete all study measures at baseline and eight weeks. A feasible intervention will be defined as class attendance of at least 75 percent (i.e., attendance in six out of eight classes)[9] and attrition rate of less than 30 percent.

Adherence. Adherence will be defined as practicing daily yoga for at least 80% of days for eight weeks (or 45 out of 56 days minimum). Each week a practice log will be provided to monitor frequency and length of yoga. The yoga facilitator will take attendance during each online class. To increase program adherence, the study coordinator will email intervention participants weekly. Six months following the completion of the intervention, participants will be asked to report the average frequency (i.e., days per month) and duration (i.e., minutes) of their yoga practices over the last seven days to evaluate long-term maintenance.

Program satisfaction. Intervention participants will complete a survey regarding overall satisfaction with their program, including satisfaction with videos and online class instruction. Videos and online classes will be deemed acceptable if at least 70% of participants are at least satisfied (i.e., rank classes as either good, great, or excellent). Participants will also indicate whether they would recommend the program to others on a scale from 1 (strongly disagree) to 7 (strongly agree) and provide feedback on how the program could be improved.

Assessment of harms. The study coordinator will screen potential participants and exclude those with any physical problems that may limit participation with yoga postures. Participants will be asked to report any adverse events experienced during the study period.

Participants with adverse events (e.g., injury resulting from the program) will be advised to consult their physician to provide care as appropriate.

Effectiveness outcomes

The primary outcome, IBS symptoms, will be measured using the *IBS-Symptom Severity Scale (IBS-SSS).* The IBS-SSS is a five-question survey that asks the severity of abdominal pain, frequency of abdominal pain, severity of abdominal distention, dissatisfaction with bowel habits, and interference with QOL over the past 10 days. Scores on the IBS-SSS range from 0 to 500 with higher scores indicating more severe symptoms. Participants can be categorized as having mild (75-175), moderate (175-300), or severe (>300) IBS. Symptom reduction of at least 50 points is considered clinically meaningful.

Secondary outcomes (*and their measures*) include quality of life (*IBS-Quality of life*), anxiety (*Generalized Anxiety Disorder-7*), depression (*Patient Health Questionnaire-9*), stress (*Perceived Stress Scale*), COVID-19 stress (*COVID-19 Stress Scale*), fatigue (*Modified Fatigue Impact Scale-21*), somatic Symptoms (*Patient Health Questionnaire-15*), and self-compassion (*Self Compassion Scale-Short Form*) (Supplementary Table 1). Intention to practice yoga will also be assessed. The intervention and control groups will be assessed on effectiveness outcomes

at baseline, four, and eight weeks. The intervention group will complete measures of effectiveness outcomes six months after the intervention.

Sample size

We will recruit twenty-five participants per group. However, assuming 30% attrition rate, we will aim to recruit 33 participants per group. Symptom reduction of at least 50 points is considered clinically meaningful, however a group difference has been shown to represent a considerable self-reported improvement [21].We calculated the sample size using a mean difference of at least 83 points on the IBS-SSS (α=0.05, β=0.80, standard deviation of 103.8)[9].

Randomization, treatment allocation, and blinding

Study flow is shown in Figure 1. The study coordinator will obtain consent from participants who will then be enrolled in the study. Participants will be randomized after baseline assessment to either the yoga intervention or the advice-only control group. A statistician blinded to the randomization key will create a computer-generated REDCap randomized sequence to allocate participants based on gender (1:1:1 male:female:other) and depression (1:1 depression:no depression). Participants will be aware of the group to which they are allocated, however, the principal investigator and data analyst will remain blinded to the randomization process.

Data management

All quantitative data will be entered into a secure REDCap database at the University of Calgary. Effectiveness outcome measures, program satisfaction, attendance, and adherence will be entered by the participants. Recruitment, attrition, and safety will be recorded by the study coordinator who is not blinded to the randomization. After the study, data will be downloaded, and patient identifiers will be removed from the data file. Data will be stored in a password-

protected file on a University of Calgary password protected computer. The interviews will be transcribed, deidentified, and uploaded to the University of Calgary's secure SharePoint site. Only the research team will have access to the data.

Statistical analysis

Descriptive analysis will summarize participant characteristics and feasibility outcomes. Univariate analysis of variance (ANOVA) will examine baseline differences between groups for variables with continuous data. Chi-square tests will examine baseline differences between groups for categorical variables. Unadjusted ANOVA and adjusted analysis of covariance (ANCOVA) models will compare differences in scores from baseline and post-intervention data within and between groups using intent to treat and per protocol analysis. A logistic regression – model examining determinants of responders (a minimum improvement of at least 50 points on the IBS-SSS scale) versus non-responders will be developed to predict a response to the intervention. This model will consider practice in minutes, baseline depression, anxiety, and IBS symptom severity scores. An α of 0.05 will be the threshold for determining statistical significance. If the frequency of missing data is >5%, we will perform additional analyses using imputation methods. Analysis will be conducted using SPSS version 26.

Post-intervention interviews

Participants who were randomized to the intervention and did not withdraw from the study will be invited by email to participate in an interview. We aim to recruit men and women and have equal representation of those who benefited from the program (i.e., experienced improvements in their IBS symptom severity) as well as individuals who did not. We anticipate needing to interview between 10 and 15 participants to reach both code and meaning saturation [22] aiming for a maximum variation sample.

Semi-structured interviews will capture participants' experiences, program satisfaction, facilitators and barriers to participation, perceptions of social support and supervised learning, perceived impact on IBS symptoms and overall physical and mental health, and input on improving future programming (Table 2). Interviews will happen virtually using Microsoft Office Teams and be approximately 30 to 45 minutes in length. The study coordinator will interview the participants, take notes during the interview, and reflect following each interview. Interview recordings will be transcribed verbatim without identifying information. Data will be coded and analyzed in duplicate using NVivo 12. Thematic analysis inductively reveals patterns and themes providing an understanding of participant experiences, with the program and their perspectives on its impact. Thematic analysis is a method for systematically identifying, organizing, and offering insight into patterns of meaning (themes) across a data set [23]. This method makes sense of shared meanings and experiences that allows the researcher to identify what data is important to the research question [24].

Discussion

The MY-IBS study aims to determine the feasibility and effectiveness of an eight-week virtual yoga and meditation program combined with home-based practice for patients with IBS. Determining feasibility will be based on study recruitment, adherence, safety, and program satisfaction. Improved IBS symptom management (the primary outcome) will determine intervention effectiveness. Secondary outcomes include quality of life, stress, fatigue, depression, anxiety, COVID-19-related stress and anxiety, and self-compassion. These findings will inform potential predictors of responders versus non-responders. Predictors may be considered in clinical practice to target the IBS patients most likely to benefit from the yoga

intervention. Interview themes and patterns will refine and inform the development of future virtual yoga programming designed for IBS patients.

To our knowledge, there are no studies of virtual yoga and meditation in the IBS population. The findings from this study may have implications for the management of IBS. The virtual delivery of yoga represents an opportunity to increase access to effective management therapies for patients with IBS. The COVID-19 pandemic has called for the reorganization of health care including utilization of virtual care. Nearly 90% of care in the United States has been delivered virtually since the pandemic[25]. Due to the COVID-19 pandemic, there is increased psychological distress and gastrointestinal symptoms among individuals with IBS[26 27] compared to individuals without IBS[28]. The present study offers a unique opportunity to examine prospectively the feasibility and effectiveness of a yoga and meditation program delivered virtually to individuals living with IBS with the COVID-19 pandemic restrictions taken into consideration. Study findings may aid in developing interventions and services tailored to patients with IBS. New insight into outcomes will be beneficial for healthcare leaders in planning how to allocate existing resources to support these services and potentially lessen the burden of IBS on both the individual and the health care system.

Ethics and dissemination

Ethics

The study protocol, informed consent form, and other study documents were reviewed and approved by the University of Calgary's ethics board. All protocol modifications will be submitted for review and approval by the ethics board. The trial participants will be informed of any modifications, and re-consented by the study coordinator, if required. Further, the trial registry for this study will be updated.

Participation is voluntary and will not influence standard clinical care. All participants will provide informed written consent and have the right to withdraw from the study at any time. Pending consent from the participant, all data collected up to the time of withdrawal will be used in the final data analyses as advised by the CONSORT guidelines [29].

Dissemination

Our targeted knowledge users and audiences will include researchers, healthcare professionals and service providers, persons with lived experiences, community groups, and professional organizations (e.g., Canadian Association of Gastroenterology). Our goal will be to increase topic area knowledge among these groups and inform future research. Our strategies will include conference presentations, publication in a peer reviewed journal, social media campaigns, development of virtually delivered tools such as mobile applications to increase accessibility and affordability and educational material distributed through the Digestive Health Foundation, IMAGINE SPOR Chronic Disease Network, and Primary Care Networks across Alberta.

Table 1. Overview of the Upa Yoga program.

Program Component	Description	Rationale
Directional Movement of the Arms	This practice involves extending the arms in four directions (sideways, front, up and down) by rotating the wrists, while consciously focusing on the inhalation and exhalation of breath with each movement.	Studies show that fibromyalgia is common among patients living with IBS [30]. This could lead to pain of the muscles and joints, fatigue, and sleep concerns. The principle behind this practice is to lubricate the fluids in the joints, increase circulation and activate the energy nodes in these joints. Doing these practices everyday can relieve muscle and joint stiffness and reduce pain over time. This practice is recommended by the Isha Foundation to increase strengths and flexibility in preparation for Yoga Namaskar.
Neck Practices	There are five sets of neck practices, each stretching the neck and final one working on the shoulder area.	The main cause of neck pain is usually muscle tension. Perceived stress can increase muscle tension. These neck exercises help relieve stress that can aggravate IBS symptoms. This practice is recommended by the Isha Foundation to increase strengths and flexibility in preparation for Yoga Namaskar.
Yoga Namaskar	This practice involves a series of seven consecutive steps of upper body stretching and squatting, aligned with breath.	This practice activates the lumbar region of the spine and strengthens the spinal muscles[31].While Yoga Namaskar has not been specifically studied in patients with IBS, yoga squatting postures have been associated with significant decrease in depression among nine individuals with IBD [20] and anxiety in a randomized self as control study in 30 healthy subjects[32].
Alternate Nostril	The participant sits cross-legged with the spine comfortably erect and eyes closed. Closing the right nostril with the thumb,	Alternate nostril breathing is traditionally considered to alleviate mental unrest and

Breathing (Nadi Shuddhi)	inhaling and exhaling through the left nostril. This is repeated on the right nostril by closing the left nostril with the ring finger.	promote physical and mental balance.[33 34] It has been demonstrated to decrease perceived stress and improve autonomic function in a randomized control trial compared to control subjects in healthy male volunteers, and decreased state anxiety in a prospective study.[35 36]
Mantra Meditation (AUM chanting)	The participants sit cross-legged, and with eyes closed, uttering each of these 3 sounds 7 times. The important aspect to this utterance is the awareness of the reverberations each of the sounds produces in the corresponding parts of the body: a - below the navel, o - mid-point of the chest, m - pit of the throat.	This mantra is thought to facilitate energy flow, and through vibratory mechanisms, creates peace and harmony leading to increased mental alertness and may improve symptoms of depression.[37 38]
Breath watching	The participants sit cross-legged with eyes closed and hold a hand gesture called the Yoga Mudra (the tips of the thumb and index finger come together forming a circle). They are instructed to maintain a gentle focus on the mid-point between both eyebrows (at the level of the pineal gland), while being conscious of the gentle movement of breath happening in their body.	Breathing in a focused manner can be used as a tool to promote positive changes to the mind, body and emotions.[39] Significant reduction in the level of state anxiety was found in a group of healthy male volunteers when they practiced breath awareness.[16]

Table 2. Semi-structured interview questions and probes.

1. **What have you done in the past to manage your IBS?**
    a. Have you tried yoga or mediation?
    b. Have you tried exercise?

2. **I would like to start by asking you what you were hoping for or expecting from the program?**
    a. Why did you join this study?
    b. Did anyone influence your decision to join?
    c. Did that meet your expectations?

3. **Next, I would like to discuss your overall experience in the MY-IBS yoga program in which you participated. Could you describe for me what participating in this program was like for you?**
    a. What did you like most about it?
    b. What didn't you like?
    c. Did this change over the course of the program?

    Sub-questions: *yoga facilitator/supervision, the timing of sessions/scheduling, length of sessions, attending with other members, online experience versus in-person, social support/other participants.*
    d. What was that like?
    e. What stood out for you?
    f. What emotions were you aware of at the time?
    g. What else do you remember about that experience?

4. **How has participating in this program affected how you manage or live with your IBS?**

    Sub-questions: *change in IBS symptoms; physical health, fatigue; mental health - stress, anxiety, depression; feeling better about myself; ability to live with my IBS.*
    a. Tell me more about that.
    b. Can you give me an example of what you mean?
    c. How has that affected you?

5. **What, if anything, has helped you to do your practices at home?**

    Sub-questions*: social support, family support, convenience*
    a. Tell me more about that.
    b. Can you give me an example of what you mean?
    c. How has that affected you?

6. **What challenges did you have, if any, doing your practices at home?**

    Sub-questions*: family, supervision/safety, schedule/time*
    a. Are you satisfied with how you did?
    b. Tell me more about that.

c. Can you give me an example of what you mean?
d. How has that affected you?

7. **What, if anything, has helped you to attend the weekly online class?**
   Sub-questions: *social support, family support, HCP support, yoga facilitator, supervision/safety, online classes, schedule/length*
   a. Tell me more about that.
   b. Can you give me an example of what you mean?
   c. How has that affected you?

8. **What challenges did you have, if any, to attend the weekly online class?**
   Sub-questions: *social support, family, yoga facilitator, supervision/safety, online classes, schedule, technical difficulties*
   a. Are you satisfied with how you did?
   b. Tell me more about that.
   c. Can you give me an example of what you mean?
   d. How has that affected you?

9. **We are interested in any ideas you have about how we might make this program better. What could we do differently?**
   Sub-questions: *content, timing, facilitator, videos, website, delivery, other supports*
   a. Would you explain that further?
   b. Can you give me an example of what you mean?

10. **Based on your experience with yoga, would you incorporate yoga to help manage your IBS? If so, how?**

11. **Before we conclude, is this anything else you would like to say about your experience with this program, that we haven't had a chance to talk about yet?**

Strengths and limitations of this study:

- Mixed methods study composed of a trial and interviews
- First virtual yoga intervention in Irritable Bowel Syndrome
- Canada-wide recruitment
- Self-reported outcome measures
- Lack of data capture on frequency of yoga practice in the control group

Authors' contributions: State how each author was involved in writing the protocol.

AD is involved in all aspects of protocol design and lead author of the manuscript. DM, JKV, YN, VR, and GM assisted with design of the protocol respective to their expertise. DM and GM assisted with the qualitative aspects of the protocol. JKV lead the statistical aspects of the protocol. YN provided their clinical expertise and patient recruitment thought the clinic. VR provided their expertise in yoga therapy. MR is the senior author on the protocol and has guided the work of this research to support AD with their training. All authors reviewed the manuscript for study design and provided critical insight into manuscript content and approved the final version for submission.

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Competing interests statement: None declared.

Data availability: Deidentified participant data will be made available upon reasonable request from the study principal investigator.

Figure 1. Participant flowchart based on the CONSORT guidelines.

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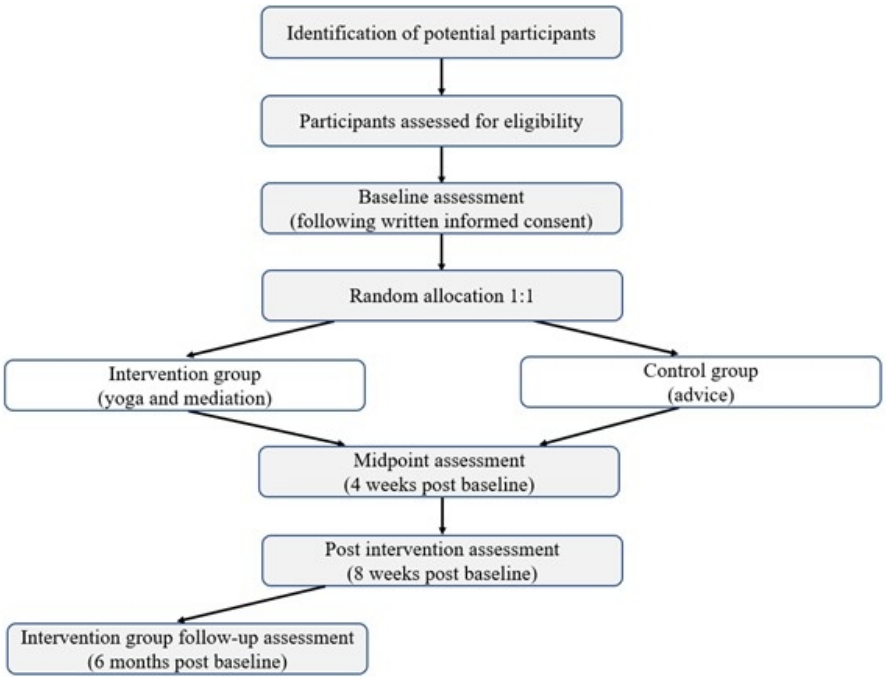

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Supplementary Table 1. Effectiveness outcomes measures.

Measure	Description	Scoring	Assessments		
Primary outcome			**Baseline**	**4 weeks**	**8 weeks**
IBS-Symptom Severity Scale (IBS-SSS)	The IBS-SSS is a five-question survey that asks the severity of abdominal pain, frequency of abdominal pain, severity of abdominal distention, dissatisfaction with bowel habits, and interference with QOL over the past 10 days. Subjects respond to each question on a 100-point visual analogue scale[22]. The IBS-SSS scale is the most frequently used severity measure for evaluating IBS severity and is commonly used as an outcome measure in clinical trials because it is highly responsive to change with treatment[22].	Scores on the IBS-SSS range from 0 to 500 with higher scores indicating more severe symptoms. Participants can be categorized as having mild (75-175), moderate (175-300), or severe (>300) IBS. Symptom reduction of at least 50 points is considered clinically meaningful; however, the primary endpoint will be the proportion of participants in each group who demonstrate a symptom reduction of 83 points or more, based on the variables used in the sample size calculation[22].	✓	✓	✓
Secondary outcomes					
IBS-Quality of life (IBS-QOL)	The IBS-QOL is a 34-item questionnaire that assesses the degree to which IBS interfered with QOL over the past 30 days. Each item is rated on a 1 to 5 Likert scale, with higher values indicating a lower QOL[25]. The IBS-QOL is currently the most validated and highly responsive self-reported QOL measure specific to IBS that can be used to assess the impact of IBS and its treatment[25].	The individual responses to the 34 items are summed and averaged for a total score and then transformed to a 0-100 scale for ease of interpretation with higher scores indicating better IBS specific QOL[25]. An increment of at least 14 points on the IBS-QOL scale from baseline will demonstrate efficacy.	✓	✓	✓
Generalized Anxiety Disorder (GAD-7)	GAD-7 is seven items, score from 0 (not all at) to 3 (nearly every day), providing a severity score between 0-21. Scores of 5, 10, and 15 represent cut points for	A 5-point change on the GAD-7 is considered clinically significant.	✓	✓	✓

	mild, moderate, and severe anxiety. The GAD-7 also is effective at identifying the presence of other anxiety disorders including panic disorder, social anxiety disorder, and post-traumatic stress disorder[26].				
Physical Health Questionnaire (PHQ-9)	The PHQ-9 is a 9-item survey with each item scored from 0 (not at all) to 3 (nearly every day) totalling from 0 to 27 points. Scores of 5, 10, 15, and 20 represent cut points for mild, moderate, moderately severe and severe depression. The PHQ assesses major depressive disorder, panic disorder, and anxiety disorder[27].	A 5-point change is considered clinically significant.	✓	✓	✓
Perceived Stress Scale (PSS)	The PSS is a 14-item survey that measures perceived stress, or the degree to which situations in one's life are appraised as stressful, on a four-point scale (0=never, 4=very often) over the last 30 days. The PSS is the most widely used psychological instrument for measuring the perception of stress[29].	An 11-point change is considered clinically significant [28].	✓	✓	✓
COVID-19 Stress Scales (CSS)	COVID-19 related stress and anxiety will be measured using the 36-item CSS survey on five scales: (1) COVID danger and contamination fears, (2) COVID fears about economic consequences, (3) COVID xenophobia, (4) COVID compulsive checking and reassurance seeking, and (5) COVID traumatic stress symptoms[33].	Not reported.	✓	✓	✓
Modified Fatigue Impact Scale-21.	This is a self-reported questionnaire consisting of 21 statements that reflect the perceived impact of fatigue on cognitive, physical, and psychosocial	A 16-point change is considered clinically significant[30].	✓	✓	✓

	functioning. Participants are asked to rate the extent to which fatigue has caused problems for them during the last four weeks. Each item is rated on a 5-point scale reflecting how often the person is limited in activities by fatigue, ranging from 0 (never) to 4 (almost always)[31].				
Patient Health Questionnaire-15 (PHQ-15)	The PHQ-15 measures the severity of 15 somatic symptoms (e.g., fatigue, energy, sleeping trouble, and pain) during the past 4 weeks for a score of 0 to 30. Items can be scored as 0 (not at all), 1 (bothered a little), or 2 (bothered a lot). PHQ-15 scores of 5, 10, and 15 represent cut points for low, medium, and high somatic symptom severity, respectively[32].	A 5-point change on the PHQ-15 is considered clinically significant.	✓	✓	✓
Self-Compassion Scale – Short Form (SCS-SF)	Participants will be asked to complete a 12-item self-reported scale measuring their self-compassion, including self-kindness, self-judgement, humanity, isolation, and mindfulness subscales. To encourage their practice and feelings of self-compassion, participants will receive self-compassion messages weekly by email.	Subscale scores are computed by calculating the mean of subscale items responses. Participants will indicate how often they behave in the stated manner, using a scale from 1 (almost never) to 5 (almost always) for a total of 60 points with lower scores indicating more self-compassion[34].	✓	✓	✓

SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description
Administrative information		
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym **(PG 1)**
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry **(PG 3)**
	2b	All items from the World Health Organization Trial Registration Data Set **(N/A)**
Protocol version	3	Date and version identifier **(N/A)**
Funding	4	Sources and types of financial, material, and other support **(PG 20)**
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors **(PG 1, 2, 20)**
	5b	Name and contact information for the trial sponsor **(N/A)**
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities **(N/A)**
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee) **(N/A)**
Introduction		
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention **(PG 4, 5)**
	6b	Explanation for choice of comparators **(PG 7, 8)**
Objectives	7	Specific objectives or hypotheses **(PG 5)**
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory) **(PG 5)**

Methods: Participants, interventions, and outcomes

Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained **(PG 6)**
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists) **(PG 6)**
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered **(PG 7, 8)**
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease) **(PG 7)**
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests) **(PG 7, 8)**
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial **(N/A)**
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended **(PG 8, 9, 10)**
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure) **(PG 7, 8, 9. Please see supplementary material Table 1.)**
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations **(PG 10)**
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size **(PG 6, 7)**

Methods: Assignment of interventions (for controlled trials)

Allocation:

Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions **(PG 11)**
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned **(PG 11)**
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions **(PG 11)**
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how **(PG 11)**
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial **(N/A)**
Methods: Data collection, management, and analysis		
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol **(PG 8, 9. Please see supplementary material Table 1.)**
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols **(Please see supplementary material Table 1.)**
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol **(PG 11)**
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol **(PG 11, 12)**
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses) **(PG 11, 12)**

	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation) **(PG 12)**
Methods: Monitoring		
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed **(N/A)**
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial **(N/A)**
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct **(N/A)**
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor **(N/A)**
Ethics and dissemination		
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval **(PG 14)**
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators) **(PG 14)**
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) **(PG 14)**
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable **(N/A)**
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial **(PG 11)**
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site **(PG 20)**
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators **(PG 20)**

Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation **(Please see the study consent form.)**
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions **(pg 14, 15)**
	31b	Authorship eligibility guidelines and any intended use of professional writers **(N/A)**
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code **(N/A)**
Appendices		
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates **(Please see the study consent form.)**
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable **(N/A)**

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.