PROTOCOL TITLE:

MYPAICE- Mindfulness and Yoga for Pain with Interstitial Cystitis Evaluation

PRINCIPAL INVESTIGATOR:

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VERSION NUMBER:

2

DATE:

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REGULATORY FRAMEWORK:

Please indicate all that apply:

☐	DOD (Department of Defense)
☐	DOE (Department of Energy)
☐	DOJ (Department of Justice)
☐	ED (Department of Education)
☐	EPA (Environmental Protection Agency)
☐	FDA (Food and Drug Administration)
X	HHS (Department of Health and Human Services)
☐	VA
☐	Other:

FUNDING:

Pelvic Floor Disorders Research Foundation American Urogynecologic Society Grant

UNM Department of OB/GYN Henrietta Lacks Grant

CLINICAL TRIALS

Is this a clinical trial per the NIH definition of a Clinical Trial? X Yes ☐ No

NIH Definition of a Clinical Trial:

A research study in which one or more human subjects are prospectively assigned to one or more interventions. An "intervention" is defined as a manipulation of the subject or subject's environment for the purpose of modifying one or more health-related biomedical or behavioral processes and/or endpoints. Examples include: drugs/small molecules/compounds; biologics; devices; procedures (e.g., surgical techniques); delivery systems (e.g., telemedicine, face-to-face interviews); strategies to change health-related behavior (e.g., diet, cognitive therapy, exercise, development of new habits); treatment strategies; prevention strategies; and, diagnostic strategies (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.

Use the following four questions to determine the difference between a clinical study and a clinical trial:

1) Does the study involve human participants? X Yes ☐ No
2) Are the participants prospectively assigned to an intervention? X Yes ☐ No
3) Is the study designed to evaluate the effect of the intervention on the participants? X Yes ☐ No
4) Is the effect being evaluated a health-related biomedical or behavioral outcome? X Yes ☐ No

Note that if the answers to the 4 questions are yes, your study meets the NIH definition of a clinical trial, even if…

- You are studying healthy participants
- Your study does not have a comparison group (e.g., placebo or control)
- Your study is only designed to assess the pharmacokinetics, safety, and/or maximum tolerated dose of an investigational drug
- Your study is utilizing a behavioral intervention

If yes to all 4 questions, please confirm that the research team is familiar with and agrees to comply with the investigator requirement to register the study on the ClinicalTrials.gov database. Additionally, the approved consent document(s) must be uploaded to the ClinicalTrials.gov database X Yes ☐ No

For any assistance with registration of your trial or the requirements, please contact HSC-CTSCResearchConcierge@salud.unm.edu

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1. Objectives

1.1 The objective of this research is to perform a non-masked, randomized clinical trial to assess pain levels and function and level of care required by patients with interstitial cystitis/painful bladder syndrome (IC/BPS) randomized to treatment with mindfulness and yoga + standard of care compared to standard care alone. Standard of care for IC/BPS is defined as treatments recommended in the American Association of Urology (AUA) guidelines (see Table 1). The target population is patients who have IC/BPS and are willing to be randomized to mindfulness/yoga therapy or standard of care therapies

Table 1: AUA Treatment Guidelines for IC/PBS

First Line	General relaxation/ Stress management, pain management, patient education, self-care, behavioral modification
Second Line	Appropriate manual physical therapy techniques, oral agents including: amitriptiline, cimetidine, hydroxyzine, PPS, intravesical instillation of DMSO, heparin, lidocaine.
Third Line	Cystoscopy under anesthesia with hydrodistension, treatment of Hunner's lesions if found.
Fourth Line	Intradetrusor Botulinum Toxin A, Neuromodulation.
Fifth Line	Cyclosporine A
Sixth Line	Diversion with or without cystectomy, substitution cystoplasty

1.2 Our central hypothesis is that IC/BPS participants treated with yoga and mindfulness will have greater improvement in their symptoms than those treated with standard of care alone. Specifically:

1.3 Outcomes & Hypotheses:

i) IC/BPS participants treated with mindfulness and yoga will assess their response to treatment based on the Graded Response Assessment (GRA) scale (described below) at 3 months compared to standard care participants. *Hypothesis: IC/BPS participants treated with mindfulness & yoga + Standard of care will have superior scores on the GRA scale compared to those treated with Standard of Care alone.*

ii) Participants will start with 1st and 2nd Line therapy as recommended by the AUA guidelines (AUA guidelines categorize treatments as 1st through 6th Lines of care) and we will record the numbers of participants that accelerate to higher lines of therapy. *Hypothesis: IC/BPS participants treated with mindfulness & yoga + Standard of care will have fewer participants who accelerate to higher Lines of care compared to those treated with Standard of care alone.*

iii) Participants will record pain, function and other IC/BPS symptoms using validated questionnaires at baseline and at follow-up (approximately at 6 and 12 weeks of treatment). *Hypothesis: IC/BPS participants treated with mindfulness & yoga + Standard of care will have greater improvement in pain, function and other IC/BPS symptoms compared to participants treated with Standard of care alone, based on validated questionnaires.*

iv) Cost-analysis will be performed comparing treatment groups. *Hypothesis: Cost analysis will find that those treated with mindfulness & yoga + Standard of care will incur less cost than Standard of care alone.*

v) Qualitative outcomes will be obtained with an optional response during the weekly interviews to see how participant's feel their treatment is going. At a later time we may go back and enter quotes into qualitative software for analysis of themes. *Hypothesis: Patients in the mindfulness& yoga + Standard of care may feel more empowered about their health.*

2. Background

IC/PBS is a chronic urologic pain disorder associated with significant morbidity. It is defined by the American Urogynecological Association (AUA) as "a complex sensation (pain, pressure, or discomfort) perceived to be related to the urinary bladder, associated with lower urinary tract symptoms of more than 6 weeks duration, in the absence of infection or any other identifiable cause[i]." A 2015 survey of 1,982 patients with IC/BPS noted that, of the 180 treatment modalities, none were truly effective. In the survey, patients were surveyed about their usage of complementary and alternative medicine (CAM). Of those who responded, 84.2% had tried CAM and 55% had been recommended CAM by their physicians[ii]. There are many reasons as to why patients turn to CAM, including side effects experienced from traditional therapies, lack of efficacy and frustration with providers[iii].

Some of the more widespread CAM modalities recommended in medicine include yoga and mindfulness, as these have gained popularity for chronic pain disorders. Yoga has been shown to improve outcomes in such pain disorders as low back pain, primary dysmenorrhea, endometriosis, and fibromyalgia[iv]. This is likely secondary to the physical components of holding poses and mindfulness of breath. However, no studies have been performed to evaluate the impact of yoga on patient's perception of pain with IC/BPS.

Indeed, there have been few RCTs evaluating its effects, and thus many recommendations for yoga come from expert opinion.

Mindfulness is also gaining popularity for treatment of chronic pain disorders. Using the biopsychosocial model it is postulated that there is a central pain mechanism that further induces pain. Patients with chronic pain conditions also often have musculoskeletal pain. Patients' overall perception of pain may be increased with chronic stress, anxiety and allodynia[v]. However newer apps such as Headspace and Calm have proven beneficial for improvements in the affect, stress and irritability associated with chronic pain in as little as 8 weeks[vi]. One systematic review even noted that an 8 week mindfulness course induced brain changes similar to traditional long term meditation practice on functional MRI[vii].

Mind/body interventions have successfully treated chronic pain conditions such as low back pain[viii], irritable bowel syndrome[ix] and fibromyalgia[x]. Reports regarding treatment response using mind/body therapies for patients with IC/BPS are fewer, thus our aim was to assess the impact of yoga and mindfulness practice+ Standard of care compared to Standard Care alone. Standard of care treatments for IC/BPS have been well defined by American Urologic Association Guidelines (see Table 1). Our hypothesis is that patients who undergo mindfulness & yoga therapy + Standard of Care compared to Standard of care alone, will have improved response to treatment. We also hypothesize that they will have greater improvement in their pain, activities and require fewer treatment interventions. If funding allows, we will also compare cost of treatment between groups.

3. Study Design

We will perform an unmasked, randomized controlled trial comparing yoga and mindfulness impact on 1) treatment response 2) level of treatment required 3) pain, activity and quality of life for patients with IC/BPS compared to standard care alone as recommended by the AUA (Table 1). The target population will be those patients with IC/BPS who are cared for by the urogynecology, gynecology and urology specialties. After obtaining informed consent, women will be randomized to either yoga & meditation + Standard of care compared to Standard of care alone. Masking is not possible with this study design, as participants randomized to the yoga/mindfulness versus standard of care will clearly know their treatment arm.

4. Inclusion and Exclusion Criteria

4.1 We will recruit patients who present with IC/BPS per the AUA definition. To confirm the diagnosis of IC/PBS,.We will also administer the O'Leary-Sant Interstitial cystitis Symptom Index and Problem Index to determine if patients are candidates for the study. We will also require that they have a physical exam performed in the past 2 years. As documented by others, a domain score of >6 will indicate applicability for enrollment in either symptom or problem domain[xi]. Additional inclusion criterion include: evidence of an absent UTI (e.g. negative urine

dipstick, a negative urinalysis or urine culture) within 2 months of enrollment as well as ability to speak and understand English or Spanish. We will recruit only patients who will be undergoing first-line and second-line treatment, as defined by AUA and who have not made treatment changes to their regimen in the past 4 weeks.

Patients will be excluded if they have:

- unevaluated hematuria,
- a history of recurrent urinary tract infection (UTI), as defined by AUA criteria as >2 culture-proven UTIs in 6 months or 3 UTIs in one year within the last 5 years,
- urinary retention, defined as a post-void residual (PVR) of >150 mL confirmed by bladder scan or catheterization,
- a history of augmentation cystoplasty or urinary diversion,
- a history of cyclosporine A use
- a history of pelvic radiation or chemotherapy in the past 2 years
- history of radiation induced cystitis
- if patients are currently pregnant or lactating or planning on becoming pregnant in the next 3-4 months
- have demonstrated Hunner's ulcers on cystoscopy, treated or untreated by fulguration or steroid injection, within the last 6 months
- As our intervention requires Smartphone utilization and video usage, we will be excluding patients whose hearing or vision would interfere with ability to use the yoga video or meditation app.
- Neurogenic bladder (e.g. secondary to CVA with residual deficits, Multiple Sclerosis, Parkinsonism)
- Severe mobility impairment or physical conditions that would interfere with their ability to perform yoga as they would be unable to perform certain Yoga postures.
- Inability to speak/understand English or Spanish
- Inability to perform study follow up

4.2 Main inclusion criteria is as follows:

- Female subjects≥18 years old

- IC/BPS clinical diagnosis, which requires >6 weeks of symptoms consistent with IC/BPS and lack of other bladder pathology (such as radiation exposure, active urinary tract infection, pelvic trauma, etc.) that would explain symptoms
- English or Spanish reading/writing
- Own a Smartphone to be able to watch an online video or use Smartphone meditation app.
- Ability/willingness to participate in follow up questionnaires
- O'Leary-Sant ICSI/ICPI >6

4.3 As noted above: Adults unable to consent, pregnant women, and prisoners will not be included in this study.

4.4 As noted above: We will include English and Spanish speaking populations only. We are excluding men as we are a Urogynecology practice and therefore do not have access to that population, and the vast majority of sufferers from IC/BPS are women[xii]. Unfortunately, we do not have the ability to recruit in other languages beyond English and Spanish, as our primary outcome measures have not been validated in other languages.

5. Number of Subjects

5.1 This is a single-center study at University of New Mexico, so the total number of subjects at the University of New Mexico is the total number of subjects for the study.

5.2 The total number of subjects to be recruited at this site is 60-120 patients.

5.3 Sample size calculation: The primary outcome for this study is a linear mixed model of GRA variation over time. Weekly GRA and O'Leary-Sant values will be obtained on all participants. We will then further characterize patients as either treatment responder or non-responders, with treatment response defined as "moderate (+2)" or The primary outcome for this study is a linear mixed model of GRA variation over time. Weekly GRA and O'Leary-Sant values will be obtained on all participants. We will then further characterize patients as either treatment responder or non-responders, with treatment response defined as "moderate (+2)" or "marked (+3)" improvement on the GRA. We used previously reported outcomes from an RCT regarding impact of medication on ICBPS symptoms.
Given that we will be performing a linear mixed model, we powered our study to detect a 30% change in treatment response between groups on the GRA, with baseline response rate of 26%. We require 41 participants/group (total N=82) to obtain 80% power (α=0.05), assuming an effect size of 0.85. Allowing for a dropout rate of 15%, we aim to randomize 94 women (47/group). We will be able to recruit the required number of participants. We see 12-15 new patients with ICBPS per month and should

be able to adequately recruit 6-7 patients/month, allowing us to meet the necessary sample of patients within 14 months of study initiation. Despite COVID-19, we still continue to care for this number of patients. The study has maximized digital & phone contact and minimized in-person contact. We foresee that we should meet our recruitment aims despite the pandemic's restrictions.

6. Study Timelines

6.1 Based on current clinic volume in the UNM division of the Urogynecology, from which we are recruiting, we estimate that recruitment of 60-120 patients will be feasible over approximately 2-3 years. Per chart review, the urogynecology division sees patients who meet criteria for this study at the rate of 10-20 per month. Assuming that approximately 25% of patients will agree to study participation (due to issues of time commitment and eligibility criteria), we believe that we will be able to recruit an appropriate number of patients in approximately 2-3 years. We believe that an additional 3 months will be needed for follow up data. We anticipate that data analysis and manuscript writing will take an additional 6-9 months.

7. Study Endpoints

7.1 The **primary endpoint** of our study is to determine the 3 month Global Response Assessment (GRA) in patients who perform yoga & mindfulness + Standard of care compared to patients who undergo Standard of Care alone, as well as a linear mixed model analysis of the GRA over time. Our **secondary endpoints** include: (i) proportion of patients in each group using accelerated lines of treatment (2-6) based on the AUA guidelines (i) the following validated questionnaires:)), O'Leary-Sant Symptom and Problem Index (OSPI/OSCI), patient self-efficacy questionnaire (PSEQ-2), the PROMIS- Pain Interference Short Form 6b (PROMIS-PI and a visual analog scale, and the hospital anxiety and depression scale (HADS-A/D) (iii) Cost analysis potentially using, for example, the QALY scale if funds are found to support this.

7.2 We will not have any primary or secondary safety endpoints for which the study will be powered, as the interventions are extremely low risk (mindfulness and yoga).

7.3 Our **exploratory endpoints** are to investigate compliance to mindfulness and yoga treatment. Due to the extremely low-risk nature of therapeutic interventions, we do not have any safety endpoints.

8. Research Setting

8.1 The study will be performed at the University of New Mexico (UNM) Eubank Women's Primary Care Clinic and Sandoval Regional Medical Center (SRMC) Urogynecology clinics. These Urogynecology clinics are dedicated to care of women with pelvic floor disorders such as interstitial cystitis/bladder pain syndrome (IC/BPS), the target population for this study.

8.2 Potential subjects will be recruited in the UNM Eubank and SRMC clinics when they present for care for IC/BPS, either in person or virtually via telephone or Zoom care visits. All patients will have a history and physical taken to determine their study eligibility, as well as a baseline BPIC-SS. Recruitment will take place either in private exam rooms at these clinics or over HIPAA-compliant telephone or Zoom conversation, and informed consent conversations regarding these clinics will take place via the same means.

8.3 There are no other laboratory tests in this trial other than would be routinely collected in the work up of IC/BPS.

8.4 There will not be involvement of any community advisory board.

8.5 There will not be any research conducted outside of the UNM HSC and its affiliates.

9. Resources Available

9.1. Qualifications of PI and study staff: Dr. Kate Meriwether is a board certified subspecialist in Urogynecology and will serve as the primary investigator (PI) for this study. She is an experienced researcher at UNM and eligible PI at UNM, in addition to serving on an HRRC at the UNM HSC Institutional Review Board, which makes her familiar with ethical and compliant practices. She has been the PI on multiple research trials and has successfully completed randomized control trials both as a fellow and now as faculty at UNM. Dr. Yuko Komesu, a co-investigator on this project is an experienced researcher at UNM and has previously evaluated mind/body therapies in both IC/BPS and urgency urinary incontinence based on RCTs. She is a tenured professor and the vice-chair of research for the department of OB/GYN, which makes her very familiar with ethical and compliance practices. She is also a Howard Friedman endowed professor in OB/GYN. Dr. Sierra M. Jansen, a co-investigator on this project, is the fellow who has a total of 12 months of protected research time during her fellowship in order to complete this study.

9.2 This trial does not require any medical decision-making or ordering of therapeutics due to research protocols.

9.3 Resources available to conduct the research: The University of New Mexico (UNM) Urogynecology division operates at two main locations. UNM Eubank Urogynecology Clinic located in Northeast Albuquerque provides a full range of services for women with pelvic floor disorders. The Eubank clinic consists of 8 examination rooms, 2 treatment rooms, and 2 physical therapy rooms. Our second location is at Sandoval

Regional Medical Center (SRMC), a community-based facility located in Rio Rancho, New Mexico, a large suburb located outside of Albuquerque.

Research Staff: The Urogynecology Division employs a clinical research specialist as well as research coordinators. Our research staff has extensive experience conducting multi-center investigations and recruiting patients to clinical studies, with special expertise in community-based research and quality of life studies.

Research Experience: The Urogynecology Division at UNM has a strong history of conducting high quality research and collaboration with other investigators in the US and abroad, and has consistently met or exceeded recruitment goals on time. We have been members of the NICHD-sponsored Pelvic Floor Disorders Network (PFDN), and have met recruitment goals with high rates of follow-up and accurate data collection. In addition to PFDN research, Dr. Kate Meriwether has mentored and has been the PI on multiple clinical trials and contributes multiple publications in peer-reviewed journals. Her Curriculum Vitae is attached.

Our group is well versed in the importance of adherence to protocols, timely completion of regulatory requirements, effective recruitment strategies, and the importance of the inclusion of minority subjects. Research is integral to all aspects of Divisional work; importantly, all members of the clinical team participate in research efforts. There are weekly research meetings to discuss the progress of the ongoing studies within the department, and it is an excellent forum to ensure that all involved are adequately informed of their duties, of the protocol, and of the procedures.

We do not anticipate that emergency care will be needed for this study; the urogynecology physicians are available on a 24 hour basis, 7 days per week for their patients requiring emergency care.

10. Prior Approvals

The only approval prior to commencing research will be with Dustienne Miller, PFPT. She is a certified yoga teacher and a pelvic floor physical therapist with extensive background in making online yoga tutorials. She is designing this yoga sequence for our study (see supplemental materials). This study was presented to Dr. Eve Espey for approval, and the signed Departmental Review Form can be found in the "Supporting Documents" Section.

This study does not include ionizing radiation, biological specimens, or drugs.

11. Multi-Site Research

This is not a multi-site research study.

12. Study Procedures

This non-blinded randomized control trial will be conducted at the UNM Eubank clinic and SRMC Urogynecology clinic. We will recruit participants and plan to randomize approximately 60-120 participants from these sites. Collaborating investigators will be members of the urogynecology division at UNM HSC.

Our primary aim is to determine whether the participants assess themselves as improving following the interventions based on the GRA at 3 months. The target population will be patients with IC/BPS who are seeking care. The current recommendation is to advise patients to undergo conservative management with self-care, behavioral modification techniques. If a patient is interested in this and fulfills study inclusion criteria then we will offer her the choice of volunteering for the study. All women will give consent prior to their enrollment, after they have had time to carefully consider whether they want to participate in the study. Research staff and clinicians will obtain consent either in clinic or via zoom. After enrollment, participants will fill out baseline surveys including:)the O'Leary-Sant Symptom and Problem Index (OSPI/OSCI)Patient Self Efficacy Questionnaire-2 (PSEQ-2), Hospital Anxiety and Depression Scale (HADS-A/D), PROMIS- Pain Interference Short Form 6B (PROMIS-PI), and a visual analog scale

In addition to the above outcomes, we will collect patient demographics, medical/surgical history and information regarding their IC/BPS (e.g. time since IC/BPS diagnosis, previous treatments for IC/BPS tried) and patient contact information. Once this information is collected, patients will also fill out an attestation of use, which they will sign/e-sign in REDCap, an affidavit that if they are randomized to mind/body they will use these daily to the best of their ability.

Randomization: Randomization assignment will be generated by computer generated randomization scheme used by appropriate personnel such as a statistician. Participants will be randomized in a 1:1 ratio by a computer generated sequence at enrollment. Randomization assignments will be completed via REDCAP. Randomization will only occur after consent has been obtained and all baseline data has been obtained.

Interventions:

Yoga & mindfulness meditation + Standard of care: Women will be asked to perform mindfulness meditation via a commercially available smartphone app and yoga through an online video tutorial (designed by a Physical Therapist expert in IC/BPS care and designed specifically for IC/BPS patients). Our online tutorial is currently in the process of being formatted however see supplemental materials for yoga flow. Patients will be instructed to perform

approximately 10 minutes of meditation daily via a commercially available app (either Calm App or Headspace App, both of which are commercially readily available) and approximately 15 minutes of yoga via the online tutorial. Yoga & use of the meditation app is estimated to take approximately 30 minutes per day. Patients may engage in any other of the 1st Line AUA therapies as well taking over the counter medications (Table 1). Patients will be called weekly to ascertain treatment compliance and monitor their progress. If symptoms are not improving there will be the option to discuss other treatment options (e.g. accelerate to higher lines of therapy based on AUA guidelines) at 6 weeks.

Women assigned to the Standard of Care alone group will receive any 1st Line and 2nd Line treatments (excluding use of the online yoga and meditation app). Patients will also be called weekly to monitor progress and to ensure no treatment effect secondary to phone calls. If symptoms are not improving there will be the option to discuss other treatment options (e.g. accelerate to higher lines of therapy based on AUA guidelines) at 6 weeks. At the termination of the study women in the standard of care group will receive 3 months of Calm App.

At the 6 week follow-up phone call patients will be given the option for escalation of therapy. Patients will be given the opportunity to escalate their treatment for IC/PBS to higher lines of treatments: use of intravesical Botox or use of sacral neuromodulation. We will record any accelerated therapy used by the patient that may be added during study participation.

For participants who have completed the study but treatment escalation data was not properly captured in RedCap surveys, These participants will be notified via email through RedCap to complete this additional survey.

Outcome measures:

GRA: The Global Response Assessment is a validated tool to assess response to treatment. It is comprised of a single question and has been utilized widely in IC/BPS[xiii]. This will be collected weekly. However, the primary outcome is the 12 week (3 month) result.

THERAPY ESCALATION: We will record when and what women use that is greater than 1st line and 2nd line therapies during their participation in the study. They will discuss escalation of therapy with their provider and study personnel will record the additional therapy as an outcome measure. This will be utilized to perform cost utility analysis to determine if the intervention is cost-effective.

PSEQ-2: The Patient Self-Efficacy Questionnaire Short Form is a 2 question questionnaire that has been used in multiple chronic pain conditions to

document feelings of self-efficacy. The Short form is validated in chronic pelvic pain[xiv]. This will be collected at baseline and at 12 weeks.

PROMIS-PI: The PROMIS-Pain interference short form 6B is an NIH PROMIS measure that measures the extent that pain interferes with daily activities. It is comprised of 6 questions[xv]. This measure will be collected weekly.

HADS: This is formally called Hospital Anxiety/Depression Scale. This is a 7 item inventory that assesses generalized anxiety including: tension, worry, fear, difficulty relaxing and restlessness[xvi]. This measure will be collected at baseline and at 12 weeks.

Euroqol-5d. (EQ-5d) This is a validated measure utilized to measure health states[xvii].

O'Leary-Sant Interstitial Cystitis Symptom and Problem Index:

This validated survey assesses severity of symptoms and bother in IC/BPS and is commonly used for IC/BPS trials. Symptom index, which has been explicitly analyzed in a prospective trial to detect change, and problem index are to be separately analyzed[xviii]

Data Analysis

Data Analysis: Between and within group differences will be evaluated using chi-square analysis as deemed appropriate by the statistician involved in study analysis (e.g. Fisher's Exact test for non-normal distributions of categorical variables and T-test for continuous variables). Differences between groups will be evaluated using Chi-square analyses for categorical variables as deemed appropriate by the statistician involved in study analysis (e.g. Fisher's Exact test for non-normal distributions). T-tests will be utilized for continuous variables, with comparison by Mann Whitney U for non-normal distributions. Within-group differences over time will be analyzed using the McNemar's test. If any baseline differences exist between the groups, a regression or multivariable analysis will determine the contribution of these differences to observed differences between groups. As the GRA and O'Leary-Sant will be collected more frequently, we plan to analyze these results with linear mixed models analysis.

Power Analysis: Power analysis was performed based on previously reported means and standard deviation from treatment effect based on GRA We assumed that 41 patients in each arm (total 82) would be required to find a difference of 30% between group's pain scores (the primary outcome) with 80% power and alpha of 0.05. In order to achieve power we will need a total of 82 patients. Assuming an approximate 20-25% dropout or loss to follow-up rate, we will plan to randomize approximately 60-120 patients.

13. Provisions to Monitor the Data to Ensure the Safety of Subjects

A DSMB will not be monitoring safety of these procedures as the study risks are low. The intervention arm includes mindfulness and yoga, both of which have been shown to be low-risk interventions with minimal adverse events[xix]. The control group will undergo standard of care treatments. Theoretically, there could be increased muscle soreness noted in patients in yoga treatment arm. There are no documented adverse events with mindfulness practice.

We will track adverse events when patients bring up these events during the course of the study with their providers or study coordinators. Because neither of the studied treatments are experimental or associated with above average risk, we do not anticipate any serious adverse events; nonetheless, these will be tracked. Participants will have access to a 24/7 phone number to reach research or clinical staff with concerns. All adverse events will be recorded and reported to the study PI.

We do not anticipate any conditions that would trigger a suspension or termination of the research.

14. Withdrawal of Subjects

Participants may withdraw from the study at any time without penalty and will continue to receive the clinical standard of care. A subject may be withdrawn from the study without her consent at the discretion of the physician and study staff if they believe she no longer meets study inclusion criteria or if she meets exclusion criteria, or if they believe that it is not in her best interest to continue study participation i.e., desire to undergo surgical treatment. Investigators may withdraw a subject if the subject is not following the study protocol. If a woman is withdrawn from the study either at her own discretion or that of the research staff, she may continue with conservative or surgical management of her IC/BPS in the usual fashion. We will collect a withdrawal Global Response Assessment to use for her progress and will utilize her data up until the time point that she is withdrawn from the study.

To minimize withdrawal from the study, patients will be randomized after they have had what they feel to have been adequate time to consider whether or not they would like to participate in the study and they provide consent. We will document reasons for withdrawal from the study if the participant willingly provides this information. We will report eligibility criteria not met or reasons for declining participation in the study if the participant willingly provides this information. The withdrawal procedure is clearly documented in the study consent.

15. Data Management/Confidentiality

Participants will be given a de-identified study subject number. Data collection sheets and questionnaires will contain the subject number. No other patient identifiers will be collected on study forms. PHI including patient name, date of birth, phone number, and medical record number will be collected to track appointments and ensure patient follow-up. The data collection, HIPAA and consent forms will be maintained in a locked file cabinet in the locked Eubank research office. A separate folder will be designated for each participant. PHI will not be entered into the study database. The link between PHI and study IDs will be kept on a password protected computer on a secure UNM OBGYN department server.

The study database does not include sensitive information or information requiring additional protection.

Study binders will be kept in a locked cabinet in the research administrative area. In order to further ensure patient confidentiality, the identifying information will be kept separately from the numbered study files in a locked cabinet.

Electronic data entry will be performed on REDCAP, using the de-identified subject study number. The electronic data and subject link will be encrypted, password protected, and stored on the secure UNM OBGYN department server. This server's electronic security is monitored / maintained by the Health Sciences Library and Informatics Center (HSLIC). A REDCAP database will be created to collect, store and manage the data. REDCAP databases are reposed securely and all data entered is de-identified. The REDCAP database is only accessible using an individual unique login and password and access is only provided to co-investigators. Access is restricted to co-investigators and research staff and will be protected using the unique REDCAP login and password provided to each co-investigator.

Access to the files and REDCAP will be restricted to research personnel and Investigators and will be locked or protected using the unique REDCAP login and password provided to each co-investigator. The data will be stored for 5 years after completion of analysis and then will be destroyed.

A Certificate of Confidentiality will not be used to protect data from forced release. No identifying or study related data will be transported to outside locations. There will be no audio or video recordings or photographs taken.

16. Data and Specimen Banking

As stated above, the data collection, HIPAA and consent forms will be maintained in a locked file cabinet in the Eubank research area. A separate file will be designated for each participant. A key matching study number to subject's name will be stored on a password protected computer on a secure UNM OBGYN department server. In order to further ensure patient confidentiality, the identifying information will be kept separately from the numbered study files in a locked cabinet. The data will be maintained for 5 years after completion of the study and then destroyed.

No specimens will be archived for future use.

17. Risks to Subjects

Risks of enrollment in the study include loss of confidentiality. We will take every measure to try to ensure the security and confidentiality of participants. Participants will be recruited in a private room or in a private location via phone or HIPAA compliant ZOOM and will have ample time to consider whether they want to participate in the study. Also, locked cabinets will be used to protect patient consent information and collected data. The link identifying patients and their study numbers will be also stored on a password protected computer on a secure UNM OBGYN department server.

There are minimal risks with the intervention arm of this RCT (yoga and mindfulness). Yoga therapy is associated with low risks, such as muscle discomfort or strain though this is rare. Emotional discomfort due to the reflective nature of this therapy is also possible. Both treatment randomizations in this study are well established as options for IC/BPS with an excellent safety profile.

Pregnant women will not be included in the study, so there is no risk to embryos/fetuses. Participants will need to have a negative urine pregnancy test in the last 3 months prior to enrollment or have documentation of a hysterectomy or tubal ligation. If they are pregnant, the patient meets exclusion criteria and will be ineligible to participate.

There are no risks to those who are not subjects.

18. Potential Benefits to Subjects

The patients enrolled are already opting for first line treatment of their IC/PBS and potential use of over the counter medications. Participation in this study may help to improve an individual participant's condition, but it is also possible that the condition may not improve. There is no guarantee that any individual will personally benefit by participating in this research study. Women assigned to the yoga and meditation group will also receive 1) a video that will instruct them on use of yoga that may help with IC/BPS symptoms (designed by a physical therapist who specializes in caring for IC/BPS patients) and 2) a meditation app. that will be provided to the patient for approximately 3 months (the study will pay for it for that length of time). Participation in this study may provide information that may help other people who have a similar medical problem in the future. The literature supports improvement of QOL in similar conditions such as endometriosis or primary dysmenorrhea.

19. Recruitment Methods

The Urogynecology clinics at UNM Eubank, and SRMC have a large referral population of patients with pelvic floor conditions such as IC/BPS. Subjects will be identified in the clinics at UNM Eubank clinic and SRMC by investigators

when thy present either in person or virtually (telephone or Zoom visits) for visits for IC/BPS care. The patients will be counseled about possible treatment options for IC/BPS and they will be introduced to the study and provided with written information that may help them decide if participation in the study is right for them. Subjects are encouraged to consult with family, friends, and primary health care providers, as well as communicate any questions they may have before beginning the written consent process. We will request a waiver of HIPAA authorization for recruitment purposes.

If a woman declines to participate or is withdrawn from the study either by her desire or that of the research staff, she will be offered the same treatment options. Her follow up appointments will be the same regardless of participation in the study.

Potential participants may also self-identify through a recruitment material flyer that will be placed in Eubank clinic restrooms, waiting area and in the OB/GYN department at UNM. The proposed recruitment flyer is uploaded in the supplemental materials section. We will also plan to recruit using social media and at IC/BPS support groups, and over the radio. The proposed wording is included in the website advertisement in the supplemental materials section.

20. Provisions to Protect the Privacy Interests of Subjects

Privacy concerns are taken into account with every patient seen at the UNM and SRMC clinics. Participants approached and/or interviewed in the clinic setting will be in either private offices or examination rooms in the clinics, personal Zoom or on telephone calls that are HIPAA compliant. All staff, including research staff, are well-versed in sensitive health care discussions and procedures. Telephone interviews for recruitment and study data gathering are conducted in the research staff area or private physician offices, where all staff have received CITI Training. The office area designated for the entire Urogynecology research staff is isolated from the clinical administrative staff area, providing protection for participants and potential participants during screening, recruitment, study-designated calls, and data entry. All study sheets used to collect patient information will be de-identified.

At all times throughout the clinical investigation, confidentiality will be observed by all parties involved. All data will be secured against unauthorized access. Privacy and confidentiality of information about each subject will be preserved in study reports and in any publication. Each subject participating in this study will be assigned a unique identifier. An IRB-approved HIPAA authorization within the consent is required to be given to the patient. All documents containing personal health information (screening logs, consent documents, data forms) are maintained in locked cabinets with access available only to research staff and investigators. Data is entered into a password protected system. No individual identifiers are entered into the system. The sole link with personal information is maintained by the research team on a password protected computer on a secure UNM OBGYN department server with access limited to authorized research staff and investigators. This information is only to be used at the study center.

21. Economic Burden to Subjects

There are no study costs to the participant outside of what would be recommended for standard care. The meditation app will be provided in kind from UNM if funds are available. There is the need for a small amount of data for Calm App, however as part of the study we will not be offering to compensate for this.

Due to COVID-19 our initial visits are remote, as will be our follow up visits thus no transportation costs will be incurred. We will plan on using a prior physical exam performed by a trained gynecologist or urogynecologist in the last 2 years as a baseline exam.

Research Procedures	**Number of Samples/Procedures**	**Responsible Party**	
		Study	**3rd Party Payer or Participant**
Online Yoga	1	☐	X
Calm App	3 month subscription	X	☐
Standard of Care Procedures	**Number of Samples/Procedures**	**Responsible Party**	
		Study	**3rd Party Payer or Participant**
Clinic Visit- remote	1	☐	X
Weekly phone visit- remote	11	☐	X
3 month follow up- remote	1	☐	X

22. Compensation

The patient will receive the following compensation: For completion of the study, each patient will be compensated with a merchant card worth $60 total. They will receive a $10 merchandise card at their initial study visit (enrollment) and $50 merchandise card at their 3-month follow-up visit. This payment is reasonable compensation for the inconvenience of participating in a research study due to the additional time the study questionnaires will require from the participant. Participants will receive access to the meditation app and yoga video (if in the mindfulness/intervention arm) and both groups will receive close follow-up and attention from the research staff. At the end of the study women in the standard care group will receive a 3 month subscription to the Calm App.

23. Compensation for Research-Related Injury

If participants are injured or become sick as a result of this study, which is extremely unlikely given the nature of the interventions, UNMHSC will provide emergency treatment at the study participant's cost. No commitment is made by the University of New Mexico Health Sciences Center to provide free medical care or money for injuries to participants of the study. Reimbursement for treatment for all related costs of care will be sought from the participant insurer, managed care plan, or other benefits program. The participant will be responsible for any associated co-payments or deductibles required by the insurance. Participants will be encouraged to report any illness or injury they believe to be related to the study to the investigator or research staff. Participants will be given telephone contact information for the Urogynecology office for the purpose of asking any questions or stating any concerns about the study or treatment as a research subject. They

may also be directed toward the HRPO. This language will be stated in the consent document, and reviewed during the informed consent process.

24. Consent Process

Patients will be approached about the research study at the Urogynecology clinic or via virtual consultation at UNM Eubank or SRMC during a discussion for the management of IC/PBS. Each patient undergoes counseling in a private room with a closed door to ensure privacy. The physicians in the Urogynecology division and research staff will be able to given consent letter to patients to allow for inclusion. Our division routinely treats this condition and are highly qualified to counsel patients regarding the risks, benefits, alternatives for the treatment. Care will not be withheld if they decide not to participate. If the patient prefers, she may also be counseled about study participation via ZOOM or phone following her clinic appointment by providers or study personnel.

The patients who would like to participate in the study will be given the consent letter. Given low risk intervention nature of this trial and the often virtual nature due to the pandemic a consent letter will be utilized instead of a consent form requiring participant's signature. By enrolling in the study they will be by proxy giving their consent.

Participants will have these multiple opportunities to ask any questions and they will also be provided with the clinic's contact information to get in touch with research investigators to address any additional questions or concerns.

Subjects will be reassured that participation is completely voluntary and does not affect their treatment, their relationship with their providers, or the university to minimize the possibility of coercion or undue influence. The patients will be asked that they understand the opportunity to participate and their complete freedom to decline. This will also be asked if they understand and if they have any questions. There is no minimum time period needed between informing the patient of the study and time of consent. Subjects will be encouraged to take as much time as they need.

This study will obtain HIPAA authorization prior to enrollment. HIPAA authorization will be reviewed with all participants by the physician or research staff obtaining consent. Specific information that will be obtained includes prior medical history, surgical history, reproductive health history including child bearing, drug allergies, age, and ethnicity. This information will obtained by health care providers, not research coordinators, as deemed necessary for a more complete and accurate medical history of the patient.

<u>Subjects not fluent in English:</u>

Patients will be consented with a certified translator if Spanish speaking. Spanish-speaking patients will be offered information about risks, benefits, and alternatives to study participation in a private setting and given adequate time to consider the risks and benefits of the study prior to offering consent or declining to participate. Yoga tutorial and Calm App is available in Spanish for patients. The Spanish consent will be translated from the English consent once the English consent is approved, and we will submit a modification in Huron IRB to update the study with Spanish materials in the future.

Cognitively Impaired Adults/Adults Unable to Consent/Use of a Legally Authorized Representative:

NA. Cognitively impaired subjects will not be included in this study.

Subjects who are not yet adults (infants, children, teenagers):

NA. Only subjects ≥ 18 years of age will be included in this study.

Waiver or Alteration of Consent Process (consent will not be obtained, required element of consent will not be included, or one or more required elements of consent will be altered)

NA. There will be no waiver or alteration of the consent process.

25. Documentation of Consent

a. *Describe if you plan to use a consent form to document consent.* N/A we will be using a consent letter.

b. *If the study is collecting and/or storing tissue samples, include a Tissue Banking Consent Form (and Authorization if the specimens will be accompanied by PHI).*

i. N/A we will not be collecting tissue samples.

c. *Describe if you plan to obtain consent but will be using a script, information sheet, or other mechanism. If you will obtain consent verbally, attach a consent script and information sheet, if you will be providing one. If you will be obtaining consent via an on-line survey, please use the survey cover letter consent template on the HRPO website and include your email script with your submission.*

Complete the checklist for "Waiver of Documentation of Consent" in the Checklists section of this Protocol Template. If you will be excluding or modifying one or more of the required elements of consent you will also need to request an Alteration of Consent.

We will be using a Consent letter for documentation of consent given low risk nature of study, see attached in supplemental forms.

26. Study Test Results/Incidental Findings

We do not intend to share study test or procedure results with study participants, but as all of their data collected is subjective and directly from them, they will be aware of all the data/information in the study regarding them. Additionally, we do not anticipate that the research being conducted will result in incidental findings. Every patient will receive the practice's standard of care regarding workup of IC/PBS, which may include different laboratory tests, urine culture, cystoscopy or urodynamic testing if unclear cause of pain, or imaging studies, as determined by their other active medical issues. These results are not directly a part of the research being conducted and will hence be disclosed to the patient. They will not, however, affect randomization.

27. Sharing Study Progress or Results with Subjects

We do not intend to share study progress with participants while the study is underway as not to introduce bias. We do not intend to seek out study participants to disseminate information once the study is complete. Women who are interested in the results will be provided the information where to read the manuscript once it is published. Study results for individual participants will not be shared.

28. Inclusion of Vulnerable Populations

N/A. There will not be any vulnerable populations included in this study.

29. Community-Based Participatory Research

N/A. There will be no involvement of the community in this research.

30. Research Involving American Indian/Native Populations

N/A. This research does not specifically target this population. If an American Indian woman is a candidate for the study, she will be offered participation if she is able to speak/read/write in English or Spanish.

31. Transnational Research

N/A. This study is domestic.

32. Drugs or Devices

N/A. There is no drug or device utilized in this study.

33. Principal Investigator's Assurance

By submitting this study in the Click IRB system, the principal investigator of this study confirms that:

☒ The information supplied in this form and attachments are complete and correct.

☒ The PI has read the Investigator's Manual and will conduct this research in accordance with these requirements.

☒ Data will be collected, maintained and archived or destroyed per HSC Data Security Best Practices, including:

1. **Best Practice for data collection** is for it to be directly entered onto a data collection form that is in a secured access folder on an HS drive behind a firewall, or in a secure UNM Data Security approved system such as REDCAP.
2. **Data collection of <u>de-identified data</u>**, if done in a clinical setting or other setting that does not allow direct entry into a secured system, may be done temporarily using a personal or university owned electronic storage device or hard copy document. **The important security safeguard is that no identifiers be include if the data is entered or stored using an untrusted device or storage.**
3. **Permanent (during data analysis, after study closure)** storage must reside on HSC central IT managed storage. Processing of data (aggregation, etc.) are to be carried out in such a way as to avoid creating/retaining files on untrusted storage devices/computers. Trusted devices are HSC managed and provide one or more of following safeguards: access logs, encryption keys, backups, business continuity and disaster recovery capabilities.
4. **Alternate storage media** must be approve by HSC IT Security as meeting or exceeding HSC central IT provided security safeguards.

34. CHECKLIST SECTION

This section contains checklists to provide information on a variety of topics that require special determinations by the IRB. Please complete all checklists relevant to your research.

35. Partial Waiver of Consent for Screening/Recruitment

Complete this checklist if you are requesting a partial waiver of consent so that you can review private information to identify potential subjects and/or determine eligibility prior to approaching potential subjects for consent or parental permission.

We are requesting a partial waiver of consent for screening and recruitment purposes.

A. Describe the data source that you need to review (e.g., medical records):

We would review medical records to ensure that patients have a diagnosis of IC/BPS and not an alternative diagnosis (such as recurrent UTI) that would make them ineligible for the study.

B. Describe the purpose for the review (e.g., screening):

We would need to review records for screening purposes to ensure that the patients meet eligibility criteria.

C. Describe who will conducting the reviews (e.g., investigators, research staff):

The reviews of the medical records will be by research staff and investigators in advance of patients' clinical visits, so that recruitment can be optimized.

D. Do all persons who will be conducting the reviews already have permitted access to the data source?

☒ Yes

☐ No. Explain:

i. Verify that each of the following are true or provide an alternate justification for the underlined regulatory criteria:

1. <u>The activity involves no more than minimal risk to the subjects</u> because the records review itself is non-invasive and the results of the records review will not be used for any purposes other than those described above.

☒ True

☐ Other justification:

2. <u>The waiver or alteration will not adversely affect the rights and welfare of the subjects</u> because eligible subjects will be approached for consent to participate in the research and are free to decline. Further, the information accessed during the records review will not be

disclosed to anyone without a legitimate purpose (e.g., verification of eligibility).

☒ True

☐ Other justification:

3. The research could not practicably be carried out without the waiver or alteration because there is no other reasonably efficient and effective way to identify who to approach for possible participation in the research.

   ☒ True

   ☐ Other justification:

4. Whenever appropriate, potentially eligible subjects will be presented with information about the research and asked to consider participation. *(Regulatory criteria: Whenever appropriate, the subjects will be provided with additional pertinent information after participation.)*

   ☒ True

   ☐ Other justification:

36. Partial Waiver of HIPAA Authorization for Screening/Recruitment

Complete the following additional questions/attestations if the records you will review to identify potential subjects and/or determine eligibility include Protected Health Information (PHI).

We are requesting a partial waiver of HIPAA authorization for screening/recruitment. We will review medical records of participants to ensure that they are eligible for the study, in particular to review if they have a clinical diagnosis of IC/BPS, and to ensure they don't have an alternative diagnosis that would make them ineligible.

37. Waiver of Documentation of Consent

Complete this checklist if you intend to obtain consent verbally but will not be obtaining signatures from subjects on a consent form to document consent. Waivers of documentation of consent are commonly requested when using scripts, information sheets, or email or survey introductions to present the elements of consent instead of using a traditional consent form.

A. Are you requesting a waiver of documentation of consent for some or all subjects?

   X All. Explain: When patients are unable to present in person to the clinic due to COVID restrictions, and are having all virtual visits such as HIPAA-compliant Zoom visits or telephone visits, they will be unable to provide written, documented consent. Therefore, we request the ability to email or mail them a consent letter to all patients with virtual visits or hand out a consent letter to those in person that allows us to explain the risks and benefits

of the study to them after the verbal conversation of consent, and explain to them that participation in surveys or the interventions from then forward would constitute consent.

B. Provide justification for one of the following:

i. That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern.

ii. That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

The minimal risk of mindfulness practice and yoga or usual care is such that normally, if performing these practices in everyday life, no informed consent would be required for these procedures.

C. Do you intend to provide subjects with a written statement regarding the research in lieu of a traditional consent form?

☒ Yes. Please attach a copy to your submission in Click.

☐ No

38. Alteration of Consent

Complete this checklist if you intend to obtain consent but will be eliminating or altering one or more of the required elements of consent. Alterations of consent are commonly requested for research involving deception or for minimal risk research when an abbreviated consent is desired and one or more of the required element are not relevant to the research.

Note: FDA-regulated research is not eligible for an alteration of consent.

A. Which element(s) of consent do you wish to eliminate and why?

B. Which element(s) of consent do you wish to alter and why?

C. Provide justification for each of the following regulatory criteria:

i. The research involves no more than minimal risk to the subjects:

ii. The waiver or alteration will not adversely affect the rights and welfare of the subjects:

iii. The research could not practicably be carried out without the waiver or alteration:

iv. Whenever appropriate, the subjects will be provided with additional pertinent information after participation:

N/A we are not requesting an alteration of consent.

39. Full Waiver of Consent/Parental Permission

Complete this checklist if you are requesting a full waiver of consent for all subjects or certain subject groups (e.g., retrospective cohort). Full waivers of consent are commonly requested when the research does not include any opportunity for interaction with subjects (e.g., chart review).

Note: FDA-regulated research is not eligible for a full waiver of consent using these criteria. If you believe that your FDA-regulated research may be eligible for a waiver under another mechanism, such as planned emergency research, contact the HRPO for assistance in determining what information to provide to the HRRC.

A. Are you requesting a waiver for some or all subjects?

☐ All

☐ Some. Explain:

B. Provide justification for each of the following regulatory criteria:

i. The research involves no more than minimal risk to the subjects:

ii. The waiver or alteration will not adversely affect the rights and welfare of the subjects:

iii. The research could not practicably be carried out without the waiver or alteration:

iv. Whenever appropriate, the subjects will be provided with additional pertinent information after participation:

N/A. We are not requesting a full waiver of consent/parental permission.

40. Full Waiver of Consent/Parental Permission (Public Benefit or Service Programs)

Complete this checklist if you are requesting a full waiver of consent for all subjects or certain subject groups (e.g., retrospective cohort) and the research involves the evaluation of a public benefit or service program.

A. Are you requesting a waiver for some or all subjects?

☐ All

☐ Some. Explain:

B. Provide justification for each of the following regulatory criteria:

i. The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine: (i) public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs:

ii. The research could not practicably be carried out without the waiver or alteration.

N/A. We are not requesting a full waiver of consent/parental permission.

41. Full Waiver of HIPAA Authorization (Checklist)

Complete this checklist if you are requesting a full waiver of the requirement to obtain HIPAA authorization for all subjects or certain subject groups (e.g., retrospective cohort). Full waivers of HIPAA authorization are commonly requested when the research does not include any opportunity for interaction with subjects (e.g., chart review).

A. Are you requesting a waiver of authorization for some or all subjects?

☐ All

☐ Some. Explain:

B. Describe your plan to protect health information identifiers from improper use and disclosure:

C. Describe your plan to destroy identifiers at the earliest opportunity consistent with conduct of the research (absent a health or research justification for retaining them or a legal requirement to do so):

D. Describe why the research could not practicably be conducted without the waiver or alteration:

E. The PHI accessed or recorded for identification/screening purposes will not be reused or disclosed to (shared with) any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of the PHI would be permitted under the Privacy Rule.

☐ True

☐ False

N/A. We are not requesting a full waiver of HIPAA.

42. Other Waiver Types (Checklist)

If you are seeking another waiver type (e.g., Planned Emergency Research, Waiver of Parental Permission to Protect Child Participants, Enforcement Discretion for In Vitro Diagnostics, etc. contact the HRPO office for assistance in determining what information to submit for the HRRC's consideration.

N/A. We are not requesting other waiver types.

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43. Vulnerable Populations (Checklist)

A. Adults with Cognitive Impairments

N/A. Adults with cognitive impairments will not be included in this study.

B. Children

N/A. Children will not be included in this study.

C. Pregnant Women and Fetuses

N/A. Pregnant women and fetuses not be included in this study.

D. Neonates of Uncertain Viability or Nonviable Neonates

N/A. Neonates of uncertain viability or nonviable neonates not be included in this study.

E. Nonviable Neonates

N/A Nonviable neonates will not be included in this study.

F. Biomedical and Behavioral Research Involving Prisoners

N/A. Prisoners will not be included in this study.

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44. Medical Devices (Checklist)

N/A. No medical devices will be utilized.

45. Export Control (Checklist)

N/A. There will not be any export control concerns.

46. Data Transfer/Sharing (Checklist)-

Complete this checklist if the research involves transferring/sharing of data with an external entity (institution, company, etc.).

A. Will data be transferred/shared with an external entity (institution, company, etc.)?

☐ Yes

X No. **The remainder of this section does not apply.**

47. Specimen Transfer/Sharing (Checklist)

Complete this checklist if the research involves transferring/sharing of specimens with an external entity (institution, company, etc.).

A. Will specimens be transferred/shared with an external entity (institution, company, etc.)?

☐ Yes

X No. **The remainder of this section does not apply.**

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