PROTOCOL TITLE:

Enhancing Behavioral Treatment for Women with Pelvic Floor Disorders

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VERSION DATE:

April 25, 2019

DEFINITIONS OF ACRONYMS:

BMQ = Brief Medication Questionnaire
CBT = cognitive-behavior therapy
DSM-5 = Diagnostic and Statistical Manual of Mental Disorders
HLM = hierarchical linear models
IPIP = International Personality Item Pool
MBSR = mindfulness-based stress reduction
PCL-5 = PTSD Checklist for DSM-5 with Life Events Checklist
PFDI-20 = Pelvic Floor Distress Inventory
PGI-I = Patient Global Impression of Improvement
PROMIS = Patient Reported Outcomes Measurement Information System
PTSD = posttraumatic stress disorder
RRS = Ruminative Responses Scale
UDI-6 = Urinary Distress Inventory
UP-CBT = Unified Protocol Cognitive-Behavior Therapy

1.0 Purpose of the study:

1.1 Purpose

The purpose of this proposal is to test a novel behavioral treatment – Unified Protocol Cognitive-Behavior Therapy (UP-CBT)[1] – to enhance quality of life in women with pelvic floor disorders. Emotional distress is treatable using behavioral procedures, and effective treatment would increase women's emotional health and help to reduce urinary symptoms (e.g., incontinence, frequent urination). Women with pelvic floor disorders are often seen in the urogynecology or urology clinic, which makes this setting ideal for offering additional interventions that may improve their quality of life. Unfortunately, many women with pelvic floor disorders may not receive effective behavioral treatment, such as cognitive behavior therapy, because urogynecologists, urologists, and other medical professionals may not be aware of providers in their community who offer this treatment. We will enhance treatment options by 1) providing evidence for an all-purpose cognitive-behavioral intervention (i.e., UP-CBT), 2) offering and integrating treatment in the medical clinic, maximizing convenience, and 3) improving clinical outcomes for these patients.

1.2 Specific Aims

1. To demonstrate that UP-CBT is an effective form of therapy for women with lower urinary tract symptoms.
2. To use baseline characteristics in moderation analyses to determine which women will be most likely to have a good response to therapy.
3. To use mediation analyses to test a possible causal chain of events – Does treatment lead to lower anxiety, which in turn leads to fewer urinary symptoms?

1.3 Hypotheses

1. We hypothesize that UP-CBT will reduce anxiety, and urinary symptoms in women suffering from lower urinary tract symptoms, at post treatment and follow-up.
2. UP-CBT will be compared to a control condition, supportive therapy. Supportive therapy, although often used in clinical settings (e.g., in support groups), is not expected to reduce anxiety, or urinary symptoms on average. Thus, we expect that the benefits of UP-CBT will be greater than benefits of the control therapy, supportive listening.

2.0 Background / Literature Review / Rationale for the study:

2.1 Gaps in Current Knowledge

Urinary symptoms are common health issues affecting an individual's quality of life, including mental health. Urinary symptoms include urgency, frequency, incontinence, nocturia, and overactive bladder.[2] We propose a novel behavioral intervention to improve quality of life in women suffering from urinary symptoms. Many women suffer from urinary symptoms, and these symptoms often cause emotional distress as anxiety and depression are both risk factors for developing urinary symptoms.[3] Similarly, urinary symptoms can be exacerbated by emotional distress. Urinary symptoms and pelvic floor disorders affect nearly one in four women.[4] Women with incontinence are both more likely

to have baseline emotional distress and to develop emotional distress as a result of their incontinence. Yet, current methods to treat incontinence do not address the emotional impact that urinary symptoms may have on women. In fact, one in five women will have surgery for these disorders with 30% needing a second surgery for the same condition.[5,6] Therefore, more research is desperately needed on non-surgical treatments for these problems that affect millions of women.

2.2 Background

This study addresses how treatment of overall emotional distress affects anxiety, and in turn urinary symptoms. By experimentally manipulating the trajectory of anxiety through treatment, this study will also give insight into emotional distress as a mechanism of urinary symptoms. Although there is a strong connection between emotional distress and urinary symptoms, evidence on their causal connections remain unexplored.[7-11] Furthermore, research on cognitive-behavior therapy (CBT) for people with urinary symptoms is lacking. Our study will be the first to apply an empirically-supported, transdiagnostic cognitive- and behaviorally-based treatment to women suffering from urinary symptoms, carried out in accord with high quality psychotherapy trials. The existing evidence base is limited to mindfulness-based stress reduction (MBSR)[12,13] and physical therapy techniques (e.g., pelvic floor exercises) as treatments for urinary symptoms, which did not address co-occurring symptoms of emotional distress.

Cognitive-behavior therapy has a well-developed protocol and thus can be administered to women of all ages, and of all economic backgrounds. The intervention is time-limited and low-cost, requiring only visits with the behavior therapist and a low-cost workbook that is widely available. This project will also facilitate systemic change by bringing a behavioral intervention directly to the woman, as opposed to asking the patient to schedule appointments in a different location. Delivering cognitive-behavior therapy in the medical setting, such as in primary care, has been used successfully in previous studies,[14-17] but currently does not exist at Northwestern Medicine. This study can also bring systematic change to the practice of medicine by advancing another possible treatment (i.e., UP-CBT) at the disposal of doctors who are treating women with pelvic floor disorders.

3.0 Inclusion and Exclusion Criteria:

3.1 Criteria

Women must be 18 years of age or older to participate. They must have one or more urinary symptoms, including frequency, nocturia, urgency, leakage, hesitancy, straining, or dribbling. Women who present with clinical signs of anxiety based on the physician exam, have any documented anxiety disorder in the medical record and/or are taking medication for anxiety will be eligible for the study. Women must consent to randomization to treatment, and be willing to complete 12 sessions of treatment, as well as to complete baseline and outcome questionnaires. Women that screen positively for an alcohol or substance use disorder (based on the medical record) will be excluded from the study. Any women with blood in the urine, a positive urine culture, or other signs of possible infection will be deferred until they have been evaluated and treated as needed. Women who are pregnant or who have given birth within the past 6 months will be

excluded from the study. Other exclusion criteria include serious disease that would impede participation (e.g., Alzheimer's dementia, Parkinson's disease); recent (within 6 months) pelvic or endoscopic surgery, urethral stricture, pelvic malignancy, current chemotherapy or other cancer therapy, pelvic device or implant complication; recent (within 12 months) Botox injection to the bladder or pelvic structures; or difficulties communicating in English. Women who are currently in their own psychotherapy are ineligible for the study.

In addition, participants must be willing to defer from usual treatment for urinary problems until after completing the 12-week therapy intervention. For these women with lower urinary tract symptoms, there are multiple treatment options that can be tried sequentially, including the management of anxiety. Thus, if the person consents to be in the study, they will agree to these procedures before trying an alternative management strategy. Some alternatives include physical therapy (e.g., pelvic floor therapy), which can by uncomfortable and/or painful, or even surgery, which has other complications. Thus, psychotherapy is a reasonable and viable alternative. Lower urinary tract symptoms are not life threatening, so waiting to start an alternate therapy will cause waiting for the participant, but no harm. The participant will of course have the choice not to agree to the study and pursue other treatments, or no treatment, if they wish. If a patient is eligible, they will then be given the opportunity to provide informed consent.

Table 1. Summary of Inclusion and Exclusion Criteria

Inclusion Criteria	**Exclusion Criteria**
1. Female 2. Age 18 years or older 3. Presence of one or more of the following urinary symptoms in past 12 months and currently seeking treatment: frequency, nocturia, urgency, leakage, hesitancy, straining, or dribbling 4. Willing and able to provide informed consent 5. Anxious presentation and/or history of anxiety 6. English speaking 7. Willing to defer usual treatment for urinary problems	1. Blood in the urine, positive urine culture, signs of infection 2. Pregnant, or 6 months or less postpartum 3. Psychosis, dementia, or other cognitive impairment that would preclude participation 4. Recent (within 6 months) pelvic or endoscopic surgery, urethral stricture, pelvic malignancy, current chemotherapy or other cancer therapy, pelvic device or implant complication 5. Recent (within 12 months) Botox injection to the bladder or pelvic structures 6. Currently in psychotherapy 7. Current alcohol or substance use disorder 8. Difficulty communicating in English

3.2 Special populations

This study will not include any special populations.

4.0 Sample Size:

This study will include up to 40 participants. UP-CBT has been shown to have quite large effects (Cohen's *d* values of 1.7 or greater).[18] For this study, we have chosen a slightly more conservative estimate for Cohen's *d* of 1.5, which represents 1.5 standard deviations between the treatment effect of UP-CBT versus the control group. Based on a power analysis,[19] we would require 16 women per group, in the data analyzed, to detect a treatment effect with > 98% power with a Type I error rate of $\alpha = .05$, two-tailed. Study withdrawal is estimated at roughly 20%, leaving an estimated final sample of 32 participants for data analysis (see CONSORT diagram below).

5.0 Research Locations:

Participant recruitment and consent will occur at the Northwestern Medicine Integrated Pelvic Health Program (IPHP) clinic within the Department of Obstetrics and Gynecology and through the Northwestern Medicine Urology clinic. Dr. Kenton will oversee recruitment at the IPHP and Dr. Flury will oversee recruitment at the urology clinic. Use of IPHP space has been approved by Dr. Kenton, the chief of Urogynecology. Therapist training will take place in the Griffith lab space in the Department of Medical Social Sciences (MSS). Dr. Griffith has approved use of this space for this research project. Therapy sessions will take place in the Griffith lab space in MSS and in the IPHP clinic space in the Arkes Pavillion of Northwestern Memorial Hospital. Data will be stored at the Griffith lab space, and specific secure cabinets have been designated for this study.

6.0 Multiple sites:

NA

7.0 Reliance Agreements/Single IRB:

NA

8.0 Procedures Involved:

8.1 Randomization and Study Design

This is a pilot study to test pre-post changes associated with UP-CBT, urinary symptoms, and emotional distress. Women eligible for the study will be randomized to treatment based on a predetermined list created using the blockrand package of R.[20,21] Randomization will occur by blocks, with varying block sizes, in accord with recommended methods for RCTs.[22-24] The randomization key will be linked to a unique study ID number, as well as to a treatment condition (UP-CBT or Supportive Therapy).

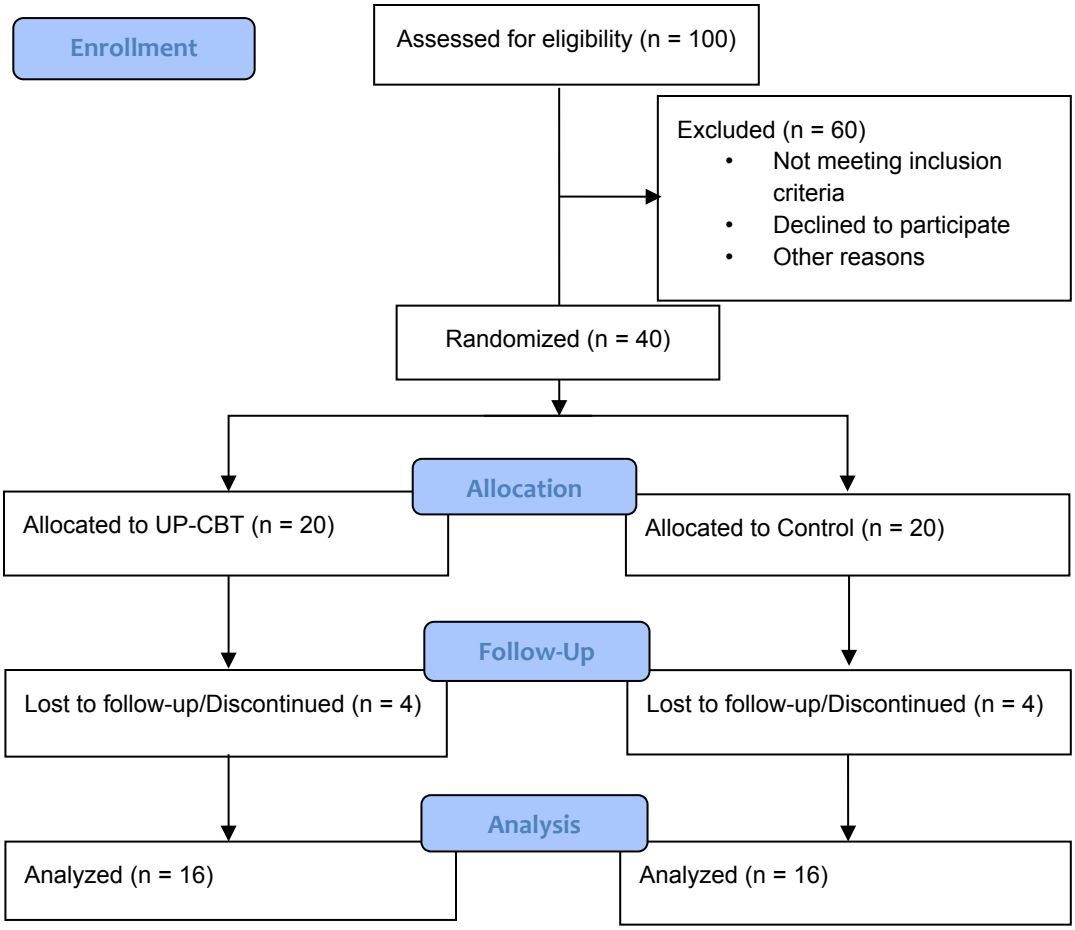

Figure 1. Study Design CONSORT Flow Diagram

8.2 Use of Electronic Medical Record

The electronic medical record (Epic) will be used to extract the following social and medical history. Demographic data (e.g., age, date of birth, gender, race/ethnicity, and insurance type) will be obtained from the patient's electronic medical record, and verified via self-report. Demographic variables will likely be used as covariates in analyses. Results of physical examinations, particularly urological and gynecological history as well as urinary symptoms, will be used to determine inclusion criteria. History and diagnoses of serious illness that would preclude study participation will be extracted to determine exclusion criteria (see section 3.2 above). In addition, substance and alcohol use history and diagnoses will be accessed through Epic to establish the exclusion criterion of substance use disorder. Lastly, mental health history and diagnoses will be pulled from Epic for inclusion/exclusion criteria, and to provide background information for therapists.

8.3 Measures

Participants will be asked to complete questionnaires at baseline, mid-treatment (after 6 sessions), posttreatment (after 12 sessions), at a 3-month follow-up, and at a 6-month follow-up. Baseline, mid-treatment, and posttreatment assessments will be completed on tablets with a link from REDcap, though participants will have the option to

respond on paper forms. Both follow-up assessments will be carried out online with a link sent via email. The primary outcome tool for this study will be the six-item Urinary Distress Inventory (UDI-6), which is a subscale of the Pelvic Floor Distress Inventory (PFDI), as measure of urinary symptoms.[25] We will also measure anxiety using a short form from the NIH Patient Reported Outcomes Measurement Information System (PROMIS), which has been shown to be reliable and valid;[26] this form is brief and easy to complete. Secondary measures include the PROMIS profile[27] (depression, fatigue, pain, physical function, sleep disturbance, and social roles), trauma history assessed with the PTSD Checklist for DSM-5 with Life Events Checklist (PCL-5),[28] the Mini-IPIP, a 20-item short form of the International Personality Item Pool measure of the Big Five personality traits,[29] the Ruminative Responses Scale (RRS) short form,[30] and the Patient Global Impression of Improvement (PGI-I) – a one item self-report assessment of improvement of urinary symptoms.[31] In addition, at both follow-up assessments, participants will be asked whether they have received any treatment outside of the study for their urinary symptoms and/or their anxiety. Any treatment participants receive outside of the study will be tracked in this manner and included in data analyses.

Table 2. Timing of Assessments

Measure	**Estimated Completion Time**	**Baseline**	**Session 6**	**Session 12**	**3 Month Post-Treatment Follow-up**	**6 Month Post-Treatment Follow-up**
Medical history and physical exam	0 (part of regular medical visit and extracted from EMR)	X				
Demographic questionnaire	1 min	X				
Single Item Literacy Screener (SILS)	< 1 min	X				
Brief Medication Questionnaire (BMQ)[32]	3-5 min	X			X	X
Primary outcome 1: PROMIS Anxiety subscale of profile (4 of 29 items below)	See below for entire profile	X	X	X	X	X
Primary outcome 2: Urinary symptoms using the Urinary Distress Inventory (UDI-6) of the Pelvic Floor Distress Inventory (PFDI)	1-3 min	X	X	X	X	X
Secondary outcomes: • PROMIS Profile (29 items) • PGI-I	5-10 min < 1 min	X	X	X X	X X	X X

Secondary correlates: • PTSD Checklist for DSM-5 with Life Events Checklist (PCL-5)	10 min	X				
• Mini-IPIP	3-5 min	X				
• Ruminative Response Scale (RRS)	1-3 min	X				
• Follow-up treatment questions	1-3 min				X	X

8.4 Therapy

Participants will be scheduled to come to an individual treatment session once per week for 12 weeks, at a convenient time for them, on the Northwestern Campus. This arrangement allows for a one-stop experience for the patient, maximizing their convenience. As described above, participants will be randomized to one of two therapy conditions: UP-CBT or supportive therapy. All sessions, in both conditions, will be 45 minutes in duration. If a participant happens to miss or cancel a session they will be rescheduled.

Unified-Protocol Cognitive Behavior Therapy (UP-CBT) is a form of therapy that draws upon various forms of cognitive-behavior therapy to "unify" the most important tools into one protocol. Cognitive-behavior therapy has been a leading treatment for depression and anxiety for decades, but historically has focused on specific disorders (e.g., major depression, social anxiety disorder, panic disorder). UP-CBT includes a variety of general-purpose techniques to help people cope more skillfully with emotionally stressful situations. This includes dealing with emotional situations by reappraising negative thoughts (e.g., "If I get nervous at work, the stress I feel will be temporary and won't kill me" rather than "I can't deal with my life"). UP-CBT focuses on dealing with stress in general, but its techniques are readily adaptable to dealing with urinary symptoms. For example, a woman might have catastrophic thinking about urine leakage ("What if someone notices that I've leaked?"). These catastrophic thoughts can result in strong fear responses, as well as potentially problematic behaviors (e.g., avoidance of social situations or even skipping work). In general, UP-CBT teaches people to track emotions, thoughts, and behavior in an effort to identify maladaptive patterns. In addition, participants learn to restructure their thoughts, and to more confidently confront situations that they find challenging. Towards the end of treatment, patients learn to prevent relapses through practice of therapy skills. Participants in the UP-CBT group will be asked to complete homework outside of the therapy session, to practice therapy skills. Homework will be completed in their therapy workbook, and they will be instructed to bring their workbook to each session. After completing the 12 sessions, participants will be able to keep their workbook.

Supportive therapy is a non-active form of psychotherapy that has been widely used as a control condition in therapy studies.[33-36] Many of the elements of supportive therapy may be beneficial to some participants, just as pill placebos benefit some participants in drug trials. As such, it is an excellent control condition because it is not merely "sham

therapy". Supportive therapy is widely-used in clinical community settings. In this condition, no cognitive-behavioral exercises will be used. Supportive Therapy allows for careful control over the number of therapy sessions and time per session. Thus, it is ideal for being able to match to UP-CBT. The protocol for supportive therapy will include 1) education about urinary symptoms, anxiety, and depression, 2) discussion of patient goals, 3) sharing of concerns in a nonjudgmental environment, 4) discussion of the possible connections between urinary symptoms and emotional distress, and 5) reflective listening. Participants in supportive therapy will *not* be given homework.

8.4.1 Therapy Progress Notes

Therapists will complete brief progress for each participant after each session in both therapy conditions. Progress notes will be used only for research purposes, and will not be added to the medical record. Progress notes will be available to participants upon their request after study completion (including completion of follow-up assessments).

8.5 Analysis Plan

Primary analyses. We will create hierarchical linear models (HLM) to test the primary hypotheses of the study. One model will determine the effect of type of therapy on anxiety. A separate model will determine the effect of type of therapy on urinary symptoms. The dependent variables for these models will be the UDI-6 subscale of the PFDI-20 and anxiety as measured by the anxiety subscale of the PROMIS Profile-29. The structure of the HLM model is shown below. Note that these models create a response profile for each person across all time points as described in the protocol.

Level 1
$Y = P0 + P1(T2) + P2(T3) + P3(T4) + P4(T5) + E$

Level 2
$P0 = B00 + B01(Condition)$
$P1 = B10 + B11(Condition) + R1$
$P2 = B20 + B21(Condition) + R2$
$P3 = B30 + B31(Condition) + R3$
$P4= B40 + B41(Condition) + R4$

The dummy variables P1-P4 are dummy codes for the five time points. These will allow us to determine the degree of change from baseline. Each of the "P" coefficients is influenced by Level-2 variables. T2 - T5 are dummy variables of the time differences from baseline. E, R1-R4 represent error terms in the model. Condition will be dummy coded (UP-CBT = 1, Supportive Therapy = 0).

Testing Key endpoints. We have two primary endpoints and therefore we will have two models. For both anxiety (PROMIS T score) and urinary symptoms (UDI-6), the full model (see above) will be compared to a reduced model with all of the terms involving condition removed (i.e., B01, B11, B21, B31, and B41). If this comparison is significant ($p < .05$), then we will test individual parameters at a Type I error rate of alpha = .05 (two-tailed). Note, these tests will only be carried out if the full-reduced model comparison is

significant. The key prediction for anxiety is that parameters B21, B31, and B41 (representing the effect of UP-CBT at post-treatment and beyond) will be significant and negative (representing fewer symptoms). The key prediction for urinary symptoms is that parameters B21, B31, and B41 (representing the effect of UP-CBT at post-treatment and beyond) will be significant and negative (representing fewer symptoms).

Missing data. All participants with baseline data will be included in the modeling using an intent-to-treat approach. The HLM approach described above can accommodate cases with missing follow-up data.

Mediation analysis. We will also carry out mediation analysis in Mplus using bias-correct bootstrapped 95% confidence intervals. We will hypothesize that these confidence intervals will not contain zero for the following mediated effects:

Condition ➔ Mid-treatment anxiety ➔ Post-treatment urinary symptoms
Condition ➔ Post-treatment anxiety ➔ 3-month urinary symptoms
Condition ➔ 3-month anxiety ➔ 6-month urinary symptoms

In addition to testing statistical significance, our hypothesis is directional. Condition (i.e., receiving UP-CBT) should lead to lower anxiety, in turn leading to lower urinary symptoms.

Exploratory analyses. Although our primary focus is anxiety and urinary symptoms, we will conduct HLM analyses on each scale of the PROMIS Profile (depression, fatigue, sleep, pain interference, pain, social function) and other subscales of the PFDI (total score, colorectal symptoms, pelvic organ prolapse symptoms). These analyses will be clearly marked as exploratory in all write-ups. We will also create a prediction model of treatment response (i.e., trajectory of symptoms) based on baseline characteristics. These will also be clearly marked as exploratory in all study write-ups.

Table 3. Project Timeline

	Months 1-2	Months 3-4	Months 5-6	Months 7-8	Months 9-10	Months 11-12	Months 13-14
IRB Approval							
Staff Training							
Recruitment							
Pilot RCT Study							
Follow-up Assessments							
Data Analysis							
Manuscript write-up							

9.0 Incomplete Disclosure or Deception:

There is no deception involved in this study. Participants will be made aware that they will be randomized to one of two therapies.

10.0 Recruitment Methods:

Participants will be recruited by research coordinators through the IPHP. If an IPHP clinician identifies a patient as meeting the eligibility criteria, a research coordinator will

be called in to speak with the participant about the study. Coordinators will follow a recruitment script. In addition, recruitment flyers and postcards will be placed in the waiting area of the IPHP, and will be shared with IPHP clinicians.

11.0 Consent Process:

The consent process will be carried out by the research coordinators at the IPHP. Written informed consent including HIPAA authorization will be obtained at same visit as screening and determination of eligibility. All participants will be asked about their understanding of their participation, and will have an opportunity to ask questions about the study prior to agreeing to participate. Participants will be free to consult with others (e.g., family members) prior to providing informed consent. Participants will provide written informed consent before beginning the study. Participants will be informed that they are free to withdraw from the study at any time without consequence. Ongoing consent will not be formally assessed after participants provide informed consent, but research team members will be trained to discuss any questions that may arise and what to do if a participant chooses to withdraw from the study. See consent form attachment.

12.0 Financial Compensation:

Each participant, irrespective of treatment group, will be compensated $100. Participant payment will occur in three blocks: once they have completed the 12 therapy sessions they will receive $70 total ($5 per session, with a $10 bonus for completing all 12 sessions), then they will receive an additional $15 for each follow-up assessment. Compensation will be prorated to $5 per session completed if the participant withdraws from the study. Payments will be provided in the form of a Stored Value Card (Visa) for therapy sessions and via virtual gift card for online follow-up surveys. If a participant withdraws from the study they will be given the option to receive their pro-rated payment either via Stored Value Card or virtual gift card based on their preference.

13.0 Audio Recording:

Audio recording of therapy sessions will be optional. For participants that provide consent for audio recordings, therapy sessions will be audio recorded to be reviewed later by the principal investigator, to ensure fidelity of treatment and for supervision of therapists. Recording devices will be stored in a locked cabinet in Dr. Griffith's lab space. Dr. Griffith and the study therapists will have keys to the cabinet. Study therapists will be required to return the recording devices to the cabinet directly after completing sessions for the day. Recordings will be destroyed one year after study completion.

14.0 Potential Benefits to Participants:

Participants will not necessarily benefit from taking part in this research. However, possible benefits include: 1) We can improve behavioral treatment for patients with lower urinary tract symptoms and comorbid emotional distress. 2) This study will provide important information about the causal link between emotional distress and urinary symptoms. 3) Participants may directly experience a reduction in their urinary symptoms and emotional distress. The potential benefits of this study should outweigh the risk to individual participants.

15.0 Risks to Participants:

Participating in this study involves minimal risks. It is possible that participants may feel some shame, emotional discomfort, distress, boredom/fatigue when completing the assessments of urinary symptoms, depression, and anxiety, or when participating in therapy. If we find that participants in the study are at risk for harming themselves or others, we will follow the protocol to connect the participant with crisis services, and document the situation accordingly. We will inform participants that their participation in this study may result in a loss of privacy. This includes data from questionnaires entered into a computerized database, questionnaires completed online, as well as written therapy notes. Several steps will be taken to protect confidentiality and minimize the above risks.

If a participant withdraws from any part of the study (e.g., does not complete one of the surveys), they are welcome to participate in other aspects of the study. If a participant chooses to withdraw from the study, data that has been collected during their participation will be analyzed unless the participant specifies otherwise.

16.0 Provisions to Protect the Privacy and Confidentiality of Participants and the Research Data:

Participants will provide written informed consent. Participants will be given a copy of the consent materials for their records. To protect confidentiality, participants will not be identified by name, but by a unique participant identification number. The key linking participant name to identification number will be stored in a password-protected file. Any other identifying information (e.g., contact information) will be kept separate from the research data. All information, data, and recordings will be kept in secure, password-protected files. Any physical data and forms (e.g., consent) will be kept in a locked cabinet in a locked room. We will inform participants that unless required by law, only the research team and representatives of the Institutional Review Board have the authority to review any study records. All parties with access to the data will be required to maintain confidentiality. Using trained graduate students as therapists will ensure that any potential safety issues are identified and referred to appropriate services. Further, therapists will be supervised by a licensed clinical psychologist. All members of the research team will complete the ethics courses required by Northwestern, including the CITI web-based course on human subjects protection.

17.0 Data Monitoring Plan to Ensure the Safety of Participants:

17.1 Data Monitoring

Each participant will be assigned an anonymous study identification number, which will be used on all study forms. A list of participant names with study IDs will be kept in a secure location separate from study materials. Participants will respond to questionnaires on tablets with a link from REDcap, but have the option to respond on paper forms if preferred, for baseline, mid-treatment, and posttreatment assessments. All paper forms will be de-identified and stored in locked storage using only study ID numbers. After the study visits where measures are given, for any surveys completed on paper the study coordinators will copy the data into REDCap. Subject name, date of birth, and copy of consent will be

entered into StudyTracker. Follow-up assessments will be completed online and connected to REDCap. Data exported from REDCap in a spreadsheet will be stored on the department shared drive (FSMFiles), where only study personnel have access. The spreadsheet will be shared between the study team via their shared drive access, REDCap access, Box.com access, or if necessary secured @northwestern email accounts. The research team will assure complete protection of all data behind Northwestern University's firewalls.

Participants will meet with a therapist on a weekly basis. Any adverse events discussed in therapy will be reported to principal investigators to determine whether the event is study related and if further assessment is needed. Moreover, at the end of the study, each participant will receive a list of referrals for therapy if they would like or need further treatment. Dr. Griffith is a licensed clinical psychologist; he can assist in connecting participants with a therapist if needed.

17.2 Risk Protocol

Should a participant endorse thoughts of harming themselves or others, the study team will intervene. The therapist will first seek consultation with the supervising psychologist (Dr. Griffith) and study physician (Dr. Kenton). If necessary, the therapist will complete a risk assessment using the Columbia- Suicide Severity Rating Scale, develop a verbal safety plan, and provide the participant with a crisis number if necessary. In the rare event that a participant endorses active suicidal or homicidal plan or intent, the therapist will escort the participant to the emergency room at Northwestern. Furthermore, in the rare event that a participant is not cooperative in this instance, the therapist would call 911.

18.0 Data, and if applicable, Specimen Banking:

Data from baseline, mid-treatment, and posttreatment assessments will be collected on tablets with a link from REDcap. If participants choose to respond via paper questionnaires, their responses will be entered onto a secure computerized database (i.e., REDCap) by trained research assistants, then forms will be stored in a locked cabinet in Dr. Griffith's lab space. Follow-up assessments will be completed online, and data will be connected to the secure computerized database. Therapy progress notes will be entered as a word processing document and then saved on a secure server.

19.0 Data Sharing:

For the purpose of open science, data may be shared as supplemental material in publications. Data will be de-identified.

20.0 Qualifications to Conduct Research and Resources Available:

This is an inter-disciplinary project being conducted by both Dr. James Griffith and Dr. Kimberly Kenton in collaboration. Dr. Griffith is listed as the PI for study contact.

PI and Supervising Psychologist: James W. Griffith, PhD. Research Assistant Professor, Department of Medical Social Sciences. Dr. Griffith is a close collaborator of Dr. Kenton (see below). They currently work together on LURN, which is focused on patient assessment, so they are well situated to execute this trial focused on treatment. He is a

recognized expert on quality-of-life issues in patients with urinary symptoms as well as advanced data-analytic techniques used for clinical trials, including growth curve models, mixed modelling, and calculating predicted probabilities of medical state. He has over 50 publications in a variety of clinical areas including urology, depression, anxiety, and cognitive difficulties. He has contributed to the design, execution, and data analyses of clinical trials and large observational studies with aggressive recruitment goals. He is also a licensed clinical psychologist with extensive experience in cognitive-behavior therapy.

Co-I and Urogynecologist: Kimberly S. Kenton, MD, MS. Professor of Obstetrics and Gynecology and Urology, Division of Female Pelvic Medicine and Reconstructive Surgery. Dr. Kenton will co-lead this project along with Dr. Griffith. She possesses advanced training in study design, participant recruitment, and statistics. Dr. Kenton and Dr. Griffith also work closely together on a variety of projects, all focused on women's health including pelvic floor disorders. As a specialist in urogynecology, Dr. Kenton is well aware of the role of anxiety in urinary symptoms, so she will oversee the study to ensure that its results can be integrated into clinical care in the future.

Project Manager and Acting PI: Bayley J. Taple, MS. Graduate student in the Northwestern University Feinberg School of Medicine Clinical Psychology PhD program, Graduate Student Research Assistant in Medical Social Sciences, and T32 Predoctoral Fellow on the Basic Science Training Grant in Urology (PI: David J. Klumpp). Ms. Taple's research is focused on precise symptom assessment of urology patients – including pain, urinary symptoms, and mental health comorbidities – in order to understand etiological mechanisms and to develop novel therapies. Her research employs rigorous statistical methods, providing her with the skills to plan and lead the analytical aspects of this project.

Urologist: Sarah C. Flury, MD. Assistant Professor of Urology. Dr. Flury will assist with participant recruitment by expanding recruitment efforts outside of the IPHP to the general Urology clinic. She will offer the option to participate in this research study to women in her clinic who meet the inclusion criteria, and refer those women to the research coordinators and/or project manager.

Study Therapists. Therapists for both treatment arms will be qualified PhD students from the Northwestern University Feinberg School of Medicine Clinical Psychology PhD program. Graduate student therapists will have current and/or prior therapy experience. Therapists will be closely supervised by Dr. Griffith (PI), a licensed clinical psychologist in the state of Illinois. This study has been approved as an additional practicum experience, thus students will earn direct clinical contact hours for their work on the study. They will have completed CITI training.

Research Coordinators. RCs will have a Bachelor's degree or a higher degree, and previous experience with clinical research. They will have completed CITI training. RCs will report directly to PIs.

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