PROTOCOL TITLE:

SQEASI: Systematized Quality Exercise Alternatives for Stress Incontinence

PRINCIPAL INVESTIGATOR:

Name: Dr. Gena Dunivan

Department: Obstetrics and Gynecology

VERSION NUMBER:

3

DATE: 10/1/18

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)
☐	HHS (Department of Health and Human Services)
☐	VA
☐	Other:

Is this a clinical trial under ICH-GCP E6? ☐ Yes ☒ No

If yes, please confirm that the research team is familiar with and agrees to comply with the investigator requirements cited in ICH-GCP E6. ☐ Yes ☐ No

ICH-GCP E6 can be accessed by copying and pasting this URL into your browser:
http://www.fda.gov/downloads/Drugs/Guidances/ucm073122.pdf

Table of Contents

1. Objectives

The objective of this research is to perform a non-blinded, non-inferiority randomized controlled trial to assess the quality of life (QOL) of women with stress urinary incontinence (leakage of urine with cough or sneeze) before and after conservative treatment with either pelvic floor physical therapy (PFPT) or home biofeedback. The target population are patients with stress urinary incontinence (SUI) who are seeking care and desire non-surgical management. Our central hypothesis is that home biofeedback will be non-inferior to pelvic floor physical therapy and both will equally improve quality of life for women with stress urinary incontinence. The specific aims are:

Aim 1: To compare quality of life, as measured by the International Consultation Incontinence Questionnaire-Short Form (ICIQ- SF), in women with stress predominant incontinence before and after PFPT versus home biofeedback application after 3 months of therapy. Secondary outcomes related to this aim include improvements in urinary incontinence severity as measured by the Incontinence Severity Index (ISI) and desire to pursue additional therapy (such as pessary or surgery) at the conclusion of the study. **Hypothesis**: Home biofeedback will demonstrate equal improvement in QOL in women with SUI compared to PFPT.

Aim 2: To perform a comparative analysis of cost between PFPT treatment and home biofeedback for stress predominant incontinence as well as patient preference for either PFPT vs home biofeedback. **Hypothesis**: Home biofeedback will be less expensive than PFPT due to decreased copays, driving to visits, with similar success rates and women will prefer to have home therapy.

Aim 3: To determine whether patients experience improvement in sexual function following treatment using the Pelvic Organ Prolapse Incontinence Sexual Questionnaire- 12 and Female Sexual Function Index (FSFI). **Hypothesis**: Both groups will report improved sexual function.

2. Background

Urinary incontinence, or accidental loss of urine, is a common problem that affects 10-30% of all women with the majority of incontinence attributed to stress urinary incontinence (SUI) or mixed urinary incontinence (MUI) (1). Prior studies have shown that pelvic floor physical therapy (PFPT) and biofeedback training are both excellent non-surgical options and are recommended as first-line therapy (2) for SUI (leaking with laugh, cough, and sneeze). Both the American Urologic Association and the International Urogynecologic Association recommend PFPT as first-line therapy for SUI (2). Many areas of the country do not have qualified PFPT and

the community outpatient rehabilitation referral is often limited for patients in rural areas that must travel to larger city centers for PFPT. Women who live far from PFPT facilities also must travel great distances to see medical providers for their incontinence and attend multiple PFPT appointments. Though physical therapists have used biofeedback for 20 years, several FDA approved devices for home biofeedback have been introduced to help treat women with SUI at home. Regarding these devices, there is limited information available comparing them to the standard of care. If home biofeedback is equivalent to standard of care PFPT for SUI, patients can obtain treatment in the privacy of their homes with a home devices that may offer similar quality of life improvements for SUI without the inconvenience of travel, cost and personal distress as PFPT. To solve the problem of limited PFPT services and the obstacles obtaining PFPT, we propose to study at home biofeedback devices versus PFPT for women with SUI. This innovative research shows promise in helping our patients overcome an embarrassing and costly condition in the privacy of their own homes on their own time.

3. Study Design

We plan to perform an unmasked, non-inferiority randomized controlled trial to determine if quality of life is improved with use of PFPT or home biofeedback linked to smartphone for stress urinary incontinence. The target population are those patients with stress urinary incontinence who present to the urogynecology clinic either at University of New Mexico Hospital (UNMH) or Sandoval Regional Medical Center (SRMC). Women will be informed which arm of the study they are randomized to as this is required for treatment. Masking is not possible with this study design, as participants either do or do not receive a biofeedback device. All women will give written consent prior to enrollment.

4. Inclusion and Exclusion Criteria

We will recruit patients who present to the University of New Mexico Urogynecology and Gynecology practices at UNM Eubank Clinic (UNM) or Sandoval Regional Medical Center (SRMC) with pure stress urinary incontinence or mixed urinary incontinence with stress predominant symptoms who have never had an anti-incontinence procedure in the past or formalized PFPT. They also cannot be currently using a pessary. To confirm diagnosis and eligibility, we will conduct a history and physical, complete with cough stress test and POP-Q pelvic examination. A cough stress test requires the patient to cough or Valsalva in lithotomy or standing position to assess for leakage of urine and is part of our routine standard of care when evaluating urogynecologic issues. Urinary leakage during this test indicates SUI. If the patent notes >50% of incontinence symptoms from SUI, she will be introduced to the study and provided with written information that may help her decide if participation in the study is right for her. All patients will be counseled about possible treatment options for stress urinary incontinence including non-surgical and surgical techniques. 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.

The rationale for targeting this population is that these are women who would routinely undergo conservative management for their condition initially. Patients will be enrolled if they meet the inclusion and do not meet the exclusion criteria.

The inclusion criteria are:

- Female Subjects >18 years of age
- SUI or Mixed UI with stress predominant symptoms and more bother by the SUI
- English speaking/reading
- Own a smartphone that can support phone application and Bluetooth for the biofeedback device and be able to upload a smartphone application with minimal instruction
- Willing to come for 4 PFPT visits over 3 months if randomized

Exclusion criteria:

- Prior anti-incontinence surgery
- Had prior pelvic floor physical therapy for SUI
- Prolapse of any compartment noted below the hymen
- Inability to speak/understand English
- Pregnant
- Decline or unable to return for frequent PT visits during study period
- Unable to be contacted for follow up by telephone
- Neurologic disorders known to cause neurogenic bladder
- Plan to continue using a pessary after potential enrollment visit

We have decided to only include adults who are capable of giving informed consent. Children, prisoners and pregnant women will not be included. Additionally, the phone app is only available in English, therefore non-English speaking patients are excluded.

5. Number of Subjects

The primary outcome of this study is improvement in incontinence quality of life as measured by the ICIQ-SF Questionnaire. We used the previously reported means and standard deviation for this questionnaire (3) from a prior RCT on biofeedback and pelvic floor exercises. We have powered the study based on a 4-point difference as significant between groups. This 4-point difference used for the power calculation is based on prior studies and the minimally important difference that has been previously established (4). To achieve power for this non-inferiority RCT demonstrating a difference between groups of less than 4 points we need 21 patients per group (biofeedback versus PFPT) to detect no difference with an alpha =0.05 and

with 80% power. Allowing for a dropout of 20% we will enroll at least 50 patients (or 25/group), but up to 75 total.

This is a not a multi-center study. Data will be housed at the Eubank clinic

6. Study Timelines

Based on current clinic volume in the UNM division of Urogynecology, we estimate recruitment of up to 75 patients would be feasible over a 12 month period. A review of our clinic calendar revealed in 1 months' time, the urogynecology division typically sees 10-20 patients who would meet criteria for our study. Assuming 50% enrollment, we will be able to recruit our projected number of patients in 12 months. Additionally, as subjects will be hey are followed for 3 months after randomization, we expect it may take up to 15 months to collect 3 month follow up data. We estimate that data analysis and composition of the manuscript will take an additional 10 months.

Timeline	**July 2018- Oct 2019**	**Nov 2019-Feb 2020**	**Mar 2017-May 2020**
Subject recruitment, therapy, through 3 month follow up	◄———	———	
Data analysis		◄———	———
Manuscript preparation			◄———

7. Study Endpoints

The **primary endpoint** of our study is to determine the 3 month change in ICIQ-SF score between the women who undergo PFPT compared to those to those who undergo home biofeedback therapy for stress urinary incontinence. Our secondary endpoints include patient report of symptomatic cure or improvement and cost effectiveness between techniques and cost of intervention. Our **exploratory endpoints** are to investigate compliance with treatment between groups, preference if given choice between options, and differences in sexual function 3 months after initiation of therapy between the two groups. Desire for further treatment will also be assessed.

Given the extremely low-risk nature of the therapeutic interventions, we do not have any **safety endpoints.**

8. Research Setting

The study will be performed at the University of New Mexico Hospital (UNMH) and Sandoval Regional Medical Center (SRMC) associated urogynecology clinics. Potential subjects

will be recruited in the UNM Eubank and SRMC clinic. All patients will have a complete history and physical taken. They will undergo a pelvic exam where they will be instructed on how to perform a pelvic floor contraction correctly and a cough stress test will be performed as part of the standard of care. After recruitment, they will undergo the consent process, and fill out initial questionnaires in the outpatient offices. Patients randomized to the biofeedback group will be given their devices in clinic and research staff will assist in setting up the device and downloading the phone app. The patients randomized to physical therapy will have their PFPT at the UNM Eubank clinic. To standardize therapy for these women all of our pelvic floor physical therapists will provide women with the same set of exercises and standard schedule of one initial visit and 3 follow up appointments. All other follow-up will be performed in the above-mentioned outpatient clinics.

There are no laboratory tests in this trial other than what would routinely be collected for the workup of SUI, nor is there involvement of any community advisory board. We do not perform urodynamic studies prior to managing patients with SUI with conservative therapy, so this study will not be performed. Also, there will not be any research conducted outside of the UNM HSC and its affiliates.

9. Resources Available

Dr. Gena Dunivan 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. She has been the PI on multiple research trials and has successfully completed randomized control trials both as a fellow and now at UNM. Dr. K. Lauren Barnes is the fellow who has a total of 12 months of protected research time during her fellowship in order to complete this study.

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.

Timeline	**July 2018- Oct 2019**	**November 2019-Feb 2020**	**Mar 2017-May 2020**

Subject recruitment, therapy, through 3 month follow up	◄———	———	———
Data analysis		◄———	———►
Manuscript preparation			◄———►

Research Staff**:** The Urogynecology Division employs a program specialist, 3 research coordinators and one student research assistant. 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 PFDN, and have met recruitment goals with high rates of follow-up and accurate data collection. In addition to PFDN research, Dr. Gena Dunivan 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

There will not be any approvals obtained prior to commencing the research. The 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 any ionizing radiation, biological specimens, or drugs.

11.Multi-Site Research

This is not a multi-site research study.

12.Study Procedures

This non-blinded, non-inferiority randomized controlled trial will be conducted at the UNM Eubank Clinic and SRMC Urogynecology clinic. Each site will recruit participants and we will plan to obtain up to 75 between the two sites. Collaborating investigators will be members of the Urogynecology Division at UNM HSC.

The primary aim of our study is to determine if quality of life is improved with use PFPT versus home biofeedback therapy alone in women with SUI. The target population will be patients with SUI who are seeking care. The current recommendation is to advise patient undergo conservative management with PFPT, try an incontinence pessary, or request the patient perform exercises at home. For all patients who present for treatment of SUI, we will take a thorough history and physical (including a POP-Q pelvic examination), score vaginal muscle strength based on Modified Oxford Grading Scale, perform a cough stress test to assess for SUI, and counsel the patient on all of her options including medical and surgical interventions.

If the patient is interested in conservative management and fulfills study inclusion criteria, we will then offer her the choice of volunteering for the study. All women will give written consent prior to their enrollment at this time and fill out questionnaires in the clinic. Research staff and clinicians will obtain consent and administer study questionnaires. After enrollment, participants will fill out baseline surveys, including the International Consultation on Incontinence Questionnaire- Short form (ICIQ-SF), Incontinence Severity Index (ISI), European Quality of Life-5 dimensions (EQ-5D), Overactive Bladder Questionnaire short form (OAB-q SF) Pelvic Organ Prolapse Incontinence Sexual Questionnaire (PISQ-12), and Female Sexual Function Index (FSFI). Data collected in addition to the above outcome measures includes patient demographics, medical/surgical History, and contact information, which are attached as supporting documents. This information will be collected from the patient on the day of enrollment and we will review the patient's medical record if information is missing or unclear.

Randomization assignment will be generated by computer based randomization table and assigned by a research coordinator not otherwise involved in the study. Assignments will be kept in sealed opaque envelopes numbered sequentially. On the day of the patient's clinic visit, after signing consent and deciding to participate, the research coordinator will bring the next envelope in the sequence will be opened, randomizing the patient to PFPT or home biofeedback. The therapy allocation will then be carried out.

The biofeedback group will be given a PeriCoach© biofeedback device, which has a Bluetooth connection to a smartphone, free of charge. The smartphone application will be uploaded during the visit and linked to the device to ensure the patient understands how to

install the program. An information sheet with recommendation for exercise frequency will be given at the time of enrollment to provide recommendations for use. All participants will start as a beginner in the program and works up to a maintenance level. At the end we expect they will be doing 15 exercises, 3 times per day per manufacturer's instructions. 2 weeks following enrollment, these patients will be called to ensure they understand how device functions and are not having technical difficulties. When the patient returns for the 3 month follow up the smartphone app will be reviewed as the app records how often the patient performs the exercises. If that is not available, we will have the patient self-report her exercise frequency.

For patients randomized to physical therapy, PFPT will be scheduled for 4 sessions over 3 months, as is common practice for patients with SUI. These patients will receive instructions on how to engage their core, contract their vaginal muscles, as well as recommendations for home exercises to be performed for 3 sessions per day. The first session will be to establish the patient's baseline abilities with follow up sessions to reinforce instructions, performance of exercises and to ensure the patient is improving. Patient compliance of attending PT sessions will be recorded, as will the amount each patient spends in co-pays per session. After 3 months, regardless of the number of appointments the patient has attended, she will return for a follow up visit to assess how well she is doing.

Three months after starting active treatment, all participants will have a return visit to discuss progress, which is consistent with our standard care for these patients. If the participant had a delay in starting PFPT, the follow up visit will occur 3 months after first PT appointment. At the 3 month visit the patient will complete the ISI, ICIQ-SF, EQ-5D, OAB-q SF, PISQ-12, FSFI, and PGI-I. We will also ask the patient which treatment she would prefer if given the option, the level of satisfaction she has with the current treatment, and if she is planning any future surgical procedures or treatment for her stress incontinence. A physical exam will assess pelvic floor strength using the Modified Oxford Grading Scale and a cough stress test will be performed. If the patient is unable to return to clinic, a member of the research team will call the patient to administer the surveys over the phone. If unable to contact the patient 3 times, we will discontinue attempts and the patient will be considered lost to follow up.

Table 1: Outcomes collected at various time points

	Baseline	3 months
Demographic and medical history	X	
ISI	X	X
Revised Oxford Scale	X	X
ICIQ-SF	X	X
EQ-5D	X	X

FSFI	X	X
OAB-q SF	X	X
PISQ-12	X	X
PGI-I		X
Follow up Questionnaire		X

Our primary outcome is changes in QOL at 3 months after treatment initiation as measured by the ICIQ-SF. It is our standard of care to see patients back at 3 months following SUI treatment initiation to assess for continued leakage and offer further conservative or surgical management. Therefore, as part of a secondary aim we will assess sexual function, compliance with treatment between groups, preference between 2 options, and desire for further treatment at this 3 month time point.

Outcome Measures:

1. **Pelvic Organ Prolapse Quantification (POP-Q):** This is a validated scale adopted by IUGA/ICS and described in their 2010 joint report. It aims to measure the degree of POP where the hymen is the fixed point of reference for description. (5)
2. **Modified Oxford grading system**: This applies a 6-point scale to rate the muscle strength of the pelvic floor where, strength is as follows:
   0 = no contraction; 1 = flicker; 2 = weak; 3 = moderate; 4 = good; 5 = strong (6)
3. **The Pelvic Organ Prolapse/Incontinence Sexual Questionnaire, 12 (PISQ-12):** This is a brief validated, reliable and responsive measure of women's sexual function in those with pelvic floor disorders. (7)
4. **Incontinence Severity Index (ISI):** This is a validated questionnaire that has been shown to correlate well with pad weighing tests. (8)
5. **Patient's Global Impressions of Improvement (PGI-I):** This is a validated 1-item questionnaire rating specific condition as perceived change in her condition in response to therapy for SUI. (9)
6. **The International Consultation Incontinence Questionnaire-Short Form (ICIQ- SF)** This validated scale is a condition-specific assessing QOL of women with urinary incontinence. The most recent Cochrane review on Biofeedback recommends using this scale in trials using biofeedback for urinary incontinence. (10,11)
7. **Female Sexual Function Index (FSFI):** A brief questionnaire measure of sexual functioning in women that assesses arousal, orgasm, satisfaction and pain. (12)
8. **8. European Quality of Life-5 Dimensions (EQ-5D):** Preference-based utility index algorithm used to calculate each subject's utility index and compare change in QALYs between treatment groups (13).
9. **Overactive Bladder Questionnaire- short form (OAB-q SF):** Symptom bother scale that captures the full spectrum of OAB symptoms and health related quality of life (14).

13.Data Analysis

Data Analysis: Between and within group differences will be evaluated using Fisher's exact test for categorical variables and t-tests for continuous variables. If there are any baseline differences between groups, a multivariate analysis will determine the contribution of these differences to observed differences (if any) between groups.

Power Analysis: Power analysis was performed based on previously reported means and standard deviation for the ICIQ-SF questionnaire. The primary outcome of this study is improvement in incontinence quality of life as measured by the ICIQ-SF Questionnaire. We used the previously reported means and standard deviation for this questionnaire (10) from a prior RCT on biofeedback and pelvic floor exercises. We have assumed a change score of greater than 4 points to be significant between groups based on prior studies and the minimally important difference that has been previously established (11). To achieve significance for a non-inferiority study using these assumptions we would need 42 patients, 21 per group to detect this difference with alpha =0.05 and with 80% power. To allow for a dropout of 20% we will enroll at least 50 patients, but up to 75 to account for participants who are lost to follow up.

Comparative Cost Analysis

The cost analysis will be conducted from a societal and patient perspective and will be expressed as incremental cost required to produce one additional unit of quality-adjusted life year (QALY). Data on each subject's use of medical and non-medical resources related to stress urinary incontinence care will be collected during the follow up period. Direct and indirect costs of care in the physical therapy group will be compared to the at home biofeedback group. We plan to capture incremental direct health care, direct non-medical, and indirect resource use related to study interventions and incontinence care using surveys.

Rationale for using the EQ-5D to measure Utility Values

The European Quality of Life-5 Dimensions (EQ-5D) is a preference-based utility index algorithm will be used to calculate each subject's utility index (13). This instrument will be collected at baseline and 3 months. The EQ-5D has 5 attributes (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) with 3 levels each for a possible 243 unique health states. Using the scoring function based on time-tradeoff method we will compare change in QALYs between the two treatment groups. We are choosing to use a general scale to calculate change in utilities (rather than condition-specific) to allow for comparison of cost-effectiveness results with other interventions and diseases, and this instrument has been validated in women with pelvic floor disorders.

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

There is no DSMB that will be monitoring safety of these procedures. PFPT is a common treatment modality for SUI and standard of care. The biofeedback device is FDA approved and

we anticipate minimal safety concerns from use. Vaginal bleeding, pelvic muscle pain, bacterial vaginosis and pelvic pain could conceivably be caused by use. Additionally, we will keep track of adverse events and ask patients about adverse events at the 3 month time point. Because neither of the studied treatments are experimental or associated with above average risk we do not anticipate any adverse events. 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.

15.Withdrawal of Subjects

Any participant 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. 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 SUI in the usual fashion.

To minimize withdrawal from the study, patients will be randomized just after deciding on non-surgical management and signing consent. According to the 2010 CONSORT guidelines, we will analyze all participants assessed for eligibility within the study. We will document reasons for withdrawal from the study including failure to meet eligibility criteria or participant declining enrollment into the study. We will report eligibility criteria not met or reasons for declining participation in the study. The withdrawal procedure is clearly documented in the study consent.

16.Data Management/Confidentiality

Randomization assignment will be generated by computer based randomization table and assigned by a research coordinator not otherwise involved in the study. Assignments will be kept in sealed opaque envelopes numbered sequentially, and on the day of the patient's clinic visit a research coordinator will open the next envelope in the sequence. This de-identified study subject number will then be assigned to the patient. All data collection sheets and questionnaires will contain the subject number and day of the clinic visit. 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 kept separate from participant study data in a locked, secured office.

The data collection, HIPAA and consent forms will be maintained in a locked file cabinet in the Eubank research office. A separate folder will be designated for each participant. The offices have the additional security of being badge-access only for UNMH OBGYN department employees. A key matching study number to subject's name will be stored on a password protected computer on a secure UNM OBGYN department server. .

The only PHI collected will be patient name, date of birth, and telephone number for site use only and to ensure patient follow up. This will not be entered into the database, but it will be kept with the other identifying information.

The data does not include sensitive information or information requiring additional protection.

All data will be kept in a locked file 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 in the OBGYN administrative offices, using the de-identified subject study number. The electronic data 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 deidentified. The REDCAP database is only accessible using a individual unique login and password and access is only provided to co-investigators. Access is restricted to co-investigators 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.

17.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 folder 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.

18.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 and will have ample time to consider whether they want to participate in the study. Also, locked filing 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.

Additionally, each patient who will be offered enrollment will already have agreed to non-surgical treatment of her SUI. There are minimal risks with either study arm of this RCT. PFPT therapy could cause sore muscles or vaginal spotting after treatment, but these are rare. Emotional discomfort due to the intimate nature of this therapy is also possible. Biofeedback devices carry the same risks. Both treatment randomizations in this study are well established as options for SUI with an excellent safety profile.

Pregnant women will not be included in the study, so there is no risk to embryos/fetuses. If there is concern for pregnancy, we will test the participant on the day of enrollment. 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.

19.Potential Benefits to Subjects

The patients enrolled are already opting for non-surgical treatment of their SUI. 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 who are randomized to at home biofeedback will potentially get benefit from having a personal device they can keep. 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 with improved SUI. PFPT and biofeedback have both been successfully used to treat SUI in the past.

20.Recruitment Methods

We will recruit women from our urogynecology clinical practice and we do plan to advertise for this study, including on social media.

The urogynecology clinics at UNM Eubank, and SRMC have a large referral population of patients with pelvic floor conditions and SUI. Subjects will be identified in the clinics at UNM Eubank clinic, and SRMC by investigators. The patients will be counseled about possible treatment options for SUI including non-surgical and surgical techniques. If the patients have SUI or mixed urinary incontinence with >50% stress, 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. The proposed wording is included in the website advertisement in the supplemental materials section

21.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 private offices or examination rooms in the UNM Eubank, or SRMC clinics, where 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 is required to be signed. All documents containing personal health information (screening logs, consent documents, data forms) are maintained in locked file 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 serverwith access limited to authorized research staff and investigators. This information is only to be used at the study center.

22.Economic Burden to Subjects

Research Procedures	**Number of Samples/Procedures**	**Responsible Party**	
		Study	**3rd Party Payer or Participant**
Biofeedback Device	1 device	☒	☐
Smartphone Data	90 days	☐	☒
Standard of Care Procedures	**Number of Samples/Procedures**	**Responsible Party**	
		Study	**3rd Party Payer or Participant**
Clinic Visit	1	☐	☒
Pelvic Floor Physical Therapy	4	☐	☒
3 month follow up visit	1	☐	☒
Transportation to Physical Therapy	0-4	☐	☒
Transportation to Clinic visits	2	☐	☒

There are no study related costs to the participant outside of what would be recommended for standard care. Whether enrolled in the biofeedback device or PFPT, participants will not be

billed for the study materials. The smartphone apps are free and the biofeedback device will be provided without cost, though the biofeedback smartphone app does use data to record the workout, so it is possible that the patient will use a small amount cell phone carrier data. As part of the study, we will not be offering to compensate participants for charges from their phone companies. They have already chosen to undergo conservative management of their SUI, and they will receive prior authorization from their 3rd party payers if randomized to PFPT, or they will have worked out financial assistance, if needed. These costs will be billed to their insurance provider and costs may range from copay only to full cost of treatment.

The PeriCoach© device and associated materials will be provided free of charge by the study to those randomized to PeriCoach©.

23.Compensation

For completion of the study, each patient will be compensated with a merchant gift card worth $50 total. They will receive a $10 gift card at their initial study visit (enrollment) and $40 gift card at their 3-month follow-up visit in the form of Target gift cards. 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.

24.Compensation for Research-Related Injury

If participants are injured or become sick as a result of this study, 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 written consent document, and reviewed during the informed consent process

25.Consent Process

Patients will be approached about the research study at the urogynecology clinic at UNM Eubank and at SRMC during a discussion for the management of SUI. 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 obtain consent after the participants have been counseled about their condition. Our division routinely treats this condition and are highly qualified to counsel patient regarding the risks, benefits, alternatives for the treatment. Those recruited will have already decided to undergo conservative management of SUI. Hence, they will not be coerced into performance of any "extra" treatments. Additionally, care will not be withheld if they decide not to participate.

The patients who would like to participate in the study will be consented during their new or return visit in the urogynecology clinic. They will have these multiple opportunities to ask any questions that they may have, 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. If they decide to participate at the next visit, they will be allowed to join as long as no anti-incontinence procedure or PFPT has taken place in the interim.

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 is imbedded within the study consent form, which 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.

The HIPAA form is included in the consent attached.

Subjects not fluent in English

Spanish speaking patients will not be included in the study as the required Smartphone application is not available in Spanish. We do not anticipate enrolling subjects who have limited fluency in English.

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.

26. Documentation of Consent

We plan to document consent, and the Consent form is attached. We do not plan on collecting/storing tissue samples.

27.Study Test Results/Incidental Findings

We do not intend to share study test or procedure results with study participants. 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 SUI, which may include different laboratory tests, urine culture or urodynamic testing if unclear cause of incontinence, 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.

28.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.

29.Inclusion of Vulnerable Populations

There will not be any vulnerable populations included in this study. Those electing for treatment of SUI will not be coerced into doing so, nor will they be coerced into participating in this trial.

30.Community-Based Participatory Research

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

31.Research Involving American Indian/Native Populations

NA. This research does not specifically target this population. If a American Indian woman is a candidate for this study she will be offered participation

32.Transnational Research

NA. This study is not transnational.

33.Drugs or Devices

The PeriCoach© biofeedback device will be used to measure provide immediate patient feedback while performing the exercises at home. The device should be washed at home between uses, which will be discussed with patients at the visit. The device has already been tested and validated for measuring pelvic floor contractions and is FDA approved, hence, its safety is not being evaluated in this study.

The company PeriCoach© is in the process of changing manufacturers. As such they have added a sticker to the outside of the PeriCoach© box that state "investigational use only." This is still the same FDA approved device the sticker is intended to prevent resale of the device as it is not currently available for wholesale while they switch manufacturers.

The FDA letter is attached.

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.

I. Waivers or Alterations of Consent, Assent, and HIPAA Authorization

NA. We are not requesting alterations of consent, assent, nor HIPAA Authorization

A. Partial Waiver of Consent for Screening/Recruitment

NA. We are not requesting a partial waiver of consent for screening/recruitment.

B. Partial Waiver of HIPAA Authorization for Screening/Recruitment

We are requesting a partial waiver of HIPAA authorization for screening/recruitment. We will review medical records of participants who have any missing questionnaire data, such as medical history, physical examination and demographic data. Consent will be obtained from patients to review this information.

C. Waiver of Documentation of Consent

NA. We are not requesting a waiver of documentation of consent

D. Alteration of Consent

NA. We are not requesting an alteration of consent.

E. Full Waiver of Consent/Parental Permission

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

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

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

G. Full Waiver of HIPAA Authorization

NA. We are not requesting a full waiver of HIPAA authorization.

H. Other Waiver Types

NA. We are not requesting other waiver types.

II. Vulnerable Populations

A. Adults with Cognitive Impairments

NA. Adults with cognitive impairments will not be included in this study.

B. Children

NA. Children will not be included in this study.

C. Pregnant Women and Fetuses

NA. Neither pregnant women nor fetuses will be included in this study.

D. Neonates of Uncertain Viability or Nonviable Neonates

NA. Neither neonates of uncertain viability nor nonviable neonates will be included in this study.

E. Nonviable Neonates

NA. Nonviable neonates will not be included in this study.

F. Biomedical and Behavioral Research Involving Prisoners

NA. Prisoners will not be enrolled in this study.

III. Medical Devices

The PeriCoach© biofeedback device will be used to measure pelvic floor muscle strength and provide guidance for patients to improve their pelvic floor exercises. These devices will be

provided for the 25 patients randomized to the biofeedback arm at the cost of the investigators. The devices are Bluetooth connected to the patient's smartphone and their profile collects password protected data based on the frequency and quality of their exercises on a secure smartphone application. We will request that the patient show researchers their profile at the 3 month visit to determine the frequency and quality of their exercise performance. The device has already been tested and validated for measuring pelvic floor muscle strength and treating female urinary incontinence and hence, its safety and effectiveness are not being evaluated in this study.

The FDA letter is attached.

References:

1. Karl M Luber, MD, FACOG.The Definition, Prevalence, and Risk Factors for Stress Urinary Incontinence. Rev Urol. 2004; 6(Suppl 3): S3–S9.

2. Culbertson S, Davis AM. Nonsurgical Management of Urinary Incontinence in Women. *JAMA.* 2017;317(1):79–80

3. Bertotto A, Schvartzman R, Uchôa S, et al., Effect of electromyographic biofeedback as an add-on to pelvic floor muscle exercises on neuromuscular outcomes and quality of life in postmenopausal women with stress urinary incontinence: A randomized controlled trial. Neurourol Urodyn. 2017 Nov;36(8):2142-2147. Epub 2017 May 16.

4. Larry T. Sirls, MD1, Sharon Tennstedt, PhD2, Linda Brubaker, MD, et al. The Minimum Important Difference for the International Consultation on Incontinence Questionnaire - Urinary Incontinence Short Form in Women with Stress Urinary Incontinence. Neurourol Urodyn. 2015 February ; 34(2): 183–187.

5. Bump RC, Mattiasson A, Bø K, et al. The standardization of terminology of female pelvic organ prolapse and pelvic floor dysfunction. Am J Obstet Gynecol. 1996 Jul;175(1):10-7.

6. Ferreira CH, Barbosa PB, de Oliveira Souza F, et al. Inter-rater reliability study of the modified Oxford Grading Scale and the Peritron manometer. Physiotherapy. 2011 Jun;97(2):132-8. Epub 2010 Oct 22.

7. Rogers RG, Kammerer-Doak D, Villarreal A, et al, A new instrument to measure sexual function in women with urinary incontinence or pelvic organ prolapse. Am J Obstet Gynecol. 2001;184(4):552.

8. Sandvik H, Espuna M, Hunskaar S. Validity of the incontinence severity index: comparison with pad-weighing tests. Int Urogynecol J Pelvic Floor Dysfunct. 2006 Sep;17(5):520-4. Epub 2006 Mar

9. Schagen van Leeuwen JH, Lange RR, Jonasson AF, et al. Efficacy and safety of duloxetine in elderly women with stress urinary incontinence or stress-predominant mixed urinary incontinence. Maturitas. 2008 Jun 20;60(2):138-47.

10. Herderschee R, Hay-Smith EJ, Herbison GP, Roovers JP, Heineman MJ, Feedback or biofeedback to augment pelvic floor muscle training for urinary incontinence in women. Cochrane Database Syst Rev. 2011

11. Karantanis E, Fynes M, Moore KH, et al., Comparison of the ICIQ-SF and 24-hour pad test with other measures for evaluating the severity of urodynamic stress incontinence. Int Urogynecol J Pelvic Floor Dysfunct. 2004 Mar-Apr;15(2):111-6; Epub 2004 Jan 31.

12. Rosen R, Brown C, Heiman J, et al. The Female Sexual Function Index (FSFI): a multidimensional self-report instrument for the assessment of female sexual function. J Sex Marital Ther. 2000;26:191-208.

13. EuroQol--a new facility for the measurement of health-related quality of life. Health Policy, 1990. **16**(3): p. 199-208.

14. Coyne KS, Thompson CL, Lai JS, Sexton CC. An overactive bladder symptom and health-related quality of life short-form: validation of the OAB-q SF. Neurourol Urodyn. 2015 Mar;34(3):255-63.