Use of the LEVA® Pelvic Health System for Fecal Incontinence

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PROTOCOL TITLE:
COMPARISON OF THE DURATION OF USE OF THE LEVA® PELVIC HEALTH SYSTEM IN WOMEN WITH FECAL INCONTINENCE

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REVISION HISTORY

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	23Jan2025	Adding letter for subjects lost to follow up	No

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1.0 Study Summary

Study Title	COMPARISON OF THE DURATION OF USE OF THE LEVA® PELVIC HEALTH SYSTEM IN WOMEN WITH FECAL INCONTINENCE
Brief Summary	This study will assess whether 8 weeks of use of the Leva Pelvic Health System (Leva) is non-inferior to 16 weeks of use for the treatment of chronic fecal incontinence (symptoms >/= 3 months) in adults with a vagina. Participants will be instructed to complete pelvic floor muscle training using the Leva for 8 or 16 weeks. The hypothesis is that 8 weeks of use of Leva is non-inferior to 16 weeks of use, assessed by a validated FI symptom severity survey. Surveys will be completed at 0 weeks, 16 weeks, and 24 weeks. Long-term surveys will be completed at 1 year and 2 years from enrollment.
Number of study sites	1
Study Design	Pragmatic Non-Inferiority Randomized Control Trial
Primary Objective	To assess whether 8 weeks of use of the Leva Pelvic Health System is non-inferior to 16 weeks of use for the treatment of fecal incontinence in women assessed by the St.Mark's/Vaizey score.[1]
Secondary Objective(s)	To determine the impact of using the Leva Pelvic Health System on the following parameters and to compare these between 8 vs 16 weeks of use: • Pelvic Organ Prolapse Quantification System (POP-Q) • Brink Scale Score • Stool consistency (Bristol Stool Scale)[2] • Fecal Incontinence Quality of Life (FIQoL)[3] • Sexual Function (PISQ-IR)[4] • Patient Global Impression of Improvement (PGI-I)[5] • Patient Satisfaction[5] • Estimated Percentage of Improvement[5] • Global Pelvic Floor Symptoms (Pelvic Floor Distress Inventory – PFDI-20)[6] To assess whether 8 weeks of use of the Leva Pelvic Health System is non-inferior to 16 weeks of use for the treatment of fecal incontinence in women assessed by the St.Mark's/Vaizey score at 24 weeks. To evaluate the relationship between adherence to the Leva Pelvic Health System treatment protocol and changes in fecal incontinence symptoms To evaluate patient satisfaction and usability of the smartphone application component of the Leva Pelvic Health System (mHealth App Usability Questionnaire – MAUQ)[7] To characterize parameters of product use, including adherence, coach interaction, and pelvic floor muscle parameters (endurance, lift angle) To evaluate self-continuation of pelvic floor muscle exercises, at 16 and 24 weeks.

	To monitor and report on safety and adverse events To evaluate long-term impact 1 year and 2 years from enrollment
Research Intervention(s)/ Investigational Agent(s)	The Leva Pelvic Health System is a digital therapeutic system that is FDA-cleared for the treatment of chronic fecal incontinence (symptoms >/= 3 months), for stress, urgency, and mixed urinary incontinence, and for pelvic floor muscle strengthening, in adults with a vagina. The system includes an intra-vaginal device that pairs with a smartphone application to provide real-time visual feedback about pelvic floor muscle performance during usage. It is commercially available by prescription.
Drugs/devices used on study (including any IND/IDE #)	Leva Pelvic Health System
Study Population	Females with chronic fecal incontinence
Sample Size	38 (19 participants in each arm, accounting for 20% attrition)
Study Duration for individual participants	Approximately 24 weeks Participants will be invited to complete 1 and 2 year survey data
Study Specific Abbreviations/ Definitions	FI – Fecal incontinence Leva – Leva Pelvic Health System

2.0 Background

Fecal incontinence (FI) is defined by the involuntary loss of solid or liquid stool.[8] Prevalence estimates of FI among community-dwelling women are approximately 9% and increase with age.[9] These estimates are likely underrepresented because a majority of patients with FI do not report symptoms to a healthcare provider.[10] FI has a significant effect on quality of life and psychosocial well-being, and is associated with depression, anxiety, and social isolation.[8,11]Causes of FI are multifactorial and may be attributed to bowel disorders (i.e., constipation, diarrhea) and/or anorectal dysfunction, including pelvic floor muscle weakness, impaired rectal sensation, and poor rectal compliance.[12] Treatment options include conservative management and surgical interventions. Conservative treatment is considered first-line and consists of dietary and behavioral modifications, medications, physical supports/devices, and pelvic floor muscle training (PFMT) with or without a biofeedback component.[11]Considering the barriers to treatment and social stigma associated with FI, there is an urgent need to investigate novel conservative therapeutic modalities with remote or at-home treatment capabilities. Digital therapeutics represent a new category of therapeutic interventions that are regulated, prescription products that incorporate digital systems (i.e., smartphone applications) to prevent, manage, or treat a particular health condition.[13]The Leva Pelvic Health System (Leva) is a digital therapeutic system that is FDA-cleared for the rehabilitation and training of weak pelvic floor muscles for the first-line treatment of chronic fecal incontinence (>/= 3-month uncontrolled passage of feces) in females. It is also FDA-cleared for the rehabilitation and training of weak pelvic floor muscles for the treatment of stress, mixed, and mild-to-moderate urgency urinary incontinence, including overactive bladder and for general strengthening of pelvic floor muscles in females. The system includes an intra-vaginal device that pairs with a smartphone application to provide real-time visual feedback about pelvic floor muscle performance during use.

Pilot research examined the effectiveness of the first-generation Leva device in reducing severity of FI symptoms in a single cohort of 27 patients using the device for 10 weeks. Study participants experienced a significant reduction in symptom severity assessed by St. Mark's/Vaizey score, a validated patient-reported outcome measure. Significant improvements were also reported on three of four subscales of the Fecal Incontinence Quality of Life (FIQoL) measure, including lifestyle, coping, and depression categories, as well as the Colorectal Anal Distress Inventory (CRADI-8) and Pelvic Organ Prolapse Distress Inventory (POPDI-6) subscales of the Pelvic Floor Distress Inventory (PFDI-20). More than half experienced a 50% reduction in FI episodes on a 7-day bowel diary.[14]

Additional data includes a subset analysis of participants enrolled in an 8-week randomized controlled trial (RCT) that included 299 women with stress or mixed urinary incontinence who completed pelvic floor muscle training either with the second-generation Leva device (intervention group) or according to written and audio/visual instruction (control group). While the primary outcomes assessed during this study included measures of urinary incontinence symptoms, a secondary outcome was the CRADI-8, a validated patient reported outcome measure assessing presence and degree of bother of colorectal symptoms, including fecal incontinence. The subset analysis included 92 participants (intervention group: 44; control group: 42) who indicated they "usually lose stool beyond their control" for well-formed or loose stools with a bother of "somewhat" or greater. At 8 weeks, both groups demonstrated statistically significant improvement on CRADI-8 scores that met the minimum clinical important difference (MCID) of 5 points. While the improvement in the Leva arm was greater, there was not a statistically significant difference between the groups at 8-weeks (P=.54). However, at 6 months, the CRADI-8 symptom improvement of the Leva group was significantly greater than

the control group (p=0.01). Participants in the intervention group saw continued improvement between 8 weeks and 6 months, whereas the control group did not. Participants also experienced significant improvement in condition-specific quality of life measured by the Colorectal Anal Impact Questionnaire (CRAIQ-7) at 8 weeks. While there was no significant difference between groups at 8 weeks (p=0.39), only those in the intervention arm met the MCID at this time point. Moreover, at 6 months the CRAIQ-7 improvement reported by the Leva group demonstrated improvement that was statistically significantly greater than the control group (p=0.02).

The data presented satisfied FDA requirements for breakthrough device designation yielding the indication for Leva for chronic fecal incontinence in females (symptoms >/= 3 months). However, the precise dosage of PFMT with Leva and length of exposure to digital educational and motivational content to drive symptom improvement among women with FI is not known. Broadly, data on PFMT and biofeedback interventions in the context of FI varies; reported treatment duration ranges from 8 to 16 weeks or more. The proposed study will determine the effectiveness of Leva to improve FI symptom severity and quality of life after 8 vs. 16 weeks of use and will inform subsequent implementation of this treatment to optimize patient outcomes.

3.0 Study Objectives and Endpoints

Primary objective

To assess whether 8 weeks of use of the Leva Pelvic Health System is non-inferior to 16 weeks of use for the treatment of chronic fecal incontinence in adults with a vagina, as assessed by the St.Mark's/Vaizey score.

Secondary objectives

- To determine the impact of using the Leva Pelvic Health System on the following parameters and to compare these between 8 vs 16 weeks of use:
  - Pelvic Organ Prolapse Quantification System (POP-Q) (physical exam)
  - Brink Scale Score (physical exam)
  - Stool consistency (Bristol Stool Scale)
  - Fecal Incontinence Quality of Life (FIQoL)
  - Sexual Function (PISQ-IR)
  - Patient Global Impression of Improvement (PGI-I)
  - Patient Satisfaction
  - Estimated Percentage of Improvement
  - Global Pelvic Floor Symptoms (Pelvic Floor Distress Inventory – PFDI-20)

- To assess whether 8 weeks of use of the Leva Pelvic Health System is non-inferior to 16 weeks of use for the treatment of fecal incontinence in women assessed by the St.Mark's/Vaizey score at 24 weeks. To evaluate the relationship between adherence to the Leva Pelvic Health System treatment protocol and changes in fecal incontinence symptoms

- To evaluate patient satisfaction and usability of the smartphone application component of the Leva Pelvic Health System (mHealth App Usability Questionnaire – MAUQ)

- To characterize parameters of product use, including adherence, coach interaction, and pelvic floor muscle parameters (endurance, lift angle)

- To evaluate self-continuation of pelvic floor muscle exercises, at 16 and 24 weeks.
- To monitor and report on safety and adverse events.
- To evaluate long-term impact 1 year and 2 years from enrollment.
    - St. Mark's/Vaizey Score
    - Stool consistency (Bristol Stool Scale)
    - Fecal Incontinence Quality of Life (FIQoL)
    - Sexual Function (PISQ-IR)
    - Patient Global Impression of Improvement (PGI-I)
    - Patient Satisfaction
    - Estimated Percentage of Improvement
    - Global Pelvic Floor Symptoms (Pelvic Floor Distress Inventory – PFDI-20)
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Hypothesis:
The reduction in fecal incontinence severity measured at 16 weeks following 8 weeks of use of the Leva Pelvic Health System will be non-inferior to the reduction in fecal incontinence severity following 16 weeks of use of the Leva Pelvic Health System.

Primary endpoint

- The reduction in fecal incontinence severity measured at 16 weeks following 8 weeks of use of the Leva Pelvic Health System will be non-inferior to the reduction in fecal incontinence severity following 16 weeks of use of the Leva Pelvic Health System as measured by the St. Mark's/Vaizey score.

Secondary endpoints

- Change (improvement) from baseline to 16 and 24 weeks after 8 or 16 weeks of treatment on each of the following outcomes:
    - Pelvic Organ Prolapse Quantification System (POP-Q)
    - Brink scale score
    - Stool consistency – Bristol Stool Scale
    - Condition-specific quality of life – Fecal Incontinence Quality of Life (FIQoL)
    - Sexual function – Pelvic Organ Prolapse Incontinence Sexual Questionnaire, IUGA-Revised (PISQ-IR)
    - Global Pelvic Floor Symptoms – Pelvic Floor Distress Inventory (PFDI-20)
- Change (improvement) from baseline to 24 weeks after 8 or 16 weeks of treatment as assessed by the St.Mark's/Vaizey score
- Patient Global Impression of Improvement (PGI-I)
- Patient Satisfaction Question (PSQ)
- Estimated Percent Improvement (EPI): Adherence (%) – 100% = 2x/daily use x 7 days/week for the assigned duration
- Pelvic Floor Muscle Parameters – Endurance (# seconds), Angle change (degrees)
- Usability of the smartphone application – mHealth App Usability Questionnaire (MAUQ); Participants may also be asked open-ended questions about their experience using the Leva app (e.g., What did you like most? Like least?)
- To evaluate self-continuation of pelvic floor muscle exercises, at 16 and 24 weeks.
- To evaluate long-term impact 1 year and 2 years from enrollment.

Secondary safety endpoints
Safety data will be collected, and adverse events will be monitored and reported.

4.0 Number of Participants

Total participants to be accrued, n = 38

Patients with fecal incontinence will be solicited for interest in participation and enrolled only if they meet inclusion / exclusion criteria.
Total number of participants excluding screening failures, n = 38

Patients with fecal incontinence will be solicited for interest in participation and enrolled only if they meet inclusion / exclusion criteria. Participants will be enrolled at consent.

Total number of participants accrued, n = 38, which accounts for attrition 20%. Participants who leave the study will not be replaced.

5.0 Inclusion and Exclusion Criteria

Screening for eligibility
Patients with fecal incontinence will self-identify interest in participation through a recruitment advertisement flyer or mailing.

Interested potential participants will be pre-screened via telephone call and review of the electronic medical record to determine eligibility. They will be enrolled if meeting inclusion / exclusion criteria.

Inclusion Criteria
- Participants will be included if they meet the following criteria:
  - Adult, age ≥ 18years, assigned female at birth
  - Fecal incontinence, defined as any uncontrolled loss of liquid or solid fecal material that occurs at least monthly over the last 3 months that is bothersome enough to desire treatment
  - Able to stand to perform daily training for at least 3 minutes
  - Able to speak and read English due to Leva smartphone application availability in only English at this time
  - Have an email address, owns a smartphone, and can download an app

Exclusion Criteria
- Participants will be excluded according to the following criteria:
  - Inability to tolerate insertion of vaginal device (e.g., vaginal agenesis, vaginal stenosis, unremitting pelvic pain, within 12 weeks postpartum)
  - Current diagnosis of colorectal or anal malignancy
  - Diagnosis of uncontrolled inflammatory bowel disease
  - Current rectovaginal fistula or cloacal defect
  - Rectal prolapse (mucosal or full thickness)

- Inability to utilize smart phone technology (“app” use)
- Chronic Stool Types 6 or 7
- Fecal impaction by exam
- Stage 4 pelvic organ prolapse
- Concurrent supervised anal sphincter exercise/pelvic floor muscle training with or without biofeedback
- Pelvic floor surgery (including anal sphincteroplasty) within the past 3 months
- Currently pregnant
- Received advanced therapy (i.e. other procedure or surgery) for fecal incontinence previously such as presence of a sacral neuromodulator

Specific population

The Leva Pelvic Health System includes an intra-vaginal component that is inserted to guide and complete daily pelvic floor muscle training. Therefore, female participants only will be included in the study.

6.0 Special Populations

This study will exclude each of the populations in the below listed subsections. Criteria for enrollment in this study excludes each of the populations listed in the subsections below.

If the study will enroll OR use data from any of the populations listed in this subsection, provide justification for their inclusion and describe additional safeguards included to protect their rights and welfare. Federal regulations and/or campus policy allow inclusion of the populations in subsection 6.1 only when the research meets specific criteria.

N/A

☐ Children/Minors (HRP-416 - CHECKLIST - Children)

☐ Pregnant persons / fetuses (HRP-412 - CHECKLIST - Pregnant Persons; HRP-413 - CHECKLIST - Non-Viable Neonates; HRP-414 - CHECKLIST - Neonates of Uncertain Viability)

☐ Prisoners (HRP-415 - CHECKLIST - Prisoners)

☐ Participants with impaired decision-making capacity (HRP-417 - CHECKLIST - Adults with Impaired Decision-Making Capacity)

If the study may include any of the populations listed in subsection 6.2, provide justification for including the population(s) and describe the safeguards you will use to protect their rights and welfare. Federal regulations, state law, or campus policy may require additional review and/or specific safeguards for these populations. HRP-103 - INVESTIGATOR MANUAL, HRP-013 - SOP - LARs, Children, and Guardians and HRP-334 - WORKSHEET - Vulnerable Populations.

N/A

☐ Individuals who are receiving inpatient or outpatient services for mental illness, developmental disability, or alcohol and other drug abuse (AODA)

☐ Individuals who are protectively placed by a court in a treatment facility

☐ Veterans/Military Personnel

☐ Emancipated minors

☐ Anyone especially vulnerable to manipulation or inducements for participation as a result of their illness or socioeconomic condition

If the study recruitment process would be expected to include any of the populations listed in subsection 6.3, describe the safeguards and accommodations you will use during their participation, such as interpreters, methods for completing written assessments, etc. during study participation. See the Investigator's Manual, HRP-334, and HRP-090 - SOP - Informed Consent Process for Research.

N/A

☐ Non-English speaking participants

☐ Illiterate or Low Literacy participants

☐ Participants with visual or hearing impairments

☐ Status Relationship: Individuals with a status relationship with the PI or other study team members (e.g., employees, students, family members)

7.0 Recruitment Methods

Source(s) of participants

Patients with fecal incontinence will self-identify interest in participation through a recruitment advertisement flyer or mailing. Participants may be identified through the clinic schedule and given a letter to inform them of the study. Participants may also be identified using reports from HealthLink with diagnostic codes and given a letter to inform them of the study.

Methods that will be used to identify potential participants.

Patients with fecal incontinence will self-identify interest in participation through a recruitment advertisement flyer or mailing. Participants may be identified through the clinic schedule and given a letter to inform them of the study. Participants may also be identified using reports from HealthLink with diagnostic codes and given a letter to inform them of the study.

Fliers will be posted in University of Wisconsin's Advanced Pelvic Surgery Clinic, at the digestive health center, and senior centers.

Interested potential participants will be pre-screened via telephone call and review of the electronic medical record to determine eligibility.

Describe when, where, and how potential participants will be recruited.

Patients with fecal incontinence will self-identify interest in participation through a recruitment advertisement flyer or mailing. Participants may be identified through the clinic schedule and given a letter to inform them of the study. Participants may also be identified using reports from HealthLink with diagnostic codes and given a letter or study flier to inform them of the study. In person contact will be done by the patient's provider or a member of the care team in a private exam room in the clinic. The study staff may also mail letters to these patients if they do not have an upcoming appointment in the clinic. Letters will be mailed to up to three times to prospective participants. Follow up phone call will occur one week after the final recruitment letter is mailed. UW Urogynecology clinic patients may also be identified through Healthlink and with the assistance of the Clinical Research Data Service and will be sent informational letters notifying them of the study

Fliers will be posted in University of Wisconsin's Advanced Pelvic Surgery Clinic and at the digestive health center, and senior centers.

An email may be sent to department chairs and division chiefs in UW School of Medicine and Public Health departments. The PI may inform the chairs and chiefs about the study and ask them to disseminate the study information to their providers. The email will include the UW IRB approved flyer and letter. The study staff will also bring copies of the flyers to the clinics to give to providers. If needed, the PI will set up a meeting with chairs and chiefs to explain the study. The PI will also inform providers that they cannot discuss details of the study with patients, but can reach out to study staff listed on the flyer or letter.

A mass email will be sent to all current UW–Madison employees or all current UW–Madison students using the UW's Research Email Service. Interested individuals can contact study staff using the UW email address supplied in the email message. The mass email will follow the UW IRB guidelines for email recruitment.

Pre-screening data will not be retained for people who do not enroll in the study. Screening data will be part of the study record for participants who do enroll. Per UW policy, screening data for participants who enroll will be retained for at least seven years.

Materials that will be used to recruit participants.

Recruitment advertisement fliers and mailings will be used from the start of recruitment period, weekly, until total number of participants accrued.

Compensation:

Participant compensation will be a total of $150 over the course of the study period, and mailed to the participants:
- $50 at each in-person visit
- $50 for completion of electronic surveys at completion of electronic surveys at 24 weeks

If participants chose to participant in long-term survey completion at 1 and 2 years, they will be compensated $50 for each set of electronic surveys they complete for a total of $50 at 1 year and $50 at 2 years.

8.0 Consent/Assent Process

Who will obtain informed consent.

The study investigators and clinical research coordinators

Where the consent process will take place.

Written consent will be obtained at the University of Wisconsin's Advanced Pelvic Surgery Clinic during the initial visit.

The consent process for the 1 and 2 year follow-up portion of the study will be conducted remotely, via phone call or video visit on MyChart. Electronic consent via DocuSign will be obtained from participants that wish to participate in this portion of the study.

How the consent process will be conducted

Written consent in person, face to face will be obtained for the initial portion of the study.

The study team will reach out via phone to subjects that participated in the initial portion of the study to inform them of the 1 and 2 year follow-up portion of the study and see if they are interested in participating. If a participant expresses interest, the study team will email a copy of the consent addendum to the participant and schedule a remote visit (phone call or MyChart video visit) to reconsent the participant.

The participant will then sign the electronic consent addendum in DocuSign and the study staff will then DocuSign the same consent addendum. A copy of the signed consent addendum will then be emailed to the participant.

Waiting period
There is no designated waiting period between informing prospective participant and obtaining consent. Prospective participants can take the consent form home to review, and return for the informed consent discussion at a later visit if they are interested in participating.

Step for the potential participant's understanding
The study investigators and clinical research coordinators will be present to explain the protocol, review and obtain the informed consent, to administer initial tasks, to assist in downloading smartphone applications and provide the device.

Participants will have the opportunity to read the informed consent document (attached) and be given the opportunity to ask any questions or address any concerns.

The study investigators and clinical research coordinators will review the informed consent, and describe to the participant what the study entails, including instructions on how to end their participation in the study at any time / their right to withdraw without any repercussions, and risks, benefits, and alternatives to participating in the study.

Study investigators and clinical research coordinators will assess participant understanding of the study, as well as address any questions or concerns to the participants satisfaction.

Participants will sign the informed consent if they agree to participate and be provided with a copy of the signed document.

Any process to ensure ongoing consent.
The study team will be soliciting information from participants throughout the study and address any ongoing questions or concerns.

Follows HRP-090 - SOP - Informed Consent Process for Research.
Yes.

Non-English Speaking Participants
Participants will be included if they are able to speak and read English due to Leva smartphone application availability in only English at this time.

9.0 Process to Document Consent in Writing

HRP-091 - SOP - Written Documentation of Consent.
YES

10.0 Setting

Where research procedures will be performed.

- University of Wisconsin's Advanced Pelvic Surgery Clinic
- Participant self-guided treatment at home setting

11.0 Study Intervention

Description:

The Leva Pelvic Health System is a commercially available digital therapeutic system that is FDA-cleared for the treatment of chronic fecal incontinence (symptoms >/= 3 months) in women, for stress, urgency, and mixed urinary incontinence in women, and for pelvic floor muscle strengthening in women. The system includes an intra-vaginal device that pairs with a smartphone application to provide real-time visual feedback about pelvic floor muscle performance during use. The training protocol embedded in the device/app includes 5 cycles of 15-second contraction followed by a 15-second rest period. This 2.5-minute training protocol is completed twice daily. Participants will be instructed to follow this training regimen with the Leva Pelvic Health System for either 8 or 16 weeks. The device will be shut off remotely by Leva at the end of the allocated 8- or 16-week study period and participants will be able to keep or dispose of the device.

In addition to guiding PFMT, the Leva app also provides educational and motivational content in the form of 'daily tasks.' At each training session, participants will have the opportunity to watch a brief educational video or read a short informative message or article presented to them that describes their health condition, helpful behavioral modifications (e.g., toileting posture, breathing exercises, dietary changes), or words of support or motivation. While engagement with these tasks is optional (PFMT can be completed without completing the task), participants will be encouraged to access this content.

Drug/Device Handling

The Research assistant or Principal Investigator (PI) will familiarize the subject with the Leva Pelvic Health System, assist in downloading the app, instruct the subject in the placement, removal and use of the device and the associated smartphone application. This will be completed using a demo device in the clinic.

The Research assistant or PI will complete the designated Leva medical order form and send via secure fax to the commercial entity to notify them of new participant usage. The Leva app requires the study team to prescribe the device to allow the participant to register the device. This is part of the data sharing agreement.

As part of the registration for the device, Axena Health (The Leva Pelvic Health System) will receive a prescription form from study physician and coordinators with information about participant name, date of birth, phone number, email address, and mailing address. This information requested so that the Leva health coaches are able to provide assistance as a part of this program, and in case any replacement devices are needed during the study period in the event of device damage or failure.

The devices will be stored in the study investigator's office in double locked storage.
The Research assistant or PI will dispense the device to the participant at the initial study visit.

Each participant will receive additional instructions on device set-up and first use by the designated Leva team, as occurs with typical commercial use.

The device will be shut off at the end of the allocated 8- or 16-week study period and participants will be able to keep or dispose of the devices.

The Leva Pelvic Health System is a commercially available digital therapeutic system that is FDA-cleared for the treatment of chronic fecal incontinence (symptoms >/= 3 months) in women, for stress, urgency, and mixed urinary incontinence in women, and for pelvic floor muscle strengthening in women.

	Applicable to:		
FDA Regulation	***IND Studies***	***IDE studies***	***Abbreviated IDE studies***
21 CFR 11	***X***	***X***	
21 CFR 54	***X***	***X***	
21 CFR 210	***X***		
21 CFR 211	***X***		
21 CFR 312	***X***		
21 CFR 812		***X***	***X***
21 CFR 820		***X***	

12.0 Study Timelines

Individual participants will be actively engaged in the study for approximately 16 weeks. Long-term follow-up questionnaires will be administered at 6 months (24 weeks from study start). Study enrollment is anticipated to begin in September 2023 and is estimated to be completed within one year.

Participants will be invited to complete follow up surveys for the study at 1 year and 2 years from enrollment.

13.0 Procedures Involved

Study design

This is a prospective, pragmatic, non-inferiority randomized control trial.

Schedule of procedures:

Study Phase	Screening / Enrollment	16 week Follow Up Visit	24 week Follow Up	1 year surveys	2 year surveys
Visit Number	1	2			
Informed Consent	X				

Review Eligibility	X				
Demographics/Medical Hx	X				
Physical Exam	X	X			
Electronic Study Surveys	X	X	X	X	X
Vital Signs: BP, HR, RR	X				
Pregnancy Test, Urine	X				
Prior/Concomitant Meds	X				
Clinical Laboratory Eval	X				
Adverse Event Assessment		X			

Procedures performed to monitor participants for safety
N/A

Biospecimens
N/A

Drugs and devices
The Leva Pelvic Health System and associated smartphone application will be utilized in this research as the administered treatment to assess the primary endpoint.

Data will be collected during the study
- In office examination at first visit and 16 weeks
  - Limited Physical Examination will include the collection of the following data:
    - Vitals (height, weight, pulse, blood pressure)
    - POP-Q
    - Brink Scale Score

- Leva smartphone application surveys administered at 0,4,8,12,16 weeks
  - UDI-6
  - CRADI-8

- Administration of electronic surveys at 0, 16 weeks and 24 weeks via emailed weblink.
  - St Mark's (Vaizey)
  - Bristol Stool Scale
  - FIQoL
  - PISQ-IR
  - PGI-I
  - Patient satisfaction
  - Estimated percent improvement
  - mHealth App Usability Questionnaire (MAUQ)
  - PFDI-20

- *Questionnaires, structured interviews, or other assessments.*
  Attached

- Source records that will be used to collect data about participants.
  UW Health HealthLink Records (study team will directly access)

Long-term follow-up data

- Administration of surveys at 6 months by mail or email
  - Bristol Stool Scale
  - St Mark's (Vaizey)
  - FIQoL
  - PISQ-IR
  - PGI-I
  - Patient satisfaction
  - Estimated percent improvement
  - mHealth App Usability Questionnaire (MAUQ)
  - PFDI-20
- To evaluate self-continuation of pelvic floor muscle exercises, at 16 and 24 weeks.
- Long-term follow up data will be collected by adminstration of electronic surveys completed at 1 year and 2 years from enrollment date:
  - Bristol Stool Scale
  - St Mark's (Vaizey)
  - FIQoL
  - PISQ-IR
  - PGI-I
  - Patient satisfaction
  - Estimated percent improvement
  - PFDI-20

Regulatory status of all drugs and devices used in the study

The Leva Pelvic Health System is FDA cleared and commercially available.

14.0 Comparison of usual care and study procedures

Describe the current alternatives to participation in this research study.

If a participant chooses not to participate in this study, they can continue to receive standard clinical care, which is initiated with conservative management.

Describe standard practice or standard of care for this participant population

Standard clinical care is initiated with conservative management.

Typically, patients who are presenting for management of chronic fecal incontinence will initially be managed with medical therapy (diet supplementation with bulking agents and / or anti-diarrheal agents) to improve stool consistency.

Subsequent therapy may include biofeedback, followed by advanced therapy options, like surgery.

Typical follow up is 3-4 months.

List any research procedures that overlap with standard practice

The research procedure utilizes Leva Pelvic Health System (a digital therapeutic system that includes an intra-vaginal device that pairs with a smartphone application) to provide real-time visual feedback about pelvic floor muscle performance during use.

While the primary end point of the study is to assess non-inferiority of use of Leva for 8 weeks to 16 weeks, an overlap to standard clinical treatment is the smartphone application educational material. The Leva application provides educational and motivational content in the form of 'daily tasks.' At each training session, participants will have the opportunity to watch a brief educational video or read a short informative message or article presented to them that describes their health condition, helpful behavioral modifications (e.g., toileting posture, breathing exercises, dietary changes or supplementation with bulking agents or anti-diarrheal agents), or words of support or motivation. Engagement with these tasks is optional (PFMT can be completed without completing the task), but participants will be encouraged to access this content to ensure they are provided standard clinical education regarding chronic fecal incontinence.

Describe whether research participation would affect standard clinical care

This study is not anticipated to affect standard clinical care.

While participants will not meet with a clinician for the usual treatment of fecal incontinence, they will receive standard conservative management education through the Leva smartphone application engagement, as well as the self-guided treatment through Leva.

15.0 Withdrawal of Participants

Circumstances under which participants will be withdrawn from the research without their consent.

Removal of Participants from Study:
- Participants are free to withdraw from the study at any time, for any reason.

Participants will be asked for a reason for withdrawal. If due to any adverse event, they will be managed as appropriate and followed until resolution. Participants will be asked if collected data can be utilized or completely withdrawn. Participants will be asked if they can be contacted in the future by the study team.
Participants will be able to keep or dispose their device.

Participants may be withdrawn from the study for the following reasons:
- Participant is unable to use the Leva Pelvic Health System
- Participant experiences a severe adverse effect
- Participant does not follow the study instructions or return for follow up visits
- Participant needs a treatment not allowed while participating in the study
- If the study is stopped by researchers

Procedures for orderly termination.

Should study participants require termination from research due to any of the above listed reasons. They will be notified and instructed that they can keep or dispose of the device.

Describe procedures that will be followed when participants withdraw from the research

No future/continued data will be collected from participants who withdraw from research. The device will be kept or disposed of by the study participants.
If withdrawal is due to any adverse event, they will be managed as appropriate and followed until resolution.

Participants will be asked if they can be contacted in the future by the study team.

LOST TO FOLLOW UP
The study team will mail a Certified Letter (Must be signed for) to study participants who they have not be able to reach at one year after enrollment. The letter will be sent to the most current address on file. If the study team does not receive a response, the study team will designate them as lost to follow up and no longer attempt to reach the subject. The letter is uploaded to the Supplemental Information section.

16.0 Data Management and Confidentiality

Describe any procedures that will be used for quality control of collected data.

All Leva user's complete device registration and provide informed consent for personal and device-related data to be cloud-captured and stored in a HIPAA-compliant manner (Supplement 1). This information includes user demographics, presence and degree of bother of incontinence symptoms, and adherence (i.e., the number of training sessions completed in a given timeframe). For this study, all user data will be coded prior to analysis of user characteristics/variables and treatment outcomes.

The app will be undergoing a UW-Madison cybersecurity risk assessment, requested through OneTrust. Any recommendations that come out of the cybersecurity risk assessment would be implemented once the review is completed.

Describe the steps the researchers will take to secure the data

[x] Data will be coded, and the "key" linking identities to codes will be kept separately from the data.

[x] Only those listed as key personnel will have access to the "key."

[] Other: _____

Patient contact information will be stored separately from the study ID number, and all sensitive data collected will only be identified with study ID numbers. The electronic file linking study ID number and patient's identity will be stored in a password-protected data file on a secure shared drive accessible only to the principal investigator, research assistant, and clinical research coordinators who communicate with the participants.

Data will be collected and stored in REDCap (https://redcap.ictr.wisc.edu).

All researchers / investigators will ensure data management methods are HIPAA compliant.

All personnel with access to individual patient data will be trained in the maintenance of confidentiality of Protected Health Information as required by the Health Insurance Portability and Accountability Act (HIPAA) of 1996.

The University of Wisconsin requires all researchers working with human subjects to take online training courses provided by the Collaborative Institutional Training Initiative (CITI). The IRB proposal form will be submitted understanding that the Principal Investigator has completed the required training.

Describe how and where data will be stored and maintained

[x] Research Electronic Data Capture (REDCap) - ICTR
[x] Data will not be stored or accessed on portable devices.
[x] Portable devices will be used to access secure web-based data collection sites such as ICTR's REDCap. No data will be stored locally on the device.
[x] Screening and enrollment logs will be stored on the UW-Madison Obstetrics and Gynecology secure department server.

Management of Identifiers:

[x] Any identifiers will be destroyed at study closure or at the time of publication.

Describe any planned sharing of data outside the study team / institution

Coded Leva smartphone application usage data will be reported to study investigators and transferred to REDCap prior to statistical analyses.

Note that The Leva Pelvic Health System is an FDA-cleared and commercially available device for which users complete device registration and provide informed consent for personal and device-related data to be cloud-captured and stored in a HIPAA-compliant manner (Supplement 1). For the purposes of this study, any data shared between the University of Wisconsin researchers and Axena Health (The Leva Pelvic Health System) will be coded prior to analysis of user characteristics and treatment outcomes.

To ensure appropriate confidentiality protections, PHI will not be shared from study researchers to the Leva team.

Whether data will have all identifiers removed prior to sharing.

Patient contact information will be stored separately from the study ID number, and all sensitive data collected will only be identified with study ID numbers. The electronic file linking study ID number and patient's identity will be stored in a password-protected data file on a secure shared drive accessible only to the principal investigator and research assistant.

How data will be transmitted or transported.

Coded Leva smartphone application usage data will be reported to experimenters and transferred to REDCap prior to statistical analyses.

Describe limitations on the sharing of data, if any.

Participant data will be coded and linked to participant identifiers. There are no limitations on the sharing of data.

17.0 Provisions to Protect the Privacy Interests of Participants

Describe the steps that will be taken to protect participants' privacy interests.

[x] Procedures will be performed in a private area where others cannot see the procedures being performed or overhear the conversation between subjects and researchers.
[x] All members of the study team are up to date on their institutional HIPAA training.
[x] The study is not collecting information that could pose legal or reputational risks to participants.

Sensitive information
This study will collect information on fecal incontinence, bowel movement consistency, pelvic floor and pelvic floor musculature, satisfaction, quality of life, and sexual function. Collection of sensitive information about participants is limited to the amount necessary to achieve the aims of the research. Collection of this information from participants is justified as fecal incontinence and pelvic health are interrelated, and it is important to assess the impact of treatment on these other listed aspects of health.

Steps you will take to make the participants feel at ease with the research
Establishing rapport with participants in order to guarantee the validity and integrity of the study. Ensure participant understanding that research investigators and team will always act in accordance with ethical guidelines and solutions in order to protect the participants from risks and maintain their privacy by establishing confidentiality.

Medical records from UW Health or other sources
The study team has authorized access to electronic medical records and will access participant data as allowed by legal medical record holder. Record review will be reviewed initially at screening, after each study visit for participants who consent, and at study completion.

18.0 Sharing of Results

Describe whether results will be shared with participants or others
The results of the urine pregnancy test and physical exam results will be added to the participant's medical record.
Individual study results will not be shared. Study results will be shared with participants in aggregate as a results brief.

Describe plans to share study results with the public.
Study results have the potential to be submitted for publication to a peer-reviewed scientific journal. Study results may also be presented at professional conferences and at departmental meetings.

19.0 Data Banking

Data banked for future use
Data will be accessed in REDCap until study publication. Study investigators will have access to data. After study publication, de-identified data will be stored on a secure department server for future use.

Data to be stored
- Survey data (coded):
  a. Bristol Stool Scale
  b. St Mark's (Vaizey)
  c. FIQoL
  d. PISQ-IR
  e. PGI-I
  f. Patient satisfaction

g. Estimated percent improvement
h. MAUQ
i. PFDI-20

- Exam data (coded):
  a. Vitals (height, weight, pulse, blood pressure)
  b. POP-Q
  c. Brink Scale Score

- Coded patient demographic and relevant medical history data

Procedures to release data

Data may be shared with researchers at UW-Madison, Axena Health or other outside institutions for future research. This research will be about fecal incontinence or other types of research. Data will be kept for an unlimited amount of time after completion of this study. IRB review will be requested before data is used for research outside the scope of this protocol. PHI will be removed from the data before sharing with other researchers.

Participants may withdraw their banked data from future research use.

If a participant withdraws from the study, they will be asked if collected data can be utilized or withdrawn from the banked data. Data will still be part of the study records. Participants will be asked if they can be contacted in the future and if the study team can contact them in the future.

Participants will keep or dispose of the study device.

After any study analysis, participants will not be able to request data withdrawal. Participants will be made aware that analyzed data cannot be withdrawn.

20.0 Study Analysis

Statistical Hypotheses

This is a prospective, pragmatic, non-inferiority randomized control trial.

- Primary alternate hypothesis: 8 weeks of use of the Leva Pelvic Health System is non-inferior to 16 weeks of use for the treatment of fecal incontinence in women assessed by the St.Mark's/Vaizey score at 16 weeks follow up.

-Primary null hypothesis: 8 weeks of use of the Leva Pelvic Health System is not non-inferior to 16 weeks of use for the treatment of fecal incontinence in women assessed by the St.Mark's/Vaizey score at 16 weeks follow up.

-Secondary endpoints:
- To determine the impact of using the Leva Pelvic Health System on the following parameters and to compare these between 8 vs 16 weeks of use at 16 and 24 weeks:

- POP-Q
- Brink Scale Score
- Stool consistency (Bristol Stool Scale)
- Fecal Incontinence Quality of Life (FIQoL)
- Sexual Function (PISQ-IR)

- Patient Global Impression of Improvement (PGI-I)
- Patient Satisfaction
- Perceived Percentage of Improvement
- Global Pelvic Floor Symptoms (Pelvic Floor Distress Inventory – PFDI-20)

- To evaluate change (improvement) from baseline to 24 weeks after 8 or 16 weeks of treatment as assessed by St.Mark's/Vaizey score
- To evaluate the relationship between adherence to the Leva Pelvic Health System treatment protocol and changes in fecal incontinence symptoms
- To evaluate patient satisfaction and usability of the smartphone application component of the Leva Pelvic Health System (mHealth App Usability Questionnaire)
- To characterize parameters of product use, including adherence, coach interaction, and pelvic floor muscle parameters (endurance, lift angle)
- To evaluate self-continuation of pelvic floor muscle exercises, at 16 and 24 weeks.
- To monitor and report on safety and adverse events

Sample Size Justification:

Treatment response as length of use on symptom improvement (8 weeks vs 16 weeks) (St Mark's (Vaizey) scores of –3 ± 4.37 at 8 weeks (compared to baseline)

1. Non-inferiority test (8 weeks vs 16 weeks) with allowable difference of 1 (based on statistical considerations and clinical judgement)
2. 8 weeks vs 16 weeks of Leva use
   a. α =0.05
   b. power 80%
      i. Sample size to enroll in each group with attrition rate 20%, n= 19

Participant Population(s) for Analysis:

Non-inferiority randomized control trial comparing 8 weeks of use of the Leva Pelvic Health System to 16 weeks of use for the treatment of fecal incontinence in women assessed by the St.Mark's/Vaizey score at 16 weeks.

Each treatment arm will be matched 1:1 for 8 weeks:16 weeks use of the Leva Pelvic Health System and randomized in a permuted block randomization technique.

Statistical Methods:

The point-estimate and the fixed-margin methods are methods of analyzing non-inferiority where the margin is defined based either on the effect estimate from the historical evidence or the limit of the confidence interval of the effect estimate that is the closest to the null effect. Statistical analysis for primary objective will likely utilize the point-estimate method, as in this method, the fraction of the effect estimate that is considered clinically significant is determined based on clinical judgement.[15]

Treatment response as length of use on symptom improvement at 16 weeks (comparing 8 weeks vs 16 weeks of use of Leva) as assessed by St Mark's (Vaizey) scores.
A difference of –3 ± 4.37 is expected at 8 weeks and 16 weeks (compared to baseline), with an allowable difference of 1.

Planned Interim Analysis

No interim efficacy analysis is planned.

Device usage data and safety data will be collected throughout the study period. The anticipated risk is minimal; the study team will alert the investigator if responses to surveys about quality of life indicate concerns for participant well-being.

Complete efficacy data will be collected at 16 weeks and at 6 months from study start for comparison to baseline data.

Handling of Missing Data:

If there is any missing data, we typically assume it is missing at random.
Missing data will be documented along with reasons for this missingness.
Any impact of missing data will be calculated with sensitivity analyses.
If missing data is extensive, then an appropriate model-based approach will be utilized to estimate effects under various assumptions.

21.0 Potential Benefits to Participants

Potential benefits that individual participants may experience from taking part in the research.

Participants will participate in rehabilitation and training of weak pelvic floor muscles, which may lead to:
- Improvement in chronic fecal incontinence symptoms
- Improvement in stress, mixed, and mild to moderate urgency urinary incontinence (including overactive bladder) symptoms
- Strengthening of pelvic floor muscles

It is reasonable to consider that at least half or more participants will experience such symptom improvement, enough to be considered clinically meaningful. Based on pilot data, this symptom improvement may last 6 months or more.

22.0 Risks to Participants

Foreseeable risks, discomforts, hazards, or inconveniences

The Leva Pelvic Health System is an FDA-Cleared Class II Medical device. As such it has been tested and found to conform with the requirements of Medical Electrical Equipment - Part 1: General Requirements For Basic Safety And Essential Performance [AAMI ES60601-1:2005 +A1]Medical Electrical Equipment - Part 1: General Requirements For Basic Safety And Essential Performance [CSA C22.2#60601-1:2014 Ed.3]Medical Electrical Equipment - Part 1-6: General Requirements For Basic Safety And Essential Performance - Collateral Standard: Usability [IEC 60601-1-6:2010 Ed.3+A1]Medical Electrical Equipment Part 1-11: General Requirements For Basic Safety And Essential Performance Collateral Standard - Requirements For Medical Electrical Equipment And Medical Electrical Systems Used In The Home Healthcare Environment [IEC 60601-1-11:2015 Ed.2] In addition, a biocompatibility evaluation was performed to satisfy FDA requirements [ISO-10993-1: 2018] Biological Evaluation of Medical Devices - Part 1. All patient contact materials have passed testing for cytotoxicity,

sensitization and irritation. The results of these tests indicate that the device is safe for its intended use.

The risk of adverse events related to use of the Leva Pelvic Health System is minimal. In a pilot study evaluating the use of Leva for fecal incontinence, no significant device-related adverse events were reported.[16]

Adverse events, including vaginal irritation , pain and urinary tract infection, may occur in a small proportion of women. In a recent clinical trial examining Leva as a treatment for women with urinary incontinence, rates of vaginal irritation and urinary tract infection were 2.7% (5/182) and 1.7% (3/181), respectively.[17]

Participants who report these complaints will be evaluated for severity and desire to continue with study. Adverse events will be managed and followed to resolution. Participants may discontinue use of the device for a short timeframe or altogether.

Minimize risks of harm or discomfort.

The study inclusion and exclusion criteria have been created to allow for a pragmatic trial, but with the intention to prevent harm or discomfort for participants.
Specifically, the first exclusion criteria is 'the inability to tolerate insertion of vaginal device (vaginal agenesis, vaginal stenosis, unremitting pelvic pain, within 12 weeks postpartum).'

Participants will be monitored during the study period for any adverse events, risks or safety concerns. Any participant questions or concerns will be communicated with either the study investigators directly or Axena Health, Inc. (The Leva Pelvic Health System) directly and reported to study investigators.

Participants will be provided with surveys to complete at 4 and 6 months from study completion and will have additional opportunity to communicate any adverse events, risks or safety concerns.

23.0 Provisions to Monitor the Data to Ensure the Safety of Participants

Plan to periodically evaluate the data collected

The anticipated risk is minimal; the study team will alert the investigator if responses to surveys about quality of life indicate concerns for participant well-being.

Participants will be monitored during the study period for any adverse events, risks or safety concerns. Any participant questions or concerns will be communicated with either the study investigators directly or Axena Health, Inc. (The Leva Pelvic Health System) directly and reported to study investigators.

The Leva team will send updates to the study team every 4 weeks. If an identified concern or event is unexpected or greater than minimal risk, the study team will be notified by Leva team or participant immediately.

What data are reviewed, including safety data, untoward events, and efficacy data.

The anticipated risk is minimal; the study team will work together with the Leva team to monitor study progress and identify potential problems, risks, safety concerns, adverse events or reportable events.

The Leva team will send updates regarding safety data and usage data every 4 weeks. If an identified concern or event is unexpected or greater than minimal risk, the study team will be notified by Leva team or participant immediately.

Efficacy data will be reviewed at study completion.

The study team also conduct regular internal reviews of study data and consent forms for compliance.

How the safety information will be collected

The anticipated risk is minimal; the study team will work together with the Leva team to monitor study progress and identify potential problems, risks, safety concerns, adverse events or reportable events. Participants will also be encouraged to call on any identified potential problems, risks, safety concerns, adverse events or reportable events.

The frequency of data collection, including when safety data collection starts and ends.

Device usage data and safety data will be collected throughout the study period.
Participants will be instructed to contact study investigators or research coordinators with any questions or concerns at any time during the study.
Complete efficacy data will be collected at study completion and long-term follow up data at 6 months from study start; this data will be compared to baseline data.

Who will review the data.

The study team will review the data.

The frequency or periodicity of review of cumulative data.

The cumulative data will be reviewed at study closure.

The statistical tests for analyzing the safety data to determine whether harm is occurring

N/A - there is minimal risk associated with this study

Any conditions that trigger an immediate suspension of the research

Any unexpected change in study status by the device manufacturer, study investigator, or institution that appears to impact subject safety and/or the ability of the study to meet its original aims (e.g., halt to enrollment due to equipment malfunction or device supply issues).

Reportable event reporting requirements

The timeframes for reporting information / events will comply with the posted requirements. The research assistant or PI will report to the IRB in accordance with posted IRB reportable event reporting guidelines as outlined in the Investigator Manual.

24.0 Economic Burden to Participants

Participants are not anticipated to have any cost related to participation in this research.

25.0 Resources Available

Will the research be conducted outside School of Medicine and Public Health or UW Hospitals and Clinics (e.g. the researcher does not have an SMPH research feasibility attestation for this study)?

☐ YES (complete 25.1)

[x] NO (remove text below, but retain this section)

26.0 References

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