Tailoring Online Continence Promotion for Women

NCT05183217

4/19/2024

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Protocol Number: MRR 2021-1555
Principal Investigators: Megan Piper, PhD and Heidi Brown, MD, MAS

Funding Source: National Institute of Diabetes and Digestive and Kidney Disease

Protocol Version History

Protocol Version	Version Date	Summary of Revisions Made	Rationale
1.0	11/05/2021	Initial version	
2.0	12/10/2021	Revisions made after IRB pre-review	
3.0	10/17/2022	Updates needed due to Dr. Werner's change in location and change in location	
4.0	9/20/2023	Final revisions before launch of recruitment and updates due to Dr. Brown's change in institution	
5.0	1/3/2024	Increase enrollment number	
6.0	1/6/2024	Implementing a quality check to ensure participants are real participants	
7.0	2/6/2024	Enrollment criteria	
8.0	4/19/2024	Changes requested following post-approval monitoring review of study	

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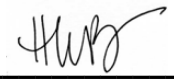
1.0 STATEMENT OF COMPLIANCE

I confirm that I have read this protocol. I will comply with the IRB-approved protocol, and applicable regulations, guidelines, laws, and institutional policies.

I agree to ensure that all staff members involved in the conduct of this study are informed about their obligations in meeting the above commitment.

Name	Signature	Date
Heidi W. Brown, MD, MAS Principal investigator		11/05/2021
Megan Piper, PhD Principal investigator		9/20/2023
Not Applicable (NIDDK) Sponsor		

2.0 LIST OF ABBREVIATIONS

BCABL	Barriers to Care-seeking for Accidental Bowel Leakage
BICS	Barriers to Incontinence Care-Seeking Questionnaire
BMI	Body Mass Index
CCC	Clinical Coordinating Center
DCC	Data Coordinating Center
DHHS	Department of Health and Human Services
DSMP	Data and Safety Monitoring Plan
EPI	Estimated Percent Improvement
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GPI	Global Perception of Improvement
GSE-UI	Geriatric Self-Efficacy Index for Urinary Incontinence
HIPAA	Health Insurance Portability and Accountability Act
HSIRB	Health Sciences Institutional Review Board
ICIQ-UI SF	International Consultation on Incontinence Questionnaire – Urinary Incontinence Short Form
IRB	Institutional Review Board
MOM	Mind Over Matter
NDE	Natural Direct Effect
NIDDK	National Institute of Diabetes and Digestive and Kidney Diseases
NIE	Natural Indirect Effect
NIH	National Institutes of Health
OHRP	Office for Human Research Protections
PFIQ-7	Pelvic Floor Impact Questionnaire Short Form
PHI	Protected Health Information
PI	Principal Investigator
PSQ	Patient Global Ratings of Satisfaction
SMIS	St. Mark’s Incontinence Score
UW	University of Wisconsin-Madison

3.0 STUDY SUMMARY

3.1 Synopsis

Full Title	Tailoring Online Continence Promotion for Women
Protocol Number	MRR 2021-1555
ClinicalTrials.gov Identifier & Summary	NCT05183217 This project seeks to understand whether, and how, tailoring an online continence intervention can increase engagement and uptake of health behaviors known to improve symptoms.
Number of Site(s)	University of Wisconsin-Madison
Main Inclusion Criteria	• Female, age ≥ 50 years • Can read and write English • Can use email • Has access to Internet-connected device (such as a computer, tablet, or smart phone) to use an online program
Main Exclusion Criteria	• Women with medical conditions for which the intervention is not medically appropriate, including: − dementia − neurologic or musculoskeletal conditions in which pelvic floor muscle exercises are contraindicated − hematuria or bloody stools within the last 6 months that have not been evaluated by a medical professional
Objective(s)	Primary Objective • To evaluate whether tailoring will increase engagement with online MOM. [Corresponds to Aim 1 of grant] Secondary Objectives • To evaluate whether tailoring will increase adoption and maintenance of health behaviors that promote continence. [Corresponds to Aim 2 of grant] • To determine the extent to which intervention engagement mediates the effect of tailoring on health behavior change. [Corresponds to Aim 3 of grant] • To determine the extent to which factors other than degree of intervention engagement mediate the effect of tailoring on health behavior change. [Corresponds to Aim 3 of grant]
Endpoints	Primary Endpoint • Proportion of participants who engage with online MOM (participation in at least one session per week during the first 4 weeks of the program) in the group with (test) and without (control) tailoring. [Aim 1 primary outcome] • Comparison of specific program use metrics (number of, minutes spent on, and average intervals between program sessions accessed weekly; number of and specific components accessed) between the two groups and cluster analyses will identify patterns of program use (such as tracking and reminders). [Aim 1 exploratory outcomes] Secondary Endpoints

	• Proportion of participants in the treatment group compared to the control group who adopt consistent pelvic floor muscle exercises at 4 weeks, defined as self-reported performance of pelvic floor muscle exercises consistently (often or always) at 4 weeks after reporting inconsistent performance of these exercises at baseline. [Aim 2 primary outcome] • Proportion of participants in the treatment group compared to the control group who maintain exercise (reporting consistent exercise performance at two consecutive time points between 4, 12, and 24 weeks). [Aim 2 exploratory outcome] • Proportion of participants in the treatment group compared to the control group who adopt other health behaviors (fiber intake of at least 21 g; caffeine intake <205 mg/day, daily fluid intake between 60 and 100 ounces, and 6-9 voids per day) at 4 weeks, defined as exhibiting these behaviors consistently (often or always) at 4 weeks after reporting inconsistent performance of these behaviors at baseline. [Aim 2 exploratory outcome] • Proportion of participants in the treatment group compared to the control group who maintain other health behaviors (fiber intake of at least 21 g; caffeine intake <205 mg/day, daily fluid intake between 60 and 100 ounces, and 6-9 voids per day), reporting consistent performance of these behaviors at two consecutive time points between 4, 12, and 24 weeks). [Aim 2 exploratory outcome] • Proportion of participants in the treatment group compared to the control group with a body mass index (BMI) >25mg/kg^2 at baseline who report weight loss of at least 2 kg at 12 or 24 weeks. [Aim 2 exploratory outcome] • Assessment of degree of program engagement (defined by program use data during the first 4 weeks) in relation to the intervention's effect on adoption of pelvic floor muscle exercises at 12 weeks. [Aim 3 outcome] • Assessment of self-efficacy (comparing change in self-efficacy measures at 4 weeks relative to baseline [0 weeks]) in relation to the intervention's effect on adoption of pelvic floor muscle exercises at 12 weeks. [Aim 3 outcome] • Assessment of incontinence symptoms and quality of life (comparing change in survey rating at 4 weeks relative to baseline [0 weeks]) in relation to the intervention's effect on adoption of pelvic floor muscle exercises at 12 weeks. [Aim 3 outcome] • Assessment of barriers to care-seeking (comparing change in survey rating at 4 weeks relative to baseline [0 weeks]) in relation to the intervention's effect on adoption of pelvic floor muscle exercises at 12 weeks. [Aim 3 outcome]
Study Design	This is a two-arm, parallel, randomized, controlled trial (RCT) comparing an online continence promotion program with standard weekly reminders (control arm) to an online continence promotion program with tailoring (treatment arm) to determine the impact of tailoring on program engagement.
Study Intervention	Women in the treatment arm will receive tailored content and digital reminders for 12 weeks based on their individual characteristics, symptoms, and behaviors assessed at baseline, with reassessment of key inputs every week resulting in re-tailored outputs.
Total Number of Participants	Up to 800 participants will be recruited for the main project. A subset of participants (N=36) will be invited to complete semi-structured qualitative interviews.
Study Population	Females aged 50 years and older in the U.S. who do not have medical conditions for which the intervention is not medically appropriate.

Statistical Methodology	The proportion of participants in the treatment versus control group who achieve engagement (primary outcome) will be compared using binomial chi-squared test with type I error rate at 0.05.
Estimated Participant Duration	The duration of the study for each participant is approximately 24 weeks.
Estimated Enrollment Period & Study Duration	Study enrollment will occur over 12 months with the total expected duration of the trial to be 18 months.

4.0 KEY ROLES

The following is a list of all key personnel and roles:

Principal Investigators	**Megan Piper, PhD** **Professor** **Department of Medicine** **University of Wisconsin SMPH** **1930 Monroe Street, Suite 200** **Madison, WI 53711** **608-265-5472** ***mep@ctri.wisc.edu*** **Heidi Brown, MD, MAS** **Clinician Researcher II** **Kaiser Permanente Research** **Division of Health Services Research & Implementation Science** **3250 Fordham Street** **San Diego, CA 92110** **619-695-4714** **Heidi.w.brown@kp.org**
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5.0 INTRODUCTION

5.1 Background

Incontinence is common, costly, and vastly undertreated in women. More than 60% of women age 65 or older suffer from urinary and/or bowel incontinence, the combined annual cost of which exceeds $30 billion in women aged 50 and older [1-3], and its prevalence is increasing, even in younger women [4]. In addition to negative impacts on quality of life, social isolation, and depression [3, 5-7], urinary and bowel incontinence increase risks for caregiver burnout, hospitalization, and nursing home placement [8-11]. Despite the existence of effective treatments [12-16], we found that over half of women with urinary incontinence and 70% of women with bowel incontinence do not seek medical care [17]. Incontinence interventions delivered in healthcare settings thus reach fewer than half of those in need.

An in-person intervention delivered in community settings, *Mind Over Matter: Healthy Bowels, Healthy Bladder (MOM)* improves bladder and bowel incontinence and increases adoption and maintenance of pelvic floor muscle exercises in women age 50 and older [18]. This program was developed and tested during the PI's career development award. Based on the Health Action Process Approach (Figure1) [19, 20], in-person MOM consists of three 2-hour sessions over 4 weeks during which eight to 12 women learn strategies to improve symptoms, set personal goals, and overcome barriers to success. The program is delivered in the community by a trained lay-facilitator and targets both urinary and bowel incontinence, which often co-occur. Key content includes instruction about behavior changes that improve both urinary and bowel incontinence (pelvic floor muscle exercises, fluid and fiber adjustments, weight loss, and toileting strategies). MOM is innovative because it targets both urinary and bowel symptoms, can be facilitated without health expertise, and incorporates a care-seeking tool designed specifically to overcome barriers previously identified by our team [21]. In a randomized, waitlist-control trial (N=121), MOM participants had eight-fold odds of improved urinary continence and three-fold odds of improved bowel continence compared to controls [18].

Although MOM is effective, its reach remains limited because of its in-person format. Community organizations' staff and funding constraints limit their ability to offer resource-intensive, small-group programs [22]. We partnered with a state epidemiologic survey to identify women aged 50 and over with incontinence outside the healthcare setting and learned that only 17% would participate in a small-group program like MOM, whereas over 60% would participate in an online version, noting its superior convenience and privacy [23]. Community organizations can promote online programs using websites, e-newsletters, and social media without consuming precious limited resources.

With a pilot dissemination and implementation grant, we adapted the key components of the in-person MOM program to an online setting (www.healthybowelandbladder.org**).**The online MOM

program reached 15 times as many women in 3 months as the in-person MOM program reached in an entire year. In our dissemination pilot study, there were 4,471 new visitors to the online program (94% female, 27% age 55-64, 60% > 65) over a 3 month time period, versus 282 participants in the in-person program over 12 months (April 2019-2020) (unpublished data). However, the average number of program sessions completed by online participants was 1, and the proportion of users in the pilot study doing pelvic floor muscle exercises consistently four months later was only 27% (28/102) (as compared to 63% four months after participation in the in-person MOM program) [18]. This finding is similar to findings by a Swedish incontinence research group examining an Internet program to improve urinary incontinence, where only 16% of users (27/166) who started the program completed it, and only 40% of those (11/27) did pelvic floor muscle exercises consistently [24]. Unfortunately, engagement with digital health interventions is dismally low across health conditions [25, 26].

The potential public health impact of online programs is tremendous because of their relative scalability, reach, and cost-effectiveness, but they require optimization to maximize engagement and efficiency and preserve effectiveness of in-person programs. To increase engagement in other mobile/online interventions, daily digital triggers have been used [27, 28]. However, such digital triggers prompt some users to disengage, and can become subject to alert fatigue and habituation, depending on their timing, frequency, and content [29]. For example, in a mobile telehealth program for urinary incontinence specifically designed for U.S. women veterans (MyHealtheBladder) that involves daily motivational emails and program sessions, one-third of participants disengaged over 8 weeks [28]. In our qualitative interviews to understand barriers to engagement with online MOM, some users wanted email or text reminders, whereas others strongly felt such reminders would be intrusive (unpublished data). This sentiment was also described by Swedish women users of a mobile app (Tät) for stress urinary incontinence, which incorporates an optional reminder function as part of its program [30]. Similarly, while some online MOM users preferred the autonomy of the self-guided program, others wished for a guided experience where they would be directed to program features most relevant for them specifically. These diverse and conflicting user preferences and behaviors emphasize the challenges faced by one-size-fits-all interventions. In fact, NIDDK has convened multiple workshops in recent years focused on developing a science base to personalize urinary incontinence treatments [31, 32].

Table 1. Model of tailoring depth applied to online MOM program (based on [33])

Level	Input	Tailoring Strategies	Output
Deep (Health Action Process Approach) [19]	• Self-efficacy • Risk perception (and current symptoms) • Outcome expectations • Intentions • Barriers & resources	• Content matching • Evaluative feedback • Personalizing sender, content, medium for triggers	• Situation-specific action & coping plans • Digital triggers that align with user's phase (motivational vs. volitional)
Surface	• Self-reported reminder preferences • Behavior tracking • Program use	• Comparative progress • Trigger frequency, timing, intervals	• Reinforce behavior & symptom tracking • Celebrate goal attainment

Tailoring, or personalization, improves engagement with and sustained participation in electronic health promotion interventions targeting conditions such as tobacco use, obesity, and diabetes. Tailoring delivers information that is customized to be personally relevant to the user, and thus more likely to be read, cognitively processed, and acted upon [34]. Information about the individual, or "input," is used to select personalized content from an expert-developed database using a computerized algorithm [35].

That individualized content, or "output," is delivered to the individual user through multiple strategies and delivery modes, including digital triggers that can be further tailored in five domains (sender, medium, timing, frequency, and content) [29]. Table 1 depicts two tailoring levels: surface-level (based on observable factors) and deep (based on theoretical constructs) [33]. Tailoring improves engagement with and effectiveness of online programs promoting behavior changes related to physical activity, nutrition, and smoking cessation, especially when tailoring algorithms are informed by behavior change theory and conceptual models relevant to target outcomes [33-37].

5.2 Rationale

Transdisciplinary, rigorous research is needed to individualize treatment for urinary incontinence, a specific priority for NIDDK. The proposed work harnesses expertise from investigators outside urology to study whether and how tailoring electronic continence interventions can increase their potential effectiveness and reach. Our team combines diverse expertise in human factors engineering, clinical and social psychology, health communication theory, dissemination and implementation research, and urogynecology to contribute critical insight about how tailoring principles, widely used in other electronic health interventions, can be most impactful for urinary and bowel continence promotion. We anticipate that our findings will be applicable to other electronic continence promotion interventions, and may inform other incontinence treatment interventions that include pelvic floor muscle exercises as a component. This small R01 grant will provide the preliminary data required for a subsequent large-scale trial examining the impact of a novel electronic continence promotion program on urinary and bowel incontinence symptoms and evaluating dissemination strategies. Our long-term goal is to discover and enhance solutions for incontinence in women and identify optimal methods for their dissemination outside the healthcare setting. This work is directly responsive to NIDDK's mission to enhance science regarding personalized therapy for urinary incontinence. Furthermore, the intervention being studied targets another disease of interest to NIDDK: bowel incontinence.

6.0 STUDY OBJECTIVES AND ENDPOINTS

Objectives	Endpoints
Primary	
To evaluate whether tailoring will increase engagement with online MOM. [Corresponds to Aim 1 of grant]	• Proportion of participants who engage with online MOM (participation in at least one session per week during the first 4 weeks of the program) in the group with (test) and without (control) tailoring. [Aim 1 primary outcome] • Comparison of specific program use metrics (number of, minutes spent on, and average intervals between program sessions accessed weekly; number of and specific components accessed) between the two groups and cluster analyses will identify patterns of program use (such as tracking and reminders). [Aim 1 exploratory outcomes]
Secondary	

To evaluate whether tailoring will increase adoption and maintenance of health behaviors that promote continence. [Corresponds to Aim 2 of grant]	• Proportion of participants in the treatment group compared to the control group who adopt consistent pelvic floor muscle exercises at 4 weeks, defined as self-reported performance of pelvic floor muscle exercises consistently (often or always) at 4 weeks after reporting inconsistent performance of these exercises at baseline. [Aim 2 primary outcome] • Proportion of participants in the treatment group compared to the control group who maintain exercise (reporting consistent exercise performance at two time points between 4, 12, and 24 weeks). [Aim 2 exploratory outcome] • Proportion of participants in the treatment group compared to the control group who adopt other health behaviors (fiber intake of at least 21 g; caffeine intake <205 mg/day, daily fluid intake between 60 and 100 ounces, and 6-9 voids per day) at 4 weeks, defined as exhibiting these behaviors consistently (often or always) at 4 weeks after reporting inconsistent performance of these behaviors at baseline. [Aim 2 exploratory outcome] • Proportion of participants in the treatment group compared to the control group who maintain other health behaviors (fiber intake of at least 21 g; caffeine intake <205 mg/day, daily fluid intake between 60 and 100 ounces, and 6-9 voids per day), reporting consistent performance of these behaviors at two time points between 4, 12, and 24 weeks). [Aim 2 exploratory outcome] • Proportion of participants in the treatment group compared to the control group with a body mass index (BMI) >25mg/kg^2 at baseline who report weight loss of at least 2 kg at 12 or 24 weeks. [Aim 2 exploratory outcome]
To determine the extent to which intervention engagement mediates the effect of tailoring on health behavior change. [Corresponds to Aim 3 of grant]	• Assessment of degree of program engagement (defined by program use data during the first 4 weeks) in relation to the intervention's effect on adoption of pelvic floor muscle exercises at 12 weeks. [Aim 3 outcome]

To determine the extent to which psychological variables and incontinence symptoms mediate the effect of tailoring on health behavior change. [Corresponds to Aim 3 of grant]	• Assessment of self-efficacy (comparing change in self-efficacy measures at 4 weeks relative to baseline [0 weeks]) in relation to the intervention's effect on adoption of pelvic floor muscle exercises at 12 weeks. [Aim 3 outcome] • Assessment of incontinence symptoms and quality of life (comparing change in survey rating at 4 weeks relative to baseline [0 weeks]) in relation to the intervention's effect on adoption of pelvic floor muscle exercises at 12 weeks. [Aim 3 outcome] • Assessment of barriers to care-seeking (comparing change in survey rating at 4 weeks relative to baseline [0 weeks]) in relation to the intervention's effect on adoption of pelvic floor muscle exercises at 12 weeks. [Aim 3 outcome]

7.0 STUDY DESIGN

7.1 General Design

We will conduct a two-arm, parallel, randomized, controlled trial (RCT) comparing an online continence promotion program with standard weekly reminders (control arm) to an online continence promotion program with tailoring (treatment arm) to determine the impact of tailoring on program engagement. Women in the treatment arm will receive tailored content and digital reminders for 12 weeks based on their individual characteristics, symptoms, and behaviors assessed at baseline, with reassessment of key inputs every week resulting in re-tailored outputs. Participants (N=600) will be randomized and complete electronic surveys at enrollment, 4, 12, and 24 weeks. The primary outcome is the proportion of participants who engage with the program at least weekly in the first 4 weeks of the trial in the treatment versus control arms, with data collection continuing for 24 weeks to explore the impacts of tailoring over time. Cluster analysis based on machine learning principles will identify patterns of program use. Secondary outcomes will 1) compare the rates of adoption of pelvic floor muscle exercises (at 4 weeks) and maintenance (continuing to perform pelvic floor muscle exercises at 12 and/or 24 weeks) in the treatment and control groups and will explore differences in other continence-related behavior changes in these groups, and 2) will examine the extent to which program engagement in the first 4 weeks mediates the effect of tailoring on health behavior change at 12 weeks and will explore other potential mediators. To contextualize the findings from all 3 aims, a subset of participants (N=36) will be invited to complete semi-structured qualitative interviews about their engagement with the program, their adoption of health behaviors, and their perceived barriers to and facilitators of engagement and behavior change (see section 11.0).

7.2 End of Study Definition

A participant is considered to have completed the study when 30 weeks have elapsed from completion of baseline questionnaire (after electronically signing the informed consent form) (allows 6 weeks to capture final 24 week data).

8.0 PARTICIPANT SELECTION

8.1 Inclusion & Exclusion Criteria

Eligibility will be determined by inclusion and exclusion criteria below.

Inclusion Criteria
1. Willing to provide informed consent.
2. Female, age ≥ 50 years.
3. Can read and write English.
4. Can use email.
5. Has access to Internet-connected device (computer, tablet, or smart phone) to use the online program

Exclusion Criteria

• Women with medical conditions for which the intervention is not medically appropriate, including:
  • dementia
  • neurologic or musculoskeletal conditions in which pelvic floor muscle exercises are contraindicated
  • hematuria or bloody stools within the last 6 months that have not been evaluated by a medical professional

• Not suitable for study participation due to other reasons at the discretion of the investigators.

8.2 Vulnerable Populations

Recruited participants may meet the definition of “older adults” (65 years of age or older) or “elderly individuals,” a vulnerable population. No other vulnerable populations will be recruited or eligible for the study. Women with medical conditions for which the intervention is not medically appropriate will be excluded (dementia, neurologic or musculoskeletal conditions in which pelvic floor muscle exercises are contraindicated, recent hematuria or bloody stools that have not been evaluated by a medical professional). Specific efforts will be made to optimize recruitment of women in rural areas and underrepresented minority groups.

8.3 Participant Identification

Potential participants may self-identify by responding to IRB-approved recruitment efforts, such as web postings, posters/flyers, social media ads, newsletter ads, mass mailings, email blasts, etc. IRB-approved

screening scripts, eligibility questionnaires, and email response templates will be utilized when communicating with potential participants who respond to these recruitment methods.

Information collected is to be limited to protect the potential participant's privacy and information collected from potential participants who fail pre-screening or decline to participate. Any information collected from potential participants who fail pre-screening or decline to participate will be stored anonymously (no identifiers retained). Indirect recruitment materials and response communications will not contain participant health information.

8.4 Participant Recruitment

We will recruit participants using the methods we have used successfully in the past: email list solicitation, electronic dissemination by community agencies and paid advertisements on social media. All of the recruitment materials that the research team will use to recruit participants have been uploaded to ARROW. The research team will not recruit participants by phone. However, if individuals have questions regarding the study, they may contact the research team by phone or email. The research team will use the Basic Introductory Telephone Script guidance when communicating with participants via phone about the study.

We have previously found that advertising via Facebook was particularly effective, supporting the feasibility of using these recruitment strategies for the proposed work. Program engagement was higher among those who enrolled in online MOM through a link on a community organization's website (mean session time 6 minutes, 4.8 pages) than among those who clicked on a Facebook advertisement (mean session time 58 seconds, 1.7 pages).

To optimize recruitment of women in rural areas and under-represented minority groups, we will specifically advertise with community agency partners that serve those communities. Each partner agency will disseminate recruitment advertisements and promote participation under its own banner, via the usual electronic and social media channels by which it routinely communicates with its constituents. Alongside targeted advertisements from the study team itself, this messaging from trusted sources will increase visibility and improve receptiveness among under-represented participants. Interested potential participants will visit the study website to be screened via electronic questionnaire and provide electronic informed consent before being directed to the baseline survey.

Recruitment for this study will occur online, so targeted outreach to specific populations is not hindered by geography. Social media advertising will be focused on members in areas with a high prevalence of Black, Indigenous, and Persons of Color (BIPOC). We have successfully recruited research participants from rural areas in prior studies through partnerships with trusted community agencies that serve rural areas. We will expand our recruitment partnerships for this study to include community agencies that serve BIPOC, including financial compensation for their time and partnership. Outreach materials will reflect the diversity of those we hope to recruit.

8.5 Remuneration and Retention Strategies

Participants will receive $25 after completing each survey (time 0, 4, 12 and 24 weeks). Surveys and payments will be emailed rather than embedded in the intervention so that payment is not misinterpreted as being related to program use. A subset will have the opportunity to be compensated an additional $25 for completing a semi-structured interview (see Section 11.0). We will also distribute educational materials (infographic and video) via email and on the study website that build research literacy and inform participants of their power to improve the quality of the science by providing complete data. Using these strategies – payment after each survey and the educational materials – our attrition rate in the RCT of the in-person MOM program was only 6%. Education materials will not contain individual's health information.

8.6 Early Termination and Withdrawal

Participants are free to withdraw from participation in the study at any time upon request.

Participants who sign the electronic informed consent form and are randomized but do not receive the study intervention will be replaced. Participants who sign the informed consent form, are randomized and use the study program, and then subsequently withdraw, or are withdrawn or discontinued from the study, will be analyzed in the intent-to-treat arm.

When participants withdraw, they will be instructed to no longer use the program and they will not receive additional communications from research personnel.

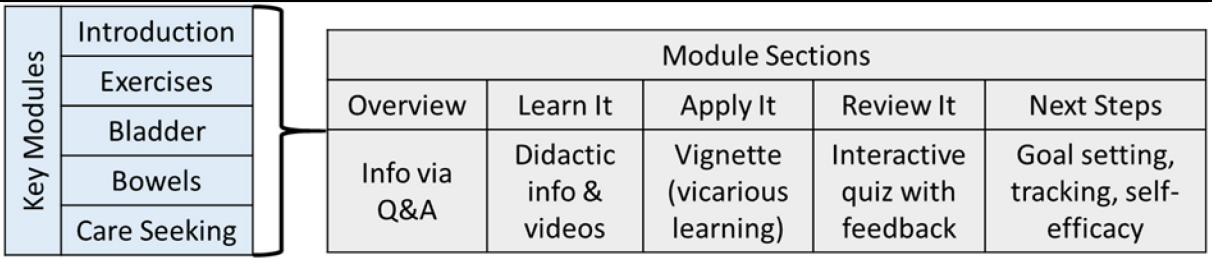
All participants will be asked to complete an identity verification survey. The answers participants to provide to this survey will be compared to the information they provided in the screening survey. If participants answers significantly differ (ie. different name, different addresses, etc), the participant will be removed from the study. Participants will also be removed if they spent six minutes or less completing the baseline survey, if the phone number they provided is invalid, has a fraud score greater than 85, and is flagged as risky, and if the mailing address they provided is invalid.

9.0 PROCEDURAL INTERVENTION

9.1 Study Procedural Intervention and Control Description

Mind Over Matter: Healthy Bowels, Healthy Bladder (MOM; both arms). This online program has five key modules, each of which is subdivided into five sections (Figure 1). The Introduction module provides a program orientation and overview, including its evidence base and additional resources. “Exercises” contains pelvic floor muscle exercise regimens for specific skill levels and symptoms. “Bladder” covers types of urinary incontinence and behavior changes (weight loss, fluid modifications, toileting behaviors) that improve symptoms; “Bowels” covers constipation, bowel incontinence, fiber modifications, and toileting behaviors. “Care Seeking” provides information about healthcare providers and other available treatment options. Each module has five sections that build knowledge, self-efficacy, and skills to set action and coping plans relevant to a participant’s symptoms.

Figure 1. Online Mind Over Matter: Healthy Bowels, Healthy Bladder (MOM) Program Structure



9.1.1 Description of Treatment Group Intervention

Participants allocated to the test arm will receive an email inviting them to create a login and password to access the online MOM program content and will additionally receive tailored “output” (personalized cues, emphasis on relevant content, individualized and tailored reminders about their goals) based on a computer algorithm incorporating unique user “inputs” (individual factors). Inputs include: (1) program use data; (2) self-reported data (demographics, symptoms, communication preferences, risk

perception, outcome expectations, self-efficacy, motivation, intention, behaviors, barriers, and facilitators). Inputs will be reassessed every week for retailoring so that personalization evolves over the course of the intervention. Tailored output will include personalized action, coping, and tracking plans; digital triggers to engage with content specific to the user's unique symptoms, behavioral intentions, and expected outcomes; periodic reminders in the user's preferred format and frequency; and behavioral reinforcements and acknowledgements upon completion of recommended tasks and achievement of goals. For example, a smartphone user with stress urinary incontinence who set a goal of doing pelvic floor muscle exercises daily and has not accessed the program for two days might receive this email: "Is your action plan working? Click here for a refresher on the 'Squeeze before you Sneeze!' exercise," sent at the same time of day when she has accessed the program previously.

9.1.2 Description of Active Control Group

Participants allocated to the active control group will receive an email inviting them to create a login and password to access the online MOM program. They will receive automated weekly reminders via email reminding them to re-visit the program, regardless of their individual user activity.

9.2 Method for Assigning to Treatment Groups - Randomization

Randomization will be performed following identity verification completion. Participants will be blinded to their allocation. REDCap will randomize participants to one of the two study arms. The research team will not be blinded to participants study arm, as the research team must manually tailor weekly emails to participants allocated to the treatment arm. After a participant electronically consents and completes her identity verification, the study coordinator will confirm the participant is a real participant and determine what the next randomization allocation is, as made available by the statistician. The participant will receive an email with a link to the study website one week after completing their informed consent. She will also receive an email with instructions about how to save the program as an app on her mobile device. Those who do not access the website within three days will receive another email and then up to three telephone calls from the study team. The research specialist will offer assistance with signing into the program when calling. Only those participants who access and sign-up on the study website will be considered randomized. Participants must also complete a quality survey to confirm their identity. This short questionnaire will have participants confirm information that they provided in the screening questionnaire. Participants who are not able to confirm their identity will be removed from the study. If a participant was randomized prior to January 5th, 2024, they will be sent the identity verification survey and asked to confirm their identity. Participants who are going to be randomized after January 5th, 2024, will be asked to complete the identity verification prior to randomization. If the participant is not able to verify their identity and provide a valid phone number and mailing address they will be removed from the study.

10.0 STUDY PROCEDURES

10.1 Screening, Informed Consent, and Enrollment

10.1.1 Screening

The study website will include information about the program and the research study itself including requirements for study participation. For potential participants who are interested in study participation, they will be directed to a screening webpage in which they will be asked their age, gender, whether they read and write English, if they have access to an Internet-connected device (like a computer, tablet, or smartphone), and whether they use email. If the study website begins to be infiltrated by bots, potential participants will be directed to email women.on.*the.go@ctri.wisc.edu* to schedule a phone call with a member of our study team before being sent a direct link to the screening webpage. They will also be asked if they have been diagnosed with the following medical conditions: dementia, neurologic or musculoskeletal conditions in which pelvic floor muscle exercises are contraindicated, or recent

(within last 6 months) hematuria or bloody stools that have not been evaluated by a medical professional. Potential participants who do not qualify for the study will be informed of that. Those who do qualify will be invited to participate and will be directed to an electronic informed consent form page.

10.1.2 Informed Consent

After participants screen into the study, the research team will immediately direct participants to the informed consent form. Participants will complete the informed consent electronically, with all consent information provided in the form. In compliance with university guidance on electronic informed consent, participants will be asked to type their name with an accompanying check box and statement noting an intent to affix a legal signature. The informed consent (informed consent form uploaded in ARROW) will provide participants with all study information. The informed consent process will make clear that participation in any and all aspects of the study are voluntary, and that participants may end their participation at any time. The informed consent process will include contact information for the principal investigator, Dr. Piper, who can be contacted if participants or potential participants have questions or concerns; However, we will also indicate that the PI and study team cannot decide if an individual is medically able to participate, and that it is up to individuals and their healthcare providers to decide whether they can do the exercises and make changes to their diets. Those with concerns will be encouraged to contact their healthcare provider.

10.1.3 Enrollment

A research participant will be defined as “enrolled” in the study when they meet the following criteria:

- The participant has provided electronic informed consent.
- The participant and study staff have completed all screening documentation.
- The research team has verified that the participant meets all of the inclusion criteria.
- The research team has verified that participant meets none of the exclusion criteria.
- The participant has been assigned to the protocol by study staff.
- The participant has completed the identity verification survey. Participants who were previously randomized who do not confirm their identity will be removed from the study. Participants who are eligible to be randomized after January 5th, 2024, must complete the identity verification survey and must not significantly differ in answer responses from the screening survey, per 8.6 prior to being randomized in the study.
- The participant has spent more than six minutes completing the baseline survey.
- The participant has a valid phone number, with a fraud score less than 85 and not flagged as risky.
- The participant has provided a valid mailing address.
- The participant has been randomized.

10.1.4 Screen Failure and Re-enrollment

Individuals who do not meet the criteria for participation in this trial (screen failure) will not be rescreened.

10.2 Study Questionnaires and Surveys

The following questionnaires and surveys will be administered at one or more times during the study. Participants will be sent questionnaires and surveys via their email address at baseline, and 4, 12, and 24 weeks into the program. The study questionnaires will utilize the REDCap reCAPTCHA feature to ensure enrollees are not bots. The Study Calendar in section 10.3 details when specific questionnaires and surveys are administered.

10.2.1 Demographics Questionnaire

Participants will be asked their age, race, ethnicity, height, weight, highest grade achieved, work status, marital status, living status, what other medical conditions they may have, and if they have health insurance and a primary care provider.

10.2.2 Pelvic Floor Muscle Exercise Frequency

Participants will be asked to answer the question, “How often do you do Kegel squeezes, or pelvic floor muscle exercises?”, on a 5-point Likert scale with the following descriptors—1: less than once per month; 2: a few times per month; 3: at least once per week; 4: several times per week; 5: almost every day. Participants will also be asked about number and type of panty liners, pads, or undergarments used daily, and the cost of these products weekly.

10.2.3 Fiber Food Frequency Questionnaire

Participants will be asked to individually estimate their daily fiber intake of specific foods on a scale from 1 (<1 severing per week) to 6 (2+ servings per day). Foods include fruit (not juice), green salad, potatoes or oatmeal, vegetables, vegetable juice, vegetable soup/stew, fiber cereal (Raisin Bran, Bran Buds, Fruit-n-Fiber), whole wheat/rye bread, brown rice, whole wheat pasta, barley, couscous, quinoa, and beans.

10.2.4 Fluid and Voiding Questionnaire

Participants will be asked to individually estimate their daily water, caffeinated beverage (coffee, tea, soda), and other decaffeinated beverage (milk, herbal tea, decaf) intake. Participants will also be asked to estimate their weekly intake of 8 ounce servings of alcohol and diet soda. The Bristol Female Lower Urinary Tract Symptoms-Filling Symptoms (BFLUTS-FS) and the Bristol Female Lower Urinary Tract Symptoms-Voiding Symptoms (BFLUTS-VS) will be used to assess urinary symptoms [38]. Participants will be asked about their bowel movements, including in the use of the Bristol Stool Chart [39].

10.2.5 Geriatric Self-Efficacy Index for Urinary Incontinence

The Geriatric Self-Efficacy Index for Urinary Incontinence (GSE-UI) [40] is a validated and clinically responsive [40, 41] instrument for older women with urinary incontinence. Participants select a 0-10 score for each of the 12 items, with total scores ranging from 0-120. A higher score is indicative of a higher level of self-efficacy related to urinary incontinence.

10.2.6 Generalized Self-Efficacy Scale adapted for MOM program

In consultation with Dr. Ralf Schwarzer, Health Action Process Approach [19, 20] developer, we adapted the Generalized Self-Efficacy Scale [42] for behaviors related to continence promotion (such as pelvic floor muscle exercises).

10.2.7 Program-Specific Survey of Other Health Action Process Approach Components

Program-specific survey of other Health Action Process Approach components (risk perception, outcome expectations, intentions, action / coping plans, barriers, facilitators).

10.2.8 Barriers to Incontinence Care-Seeking Questionnaire

The Barriers to Incontinence Care-Seeking Questionnaire (BICS-Q) [43] contains 14-items framed on a 4-point Likert scale and is validated in women with urinary incontinence.

10.2.9 Barriers to Care-seeking for Accidental Bowel Leakage

The Barriers to Care-seeking for Accidental Bowel Leakage (BCABL) [21] has been validated by our team in women with bowel incontinence. BCABL contains 16 questions framed on a 4-point Likert scale with the following descriptors-1: strongly disagree; 2: somewhat disagree; 3: somewhat agree; 4: strongly agree.

10.2.10 International Consultation on Incontinence Questionnaire – Urinary Incontinence Short Form

The International Consultation on Incontinence Questionnaire – Urinary Incontinence Short Form (ICIQ-UI SF) [44] is a widely used validated instrument with an established minimum clinically important difference [45]. Its score translates to mild (1-5), moderate (6-12), severe (13-18), and very severe (19-21) symptoms of incontinence [46].

10.2.11 St. Mark's Incontinence Score

St. Mark's Incontinence Score (SMIS) [47], also referred to as Vaizey Score, generates a scale between 0 (continent) and 24 (completely incontinent), and is widely used in urogynecology and colorectal surgery to assess bowel incontinence severity.

10.2.12 Pelvic Floor Impact Questionnaire Short Form

The Pelvic Floor Impact Questionnaire Short Form (PFIQ-7) [48]) is a widely-used validated instrument that assesses condition-specific quality of life.

10.2.13 12-item Short Form Health Survey (SF-12)

The 12-item Short Form Health Survey (SF-12 [50]) is a validated questionnaire for patients with chronic conditions.

10.2.14 Symptom Improvement and Program Satisfaction

The Symptom Improvement and Global Satisfaction Questionnaire is a validated three-item questionnaire that assesses global satisfaction and approximates symptom improvement that has been validated in other studies of conservative interventions to improve incontinence [49]. The items are Patient Global Ratings of Satisfaction (PSQ), Global Perception of Improvement (GPI), and Estimated Percent Improvement (EPI) [49]. PSQ is rated on a 3-point Likert scale with the following descriptors-1: completely; 2: somewhat; 3: not at all. GPI is rated on a 5-point Likert scale with the following descriptors-1: much better; 2: better; 3: about the same; 4: worse; 5: much worse. Participants EPI is a free-text response allowing for a numerical response between 0 and 100.

10.2.15 Behavioral Intention to Use Scale

The Behavioral Intention to Use Scale was developed by our research team in expertise in human factors engineering. The questionnaire will ask participants if and how they will use the online program in the future to prevent and manage their incontinence symptoms. In addition, questions will ask participants how the research team can improve the online program to improve the experience for women who may use it in the future.

10.3 Study Calendar

The procedures/surveys performed at each time point are listed in the table below. Key measures related to health behaviors and incontinence symptoms are assessed at all four time-points. Data regarding core

constructs within the Health Action Process Approach will be assessed at baseline, 4 weeks (for the mediator analyses), and 24 weeks (final data collection time-point). Barriers to care-seeking for incontinence will be assessed at baseline and 24 weeks. Patient global ratings of satisfaction (PSQ), global perception of improvement (GPI), and estimated percent improvement (EPI) will be assessed at 4 weeks (conclusion of active program engagement) and 24 weeks (final data collection time-point).

	0	4 w	12 w	24 w
Screening/Review Eligibility Criteria	X			
Informed Consent	X			
Demographics	X			
Behavioral Intention to Use Scale	X	X	X	X
Health Behaviors				
Pelvic floor muscle exercise frequency	X	X	X	X
Fiber food frequency questionnaire	X	X	X	X
Fluid and voiding questionnaire	X	X	X	X
Self-reported weight	X	X	X	X
Core Constructs within the Health Action Process Approach				
Geriatric Self-Efficacy Index for Urinary Incontinence (GSE-UI) [40]	X	X	X	X
Generalized Self-Efficacy Scale adapted for MOM program [42]	X		X	
Program-specific survey of other Health Action Process Approach components (risk perception, outcome expectations, intentions, action / coping plans, barriers, facilitators)	X	X	X	X
Barriers to Incontinence Care-Seeking Questionnaire (BICS-Q) [43]	X		X	
Symptoms & Quality of Life				
International Consultation on Incontinence Questionnaire – Urinary Incontinence Short Form (ICIQ-UI SF) [44] (Urinary Incontinence)	X	X	X	X
St. Mark's Incontinence Score (SMIS) [47] (Bowel Incontinence)	X	X	X	X
Pelvic Floor Impact Questionnaire Short Form (PFIQ-7) [48]	X		X	
12-item Short Form Health Survey (SF-12) [50]	X	X	X	X
Patient global ratings of satisfaction (PSQ), global perception of improvement (GPI), and estimated percent improvement (EPI) [49]		X	X	X

11.0 SPECIAL STUDY – QUALITATIVE INTERVIEWS

To contextualize the findings from all 3 aims of the grant, a subset of participants (N=36) will be invited to complete semi-structured qualitative interviews about their engagement with the program, their adoption of health behaviors, and their perceived barriers to and facilitators of engagement and behavior change.

11.1 Assessments and Data Collection Procedures

We will purposively sample to recruit participants for semi-structured qualitative interviews from three groups of anticipated user categories. These categories include: (1) frequent online program users (e.g. >3 times per week) who adopt target health behaviors (N=12); (2) infrequent online program users (e.g. <3 times per week) who adopt target health behaviors (N=12); and (3) users who neither engage with the

program nor adopt target health behaviors (N=12). Namey and colleagues found that a median sample size of 16 (range 11-26) achieves 90% saturation [51]; we will continue to conduct interviews until we reach saturation in each group [52]. Interviews will be conducted by phone or video conference and will be audio-recorded and transcribed verbatim. Recordings and transcription files will be collected and recorded in REDCap and deidentified and stored on a secure department server.

11.2 Analytic Plan

Measures: The semi-structured interview guide will be developed using input from the transdisciplinary team, with question domains based on the objectives of each specific aim of the grant:

- User experience, program engagement, barriers to and facilitators of engagement (Aim 1)
- Behaviors changes made/attempted, barriers to and facilitators of behavior change (Aim 2)
- Benefits and disadvantages of program, perceived impact on confidence, symptoms / quality of life, plans to seek care (Aim 3)

Analysis: Telephone or video conference interviews will be recorded, transcribed, and uploaded to NVivo software (QSR International) for analysis. Qualitative analysis will complement quantitative findings by providing additional insight based on participants' perceptions of using online MOM. We will use an inductive and deductive content analysis approach guided by the Health Action Process model [19, 20] and allowing key constructs to emerge from the data [53]. The research team will come to consensus on emergent codes and their definitions. Transcripts will be dual coded and agreement calculated. Qualitative analysis will be iterative; findings after five interviews will be brought to consecutive participants for member checking. Qualitative findings will be triangulated with quantitative analyses of online MOM program use data and self-report measures.

11.3 Qualitative Rigor

We will use Patton's checklist [54] for ensuring and evaluating qualitative rigor across *four criteria* [55]. We will address (1) credibility, related to the quantitative method construct of internal validity, using strategies of member checking [56], methods and analyst triangulation [57], and deviant case analysis [56, 58]. We will address (2) transferability, the scope to which results are applicable to other contexts, by providing detailed descriptions of the context in which we are collecting data [59] and by purposively sampling to represent the range of diversity in engagement experiences [60]. We will address (3) dependability, or the ability to achieve consistent findings if the study is conducted as described, by creating and reporting a detailed audit trail of our process [61]. Finally, we will address (4) confirmability, requiring evidence for findings that come directly from participants rather than from a researcher's bias, through triangulation of sources (interviewing multiple engagement perspectives) and analysts [57] as well as through multidisciplinary team reflexivity [56, 62].

12.0 DATA HANDLING AND RECORD KEEPING

12.1 Data Collection and Database Management

Study participants will need to create an account for our program, hosted by Orbita Inc. (formerly known as Wellbe, Inc.), providing their first name, last name, and email address. Individual program use data (Aim 1) will be collected from the user's device and stored on Amazon Web Services (AWS) with failover at two data centers located 2,000 miles apart. Amazon provides a series of guarantees of reliability and security through a wide variety of certifications, including guaranteed uptime of 99.9%. Current copies of these certifications can be viewed at https://aws.amazon.com/compliance/. Data is encrypted in transit and at rest and governed by a set of security policies consistent with the HITRUST framework for healthcare data security. Amazon will not be able to access participant data stored on AWS. The research specialist will

receive a secure link daily provided by Orbita Inc. (formerly known as Wellbe, Inc.) and data from that secure link will be uploaded into the data repository in REDCap and then deleted.

Engagement metrics will be derived from user device data monthly and merged with self-reported data. Participants will complete electronic surveys emailed via REDCap (https://redcap.ictr.wisc.edu) at baseline, 4, 12, and 24 weeks to collect demographic and relevant health history data at baseline and the measures for Aims 2 and 3 at the intervals outlined in the Study Calendar (10.3).

Study data will be organized by unique study identifier (ID) number and stored on REDCap and a password-protected server maintained by the Biomedical Computing Group in the Department of Biostatistics and Medical Informatics of UW-Madison for analysis. After participants complete the screening questionnaire, a unique study identifier (ID) number will be generated and documented in a linking file. The file linking study ID number to participant identifiers will be kept in REDCap and a password-protected file on a Department of Medicine secure server accessible only to the principal investigator and the research assistant who communicates with patients. 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 file linking study ID number to participant identifiers will be destroyed three years after study closure.

12.2 Confidentiality and Privacy

Participant confidentiality and privacy are strictly held in trust by the participating investigators, their staff, and the sponsor(s) and their agents. This confidentiality is extended to cover the clinical information relating to participants. Therefore, the study protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party without prior written approval of the sponsor.

All research activities will be conducted in as private a setting as possible.

All study staff engaged in the conduct of this project have completed training on the protection of human participants and the Health Insurance Portability and Accountability (HIPAA) Privacy Rule. In addition, all key personnel (i.e.., Principal Investigator, individuals involved in identifying/recruiting participants, obtaining electronic informed consent, or interacting and intervening with participants) have undergone Good Clinical Practice (GCP) training.

Information about study participants will be kept confidential and managed according to HIPAA requirements. All participants will sign a combined electronic informed consent and HIPAA authorization form that includes specific privacy and confidentiality rights. Study data will be maintained per federal, state, and institutional data policies.

The investigator(s) will ensure that the identities of participants are protected by using coded participant information. The log of participant identifying information that links participants to their study-specific identification number will be maintained by the investigators. The log and all study records will be maintained in locked rooms and access will be limited to essential study personnel. Electronic study records/files will be collected and stored on REDCap and/or a secure department server and accessed via networked computers that are password-protected with access provided only to authorized study personnel.

Authorized representatives of the following groups may need to review this research as part of their responsibilities to protect research participants: representatives of the IRB and the National Institutes of

Health and federal oversight agencies, such as the Office for Human Subjects Protection (OHRP). The clinical study site will permit access to such records.

Study staff may use e-mail to communicate with research participants, if the participant has agreed to using email in the Informed Consent form. The information contained in emails will be limited to research-related surveys and general questions. All emails to participants will be sent from UW/wisc.edu/Kaiser Permanente/Indiana University accounts; personal, home or Gmail email accounts will not be used.

To further protect the privacy of study participants, a Certificate of Confidentiality will be issued by the NIH. This certificate protects identifiable research information from forced disclosure. It allows the investigator and others who have access to research records to refuse to disclose identifying information on research participation in any civil, criminal, administrative, legislative, or other proceeding, whether at the federal, state, or local level. By protecting researchers and institutions from being compelled to disclose information that would identify research participants, Certificates of Confidentiality help achieve the research objectives and promote participation in studies by helping to assure confidentiality and privacy to participants.

12.3 Protocol Deviations

A protocol deviation is any noncompliance with the clinical trial protocol or investigational plan requirements. The noncompliance may be either on the part of the participant, the investigator, or the study site staff. As a result of deviations, corrective actions are to be developed by the site and implemented promptly.

It is the responsibility of the Principal Investigator/site investigator/study staff to use continuous vigilance to identify and report deviations. The Principal Investigator is responsible for assessing whether the deviation constitutes noncompliance as defined by the reviewing IRB and if so, reporting it within the required time frame(s). The site investigator is responsible for knowing and adhering to the reviewing IRB requirements.

12.4 Publication and Data Sharing Policies

This study will be conducted in accordance with the following publication and data sharing policies and regulations:

National Institutes of Health (NIH) Public Access Policy, which ensures that the public has access to the published results of NIH funded research. It requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/) upon acceptance for publication.

This study will comply with the NIH Data Sharing Policy and Policy on the Dissemination of NIH-Funded Clinical Trial Information and the Clinical Trials Registration and Results Information Submission rule. As such, this trial will be registered at ClinicalTrials.gov, and results information from this trial will be submitted to ClinicalTrials.gov. In addition, every attempt will be made to publish results in peer-reviewed journals. Data from this study may be requested from other researchers 3 years after the completion of the primary endpoint by contacting the Study PI, Dr. Piper.

13.0 STUDY ANALYSIS

13.1 Statistical Hypotheses

- **Primary Efficacy Endpoint(s):**

Incorporating tailoring into online MOM will double the proportion of users who engage with the program, defined as at least four program sessions in the first 4 weeks of the trial, compared to the active control group (online MOM with weekly reminder emails and no tailoring). [Associated with Aim 1 of grant]

- **Secondary Efficacy Endpoint(s):**
  Tailoring will increase adoption and maintenance of health behaviors that promote continence. [Associated with Aim 2 of the grant]
- Intervention tailoring will increase engagement with the online MOM program and that the increased engagement will result in behavior changes that improve continence. [Associated with Aim 3 of the grant]
- Other mediating variables such as increased self-efficacy, decreased symptomatology, and decreased barriers to care-seeking will result in behavior changes that improve continence. [Associated with Aim 3 of the grant]

13.2 Sample Size Justification

Our goal sample size for the quantitative analysis is based on the primary outcome of program engagement, defined for this purpose as participating in at least four online MOM sessions over the 4 weeks following enrolment. We hypothesize that tailoring will double a woman's likelihood of program engagement. We estimate that 15% of participants in the control group will meet this definition of engagement based on a similar proportion of real users engaging with an Internet program tested by a Swedish incontinence research group [24]; we estimate that 30% of participants in the treatment arm will meet this definition. To obtain 90% power with a type 1 error of .05, our goal sample size is 174 participants per treatment arm. Assuming a 40% attrition rate, we will recruit 289 participants per arm. This attrition rate is between the rate of attrition in the RCT of in-person MOM (<5%), where participants were compensated following baseline assessment and final assessment, and the higher rate of attrition in our pilot dissemination study of online MOM (42%), where participants were not compensated until the final assessment. However, since this study is more similar to that of the online MOM program (this study is solely online), we have increased the attrition rate to 40% as we anticipate attrition to be more similar to that of online MOM.

13.3 Participant Population(s) for Analysis

- Primary analyses will be performed using Intention-to-Treat (ITT): all randomized participants
- Other exploratory analyses will include:
- Modified ITT: all randomized participants that received at least one dose of study intervention and/or have some particular amount of follow-up outcome data
- Protocol-compliant Population: all randomized participants who received the required study intervention and complied with the protocol sufficiently to ensure that the data would be likely to represent the effects of the study intervention according to the underlying scientific model

13.4 Statistical Methods

13.4.1 Primary Outcome Measures and Analysis

Measures. The primary outcome for this aim is engagement with the program, defined as participation in at least one session per week during the first 4 weeks of the participation. Additional engagement metrics include number of, minutes spent on, and average intervals between program sessions accessed weekly; number of and specific components accessed; and use patterns for specific program features (such as tracking and reminders). These metrics will be derived from user device data monthly.

Data Analysis. Summary statistics will describe and compare demographic and clinical characteristics in the treatment and active control groups. The proportion of participants in the treatment versus control group who achieve engagement (primary outcome) will be compared using binomial chi-squared test with type I error rate at 0.05. We will conduct exploratory analyses to determine whether individual difference variables such as race, educational attainment, and baseline incontinence symptoms moderate the effects of tailoring on engagement using chi-square analyses and by modeling interaction effects in Cox Regression. We will compare the number of and average intervals between program sessions, number of and specific pages viewed, minutes spent per week using the program (weeks 1 through 24), and use of program features (such as tracking and reminders) between women in the treatment and control groups.

To examine patterns of program engagement, we will use the processed data and characteristics to create categorizations leveraging two popular clustering models based on machine learning. Clustering is a type of unsupervised learning algorithm to partition data into groups ("clusters") within which observations are similar to one another [63]. K-means clustering finds k clusters such that the total pairwise distance between each observation and its closest cluster centroid is minimized. Hierarchical, or agglomerative, clustering builds a hierarchy of clusters where the closest pairwise clusters are merged until there is only one cluster [63, 64]. Although we will not know a priori how the data will cluster, we will plan to use k-means and hierarchical clustering to group participants into: 1) "engagement types" based on program use metrics; 2) "behavior types" based on self-reported behavior data (described in Aim 2); and 3) "engagement-behavior types" based on both program use metrics and self-reported behavior data.

13.4.2 Secondary Outcome Measures and Analysis

13.4.2.1 Secondary Outcomes Measures Associated with Aim 2 of the Grant

Measures. Frequency of health behaviors known to improve continence (fluid changes, fiber optimization, voiding patterns) will be assessed via electronic survey at baseline, 4, 12 and 24 weeks, using the same questionnaires we used in the RCT of the in-person MOM program [18]. The primary outcome for this aim is adoption of consistent pelvic floor muscle exercise at 4 weeks, defined as self-reported performance of pelvic floor muscle exercises consistently (often or always) at 4 weeks after reporting inconsistent performance of these exercises at baseline. Secondary outcomes include exercise maintenance (reporting consistent exercise performance at two consecutive time points between 4, 12, and 24 weeks) as well as adoption and maintenance of other health behaviors. Specific self-reported health behaviors of interest for exploration include: (1) daily fiber intake of at least 21g [65]; (2) caffeine intake <205 mg/day [66]; (3) daily fluid intake between 60 and 100 ounces; and (4) 6-9 voids per day. We will also compare the proportion of participants with a body mass index (BMI) >25mg/kg^2 at baseline who report weight loss of at least 2 kg at 12 or 24 weeks between the groups who did and did not receive tailoring [67].

Analysis. Summary statistics will describe and compare demographic and clinical characteristics in the treatment and active control groups. The proportion of participants in the treatment versus control group who adopt consistent pelvic floor muscle exercises between baseline and 4 weeks will be compared using the binomial chi-squared test with type I error rate at 0.05. Exploratory analyses will determine whether individual differences such as race, educational attainment, and baseline incontinence symptoms moderate the effects of tailoring on adoption of pelvic floor muscle exercise using chi-square analyses and by modeling interaction effects in Cox Regression. For secondary outcomes, the proportion of participants in the treatment versus control group who adopt or maintain a health behavior will be compared using similar analyses to those described for the primary outcome.

13.4.2.2 Secondary Measures Associated with Aim 3 of the Grant

Measures. The primary outcome for this aim is adoption of consistent pelvic floor muscle exercise at 12 weeks, defined as self-reported performance of pelvic floor muscle exercises consistently (often or always) at 12 weeks after reporting inconsistent performance of these exercises at baseline. The primary independent variable is allocation to the treatment (tailoring) or control arm.

Potential mediators will include:

- Program Engagement: High program engagement during weeks 0 – 4 as defined through cluster analysis described in Aim 1.
- Self-Efficacy: Change in self-efficacy measures between baseline and 4 weeks on the surveys, GSE-UI and Generalized Self-Efficacy Scale.
- Incontinence Symptoms and Quality of Life: Changes between baseline and 4 weeks on the surveys ICIQ-UI SF and SMIS (incontinence), and PFIQ-7 and SF-12 (quality of life).
- Symptom improvement and program satisfaction: At 24 weeks, patient global ratings of satisfaction (PSQ), global perception of improvement (GPI), and estimated percent improvement.
- Perceived barriers to care: Changes between baseline and 4 weeks on the surveys, BICS-Q and BCABL.

Analysis. Mediation analyses as described by VanderWeele and Vansteelandt [68] will be conducted based on a regression model for behavior change (B) against the indicator of tailoring (T) and the multiple potential mediators M_1, …, M_K, i.e., B → T+M_1+…+M_K, along with K models for each mediator against tailoring, i.e., M_k → T (k=1,…, K). The natural direct effect (NDE) and natural indirect effect (NIE) through each of the mediators will be estimated and tested using proper linear combinations of the regression coefficients [68]. In addition to mediation analyses, summary statistics will describe changes in incontinence severity and impact over time in women who did and did not receive tailoring to inform design of a planned subsequent effectiveness trial. We will compare differences between 0 and 24 weeks in scores on instruments assessing barriers to care-seeking in the treatment and control groups and differences in program satisfaction and global perception of improvement between 4 and 24 weeks in the two groups. Continuous variables will be compared using the *t*-test and categorical variables using the chi-square test, both with type I error rate at 0.05.

13.5 Handling of Missing Data

We will prevent and manage missing data according to the National Research Council's Panel on Handling Missing Data in Clinical Trials guidelines. We will implement strategies that we have used successfully in the past (described in section 8.5) to minimize patient attrition (goal <20%). To evaluate missing data, we will conduct sensitivity analyses using methods appropriate for data missing at random [69] and for data missing not at random [70].

14.0 RISK/BENEFIT ASSESSMENT

14.1 Known Potential Benefits to the Participants

There are no direct benefits of participation. The potential benefits to society include information about the acceptability, usability, and effectiveness of a digital version of an effective behavioral intervention to improve bladder and bowel incontinence. This research also collects information about which implementation strategy reaches the most women at risk for or experiencing incontinence.

14.2 Known Potential Risks

There are no physical risks related to study participation, which entails completing several electronic questionnaires, and perhaps being invited to participate in a phone or video conference interview.

There is a risk that patient information could become known to someone not involved in this study. If this happens, it could result in damage to the patient's reputation, which could also affect relationships with family and friends, affect employment, or make it harder to get insurance or a job.

There are several precautions that will be used to ensure that participant privacy is protected. The study questionnaires and interviews (for some) can be completed by participants in a private location of their choosing. (The eMOM intervention can also be completed in the locations of the participants' choosing.) Collection of sensitive information about participants is limited to the amount necessary to achieve the aims of the research. Data will be collected and stored by REDCap and then de-identified and stored on a secure department server. Patient contact information will be stored separately from 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. Participants will receive $25 after completing each survey (time 0, 4, 12, and 24 weeks) and after completing a semi-structured interview, if asked to participate in an interview. Surveys and payments will be emailed rather than embedded in the intervention so that payment is not misinterpreted as being related to program use.

14.3 Risk/Benefit Analysis

The risks associated with this study are minimal, and there are potential benefits to society, including information about the acceptability, usability, and effectiveness of a digital version of an effective behavioral intervention to improve bladder and bowel incontinence.

15.0 DATA AND SAFETY MONITORING

15.1 Data and Safety Monitoring Plan

The following Data and Safety Monitoring Plan (DSMP) pertains to all research to be supported under the PAS-20-160, Small R01s for Clinical Trials Targeting Diseases within the Mission of NIDDK Award. This plan comprises research conducted directly by the University of Wisconsin-Madison (UW) investigators and all other personnel who are supported by these funds. All investigators must agree to comply with the procedures outlined in this DSMP. This DSMP does not reduce any investigator's obligation to comply with the requirements of the UW Health Sciences Institutional Review Board (HSIRB).

***Monitoring the progress of trials and the safety of participants*.** The PI of the study will be responsible for routine monitoring of the progress of the research. This monitoring includes scheduled biweekly meetings with study staff and review of written documentation of all aspects of the research project. Data that are reviewed at these meetings include the number and type of participants enrolled, the number and reasons for exclusions from enrollment, the number of participants involved in each stage of the intervention, and any participant concerns or confidentiality issues.

To facilitate participant safety, study participants must meet study inclusion and exclusion criteria. Should either excessive risk to study participants and/or lack of measurable benefit to study participants be determined, the study will be stopped and all participants notified in a manner appropriate to the nature of the risk and/or lack of benefit.

Plans for the reporting of unanticipated health events. This DSMP requires that investigators notify NIH and the University of Wisconsin IRB in a timely manner of the occurrence of any unanticipated health events, which are severe, unanticipated, and possibly related to study medication or protocol.

This study does not involve pharmaceutical agents. Examples of a serious unanticipated health event would be untoward occurrences related to study participation that result in death, are life-threatening, require hospitalization or prolonging of existing hospitalization, create persistent or significant disability/incapacity, or involve congenital abnormality/birth defects. Unanticipated health events would also include less serious problems that merit reporting because they are severe, unanticipated, and possibly related to study participation. Any serious unanticipated health event will be queried and reported as required by IRB, NIH and/or FDA rules. The PIs will be responsible for the accurate documentation, investigation, and follow-up of all study-related unanticipated health events.

Unanticipated health event assessment, recording, reporting, and investigation will be accomplished through staff training, structured/standardized assessments of untoward occurrences/events, and regular monitoring by the PI and research specialist. The Principal Investigator has ultimate responsibility for ensuring that unanticipated health events are detected and reported in a timely manner. Additionally, the IRB will receive an annual report of all serious unanticipated health events and unanticipated health events meeting the criteria listed above.

Plans for assuring that any action resulting in a temporary or permanent suspension of an NIDDK-funded clinical trial is reported to the NIDDK grant program director responsible for the grant. The NIDDK grant program director will be notified within 5 days if the PI deems it necessary to suspend the trial. In the case of a temporary suspension, the PI and Co-Is will develop a plan for continuation of the study and discuss this plan with the NIDDK grant program director in a reasonable time frame.

Plans for assuring data accuracy and confidentiality and protocol compliance. The PI, supported by regulatory staff, will refine and monitor existing protocols for assuring data accuracy and protocol compliance. Such protocols will include data verification and protocol compliance checks. The Data Manager and IT Manager will also be responsible for ensuring that the data for the project are securely stored, that storage is in compliance with University and federal regulations and that no unauthorized persons have access (electronic or physical) to any participant-identifiable data. The UW Medicine Research Office will ensure that HIPAA regulations and guidelines are currently implemented and all study staff have completed approved human participants and HIPAA training programs.

15.2 Safety Review Committee

In addition to the protections outlined in the DSMP (above), this research conforms to the NIH definition of a clinical trial. The trial proposed in this R01 application is not multicenter in nature. The DSMP specifies overall monitoring that will be conducted by the PI. Their responsibilities include timely reporting of unanticipated health events and serious unanticipated health events. Every 6 months, the Program Project-wide Safety Review Committee will convene to review the overall safety data, as well as data on safety summarized by treatment condition. The objective of these reviews will be to determine whether continued conduct of the trial poses no undue risk for participants.

The Safety Review Committee will be chaired by Jane Mahoney, MD, a Professor in the University of Wisconsin-Madison Department of Medicine. Dr. Mahoney is a very experienced physician and clinical trial researcher with no involvement in any of this R01's research activities. Dr. Mahoney will be joined on the committee by Justin Boutilier, PhD, Assistant Professor of Industrial Systems Engineering at UW-Madison and expert in data analysis related to machine learning; Angela Fidler Pfammatter, MS, PhD, an Assistant Professor of Preventive Medicine at Northwestern University and Clinical Health Psychologist with expertise in the development and testing of technology to influence health behaviors; and Kyle Rudser,

PhD, Associate Professor of Biostatistics at the University of Minnesota and expert in the design and monitoring of clinical trials. Drs. Boutilier, Pfammatter, and Rudser have no direct involvement with any of this R01's research activities. The project team will provide support for these reviews including summaries of collected data. The PI will participate in these reviews and take lead responsibility for implementing any recommended changes in procedure or protocol.

16.0 REFERENCES

1. Gorina, Y., et al., *Prevalence of incontinence among older americans.* Vital Health Stat 3, 2014(36): p. 1-33.
2. Xu, X., et al., *Economic cost of fecal incontinence.* Dis Colon Rectum, 2012. **55**(5): p. 586-98.
3. Miner, P.B., Jr., *Economic and personal impact of fecal and urinary incontinence.* Gastroenterology, 2004. **126**(1 Suppl 1): p. S8-13.
4. Litman, H.J. and J.B. McKinlay, *The future magnitude of urological symptoms in the USA: projections using the Boston Area Community Health survey.* BJU Int, 2007. **100**(4): p. 820-5.
5. Avery, J.C., et al., *Identifying the quality of life effects of urinary incontinence with depression in an Australian population.* BMC Urol, 2013. **13**: p. 11.
6. Brown, H.W., et al., *Quality of life impact in women with accidental bowel leakage.* Int J Clin Pract, 2012. **66**(11): p. 1109-16.
7. Shaw, C., *A review of the psychosocial predictors of help-seeking behaviour and impact on quality of life in people with urinary incontinence.* J Clin Nurs, 2001. **10**(1): p. 15-24.
8. Foley, A.L., et al., *Association between the Geriatric Giants of urinary incontinence and falls in older people using data from the Leicestershire MRC Incontinence Study.* Age Ageing, 2012. **41**(1): p. 35-40.
9. Tamanini, J.T., et al., *Association between urinary incontinence in elderly patients and caregiver burden in the city of Sao Paulo/Brazil: Health, Wellbeing, and Ageing Study.* Neurourol Urodyn, 2011. **30**(7): p. 1281-5.
10. Thom, D.H., M.N. Haan, and S.K. Van Den Eeden, *Medically recognized urinary incontinence and risks of hospitalization, nursing home admission and mortality.* Age Ageing, 1997. **26**(5): p. 367-74.
11. Grover, M., et al., *Survey of geriatricians on the effect of fecal incontinence on nursing home referral.* J Am Geriatr Soc, 2010. **58**(6): p. 1058-62.
12. Shamliyan, T., J. Wyman, and R.L. Kane, *AHRQ Comparative Effectiveness Reviews*, in *Nonsurgical Treatments for Urinary Incontinence in Adult Women: Diagnosis and Comparative Effectiveness*. 2012, Agency for Healthcare Research and Quality (US): Rockville (MD).
13. Makol, A., M. Grover, and W.E. Whitehead, *Fecal incontinence in women: causes and treatment.* Womens Health (Lond Engl), 2008. **4**(5): p. 517-28.
14. Wald, A., *New Treatments for Fecal Incontinence: Update for the Gastroenterologist.* Clin Gastroenterol Hepatol, 2014.
15. Goode, P.S., et al., *Incontinence in older women.* JAMA, 2010. **303**(21): p. 2172-81.
16. Lukacz, E.S., et al., *Urinary Incontinence in Women: A Review.* JAMA, 2017. **318**(16): p. 1592-1604.
17. Brown, H.W., S.D. Wexner, and E.S. Lukacz, *Factors associated with care seeking among women with accidental bowel leakage.* Female Pelvic Med Reconstr Surg, 2013. **19**(2): p. 66-71.
18. Brown, H.W., et al., *Small-Group, Community-Member Intervention for Urinary and Bowel Incontinence: A Randomized Controlled Trial.* Obstet Gynecol, 2019. **134**(3): p. 600-610.
19. Schwarzer, R., S. Lippke, and A. Luszczynska, *Mechanisms of health behavior change in persons with chronic illness or disability: the Health Action Process Approach (HAPA).* Rehabil Psychol, 2011. **56**(3): p. 161-70.
20. Schwarzer, R., *Modeling Health Behavior Change: How to Predict and Modify the Adoption and Maintenance of Health Behaviors. .* Applied Psychology: An International Review, 2008. **57**(1): p. 1-29.
21. Brown, H.W., et al., *Validation of an instrument to assess barriers to care-seeking for accidental bowel leakage in women: the BCABL questionnaire.* Int Urogynecol J, 2017. **28**(9): p. 1319-1328.

22. Dattalo, M., et al., *Essential Resources for Implementation and Sustainability of Evidence-Based Health Promotion Programs: A Mixed Methods Multi-Site Case Study.* J Community Health, 2017. **42**(2): p. 358-368.
23. Brown, H.W., et al., *Reasons Behind Preferences for Community-Based Continence Promotion.* Female Pelvic Med Reconstr Surg, 2020.
24. Bokne, K., M. Sjöström, and E. Samuelsson, *Self-management of stress urinary incontinence: effectiveness of two treatment programmes focused on pelvic floor muscle training, one booklet and one Internet-based.* Scand J Prim Health Care, 2019. **37**(3): p. 380-387.
25. Brouwer, W., et al., *Which intervention characteristics are related to more exposure to internet-delivered healthy lifestyle promotion interventions? A systematic review.* J Med Internet Res, 2011. **13**(1): p. e2.
26. Brouwer, W., et al., *Characteristics of visitors and revisitors to an Internet-delivered computer-tailored lifestyle intervention implemented for use by the general public.* Health Educ Res, 2010. **25**(4): p. 585-95.
27. Asklund, I., et al., *Mobile app for treatment of stress urinary incontinence: A randomized controlled trial.* Neurourol Urodyn, 2017. **36**(5): p. 1369-1376.
28. Goode, P.S., et al., *A mobile telehealth program for behavioral treatment of urinary incontinence in women veterans: Development and pilot evaluation of MyHealtheBladder.* Neurourol Urodyn, 2020. **39**(1): p. 432-439.
29. Muench, F. and A. Baumel, *More Than a Text Message: Dismantling Digital Triggers to Curate Behavior Change in Patient-Centered Health Interventions.* J Med Internet Res, 2017. **19**(5): p. e147.
30. Asklund, I., et al., *User Experience of an App-Based Treatment for Stress Urinary Incontinence: Qualitative Interview Study.* J Med Internet Res, 2019. **21**(3): p. e11296.
31. Chai, T.C., et al., *Future Directions of Research and Care for Urinary Incontinence: Findings from the National Institute of Diabetes and Digestive and Kidney Diseases Summit on Urinary Incontinence Clinical Research in Women.* J Urol, 2017. **198**(1): p. 22-29.
32. Norton, J.M., et al., *Individualizing Urinary Incontinence Treatment: Research Needs Identified at NIDDK Workshop.* J Urol, 2018. **199**(6): p. 1405-1407.
33. Ryan, K., S. Dockray, and C. Linehan, *A systematic review of tailored eHealth interventions for weight loss.* Digit Health, 2019. **5**: p. 2055207619826685.
34. Noar, S., et al., *Tailored Health Communication to Change Lifestyle Behaviors.* Am J Lifestyle Med, 2010. **5**(2): p. 112-122.
35. Lustria, M.L., et al., *Computer-tailored health interventions delivered over the Web: review and analysis of key components.* Patient Educ Couns, 2009. **74**(2): p. 156-73.
36. Harrington, N.G. and S.M. Noar, *Reporting standards for studies of tailored interventions.* Health Educ Res, 2012. **27**(2): p. 331-42.
37. Lustria, M.L., et al., *A meta-analysis of web-delivered tailored health behavior change interventions.* J Health Commun, 2013. **18**(9): p. 1039-69.
38. Brookes, S.T., et al., *A scored form of the Bristol Female Lower Urinary Tract Symptoms questionnaire: data from a randomized controlled trial of surgery for women with stress incontinence.* Am J Obstet Gynecol, 2004. **191**(1): p. 73-82.
39. Lewis, S.J. and K.W. Heaton, *Stool form scale as a useful guide to intestinal transit time.* Scand J Gastroenterol, 1997. **32**(9): p. 920-4.
40. Tannenbaum, C., et al., *Responsiveness and clinical utility of the geriatric self-efficacy index for urinary incontinence.* J Am Geriatr Soc, 2009. **57**(3): p. 470-5.
41. Tannenbaum, C., et al., *Creation and testing of the Geriatric Self-Efficacy Index for Urinary Incontinence.* J Am Geriatr Soc, 2008. **56**(3): p. 542-7.
42. Schwarzer, R. and M. Jerusalem, *Generalized Self-Efficacy scale.*, in *Measures in health psychology: A user's portfolio. Causal and control beliefs*, S.W. J. Weinman, & M. Johnston, Editor. 1995, GL Assessment Limited, The Chiswick Centre: London, UK. p. 35-37.
43. Heit, M., L. Blackwell, and S. Kelly, *Measuring barriers to incontinence care seeking.* Neurourol Urodyn, 2008. **27**(3): p. 174-8.

44. Avery, K., et al., *ICIQ: a brief and robust measure for evaluating the symptoms and impact of urinary incontinence.* Neurourol Urodyn, 2004. **23**(4): p. 322-30.
45. Nyström, E., et al., *ICIQ symptom and quality of life instruments measure clinically relevant improvements in women with stress urinary incontinence.* Neurourol Urodyn, 2015. **34**(8): p. 747-51.
46. Klovning, A., et al., *Comparison of two questionnaires for assessing the severity of urinary incontinence: The ICIQ-UI SF versus the incontinence severity index.* Neurourol Urodyn, 2009. **28**(5): p. 411-5.
47. Maeda, Y., C.J. Vaizey, and C. Norton, *St. Mark's incontinence score.* Dis Colon Rectum, 2007. **50**(12): p. 2252.
48. Barber, M.D., M.D. Walters, and R.C. Bump, *Short forms of two condition-specific quality-of-life questionnaires for women with pelvic floor disorders (PFDI-20 and PFIQ-7).* Am J Obstet Gynecol, 2005. **193**(1): p. 103-13.
49. Burgio, K.L., et al., *Global ratings of patient satisfaction and perceptions of improvement with treatment for urinary incontinence: validation of three global patient ratings.* Neurourol Urodyn, 2006. **25**(5): p. 411-7.
50. Ware, J., M. Kosinski, and S.D. Keller, *A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity.* Med Care, 1996. **34**(3): p. 220-33.
51. Namey, E., et al., *Evaluating bang for the buck: A cost-effectiveness comparison between individual interviews and focus groups based on thematic saturation levels.* American Journal of Evaluation, 2016. **37**(3): p. 425-440.
52. Sandelowski, M., *Sample size in qualitative research.* Research in nursing & health, 1995. **18**(2): p. 179-183.
53. Hsieh, H.-F. and S.E. Shannon, *Three approaches to qualitative content analysis.* Qualitative health research, 2005. **15**(9): p. 1277-1288.
54. Patton, M.Q., *Qualitative evaluation checklist.* Evaluation checklists project, 2003. **21**: p. 1-13.
55. Devers, K.J., *How will we know "good" qualitative research when we see it? Beginning the dialogue in health services research.* Health Services Research, 1999. **34**(5): p. 1153-1188.
56. Mays, N. and C. Pope, *Assessing quality in qualitative research.* Bmj, 2000. **320**(7226): p. 50-52.
57. Denzin, N., *Sociological methods: A source book.(2) McGraw-Hill.* New York, 1978.
58. Creswell, J.W. and C.N. Poth, *Qualitative inquiry and research design: Choosing among five approaches*. 2016: Sage publications.
59. Altheide, D.L. and J.M. Johnson, *Criteria for assessing interpretive validity in qualitative research.* 1994.
60. Coyne, I.T., *Sampling in qualitative research. Purposeful and theoretical sampling; merging or clear boundaries?* Journal of advanced nursing, 1997. **26**(3): p. 623-630.
61. Lincoln, Y.S. and E. Guba, *Naturalistic Inquiry*. 1985, Sage Publications: Newbury Park, CA. p. 880-885.
62. Barry, C.A., et al., *Using reflexivity to optimize teamwork in qualitative research.* Qualitative health research, 1999. **9**(1): p. 26-44.
63. Rokach, L. and O. Maimon, *Clustering Methods*, in *Data Mining and Knowledge Discovery Handbook*. 2005, Springer. p. 321-352.
64. Lloyd, S.P., *Least Squares Quantization in PCM*, in *IEEE Transactions on Information Theory*. 1982. p. 129-137.
65. Bliss, D.Z., et al., *Dietary fiber supplementation for fecal incontinence: a randomized clinical trial.* Res Nurs Health, 2014. **37**(5): p. 367-78.
66. Gleason, J.L., et al., *Caffeine and urinary incontinence in US women.* Int Urogynecol J, 2013. **24**(2): p. 295-302.
67. Imamura, M., et al., *Lifestyle interventions for the treatment of urinary incontinence in adults.* Cochrane Database Syst Rev, 2015(12): p. CD003505.
68. VanderWeele, T.J. and S. Vansteelandt, *Mediation Analysis with Multiple Mediators.* Epidemiol Methods, 2014. **2**(1): p. 95-115.
69. Collins, L., J. Schafer, and C. Kam, *A comparison of inclusive and restrictive strategies in modern missing data procedures.* Psychological Methods, 2001. **6**(4): p. 330-351.

70. O'Kelly, M. and B. Ratitich, *Clinical trials with missing data: A guide for practitioners*. 2014, John Wiley & Sons: West Sussex, United Kingdom.