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**Official Study Title**: Binge Eating Syndrome Treatment for Older Women (BESTOW)

**NCT number**: NCT05806788

**IRB Approval Date**: 04.10.2023

**Unique Protocol ID**: HSC20220898H

**UTHSA Clinical Trial Description**

This form is not mandatory. Other documents are acceptable if equivalent information is provided.

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|---|---|---|---|
| **UTHSCSA Tracking Number** *(internal use only)* | 20220898H | **1. Original Version Date** | |
| | | **1.1. Revision Date(s)** *add rows as needed* | |

**2. Background**

*Briefly discuss the important literature relevant to the trial and that provides background for the trial. Include the importance of the trial and any relevant treatment issues or controversies.*

As women age, biological, psychological, and lifestyle changes can contribute to nutritional disorders and related health problems. One form of nutrition pathology appears to be highly prevalent among older adult women: binge eating (BE), defined as discrete episodes of eating abnormally large amounts of food in one sitting while feeling out of control. We recently reported that nearly 20% of women aged ≥60 years struggle with BE. Older women with clinical BE (i.e., BE ≥1/week) reported poorer health span indices (e.g., depression, health-related quality of life [QOL], sleep problems) versus those without BE, controlling for BMI, indicating that BE represents a health burden for older women beyond elevated BMI. In our recent study examining the clinical phenotype of older women, we found that older women with BE have poor metabolic health, physical functioning limitations, and frequently experience clinical depression and anxiety in addition to their BE. Furthermore, we found that older women with clinical BE reported substantial emotional distress regarding their BE – especially the feeling of loss of control. Older women also identified internalized ageism as a source distress (e.g., "I'm too old for this"), which represents a unique aspect in the emotional toll of BE. Yet, older adults are underrepresented in BE treatment trials. Among 58 psychotherapy RCTs for eating disorders, only 3 even allowed patients over the age of 65; none were designed for older adults. Thus, BE appears to: 1) represent a significant health problem for older women, 2) have greater prevalence than once thought, 3) produce substantial distress for those affected, and 4) remain largely untreated in this population. Taken together, BE represents a significant public health problem for older women, for which effective treatment is needed.

Thus, the PI's primary work aims to develop a BE treatment to mee the specific needs of older women experiencing BE. Following the Method for Program Adaptation through Community Engagement (M-PACE) frame, we began the intervention-tailoring process (NIH Stage Model, Stage 1A) within the PI's Beeson Award. We conducted focus groups with older women (N=25; aged ≥60 years) with clinical BE to develop an age-tailored, theory-driven BE intervention (Stage 1A): the Binge Eating Syndrome Treatment for Older Women (BESTOW). Per the M-PACE process, participants reviewed evidence-based behavioral BE treatments for younger people. Results from this mixed-method study found that our participants frequently expressed negative views toward traditional diet or nutrition-based strategies, and instead stated strong preferences for approaches that improve mindful eating, provide concrete behavioral skills to prevent emotional eating, as well as long-term strategies that anchor health behaviors to individually held core values (e.g., health, social relationships) to emphasize QOL with age.

**3. Objectives and Endpoints** *All data points collected in the study should support an objective or have a regulatory purpose.*

*Complete the table – add rows as needed.*

| **3.1. Objective(s)** *Clearly and concisely define the primary and secondary outcomes.* | **3.2. Endpoint** *Clearly define the endpoints. (endpoints are the basis for concluding that the objective has been met).* | **3.3. Justification for Endpoint** *Briefly explain why the endpoint(s) were chosen.* |
|---|---|---|
| Determine the feasibility, acceptability, and estimated magnitude of potential impact on select outcomes of the tailored BE intervention in a beta testing trial | Completion of the beta testing trial; indices of saturation based on qualitative data | In an open feasibility beta testing trial, key outcomes are based on determining recruitment, engagement, acceptability, and feasibility that will inform future refinement and finalization of the intervention protocol for a future RCT to establish efficacy |

**4. Rationale**

| *Briefly state the reason for conducting the clinical trial.* |
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| Evidence suggests that: 1) BE affects older adult women at concerning rates, and is associated with negative health indices; 2) aging-related factors comprise a set of circumstances that influence treatment considerations for older women with BE; and 3) there is a need to tailor theory-driven interventions to directly address aging-related factors unique to older women with BE. Thus, using feedback from older women with binge eating on existing eating disorders treatment, there is a need for an age tailored binge eating treatment, with the first step being beta-testing the new treatment to determine feasibility and acceptability. |

| **5. Study Design** | | | |
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| **5.1. Number of Groups/Arms** | 1 | **Group name(s)** | BESTOW |

**5.2. Overall Design**
*Select all applicable*

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| | **Randomization** | | | | **Cluster Randomized** | | | | | | |
| | **Group-Sequential** | | | | **Adaptive Design** | | | | | | |
| | **Parallel Design** | | | | **Placebo-Controlled** | | | | | | |
| | **Superiority** | | | | **Equivalence** | | | **Non-inferiority** | | | |
| **Device** | | Pilot | | | Pivotal | | | Post-Approval | | | |
| **Drug/Biologic** | | Phase 1 | | Phase 1/2 | | Phase 2 | | Phase 2/3 | | Phase 3 | | Phase 4 |

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|---|---|---|---|
| | **Dose escalation** | *If yes, details →* | |
| | **Dose ranging** | *If yes, details →* | |
| | **Sub-studies** | *If yes, details →* | |

**5.3. Other Design Details**:
This study is a beta-testing of a new behavioral intervention treatment – all participants will be assigned to the treatment and give feedback on the treatment throughout the study.

Group Intervention ("Program"): The Binge Eating Syndrome Treatment for Older Women (BESTOW)
Subjects will be asked to attend a group session once a week for 6 weeks (for a total of 6 group sessions). Each group session will last approximately 60-90 minutes. Groups will include 3-6 women. Once the first session begins, this becomes a closed group, meaning no new persons will be added to the group for the rest of the program. The group will include the same women throughout the study. The goal of the BESTOW program is to help women improve their eating habits and to stop binge eating. The BESTOW program involves discussions as well as written and behavioral activities. You will also be asked to complete activities, or 'homework,' in between sessions that will help to stop binge eating and to improve eating habits. All group sessions will be audio recorded and transcribed to be rated for "adherence," "competence," and "fidelity," which means that we want to see how closely the BESTOW provider follows the BESTOW program.

**In summary:**
This study includes:

- Assessment Visit #1 (Today!)
  - Consent
  - 1st survey
- BESTOW Group Sessions
  - 1 session a week for 6 weeks (6 total sessions); each session 60-90 minutes
- Assessment Visit #2 (In-person OR Virtual)
  - At the END of Session #6:
    - Complete another survey (like an exit survey)
  - Within 0-7 days after the last BESTOW session, you will be asked to complete a phone interview with Dr. Kilpela to get your feedback on the intervention (30-60 minutes)
- Assessment Visit #3 (In-person OR Virtual)
  - 1 month after the last BESTOW session, you will be asked to:
    - Complete a follow-up survey

        - Complete a follow-up interview (20-40 minutes)
- Assessment Visit #4 (In-person OR Virtual)
    - 2 months after the last BESTOW session, you will be asked to:
        - Complete a final survey
        - Complete a final interview (20-40 minutes)

**Additional support available to subjects during the study and after study completion:**

This is a psychotherapy trial; therefore, participants are receiving psychotherapy delivered by a licensed clinical psychologist and eating disorders expert (PI). The PI also runs an outpatient psychotherapy program within the Dept of Psychiatry at UT Health SA and within the UT Physicians network. Therefore, participants will receive clinical care from an expert in the field. Serious comorbid psychiatric concerns are screened out, per exclusion criteria (e.g., psychosis, suicidality), which require urgent psychiatric care. UTHSCSA clinics, as well as behavioral health clinics in San Antonio offer care for these psychiatric presentations. If other mental health concerns arise, the PI is capable of assessing type, severity, and frequency of comorbid psychiatric symptoms. As a practicing psychologist at UT Health, the PI and her team have access to all referral resources available that the UTHSCSA Dept of Psychiatry has as a clinical enterprise. Furthermore, there is no treatment of this kind available in San Antonio (i.e., specialty treatment for older adults with eating disorders). Thus, for the treatment of eating disorders in older adults, patients will be receiving care from an expert in the field. If, once the study is over, participants want additional resources for mental health services, UTHSCSA Dept of Psychiatry clinics have resources collated by social workers, and the PI has access to all of these resources. The PI is also able to make individualized referrals for care, since the PI will be operating within her clinical expertise.

**Assignments**

• Home activities are not used as data collection instruments, but for participants in the form of psychotherapy (which is the gold standard in evidence-based psychotherapy practices). Participants are provided with forms to complete on their own to practice the skills discussed in the session. These forms are not used for data collection. For instance, aside from what is verbally expressed during discussions in the group therapy, content of participant activities at home are not evaluated. Rather, we are tracking adherence indictors (e.g., if they report presence/absence of completing home activities) to be able to see what % of activities participants complete (i.e., % adherence by participants). This is standard in beta testing pilot trials. Outcomes include those relevant to beta testing trials, and include indicators of feasibility, acceptability, adherence, and fidelity.

- Materials and principles for this study come from published, evidence-based psychotherapy manuals :
    - Linehan, M. (2014). DBT Skills training manual. Guilford Publications.
    - Craighead, L. W. (2006). The appetite awareness workbook: How to listen to your body and overcome bingeing, overeating, and obsession with food. New Harbinger Publications.
    - Forman, E. M., Juarascio, A. S., Martin, L. M., & Herbert, J. D. (2014). Acceptance and Commitment Therapy (ACT). The Encyclopedia of Clinical Psychology, 1-7.

**6. Study Population**

| **6.1. Study Population(s) Label/Name**<br><br>*To add more populations – select a row, copy & paste* | **6.2. Identify the criteria for inclusion**<br>*The criteria that every potential participant must satisfy, to qualify for study entry.*<br><br>All individuals in this study population must meet all of the inclusion criteria in order to be eligible to participate in the study | **6.3. Identify the criteria for exclusion**<br>*The characteristics that make an individual ineligible for study participation.*<br><br>All individuals in this study population meeting any of the exclusion criteria at baseline will be excluded from study participation. |
|---|---|---|
| Older adult women with binge eating disorder (60+) | 1. Women<br>2. Age 60+<br>3. BE ≥1/week during the past ≥3 months<br>4. Community-dwelling<br>5. Able to provide informed consent | 1. Significant cognitive impairment<br>2. Nursing home, long-term care facility<br>3. Psychosis or imminent suicide risk<br>4. Current BE treatment |

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| | 6. Consistent medication regimen for three months | |

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| **6.4. Will screen failures be allowed to <u>re-screen</u> at a later date?** | | **No** | X | **Yes** *If yes, describe criteria below ↓* |
| | If the screen failure is due to duration or frequency of binge eating and/or participant age such that the screen fail would have their 60th birthday while the study is still ongoing | | | |

**7. Study Intervention(s) being tested or evaluated**
*This can include prevention, diagnostic or therapeutic interventions (e.g., drug or device) or educational, health services or basic science interventions (e.g., educational program, health care delivery model, or examining basic physiology)*

Binge Eating Syndrome Treatment for Older Women

**8. Protocol-Directed procedures, items, services or tests**
*List all procedures directed by the study plan - including items or services provided as part of routine or conventional care and those needed to diagnosis or treat research related complications.*

Important Note – The protocol directed procedures listed must match those in the Schedule of Activities (attachment)

**8.1. Drugs** *(trade and generic, dosage, route of administration)*

**8.2. Devices**

**8.3. Biologics**

**8.4. Laboratory Tests**

**8.5. Imaging Procedures**

**8.6. Other Research Procedures** *(e.g., other safety and efficacy assessments.)*

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| **8.7 Attach a Schedule of Activities (SOA) Excel File** [Download the Template here: *Schedule of Activities]* | *Check to indicate that the SOA Excel File is attached →* |

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| **9.** | **Preparation/Handling/ Storage/Accountability of Investigational Drug, Biologic, or Device** |
| N/A | *N/A - This study does not include any investigational products (e.g. drugs, devices or biologics)* |
| N/A | *N/A - An Investigator Brochure is attached* |
| N/A | *N/A - A Drug/Device Manual is attached* |

**9.1. Acquisition and accountability**

*State how the study intervention and control product will be provided to the investigator. Describe plans about how and by whom the study intervention will be distributed, including participation of a drug repository or pharmacy, and plans for disposal of expired or return of unused product.*

**9.2. Formulation, Appearance, Packaging, and Labeling**

*Describe the formulation, appearance, packaging, and labeling of the study intervention and control product, as supplied. Information in this section can usually be obtained from the IB or the package insert, or device labeling. This section should include the name of the manufacturer of the study intervention and control product.*

**9.3. Product Storage and Stability**

*Describe storage and stability requirements (e.g., protection from light, temperature, humidity) for the study intervention and control product. For studies in which multi-dose vials are utilized, provide additional information regarding stability and expiration time after initial use (e.g., the seal is broken).*

**9.4. Preparation**

*Describe the preparation of the study intervention and control product, including any preparation required by study staff and/or study participants. Include thawing, diluting, mixing, and reconstitution/preparation instructions in this section. For devices, include any relevant assembly or use instructions.*

**10. Study Intervention Additional Details**

**10.1. Measures to Minimize Bias: Randomization and Blinding**

*This section should contain a description of randomization and blinding procedures (if applicable to the study design). It should include a description or a table that describes how study participants will be assigned to study groups, without being so specific that blinding or randomization might be compromised. Plans for the maintenance of trial randomization codes and appropriate blinding for the study should be discussed. The timing and procedures for planned and unplanned breaking of randomization codes should be included. Include a statement regarding when unblinding may occur and who may unblind. Provide the criteria for breaking the study blind or participant code. Discuss the circumstances in which the blind would be broken for an individual or for all participants (e.g., for serious adverse evets (SAEs)). Indicate to whom the intentional and unintentional breaking of the blind should be reported.*

This clinical trial is an open, implementation beta-testing trial of a new tailored binge eating treatment for older women, so there is no randomization and no concern for randomization bias or need for blinding. Outcomes are related to feasibility of intervention.

**10.2. Study Intervention Compliance**

*Define how adherence to the protocol (e.g., administration of study intervention, use of device,) will be assessed, and verified (if applicable, e.g., plasma assays, electronic monitoring devices, daily diaries).*

The study team will closely track when each study takes place and ensure any protocol deviations due to scheduling issues or other causes is noted (e.g., a participant misses a session and completes a make-up session or completes a survey outside of the planned timeline).

**10.3. Permitted Concomitant Therapy**

*This section should be consistent with the medication restrictions in the inclusion/exclusion criteria previously listed. Describe how allowed concomitant therapy might affect the outcome (e.g., drug-drug interaction, direct effects on the study endpoints).*

No medication changes three months prior to starting and participants must notify us prior to starting new medication during the study.

**10.4. Rescue Medicine**

*List all medications, treatments, and/or procedures that may be provided during the study for "rescue therapy" and relevant instructions.*

**N/A** *N/A, no rescue medicine*

## 11. Study Intervention Discontinuation

### 11.1. Discontinuation of Study Intervention

*Describe the criteria for discontinuing the study intervention (e.g., halting rules), including any monitoring test(s) and associated clinical decision point(s). Include reasons for temporary discontinuation of the study intervention (e.g., type and quantity of adverse events), clearly stating the length of time, if applicable, and describe the data to be collected at the time of study intervention discontinuation and approaches for restarting administration of or re-challenging with study intervention.*

This study involves a behavioral intervention targeting healthy eating habit; thus, the risk for AEs is minimal. Nevertheless, in addition to monitoring recruitment, intervention attendance, and assessment completion, we will also monitor the rates of development and maintenance of psychological symptoms. The PI will alert the IRB and NIH if a larger than reasonably expected medical or psychological symptom development rate occurs in the intervention or control groups. We acknowledge that circumstances other than those listed may justify stopping the study.

### 11.2. Continued Follow-up Discontinuation of Study Intervention

*Describe efforts that will be made to continue follow-up of participants who discontinue the study intervention, but remain in the study for follow-up, especially for safety and efficacy study endpoints (if applicable). Reasonable efforts must be made to undertake protocol-specified safety follow-up procedures to capture adverse events (AE), serious adverse events (SAE), and unanticipated problems involving risks to subjects or others (UPIRSOs).*

Exit interviews will be done whenever possible and they will still be invited to complete the assessments.

## 12. Statistical Considerations

### 12.1. Statistical Hypotheses

*State the formal and testable null and alternative hypotheses for primary and key secondary endpoints, specifying the type of comparison (e.g., superiority, equivalence or non-inferiority, dose response) and time period for which each endpoint will be analyzed.*

We predict that the tailored intervention will be deemed feasible and acceptable, based on key statistics (e.g., recruitment, enrollment, engagement, retention, acceptability, satisfaction) gathered in the open trial. We also expect that we will achieve at least a medium effect size ($d$=.52, Cohen, 1988) on outcomes, based on within subjects analyses. We propose to enroll a total of $N$ = 25 participants into this open, implementation trial.

### 12.2. Sample Size Determination

*Include number of participants to recruit, screen, and enroll to have adequate power to test the key hypotheses for the study. Provide all information needed to validate your calculations and judge the feasibility of enrolling and following the necessary number of participants.*

We selected number of BE days in the past month as the primary efficacy outcome. We used within-group effect sizes for BE frequency at post-treatment reported by deZwaan et al. (2017), and Burton and Stice (2006), both of which observed large effects ($d$ >1.0) with cognitive-behavioral theory treatments. Power calculations were performed for a two-sided type I error rate of .05 for the pre- vs. post-treatment comparison. Although the objective of the trial is to estimate the effect size of changes in BES, the study will achieve >90% power of using Cohen's standardized mean difference with n = 25 participants and
an effect size of $d$ = 0.80. The effect size is relative to 0 change and is consistent with those demonstrated in similar studies. In studies measuring changes BE frequency, finding an effect size of 0.5 standard deviation (SD) may be considered a minimally important difference for patients who reach this threshold (i.e., a medium effect size).

### 12.3. Populations for Analyses

*Clearly identify and describe the analysis datasets (e.g., which participants will be included in each).*

All participants will undergo the intervention and be included in the analyses noted below.

### 12.4. Statistical Analyses

*Include analysis of primary efficacy endpoints, secondary endpoints, safety analyses, and any planned interim analyses*

The focus in a feasibility pilot study like this is to estimate the magnitude of potential impact. The primary outcomes are the change of Binge Eating Scale scores, Geriatric Depression Scale scores, and BMI over time, and within-subject pre-post changes will be estimated linear mixed effect models. Secondary outcomes will be evaluated using the same analytic approach. Advantages of using likelihood-based regression models over conventional analysis of variance include the ability to use data from all participants including those who have only baseline data, relaxation of the assumption of equal variances before and after treatment, and specification of data distributions other than normal such as Poisson or log-normal. Total scores on multi-item scales are often approximately normally distributed. In some cases, reasonable normality of the distributions can be achieved with transformations such as the logarithm. Summary statistics with confidence intervals will be calculated to describe average levels and trajectories of clinical outcomes over time. Baseline variables will be summarized and frequency distributions will be examined for unusual data distributions or data points. In our experience, most missing data are associated with dropout. Individual forms or entire assessments may be missed, but that is generally reasonably attributed to extraneous factors (e.g., illness) and data missing at random is not problematic for the likelihood-based analysis methods proposed. If baseline data are associated with dropout, sensitivity analyses based on case weighting and/or covariance analysis can give some insight into the impact of attrition. For example, a predictive model for attrition using baseline data can be used in inverse propensity weighted analyses, i.e., two-part models that first predict likelihood of dropout and then weight cases who resemble dropouts more heavily. Examination of attrition, along with qualitative interviews for those who dropped out will inform the attrition plan for the larger trial.