SCHEMA

Optimizing Psychosocial Intervention for Breast Cancer-related Sexual Morbidity: The Sexual Health and Intimacy Education (SHINE) Trial

Study Goal: Using the multiphase optimization strategy (MOST) framework, we will identify a sexual morbidity intervention that has been optimized for greatest impact by returning the greatest improvement in sexual morbidity for the least intervention burden.

Study Population: Partnered adult women status post treatment of Stage 0-III breast cancer experiencing sexual concerns.

Study Design: Factorial trial using the MOST framework, in which participants will be randomized to one of 16 **conditions** (2^4) to receive access to a combination of one to four SHINE **components**. Results from factorial experiments show which components work on their own (independent, or main effects), and whether combining a component with other components amplifies or reduces its effects (synergistic or antagonistic interaction effects). This design permits testing why each component works – or does not work – through mediator analyses; it also permits moderator analyses to test whether certain survivors may benefit more than others from certain components (or combinations of components).

There are four SHINE intervention **components**: (1) psychoeducation about cancer-related sexual morbidity ("Sexual Health Essentials"), (2) training for communication with clinicians ("Health Care Discussions"), (3) training for communication with partners ("Partner Conversations"), and (4) physical intimacy promotion ("Intimacy Insights"). In total, there are 16 SHINE **conditions,** or combinations of four SHINE intervention **components.** See Table 1 for the detailed list of conditions.

Table 1: Study Factorial Design

Condition	Sexual Health Essentials	Health Care Discussions	Partner Conversations	Intimacy Insights	N
1	Enhanced	On	On	On	20
2	Enhanced	On	On	Off	20
3	Enhanced	On	Off	On	20
4	Enhanced	On	Off	Off	20
5	Enhanced	Off	On	On	20
6	Enhanced	Off	On	Off	20
7	Enhanced	Off	Off	On	20
8	Enhanced	Off	Off	Off	20
9	Standard	On	On	On	20
10	Standard	On	On	Off	20
11	Standard	On	Off	On	20
12	Standard	On	Off	Off	20
13	Standard	Off	On	On	20
14	Standard	Off	On	Off	20
15	Standard	Off	Off	On	20
16	Standard	Off	Off	Off	20

Sample Size: n=320 (20 participants randomized into each of the 16 conditions)

Study Duration: 24 weeks

Primary Objective: To identify which combination of four intervention components produces the greatest benefit for survivors experiencing breast cancer-related sexual morbidity with the least intervention burden. We will determine the optimal combination of components using the 'all active components' optimization criterion that assesses effects both independently (i.e., component main effects) and synergistically (i.e., component interaction effects): the optimal combination will aim to provide survivors the best-expected effect on sexual morbidity (i.e., change in sexual distress as measured by the Female Sexual Distress Scale – Desire, Arousal, Orgasm (FSDS-DAO) and sexual functioning as measured by the Female Sexual Function Index (FSFI) from baseline to 24-week follow-up assessment) with the least intervention burden (i.e., fewest components).

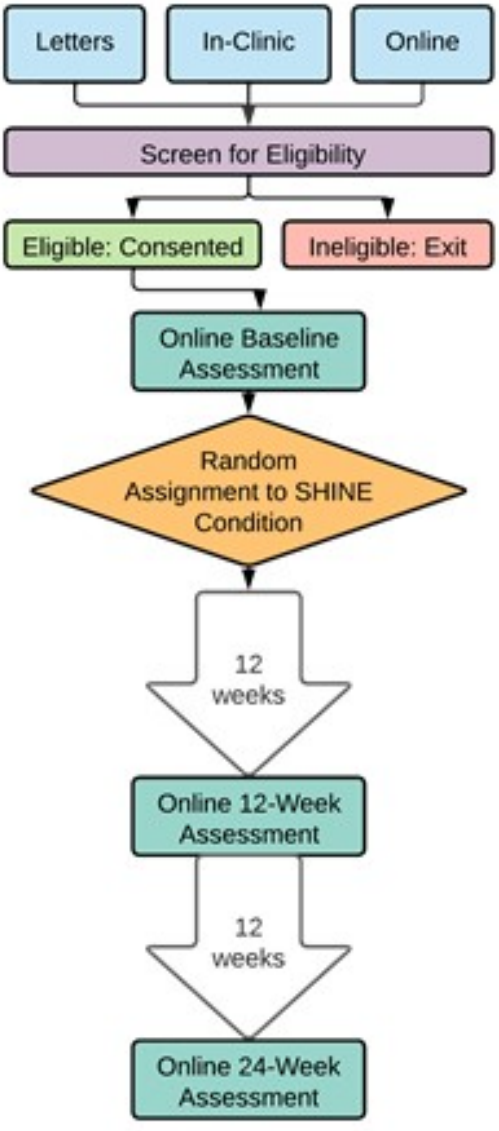
Assessments:

Participants will complete online assessments (questionnaire batteries and open-ended responses to qualitative prompts) at baseline (pre-assessment), 12-weeks post-baseline (post-assessment), and 24-weeks post-baseline (follow-up) time points.

Brief Eligibility Criteria:

- History of Stage 0 -III breast cancer diagnosis.
- ≥12 weeks following last primary cancer treatment (defined for this protocol as chemotherapy, cytotoxic antibody-drug conjugates, checkpoint inhibitors, radiation, and surgical procedures intended to remove malignant tissue). Ongoing adjuvant endocrine therapy (e.g., tamoxifen, aromatase inhibitors), adjuvant cdk 4/6-inhibitors (e.g., abemaciclib), HER2-based Monoclonal antibody therapy (e.g., trastuzumab, pertuzumab), HER2 targeted Tyrosine Kinase inhibitors (e.g., neratinib) and/or pending breast reconstructive surgery are allowed.

  Age ≥18 years at the time of study enrollment.



Following are self-reported on the ***Self-reported Eligibility Screener***:

- Cisgender female (i.e., assigned female at birth, female gender identity);
- Currently in an intimate relationship, as reported on the PROMIS SexFS screener[1] (this relationship may be with an individual of any sex and gender identity);
- Endorse being at least "somewhat" bothered by ≥1 of the following during the last 30 days: (lack of) interest in sexual activity, vaginal dryness, pain during sexual activity, or (in)ability to orgasm, as reported on the PROMIS SexFS Bother Regarding Sexual Function[1] screener;
- Endorse that ≥1 of the bothersome sexual symptoms, from the PROMIS SexFS Bother Regarding Sexual Function[1] screener is related to their breast cancer;
- Has reliable access to the Internet or is willing to participate in the study tablet lending program.
- Has a working email address (or willing to create one) and receive emails from the study.

4.0 PARTICIPANT SELECTION

4.1 Inclusion Criteria

4.1.1 History of Stage 0-III breast cancer diagnosis. History of non-breast malignancies are permitted.

4.1.2 ≥12 weeks following last primary cancer treatment. For this protocol, primary cancer treatments are defined as chemotherapy, cytotoxic antibody-drug conjugates, checkpoint inhibitors, radiation, and surgical procedures intended to remove malignant tissue. Ongoing adjuvant endocrine therapy (e.g., tamoxifen, aromatase inhibitors), adjuvant cdk 4/6-inhibitors (e.g., abemaciclib), HER2-based Monoclonal antibody therapy (e.g., trastuzumab, pertuzumab), HER2 targeted Tyrosine Kinase inhibitors (e.g., neratinib), and/or pending breast reconstructive surgery are allowed. (There is no upper limit on time since treatment. This is due to criterion 4.1.7 below – participants must endorse current sexual morbidity that they believe is related to their breast cancer. Breast cancer-related sexual morbidity often persists, or even worsens, years following treatment.[26])

4.1.3 Age ≥18 years at the time of study enrollment.

Items below will be asked on the ***Self-reported Eligibility Screener*** to the patient directly**:**

4.1.4 Cisgender female (i.e., assigned female at birth, female gender identity);

4.1.5 Currently in an intimate relationship, as reported on the PROMIS SexFS screener[1] (this relationship may be with an individual of any sex and gender identity);

4.1.6 Endorse being at least "somewhat" bothered by ≥1 of the following during the last 30 days: (lack of) interest in sexual activity, vaginal dryness, pain during sexual activity, or (in)ability to orgasm, as reported on the PROMIS SexFS Bother Regarding Sexual Function[1] screener;

4.1.7 Endorse that ≥1 of the bothersome sexual symptoms, from the PROMIS SexFS Bother Regarding Sexual Function[1] screener (see 4.1.6) is related to their breast cancer;

4.1.8 Has a working email address (or willing to create one) and receive emails from the study.

4.2 Exclusion Criteria

4.2.1 Planned cancer treatment for residual, progressive, or recurrent disease within the 24 weeks following enrollment (defined as chemotherapy, cytotoxic antibody-drug conjugates, checkpoint inhibitors, radiation, and/or surgical procedures intended to remove malignant tissue). Ongoing adjuvant endocrine therapy (e.g., tamoxifen, aromatase inhibitors), adjuvant cdk 4/6-inhibitors (e.g., abemaciclib), HER2-based Monoclonal antibody therapy (e.g., trastuzumab, pertuzumab), HER2 targeted Tyrosine Kinase inhibitors (e.g., neratinib), and/or pending breast reconstructive surgery are allowed.

4.2.2 Unable to read and comprehend English (SHINE intervention currently only available in English) as indicated by being unable to complete the Self-reported Screening Questionnaire independently.

Items below will be asked on the ***Self-reported Eligibility Screener*** to the patient directly**:**

4.2.3 Does not have reliable access to Internet (e.g., by home broadband, public network, personal data plan) by computer, tablet, smartphone etc. and is not willing to participate in the tablet lending program for this study.

4.2.4 Recent serious mental illness, as defined by reporting an inpatient psychiatric hospitalization within the past 12 months.

4.2.5 Currently participating in couple, marital, or sex therapy.

4.2.6 Currently pregnant (Pregnant women are excluded from this study because childbirth is accompanied by significant biological, psychological, and environmental changes that alter a woman's sexual functioning. Intervention content may not be medically appropriate for women who have recently given birth, given that medical providers commonly recommend that women avoid sexual contact for at least four to six weeks post-partum while healing.).