



Efficacy of a web-based women's health survivorship care plan for young breast cancer survivors: a randomized controlled trial

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Abstract

Purpose Breast cancer survivorship care plans (SCP) have limited content addressing women's health issues. This trial tested if young breast cancer survivors who receive a web-based, women's health SCP were more likely to improve on at least one of the four targeted issues (hot flashes, fertility-related concerns, contraception, and vaginal symptoms) compared to attention controls.

Methods A randomized controlled trial recruited female survivors ages 18–45 at diagnosis, 18–50 at enrollment, completed primary cancer treatment, and had a significant women's health issue: moderate or higher fertility-related concerns; ≥ 4 hot flashes/day with ≥ 1 of moderate severity; ≥ 1 moderate vaginal atrophy symptoms; or not contracepting/using less effective methods. Survivors underwent stratified, block randomization with equal allocation to intervention and control groups. The intervention group accessed the online SCP; controls accessed curated resource lists. In intention-to-treat analysis, the primary outcome of improvement in at least one issue by 24 weeks was compared by group.

Results 182 participants (86 intervention, 96 control), mean age 40.0 ± 5.9 and 4.4 ± 3.2 years since diagnosis, were randomized. 61 intervention group participants (70.9%) improved, compared to 55 controls (57.3%) (OR 1.82, 95% CI 0.99–3.4, $p=0.057$). The following issue-specific improvements were observed in the intervention versus control arms: fertility-related concerns (27.9% vs. 14.6%, OR 2.3, 95% CI 1.1–4.8); hot flashes (58.5% vs. 55.8%, OR 1.1, 95% CI 0.57–2.2); vaginal symptoms (42.5% vs. 40.7%, OR 1.1, 95% CI 0.6–2.0); contraception (50% vs. 42.6%, OR 1.4, 95% CI 0.74–2.5).

Conclusions In young breast cancer survivors, a novel, web-based SCP did not result in more change in the primary outcome of improvement in at least one of the four targeted women's health issues, than the attention control condition. The intervention was associated with improved infertility concerns, supporting efficacy of disseminating accessible, evidence-based women's health information to this population.

Keywords Breast cancer · Survivorship care plan · Fertility · Reproductive health · Randomized controlled trial

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Background

Young breast cancer survivors undergo chemotherapy and/or endocrine therapy, treatments that impair ovarian function and result in significant women's health issues in survivorship [1]. These include infertility and pregnancy concerns, limited contraception choices, hot flashes, and sexual dysfunction, which negatively impact quality of life [2–12]. Despite substantial evidence from research, practice guidelines, and clinical expertise on women's health screening and symptom management, many survivors have limited access to high-quality information throughout the cancer continuum; in particular, there are substantial unmet informational needs during the prolonged time after primary cancer treatment when fertility concerns are revisited and symptoms are experienced [13–17].

Survivorship care plans (SCPs) aim to inform cancer survivors about the effects of cancer and cancer treatment, guide follow-up care and improve care coordination [18]. As general and breast cancer SCPs have limited women's health guidance, the investigators developed an evidence-based guide for women's health care for young breast cancer survivors who have completed primary cancer treatment. The web-based SCP intervention was developed by conducting systematic reviews of women's health management strategies, critical appraisal of professional practice guidelines and online resources, and generation and refinement of the prototype with stakeholders, including survivors and their healthcare providers (providers) [19].

The SCP intervention was designed to be web-based and accessible to both survivors and the provider of their choice, as survivors actively seek health information from their providers and on the Internet [20, 21]. Oncology and primary care providers are the most common providers for this population, yet many do not have women's health expertise specific to young breast cancer survivors [22]. Hence, a randomized controlled clinical trial (RCT) was conducted to test the hypothesis that young breast cancer survivors who received the SCP intervention were more likely to improve on at least one of the four targeted women's health issues, i.e., hot flashes, fertility-related concerns, contraception, and vaginal symptoms, compared to attention controls who did not receive the intervention.

Methods

Study design and young breast cancer survivor participants

The RCT tested the efficacy of a web-based intervention in improving four women's health issues in female young breast cancer survivors. The full protocol has been published previously [23]. Eligible survivors were diagnosed with stages 0–III breast cancer between ages 18 and 45, completed primary cancer treatment (surgery, chemotherapy, and/or radiation), were ages 18–50 at study enrollment, and reported a clinically significant women's health issue. Clinically significant issues were defined as ≥ 4 hot flashes per day, ≥ 1 at least moderate in severity; moderate to high fertility-related concerns; at risk of unintended pregnancy; ≥ 1 vaginal symptom at least moderate in severity [24–27]. Survivors were able to enter the study any time after completion of primary cancer treatment.

The trial was conducted remotely in entirety. Survivors were recruited via emails and social media in partnership with Young Survival Coalition, the Susan G. Komen Foundation–San Diego, Army of Women, and Research Match; provider referrals; and emails to participants of the investigators' prior observational studies [28]. Individuals were screened for eligibility, consented, completed study baseline questionnaires, and nominated a provider through the study website. Informed consent was obtained from all individual participants included in the study. Recruitment occurred between March 2016 and June 2017. The study was approved by the institutional review board of the University of California, San Diego (NCT02667626).

Randomization, follow-up, and intervention

Survivors were randomized in a 1:1 ratio to the intervention or attention control arms and followed for 24 weeks. Computerized, block randomization was stratified by the four women's health issues. Participants in the intervention arm received access to the full web-based SCP intervention, as frequently as they desired, and twice weekly text message women's health action prompts. The SCP intervention encompassed four sections for each of the four issues: (1) a two-page SCP framed in a question and answer format; (2) a detailed summary of the systematic review results, including hyperlinks to primary research articles; (3) a description of relevant clinical guidelines with hyperlinks to them; (4) curated web-based resources for survivors and providers (Supplemental Material). Text messages with reproductive health prompts encompassed tips for managing a reported symptom. An example is,

“Anti-depressants like venlafaxine (75 mg daily) have been shown to reduce hot flash frequency and severity. Contact your healthcare provider this week to discuss venlafaxine.”

Participants in the attention control arm received access to only the curated web-based resource lists and twice weekly study adherence text messages, to standardize the number of contacts between groups. An example of an attention control text messages is, “Please take a look at (*Study Web Link*) to complete your study tasks.”

The two groups underwent equivalent numbers of contacts and study duration, but varied in the content of the web-based materials. All participants completed questionnaires at enrollment, 12 and 24 weeks and reported daily hot flashes via text messaging for 24 weeks. Daily, two text messages were pushed to all YBCS participants to ascertain hot flash frequency and severity.

Healthcare provider participants

Providers nominated by survivors as their preferred provider for managing women’s health issues were contacted by email, phone, fax, and mail for study recruitment. Interested providers were directed to the study website for eligibility screening, consent, completion of the enrollment questionnaire, and access to their patient’s intervention materials, i.e., full web-based SCP intervention versus curated web-based resource lists. Providers then completed a 24-week questionnaire. Providers were also able to complete all study procedures (consent, questionnaires) and access intervention materials in paper format.

Blinding

Study staff and survivor and provider participants were blinded to treatment allocation. To preserve blinding of participants, consent forms stated that participants would receive information and tools on self-care of reproductive health symptoms but did not detail content of the SCP or state how this information differs between the intervention and control groups. Upon study completion, the website accounts of survivor and provider participants assigned to the attention control arm automatically changed to allow access to the full SCP intervention.

Assessment of study outcomes

Study outcomes were assessed by self-report at 12 and 24 weeks. Hot flash frequency and severity over the prior 24 h were assessed, and the hot flash score was calculated [25]. Fertility-related concerns were measured using the fertility potential and pregnancy subscales of the Reproductive Concerns After Cancer scale (RCAC), a multidimensional scale with good internal consistency ($\alpha=0.82$) and construct

validity [26]. Scores > 3 indicated moderate to high concern and are associated with depression [10]. Using questions and definitions derived from the National Survey for Family Growth, [27] contraception outcomes were calculated in participants at risk of unintended pregnancy, defined as having a uterus and at least one ovary, sexually active, ≤ 45 years old, and not attempting pregnancy. Sexual health was measured using the Vaginal Atrophy Symptoms Score, a four-item scale on vaginal dryness, soreness, irritation, and dyspareunia experienced in the prior 4 weeks [24]. The scale was summarized by averaging responses with higher scores indicating a greater level of vaginal atrophy.

For each issue, participants were also asked whether they undertook actions to improve the symptom. These actions were part of the SCP content and text message reproductive health tips for the intervention group. For example, for hot flashes, the stem of the question read, “During the past 12 weeks, have you used any of the following self-care methods or medications to help with hot flashes?” and examples of responses included: I have not had hot flashes, dress in layers, keep a small fan with you during the day, acupuncture, and anti-depressant medications, such as venlafaxine, citalopram, or paroxetine.

Providers reported preparedness and confidence in talking to their patients about each of the four issues. Each preparedness item had a four-point Likert scale response (very unprepared, prepared, unprepared and very prepared). Each confidence item had a seven-point Likert scale response (not at all, slightly, somewhat, moderately, quite, very, and extremely confident).

Statistical analysis

The primary analysis was intent-to-treat. McNemar’s test with continuity correction was used to test for differences in provider-reported preparedness and confidence. The primary composite outcome was survivor-reported improvement in at least one outcome over the 24-week study, defined as 50% decrease in enrollment hot flash score; fertility and pregnancy concern scale scores ≤ 3 ; use of highly effective contraceptive methods (intrauterine devices, female sterilization, male partner sterilization, combined hormonal contraception, progestin implants, or injections); or 50% decrease in enrollment vaginal atrophy symptom score. Linear and logistic mixed effect models were used to impute missing outcomes for the primary composite outcome for ten participants (5.5%). Logistic regression models were used to test for differences by intervention versus control arm; odds ratios (OR) with 95% confidence intervals (CI) for intervention effect are reported.

To quantify intervention effects on each women’s health issue, secondary analyses were performed to compare changes in each issue with only participants who met the

enrollment criterion for that issue were included. We compared each outcome between the intervention and control groups using linear mixed effect models for the continuous outcomes (hot flash score, vaginal atrophy symptom score, fertility-related concerns score) and logistic mixed effects models for binary outcomes (use of effective contraceptive method). Two-sided *p* values < 0.05 were considered statistically significant.

A priori sample-size calculations were based on detecting clinically relevant changes in hot flash score [25]. With a sample size of 50 per arm, there was 80% power to detect a 0.57 effect-size between groups on hot flash score changes from baseline to 24 weeks based on a two-sided *t* test with alpha as 0.05. Sample size was inflated for potential clustering effect from participants having the same provider via an intraclass correlation of 0.1, 20% loss during run-in, and 20% drop-out for a total enrollment of 196 participants.

Results

Participant flow

318 individuals underwent eligibility screening, the majority of whom (82.7%) met criteria for at least one women’s health issue (Fig. 1). 182 survivors underwent randomization, 86 to the intervention arm, and 96 to the control arm. Participants were from 38 states in the US and were recruited from cancer advocacy organizations (61.5%),

previous investigator-led observational studies (13.7%), ResearchMatch (5.5%), provider referrals (3.9%), word of mouth (3.9%), and other sources (11.5%). During 6 months of follow-up, one participant (0.5%) left the study due to health reasons. Two participants in each of the intervention group and the control group did not complete at least one follow-up (2%).

Baseline characteristics of survivors and providers

Table 1 depicts baseline characteristics of survivor participants. The mean age (standard deviation) at enrollment was 40.0 (5.9) years. The majority was white (86%), non-Hispanic (95%), and college graduates (89%). Mean age at breast cancer diagnosis was 35.6 (5.4) years, with the majority of participants undergoing surgery, chemotherapy, radiation, and endocrine therapy. Significant hot flashes, fertility-related concerns, vaginal symptoms, and inadequate contraception were reported by 50–62.1% of participants (Fig. 2), with 71% reporting more than one issue. Randomization led to similar distributions of baseline characteristics and women’s health issues between the intervention and control arms (Table 1, Fig. 2).

Survivor participants nominated 165 unique providers, of which 54 (33%) enrolled with up to five recruitment attempts. Only three providers were nominated by more than one survivor participant, with each of these providers associated with survivor participants who were randomized to the same study arm. Table 2 depicts baseline

Fig. 1 Consort diagram of study flow

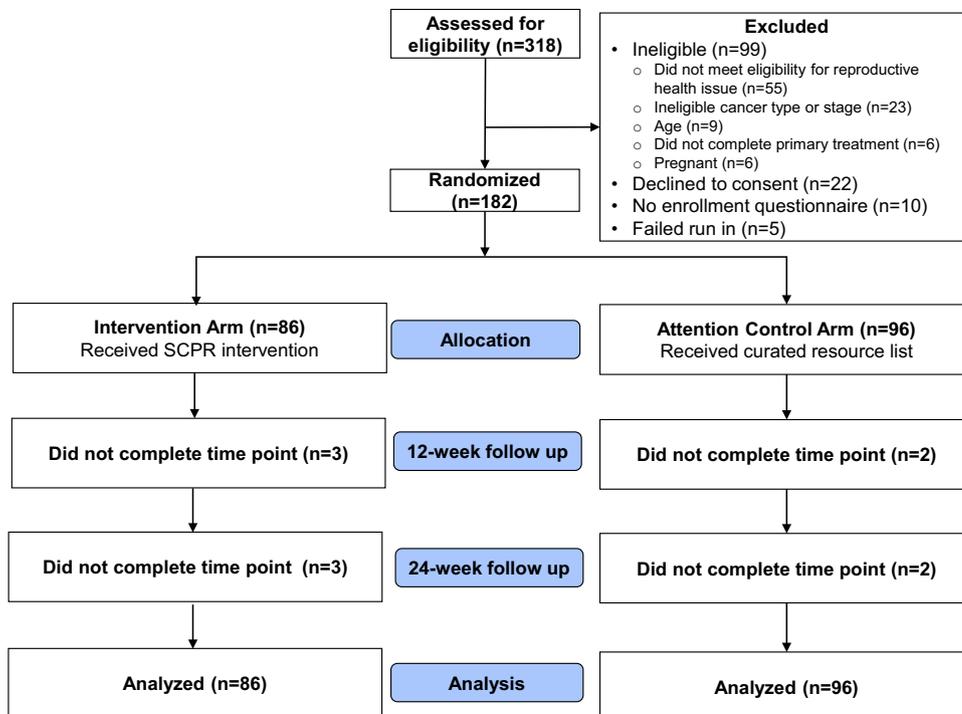


Table 1 Breast cancer survivor participant baseline characteristics by intervention arm

Characteristic	Overall <i>N</i> (%) (<i>N</i> =182)	Intervention <i>N</i> (%) (<i>N</i> =86)	Attention control <i>N</i> (%) (<i>N</i> =96)
Age at enrollment (years)			
25–35	51 (28.0)	25 (29.1)	26 (27.1)
35–40	48 (26.4)	20 (23.3)	28 (29.2)
41–45	54 (29.7)	27 (31.4)	27 (28.1)
46–50	29 (15.9)	14 (16.3)	15 (15.6)
Race			
White	157 (86.3)	77 (89.5)	80 (83.3)
Asian	7 (3.8)	4 (4.7)	3 (3.1)
Black or African American	8 (4.4)	1 (1.2)	7 (7.3)
American Indian or Alaskan Native	2 (1.1)	2 (2.3)	0 (0.0)
Mixed and other race	8 (4.4)	2 (2.3)	6 (6.3)
Hispanic ethnicity	10 (5.5)	4 (4.7)	6 (6.3)
Partnered relationship status	149 (81.9)	74 (86.0)	75 (78.1)
Education			
Did not complete college	20 (11.0)	9 (10.5)	11 (11.5)
College graduate	162 (89.0)	77 (89.5)	85 (88.5)
Income^a			
<\$51,000	25 (14.6)	10 (11.8)	15 (17.4)
≥\$51,000	146 (85.4)	75 (88.2)	71 (82.6)
Current smoker	7 (3.8)	5 (5.8)	2 (2.1)
Co-morbidities			
Hypertension	12 (6.6)	7 (8.1)	5 (5.2)
Diabetes	7 (3.8)	5 (5.8)	2 (2.1)
Mood disorder	59 (32.4)	30 (34.9)	29 (30.2)
Osteopenia or osteoporosis	28 (15.4)	13 (15.1)	15 (15.6)
Cancer characteristics			
Age at breast cancer diagnosis (years)			
18–24	4 (2.2)	2 (2.3)	2 (2.1)
25–35	86 (47.2)	40 (46.5)	46 (47.9)
36–45	92 (50.6)	44 (51.2)	48 (50.0)
Years since diagnosis			
<1	20 (11.0)	9 (10.5)	11 (11.5)
1–2	52 (28.6)	27 (31.4)	25 (26.0)
3–5	47 (25.8)	18 (20.9)	29 (30.2)
>5	63 (34.6)	32 (37.2)	31 (32.3)
Cancer surgery	180 (98.9)	85 (98.8)	95 (99.0)
Radiation	124 (68.1)	54 (62.8)	70 (72.9)
Chemotherapy	156 (85.7)	72 (83.7)	84 (87.5)
Biologic therapy	48 (26.4)	22 (25.6)	26 (27.1)
Hormone therapy	142 (78.0)	67 (77.9)	75 (78.1)
Cancer stage^a			
0	10 (5.6)	8 (9.5)	2 (2.1)
1	49 (27.2)	21 (25.0)	28 (29.1)
2	81 (45.0)	38 (45.3)	43 (44.8)
3	40 (22.2)	17 (20.2)	23 (24.0)
Cancer recurrence	7 (3.8)	6 (7.0)	1 (1.0)
Reproductive characteristics			
Hysterectomy	19 (10.4)	9 (10.5)	10 (10.4)
Bilateral oophorectomy	32 (17.6)	13 (15.1)	19 (19.8)

Table 1 (continued)

Characteristic	Overall <i>N</i> (%) (<i>N</i> =182)	Intervention <i>N</i> (%) (<i>N</i> =86)	Attention control <i>N</i> (%) (<i>N</i> =96)
Menses past year			
0	78 (42.9)	36 (41.9)	42 (43.7)
1–3	35 (19.2)	16 (18.6)	19 (19.8)
4–9	36 (19.8)	18 (20.9)	18 (18.8)
10–12	33 (18.1)	16 (18.6)	17 (17.7)
Prior live birth	100 (55.0)	52 (60.5)	48 (50.0)
Desires another baby in the future	77 (42.3)	40 (46.5)	37 (38.5)
Sexually active with male partner	162 (89.0)	79 (91.9)	83 (86.5)
Fertility concerns score, mean (SD)	3.2 (1.1)	3.3 (1.1)	3.2 (1.1)
Pregnancy concerns score, mean (SD)	3.0 (1.0)	3.0 (0.9)	2.9 (1.1)
Hot flash frequency, mean (SD)	3.4 (5.2)	3.4 (4.7)	3.3 (5.6)
Hot flash score, mean (SD)	7.1 (13.5)	7.1 (12.4)	7.1 (14.6)
Vaginal atrophy symptom score			
Mean (SD)	3.3 (2.5)	3.4 (2.6)	3.3 (2.3)
Median (range)	3.0 (0–12)	3.0 (0–12)	3.0 (0–10)
Birth control			
Not using	52 (28.6)	24 (27.9)	28 (29.1)
WHO class I/II	85 (46.7)	40 (46.5)	45 (46.9)
WHO class III/IV	45 (24.7)	22 (25.6)	23 (24.0)

WHO World Health Organization

^aNumbers do not sum up to 182 for some variables due to missing data

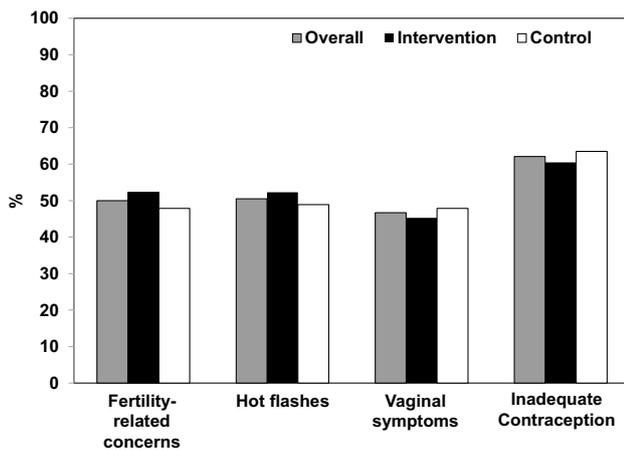


Fig. 2 At enrollment, proportions of breast cancer survivor participants ($n=182$) with hot flashes, fertility-related concerns, vaginal symptoms, and inadequate contraception, by intervention arm

characteristics of provider participants. Most providers were female (81%), white (83%), and a physician in oncology (46.3%) or gynecology (27.8%). Mean time in clinical practice was 15.4 ± 8.2 years.

Preparedness for talking with their patient about each women's health issue was dichotomized as prepared, versus unprepared (Table 2). The majority of providers reported

that they were prepared across all four issues, but providers were significantly less likely to report preparedness in discussing fertility-related issues, compared to hot flashes ($p=0.001$), vaginal symptoms ($p=0.009$), and contraception ($p=0.016$).

Confidence in discussing each women's health issue was dichotomized as quite confident, versus moderately confident or less. Only 50% of providers reported confidence in discussing fertility-related issues, significantly lower than proportions for hot flashes ($p=0.015$), vaginal symptoms ($p=0.016$), and contraception ($p=0.002$). Randomization of survivors led to similar distributions of baseline characteristics, preparedness, and confidence among provider participants by intervention arm.

Outcomes

Among 182 survivor participants, 61/86 (70.9%) women in the intervention arm improved in at least one women's health issue, compared with 55/96 (57.3%) of women in the control arm, OR 1.82, 95% CI 0.99–3.4, $p=0.057$ (Fig. 3). For each issue, the following improvements were observed in the intervention versus control arms: 50% decrease in hot flash score (58.5% vs. 55.8%, OR 1.11, 95% CI 0.57–2.18, $p=0.75$); fertility-related concerns scale scores ≤ 3 (27.9% vs. 14.6%, OR 2.27, 95% CI 1.1–4.84, $p=0.03$); 50%

Table 2 Healthcare provider baseline characteristics assigned to their breast cancer patient, by intervention arm

Characteristic	Overall <i>N</i> (%) (<i>n</i> = 54)	Intervention <i>N</i> (%) (<i>n</i> = 31)	Attention control <i>N</i> (%) (<i>n</i> = 23)
Age (y)			
30–39	12 (22.2)	8 (25.8)	4 (17.4)
40–49	20 (37.0)	10 (32.3)	10 (43.5)
50–59	17 (31.5)	10 (32.3)	7 (30.4)
≥ 60	5 (9.3)	3 (9.6)	2 (8.7)
Female	44 (81.5)	26 (83.9)	18 (78.3)
Race			
White	45 (83.3)	26 (83.9)	19 (82.6)
Asian	5 (9.3)	2 (6.5)	3 (13.0)
Black or African American	2 (3.7)	1 (3.2)	1 (4.4)
American Indian or Alaskan Native	0 (0.0)	0 (0.0)	0 (0.0)
Mixed and other race	2 (3.7)	2 (6.4)	0 (0.0)
Profession			
Physician	45 (83.4)	26 (83.9)	19 (82.6)
Nurse practitioner, physician assistant, or nurse	9 (16.6)	5 (16.1)	4 (17.4)
Specialty			
Oncology	25 (46.3)	12 (38.7)	13 (56.5)
Family or internal medicine	12 (22.2)	9 (29.0)	3 (13.0)
Obstetrics/Gynecology	15 (27.8)	9 (29.0)	6 (26.1)
Psychiatry/Psychology	2 (3.7)	1 (3.3)	1 (4.4)
Number of breast cancer patients seen per year			
≤ 20	23 (42.6)	15 (48.4)	8 (34.8)
21–40	10 (18.5)	6 (19.3)	4 (17.4)
> 40	21 (38.9)	10 (32.3)	11 (47.8)
Preparedness ^a for discussing			
Hot flashes	49 (90.7)	29 (93.5)	20 (87.0)
Fertility-related concerns	37 (68.5)	22 (71.0)	15 (65.2)
Vaginal symptoms	47 (87.0)	29 (93.5)	18 (78.3)
Contraception	47 (87.0)	30 (96.8)	17 (73.9)
Confidence ^b in discussing			
Hot flashes	38 (70.4)	21 (67.7)	17 (73.9)
Fertility-related concerns	27 (50.0)	16 (51.6)	11 (47.8)
Vaginal symptoms	37 (68.5)	21 (67.7)	16 (69.6)
Contraception	40 (74.1)	23 (74.2)	17 (73.9)

^aPreparedness indicates very prepared or prepared, versus very unprepared/unprepared

^bConfidence indicates extremely confident, very confident, or quite confident, versus not at all/slightly/somewhat/moderately confident

decrease in vaginal atrophy symptom score (42.5% vs. 40.7%, OR 1.08, 95% CI 0.59–1.99, $p=0.81$); use of highly effective contraception (50% vs. 42.6%, OR 1.35, 95% CI 0.74–2.46, $p=0.32$).

In secondary analysis, 92 survivors reported ≥ 4 daily hot flashes, with ≥ 1 moderate in severity. Among these participants, 26/45 (57.8%) in the intervention group experienced a 50% decrease in hot flash score, compared with 24/47 (51.1%) of controls (OR 1.31, 95% CI 0.58–3.01, $p=0.52$), with no significant time by intervention effect. Seventy three percent in the intervention and 42.2% in the

control group reported doing a suggested tip for hot flash management ($p=0.004$).

Ninety-one survivors had moderate or high fertility-related concerns. In the intervention group, 24/45 (53.3%) improved with no or low fertility or pregnancy concerns, compared with 14/46 (30.4%) in the control group (OR 2.61, 95% CI 1.12–6.29, $p=0.03$). In the intervention group, 40/86 (46.5%) desired another baby in the future, compared to 37/96 (38.5%) in the control group ($p=0.28$). Thirteen percent in the intervention and 21.4% in the

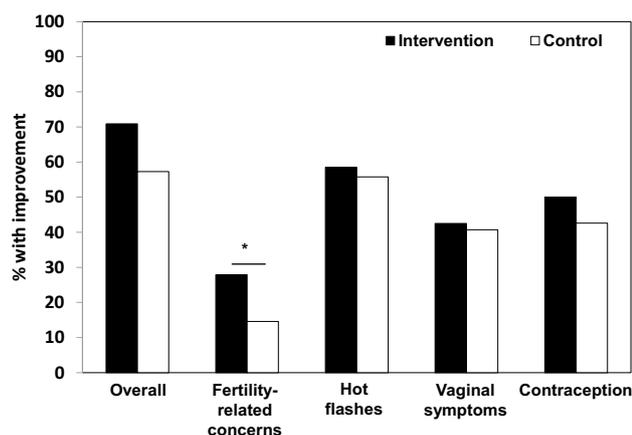


Fig. 3 By 24 weeks, proportions of breast cancer survivor participants ($n=182$) with improvement in their women's health issue(s) by intervention arm, *denotes $p < 0.05$

control group reported doing a suggested tip for fertility concerns ($p = 0.34$).

Eighty-five survivors reported vaginal symptoms over the prior 4 weeks as at least moderate in severity. In the intervention group, 10/39 (25.6%) experienced a 50% decrease in vaginal atrophy symptom score, compared with 11/46 (23.9%) in the control group (OR 1.1, 95% CI 0.4–2.96, $p = 0.85$). 44% in the intervention and 26.2% in the control group reported doing a suggested tip for vaginal symptom management ($p = 0.09$).

Among participants, 113 had a uterus and at least one ovary, were sexually active and ≤ 45 years. In the intervention group, 23/52 (44.2%) reported using a highly effective birth control method over follow-up, compared with 21/61 (34.4%) in the control group (OR 1.51, 95% CI 0.71–3.25, $p = 0.29$). Ten percent in the intervention and 8.6% in the control group reported doing a suggested tip for birth control management ($p = 0.86$).

There were no significant interactions between time since cancer diagnosis and intervention for both primary and secondary outcomes (data not shown). While provider visits were not required, 69% of participants reported seeing a provider to manage reproductive health issues by 24 weeks (22% in the intervention group and 13% in the control group by 12 weeks [$p = 0.13$]; 66% in the intervention group and 71% in the control group by 24 weeks, $p = 0.34$).

Discussion

This RCT is first to test the effects of a SCP intervention focused on fertility-related concerns, contraception, hot flash, and vaginal symptom outcomes in young breast cancer survivors. Clinical improvements were observed in both

the intervention and attention control arms across all four issues. The web-based SCP did not result in the hypothesized change in the primary outcome of improvement in at least one of the four targeted women's health issues, over the attention control condition. For infertility concerns, the intervention group had significantly higher odds of experiencing low concerns by the end of 6 months, a clinically meaningful improvement as fertility-related distress is related to poorer quality of life and depression [29].

The finding on fertility-related concerns was consistent with provider participants' report of less preparedness and confidence in managing fertility; where the vast majority of providers expressed confidence in managing hot flashes, contraception, and sexual health, only half felt confident in discussing fertility-related concerns. The gap in fertility care among survivors is well-described, despite longstanding oncology and reproductive medicine society guidelines and quality measures for fertility care [30–33]. Importantly, this care is needed not only at diagnosis, but also after cancer treatment because of persistent and prevalent infertility concerns and misperceptions on fertility and pregnancy risks [9, 34]. Optimal strategies to meet fertility-related concerns in survivorship have not been defined, [35] but this study supports that provision of concise, evidence-based information on fertility and pregnancy after breast cancer meets more of the informational needs than recommended resources alone. Given the observed positive effect of the fertility-related SCP, future studies can leverage the materials as one implementation strategy for fertility care.

The finding of improvement across arms may result from effective materials presented to both groups. Intervention materials were designed to improve self-efficacy by providing concise and up-to-date evidence, actionable steps for symptom management, in addition to hyperlinks to primary studies, clinical guidelines, and curated resources. However, controls had access to the curated resources, which contained hyperlinked online resources from professional organizations that investigators selected for valid and specific content on managing these issues. It is possible that these resources alone impacted participant engagement and education. Moreover, participants were engaged in daily text messaging, which may have served as a motivational prompt. However, natural remission of symptoms, with individuals entering trials when they are most symptomatic, and regression to the mean cannot be excluded [36].

The intervention did not result in more improvements in hot flashes or vaginal symptoms than access to curated resources. However, the majority of participants who had hot flash or vaginal symptoms at enrollment had at least 50% decrease in symptom scores during follow-up. This proportion for hot flash improvement is higher than the observed 1/2–1/3 in the placebo arms of many hot flash trials [25]. Many participants reported doing a suggested tip to improve

symptoms during the study, supporting that a health behavior was undertaken on study. A limitation is that details on dose and duration of patient behaviors to improve these symptoms were not collected.

Highly effective contraceptive methods were not undertaken by most participants, even when restricted to participants at risk of unintended pregnancy. Non-contraception among cancer survivors is high compared to the general US population, and may result from limited contraception choices and misperceptions of infertility risk [17, 34]. While hormone-free intrauterine devices are highly effective, reversible, and minimally invasive, low uptake by the end of this study supports that delivering educational materials alone is unable to address other implementation barriers such as provider access and cost [37].

The trial contributes new knowledge on the efficacy of cancer SCPs. A recent systematic review summarized 13 randomized studies on SCPs, observed heterogeneous interventions, timing, and outcome measures, and noted largely null effects on physical and psychological health outcomes [38]. Positive findings included increased implementation of survivorship care [38–40]. For general survivorship care, trials suggest that the addition of a SCP document does not augment the care delivered by an oncology provider [41–43]. In contrast, the current study focused on women's and reproductive health, an area less commonly managed by oncology providers, and the data support this SCP as an effective strategy for delivering specialty expertise to young breast cancer survivors. As our intervention did not require provider counseling, it is unknown whether provider review of the intervention with their patient would result in more clinical improvement [44]. Importantly, the study supports a tailored approach to delivering information to survivors; secondary analyses showed larger effect sizes when restricted to participants who met criteria for that particular health issue.

The study's primary strength is in intervening on women's health, an unmet survivorship care needed for young breast cancer survivors. Additional strengths include use of valid and clinically relevant outcome measures, use of a web-based format to increase reach, collaboration with breast cancer patient advocacy groups for intervention generation and study recruitment, high follow-up rates, and intent-to-treat analysis to minimize bias. All aspects of the study were conducted remotely, from screening for symptoms to delivering evidence-based information, rendering future dissemination of such a tailored intervention for young survivors feasible.

A limitation of the study is that the population was primarily white and highly educated, impacting generalizability of findings to under-represented minority women and lower SES women. The attention control condition may have been active, which may result in larger than expected change in control outcomes. The enrolled provider sample was modest,

limiting provider reinforcement of survivors' actions, but similar to other survivorship care or physician–patient dyad studies [45, 46]. Even with this limitation, having a similar distribution in provider characteristics at baseline between survivors in the intervention and control arms would minimize treatment bias that could result from differences in baseline provider confidence and preparedness. We did not embed measures of the dose of use of study materials in the study platform, ask participants about how much they used these materials, or measure change in knowledge, which may be observed via usage statistics in future work. While the content did not have patient-specific treatment summaries, breast cancer treatment and management of women's health issues are fairly homogeneous. Future studies on the women's health SCP will need to address these limitations and how content is to be modified to retain all four issues or limit to addressing fertility alone.

The low-cost, web-based intervention did not result in a statistically significant increase in the composite outcome across four targeted women's health issues, compared to the attention control condition. The intervention was associated with greater improvement in infertility concerns. Follow-up work is needed on how the intervention can help to disseminate evidence-based women's health information to more survivors with the goal of meeting the reproductive health and quality-of-life needs of this population.

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Compliance with ethical standards

Ethical approval The clinical trial complies with the current laws of the United States. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Conflicts of interest All authors declare that they have no conflict of interest.

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