Original Article

A telehealth intervention for symptom management, distress, and adherence to adjuvant endocrine therapy: A randomized controlled trial

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BACKGROUND: Patients taking adjuvant endocrine therapy (AET) after breast cancer face adherence challenges and symptom-related distress. We conducted a randomized trial to evaluate the feasibility, acceptability, and preliminary efficacy of a telehealth intervention (Symptom-Targeted Randomized Intervention for Distress and Adherence to Adjuvant Endocrine Therapy [STRIDE]) for patients taking AET. **METHODS:** From October 2019 to June 2021, 100 patients reporting difficulty with AET were randomly assigned to either STRIDE or a medication monitoring (MedMon) control group. STRIDE included six weekly small-group videoconferencing sessions and two individual calls. We defined feasibility as having >50% of eligible patients enroll, >70% complete the 12-week assessment, and > 70% of STRIDE patients complete ≥4/6 sessions. We monitored adherence with the Medication Event Monitoring System Caps (MEMS Caps). At baseline and 12- and 24-weeks after baseline, patients self-reported adherence (Medication Adherence Report Scale), AET satisfaction (Cancer Therapy Satisfaction Questionnaire), symptom distress (Breast Cancer Prevention Trial-Symptom Checklist), self-management of symptoms (Self-efficacy for Symptom Management-AET), coping (Measure of Current Status), quality of life (QOL; Functional Assessment of Cancer Therapy-Breast), and mood (Hospital Anxiety and Depression Scale). We used linear mixed effects models to assess the effect of STRIDE on longitudinal outcomes. **RESULTS:** We enrolled 70.9% (100/141) of eligible patients; 92% completed the 12-week assessment, and 86% completed ≥4/6 STRIDE sessions. Compared with MedMon, STRIDE patients reported less symptom distress (B[difference] = −1.91; 95% CI, −3.29 to −0.52; p = .007) and better self-management of AET symptoms, coping, QOL, and mood. We did not observe significant differences in AET satisfaction or adherence. **CONCLUSIONS:** STRIDE is feasible and acceptable, showing promise for improving outcomes in patients taking AET after breast cancer. ***Cancer* 2022;128:3541-3551**. © *2022 American Cancer Society.*

LAY SUMMARY:

- Patients taking adjuvant endocrine therapy (AET) after breast cancer may face challenges while following their treatment regimen.
- In this randomized controlled trial of 100 patients taking AET, a brief, small-group virtual intervention (STRIDE) was well-received by patients and led to improvements in how upset patients were due to symptoms, how confident they were in managing symptoms, and how well they could cope with stress. Thus, STRIDE is a promising intervention and should be tested in future multi-site trials.

KEYWORDS: adherence, breast cancer, distress, endocrine therapy, psychosocial intervention, side effects, symptoms, telehealth.

INTRODUCTION

Although breast cancer is the second leading cause of cancer-related deaths among women,[1] adjuvant endocrine therapy (AET) is a lifesaving treatment for early-stage, hormone-sensitive breast cancer.[2] Up to 80% of breast malignancies are hormone sensitive[3] and treated with AET (e.g., tamoxifen or an aromatase inhibitor) for 5 to 10 years, effectively reducing patients' recurrence risk by 40% to 50%[3,4] and improving 15-year survival by one third.[4] Despite these benefits, patients live with AET-related physical and emotional sequelae that interfere with quality of life (QOL) and ability to take the medication daily as prescribed. The most prominent symptoms include myalgias/arthralgias, hot flashes, sleep disturbances/insomnia, sexual dysfunction, fatigue, weight gain, cognitive impairment, and mood fluctuations.[5–10] Given patients' difficulties managing these symptoms, adherence to AET (i.e., taking medication as prescribed) is alarmingly low and presents an ongoing concern in breast cancer care.[11–13]

Up to 59% of patients are not adherent to their AET regimen,[14,15] and adherence declines each year following treatment initiation.[16] The negative effects of AET nonadherence have been consistently documented, including increases in breast cancer recurrence,[17] breast cancer mortality,[18] and overall mortality.[19] Accordingly, the American Society of Clinical

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Oncology recommends that clinicians manage AET-related symptoms to reduce barriers to medication-taking and enhance adherence.[3,5] However, efficacious interventions to improve adherence to AET are lacking, and only five published trials have targeted this behavior. The limitations of prior trials and interventions are well-documented and include the lack of focus on improving self-management of AET symptoms as the primary barrier to adherence and the absence of theory informed and evidence-based intervention strategies.[20–22]

To address this need, we followed the National Institutes of Health Stage Model for Behavioral Intervention Development[23] to develop an evidence-based, telehealth intervention: Symptom-Targeted Randomized Intervention for Distress and Adherence to Adjuvant Endocrine Therapy (STRIDE).[24,25] We conducted a single-center pilot randomized controlled trial to examine the feasibility and acceptability of the STRIDE intervention, compared with a medication monitoring (MedMon) control condition, as well as explore preliminary effects of the intervention.[26]

METHODS

Study design

We conducted a randomized controlled pilot trial of a brief, small-group telehealth intervention (STRIDE) for patients taking AET after breast cancer, compared with a MedMon control group (clinicaltrials.gov identifier: NCT03837496). This study took place at the Massachusetts General Hospital Cancer Center in Boston, Massachusetts, and three community affiliates. The Dana-Farber Harvard Cancer Center institutional review board reviewed and approved the study protocol before initiation.

Participants

Eligible patients were female, aged ≥21 years, diagnosed with early-stage hormone receptor–positive breast cancer (stage 0-IIIB), finished with primary treatment, within 1 week to 36 months of starting AET, and English speaking. They also had to have an Eastern Cooperative Oncology Group performance status of ≤2. Patients completed an adapted National Comprehensive Cancer Network distress thermometer[27] and were eligible if they scored ≥4 (range, 0–10) on any of three questions: (1) How upset are you by having to take hormonal therapy? (2) How bothered are you by the symptoms? (3) How difficult is it for you to take your hormonal therapy medication every day? Patients were not eligible if they were enrolled in a clinical trial, psychosocial intervention study, or other group psychotherapy; were undergoing primary treatment for another cancer; or had a condition that would affect study participation (e.g., uncontrolled psychosis, active suicidal ideation, psychiatric hospitalization within the year, or cognitive impairment). Patients without access to an electronic device (e.g., smartphone, computer) for the virtual study sessions were offered a study tablet.

Study procedures

From October 12, 2019, to June 4, 2021, study staff reviewed the electronic health records of patients in the breast oncology clinic and called potentially eligible patients after obtaining permission from their oncology clinician. Interested patients with AET-related distress ≥4 were offered participation. Study staff obtained informed consent electronically via REDCap, a HIPAA-approved online survey tool. We paused recruitment from mid-March 2020 through May 2020 due to the COVID-19 pandemic. Once consented, all patients completed baseline questionnaires electronically and received the Medication Event Monitoring System pill bottle and cap (Medication Event Monitoring System Caps [MEMS Caps])[28] by mail. After storing AET in the MEMS Caps for a 1-week period to capture a baseline adherence rate, patients were randomized 1:1 to the STRIDE intervention or the MedMon control group using a computer-generated randomization scheme. We stratified randomization by level of distress on the baseline Hospital Anxiety and Depression Scale subscales[29] (HADS; high [≥8] vs. low [<8]). Patients randomly assigned to STRIDE were placed in small groups of two to three participants based on scheduling availability. All patients repeated questionnaires at 12 weeks and 24 weeks after baseline and continued using the MEMS Caps throughout the study. They were remunerated $20 per completed assessment.

MedMon control

Patients randomly assigned to MedMon received care as usual and monitored their medication-taking using the MEMS Caps throughout the study. They were offered the STRIDE workbook after their final study assessment.

STRIDE intervention

Patients randomly assigned to STRIDE also received care as usual and monitored their medication-taking using the MEMS Caps throughout the study. STRIDE is a brief, manualized, telehealth intervention. A description of STRIDE is summarized in Table 2 and published elsewhere.[24] Using the National Institutes of Health Stage Model for Behavioral Intervention Development,[23] we developed STRIDE based on (1) our systematic review of interventions for oral anticancer therapy adherence,[30] (2)

our qualitative analysis of patients' perceptions of AET,[25] (3) efficacious interventions for treatment adherence[31] and stress management in breast cancer,[32] (4) theoretical models including Murray's Framework for Medication Adherence[33] and the Cognitive Model for Menopausal Symptoms,[34] (5) expert input from breast oncologists and behavioral scientists, and (6) an open pilot study.[24]

Those randomly assigned to STRIDE received usual care in addition to six weekly 1-hour virtual sessions in small groups of two to three participants and two individual 20-minute phone calls at 4 and 5 months after baseline, respectively. The two phone calls served as brief booster sessions to review ongoing use of skills and to determine the need for any additional referrals (e.g., nutrition, psychiatry, rehabilitation medicine). These were conducted individually for ease of scheduling and to maximize efficiency when offering referrals and skills' review. Licensed clinical psychologists or psychology fellows delivered sessions via a Health Insurance Portability and Accountability Act–compliant videoconferencing software (Zoom). Patients were encouraged to practice skills using audio recordings between sessions, and therapists rated patients' homework completion (0 = not complete; 7 = complete). Therapists participated in weekly supervision. To assess fidelity, study staff reviewed 10% of sessions, stratified by a therapist, for content with a goal of >90% of topics covered per session.

Measures

At baseline, study staff reviewed the electronic health records to obtain clinical information about breast cancer and treatment, whereas patients self-reported sociodemographic characteristics. To assess intervention acceptability, patients in STRIDE completed the Client Satisfaction Questionnaire (CSQ-3).[35]

We administered the Medication Adherence Report Scale (MARS-5)[36] to assess self-reported adherence to AET, as well as the MEMS Caps for an objective measure, which electronically records bottle openings as a proxy for taking medication.[25] Patients used a medication diary as a supplement. Study staff documented medication breaks or changes per patient report. We administered the Cancer Therapy Satisfaction Questionnaire (CTSQ)[37] to assess satisfaction with AET, the Breast Cancer Prevention Trial Symptom Scale (BCPT)[38] with corresponding subscales (e.g., hot flashes) to measure symptoms distress, and the Functional Assessment of Cancer Therapy-Breast Cancer (FACT-B)[39] to examine QOL, and the HADS[29] to evaluate mood (i.e., anxiety and depressive symptoms). We assessed perceived ability to cope with stress via relaxation and cognitive skills using the Measure of Current Status (MOCS-A)[40] and patients' confidence in their ability to manage AET symptoms with the Self-Efficacy for Managing AET Symptoms Questionnaire (SESM-AET).[41] See Supplemental Material for full measure descriptions.

Statistical analysis

We performed statistical analyses using SAS version 9.4. We used an intention-to-treat approach for all randomized patients. Data were assessed for patterns of normality, statistical assumptions, and missingness.[42] We defined feasibility based on rates of enrollment (>50%), retention (i.e., assessment completion >70%), and intervention attendance (≥70% of patients attending ≥4 of 6 sessions). Acceptability was defined as >75% of patients reporting satisfaction scores greater than the midpoint of the CSQ-3.[35] With feasibility as the primary end point, power calculations were conducted based on a sample of 80 patients, with an anticipated enrollment rate of at least 60% and retention and attendance rates of 80%. With these estimates, if 134 patients were approached and 80 were enrolled, the lower limit for an exact, one-sided 95% CI for the enrollment rate would be 53%, and 71% for retention and attendance rates. After 14 months of recruitment, we expanded the accrual goal to 100 patients to ensure that at least 40 patients per group completed the study.

For secondary outcomes, we first generated descriptive statistics for baseline characteristics and identified any group imbalances. We then conducted analysis of covariance to compare mean scores between groups on patient-reported outcomes at 12 weeks, controlling for baseline values of the outcome, distress level (given that the sample was stratified by distress[43]), and ovarian suppression (given group imbalance). We considered two-sided p values $< .05$ to be statistically significant and calculated effect sizes (Cohen's d) for changes in outcomes. Next, we fit linear mixed effects models with random intercepts to examine differences between groups in average outcome trajectories across the baseline and 12- and 24-week assessments, adjusting for the same covariates. Finally, we computed a weekly and monthly adherence score (% of days that AET was taken) for each patient using the MEMS Caps data of daily openings and fit linear mixed models to examine the between group differences in adherence trajectories across the 24 weeks.

RESULTS

Baseline characteristics

Between October 2019 and June 2021, we offered participation to 141 eligible patients with AET-related distress,

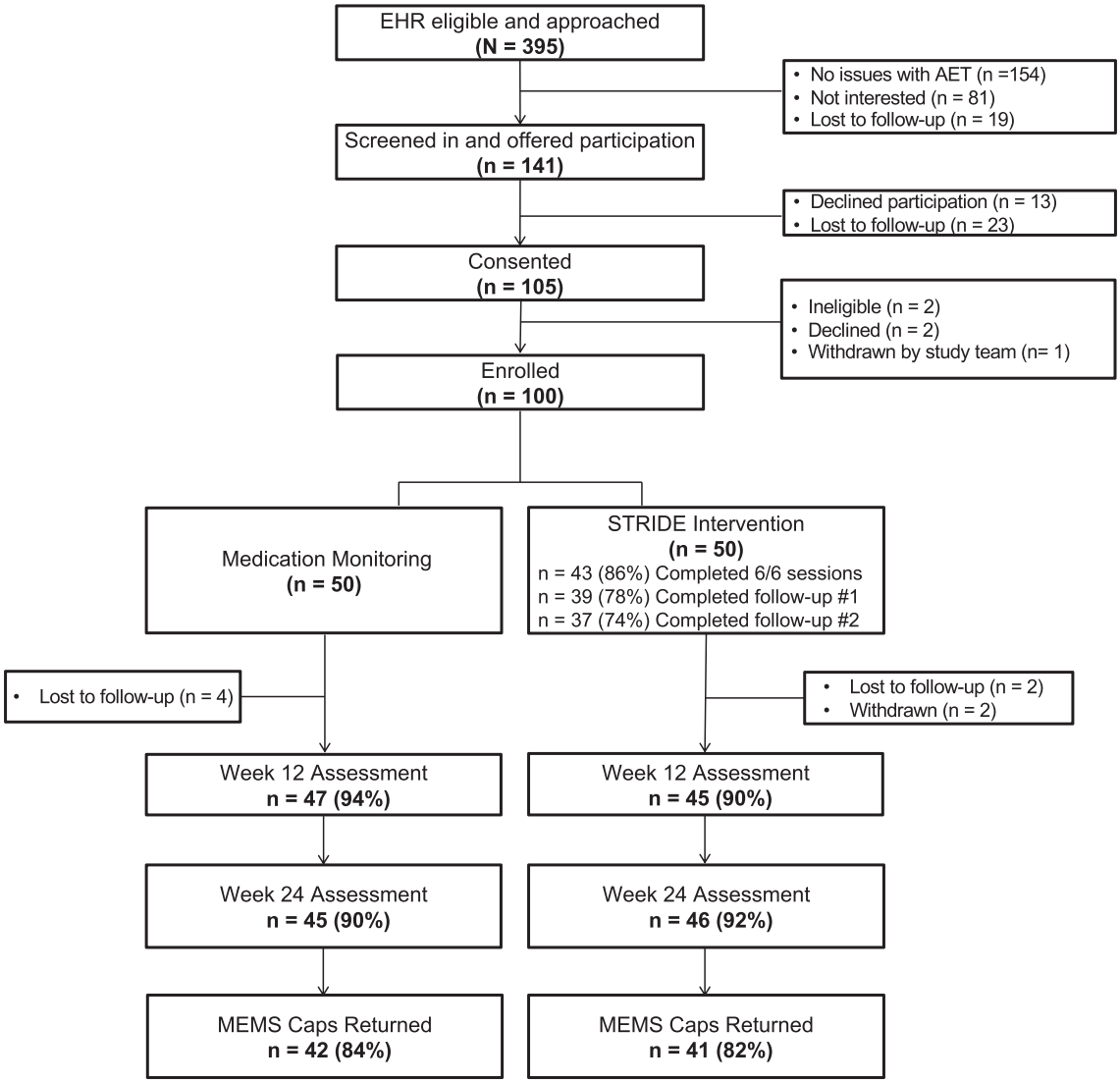

Figure 1. Study flow diagram. Screened-in: patient scored ≥4 on at least one of the adapted National Comprehensive Cancer Network distress thermometer questions. Ineligible postconsent: one patient did not complete the baseline assessment within window and became ineligible to reconsent due to her length of time on AET (>36 months). One patient became ineligible because of changes to restrictions regarding providing virtual care to out-of-state patients. Declined postconsent: two patients declined to enroll after consenting (one because of feeling too overwhelmed and one because of new health issues that prevented her from participating). Withdrawn postconsent by study team: one patient signed consent after the accrual goal was reached resulting from a staff error.

and 70.9% (100/141) enrolled (Fig. 1). Most patients were White (91%) and partnered (73%). On average, they were 56 years old (SD = 10.9, range, 31–81) and had been taking AET for approximately 18 months (SD = 8.64; Table 1). More patients in the MedMon control were receiving ovarian suppression compared with those in STRIDE (Fisher exact test = .998, $p = .014$). All enrolled patients had access to their own technology for the virtual sessions; therefore, no one required a study tablet. Enrolled patients did not differ from those who declined study participation with respect to age, cancer stage, or AET type.

Feasibility and acceptability

We enrolled 70.9% (100/141) of eligible patients in the study. Of these 100 patients, 92% completed the 12-week and 91% completed the 24-week assessment. Of the patients randomized to STRIDE ($n = 50$), 86% (43/50) completed six of six sessions. A total of 78% (39/50) and 72% (36/50) completed the first and second follow-up calls, respectively. Eighty-three patients (83%) returned the MEMS bottle at study close (MedMon = 41; STRIDE = 42). Most patients in STRIDE were placed in groups of two because of availability, and five patients

TABLE 1. Sociodemographic, Clinical, and Treatment Characteristics at Baseline

	STRIDE intervention $N = 50$	Medication monitoring $N = 50$	Full sample $N = 100$
		Mean (SD)	
Age (y; range, 31–81)	57.2 (10.6)	54.9 (11.2)	56.1 (10.9)
Months on AET (AET start to enrollment)	17.70 (8.87)	18.13 (8.49)	17.91 (8.64)
		N (%)	
Sex			
Women	50 (100)	50 (100)	100 (100)
Race			
White	47 (94)	44 (88)	91 (91)
Asian	0 (0)	4 (8)	4 (4)
Black or African American	1 (0)	0 (0)	1 (1)
Other	1 (2)	2 (4)	3 (3)
Not reported	1 (2)	0 (0)	1 (1)
Ethnicity			
Hispanic or Latino/a	1 (2)	2 (4)	3 (3)
Not Hispanic or Latino/a	47 (94)	47 (94)	94 (94)
Not reported	2 (4)	1 (2)	3 (3)
Education			
Advanced professional degree	3 (6)	6 (12)	9 (9)
Master's degree	16 (32)	16 (32)	32 (32)
College graduate	19 (38)	15 (30)	34 (34)
Some college/technical school	9 (18)	7 (14)	16 (16)
High school graduate/GED	3 (6)	5 (10)	8 (8)
11th grade or less	0 (0)	1 (2)	1 (1)
Relationship status			
Married/cohabitating	38 (76)	35 (70)	73 (73)
Noncohabitating relationship	1 (2)	2 (4)	3 (3)
Single, never married	5 (10)	4 (8)	9 (9)
Divorced/separated	6 (12)	6 (12)	12 (12)
Loss of long-term partner/widowed	6 (12)	3 (6)	9 (9)
Employment status			
Full-time/part-time work or student	33 (66)	29 (58)	62 (62)
Caring for home or family	4 (8)	6 (12)	10 (10)
Unemployed	1 (2)	3 (6)	4 (4)
Not working because of illness/disability	0 (0)	2 (4)	2 (2)
Retired	9 (18)	9 (18)	18 (18)
Other or missing	3 (6)	2 (4)	5 (5)
Income			
$25,000–$49,999	2 (4)	5 (10)	7 (7)
$50,000–$99,999	11 (22)	11 (22)	22 (22)
$100,000–$149,999	9 (18)	9 (18)	18 (18)
>$150,000	27 (54)	23 (46)	50 (50)
Declined to respond	1 (2)	2 (4)	3 (3)
Breast cancer stage			
0	5 (10)	3 (6)	8 (8)
I	36 (72)	41 (82)	77 (77)
II	6 (12)	10 (20)	16 (16)
III	3 (6)	2 (4)	5 (5)
Type of AET			
Aromatase inhibitor	28 (56)	32 (64)	60 (60)
Tamoxifen	22 (44)	18 (36)	40 (40)
Primary treatment type			
Surgery only	10 (20)	13 (26)	23 (23)
Surgery and radiation	25 (50)	23 (46)	48 (48)
Surgery and chemotherapy	2 (4)	6 (12)	8 (8)
Surgery, chemotherapy, and radiation	--	8 (16)	21 (21)
Node status			
Node positive	10 (20)	12 (24)	22 (22)
Node negative	36 (72)	34 (68)	70 (70)
Not evaluated	4 (8)	4 (8)	8 (8)
Menopausal status			
Pre- or perimenopausal	18 (36)	18 (36)	36 (36)
Postmenopausal	25 (50)	23 (46)	48 (48)
Not reported	7 (14)	9 (18)	16 (16)

(Continued)

TABLE 1. *Continued*

	STRIDE intervention $N = 50$	Medication monitoring $N = 50$	Full sample $N = 100$
HER2/neu status			
HER2/neu positive	5 (10)	8 (16)	13 (13)
HER2/neu negative	40 (80)	40 (80)	80 (80)
Not reported	5 (10)	2 (4)	7 (7)
Ovarian suppression			
Receiving ovarian suppression	8 (16)	20 (40)	28 (28)
Not receiving ovarian suppression	42 (84)	30 (60)	72 (72)

Abbreviations: AET, adjuvant endocrine therapy; STRIDE, Symptom-Targeted Randomized Intervention for Distress and Adherence to Adjuvant Endocrine Therapy.

TABLE 2. STRIDE Intervention Content, Targets, and Underlying Theoretical Frameworks

Session Theoretical framework	Behavioral targets	Topics
Session 1	AET psychoeducation	• Introduce program; assess AET adherence barriers/facilitators
MFMA	Optimize adherence	• Conduct motivational interviewing
CMMS	Relaxation training	• Explain relaxation rationale; introduce diaphragmatic breathing
Session 2	Cognitive reframing of AET-related thoughts/beliefs	• Understand thoughts, feelings, behaviors cycle
CMAC		• Identify and challenge accuracy of automatic thoughts/beliefs
		• Cognitively reframe unhelpful and inaccurate thoughts/beliefs
Session 3	Coping effectiveness and mindfulness for AET distress	• Teach coping effectiveness (problem- vs. emotion-focused)
CMAC		• Raise awareness of the present and intentional coping choices
CMMS		• Practice observing and describing thoughts nonjudgmentally
Session 4	AET side effect self-management	• Identify interfering and prominent AET symptoms
CMMS	Relaxation training	• Teach behavioral strategies to self-manage AET symptoms
MFMA		• Introduce progressive muscle relaxation
Session 5	AET side effect self-management	• Identify interfering and prominent AET symptoms
CMMS	Acceptance skills	• Teach behavioral strategies to self-manage AET symptoms
CMAC		• Explore acceptance-oriented techniques for tolerating distress
MFMA		• Strategize how to communicate effectively with health care team
Session 6	AET side effect self-management	• Identify interfering and prominent AET symptoms
CMMS	Coping w/uncertainty	• Teach behavioral strategies to self-manage AET symptoms
CMAC		• Explore skills for managing fears of recurrence & uncertainty

Abbreviations: CMAC, Cognitive Model of Adjustment to Cancer; CMMS, Cognitive Model for Menopausal Symptoms; MFMA, Murray's Framework for Medication Adherence; STRIDE, Symptom-Targeted Randomized Intervention for Distress and Adherence to Adjuvant Endocrine Therapy.

completed the sessions individually ($n = 3$ because of scheduling conflicts; $n = 2$ because of personal preference after sessions had begun).

On the CSQ-3, 41/43 (95%) patients reported an average satisfaction score ≥ 2 (the scale's midpoint). Forty-two patients (98%) indicated that most or almost all their needs were met by the program. Forty patients (93%) were mostly or very satisfied with the program, and 40 (93%) would return to the program if needed. The weekly sessions were 58 minutes long, on average. Sixty-three percent of patients randomized to STRIDE received a score ≥ 5 (range, 0–7) for homework completion. In terms of intervention fidelity, an average of 91% of topics were covered across sessions (range, 83%–96%).

Patient-reported outcomes

Compared with patients assigned to MedMon, those assigned to STRIDE reported less symptom distress related to hot flashes (BCPT-Hot Flashes; adjusted $M_{diff} = -0.72$; 95% CI, −1.43 to −0.01; Cohen's d = .31; $p = .048$) and better ability to use stress coping skills (MOCS; adjusted $M_{diff} = 4.41$; 95% CI, 1.39–7.43; Cohen's d = .48; $p = .005$) at the 12-week follow-up. Those assigned to STRIDE also reported marginally better QOL (FACT-B; 95% CI, −0.11 to 8.67) and ability to self-manage symptoms (SESM-AET; 95% CI, −0.05 to 1.41]), compared with patients assigned to MedMon (Table 3 for all 12-week results); however, these differences did not reach statistical significance. On the individual SESM-AET items, patients assigned to STRIDE did report significantly greater self-efficacy for managing specific symptoms at 12 weeks, such as hot flashes ($p = .019$), sleep difficulties ($p = .016$), and weight gain ($p = .010$). We did not observe 12-week group differences in self-reported adherence (MARS-5), satisfaction with AET (CTSQ), or mood (HADS).

Using linear mixed effects models to examine group differences across the entire 24-week study period (Table 4), patients assigned to STRIDE reported lower AET symptom-related distress (difference in slope per 12 weeks = −1.91; 95% CI, −3.29 to −0.52; $p = .007$), including distress related

TABLE 3. Effect of the STRIDE Intervention on Patient-Reported Outcomes at 12 Weeks: Results of Analysis of Covariance Models (n = 92)

Patient-reported outcome	Adjusted mean at 12 weeks (95% CI)		Beta (95% CI)	Cohen's d	p
	Medication monitoring	STRIDE intervention			
Self-Reported Adherence (MARS-5)	23.86 (23.49–24.23)	23.99 (23.61–24.36)	0.13 (–0.40 to 0.66)	0.07	.630
Symptom Distress (BCPT)	20.67 (18.82–22.53)	19.89 (17.98, 21.79)	–0.79 (–3.49 to 1.91)	0.08	.562
Hot Flashes Distress (BCPT)	3.38 (2.89–3.87)	2.67 (2.17–3.17)	–0.72 (–1.43 to –0.01)	0.31	.048*
Satisfaction with Therapy (CTSQ)	63.94 (61.30–66.58)	66.53 (63.82–69.23)	2.58 (–1.27–6.44)	0.21	.186
Quality of Life (FACT-B)	107.68 (104.66–110.71)	111.96 (108.88–115.04)	4.28 (–0.11–8.67)	0.23	.056+
Coping Skills (MOCS-A)	28.49 (26.42–30.57)	32.90 (30.78–35.02)	4.41 (1.39–7.43)	0.48	.005**
Symptom Self-Management (SESM-AET)	5.34 (4.84–5.85)	6.03 (5.51–6.54)	0.68 (–0.05 to 1.41)	0.35	.067+
Depressive Symptoms (HADS-D)	4.26 (3.56–4.96)	3.87 (3.17–4.58)	–0.38 (–1.39 to 0.63)	0.12	.451
Anxiety Symptoms (HADS-A)	6.59 (5.66–7.51)	6.54 (5.61–7.47)	–0.05 (–1.38 to 1.29)	0.01	.946

All analyses are adjusted for Ovarian Suppression Receipt (yes vs. no), Baseline Distress Level (elevated vs. not elevated [elevated = HADS anxiety or depression subscale ≥8]), and baseline value of the outcome of interest.
Abbreviations: BCPT, Breast Cancer Prevention Trial Checklist; beta, difference in adjusted mean score (STRIDE minus medication monitoring); CTSQ, Cancer Therapy Satisfaction Questionnaire; FACT, Functional Assessment of Cancer Therapy (Breast);
HADS, Hospital Anxiety and Depression Scale (A = Anxiety; D = Depression); MARS, Medication Adherence Rating Scale; MOCS-A, Measure of Current Status Part A; SESM-AET, Self-Efficacy for Managing Symptoms of Adjuvant Endocrine Therapy; STRIDE, Symptom-Targeted Randomized Intervention for Distress and Adherence to Adjuvant Endocrine Therapy.
+p < .1; *p < .05; **p < .01; ***p < .001.

TABLE 4. Longitudinal Effects of the STRIDE Intervention on Patient-Reported Outcomes Over 24 Weeks: Results of Mixed Linear Effect Models

Patient-reported outcome	Rate of change per 12 weeks (Slope) (95% CI)		Difference in slope (beta)	95% CI	p
	Medication monitoring	STRIDE intervention			
Self-Reported Adherence (MARS-5)	–0.01 (–0.25 to 0.24)	0.03 (–0.21 to 0.28)	0.04	–0.31 to 0.39	.833
Symptom Distress (BCPT)	0.40 (–0.58 to 1.38)	–1.50 (–2.48 to –0.53)	–1.91	–3.29 to –0.52	.007*
Hot Flashes Distress (BCPT)	0.05 (–0.22 to 0.31)	–0.43 (–0.69 to –0.16)	–0.47	–0.84 to –0.10	.013*
Satisfaction with Therapy (CTSQ)	0.19 (–1.39 to 1.78)	1.88 (0.30–3.46)	1.68	–0.55 to 3.92	.139
Quality of Life (FACT-B)	–0.78 (–2.47 to 0.91)	3.89 (2.21–5.57)	4.66	2.28–7.05	<.001***
Coping Skills (MOCS-A)	0.35 (–0.66 to 1.35)	2.59 (1.59–3.60)	2.25	0.83–3.67	.002**
Symptom Self-Management (SESM-AET)	0.27 (–0.02 to 0.56)	0.66 (0.37–0.94)	0.39	–0.02 to 0.79	.060+
Depressive Symptoms (HADS-D)	–0.01 (–0.35 to 0.33)	–0.45 (–0.79 to –0.11)	–0.44	–0.92 to 0.04	.071+
Anxiety Symptoms (HADS-A)	–0.22 (–0.69 to 0.25)	–0.99 (–1.46 to –0.52)	–0.77	–1.44 to –0.10	.024*

All analyses use maximum likelihood estimation to account for missing data. Analyses are adjusted for Ovarian Suppression Receipt (yes vs. no), Baseline Distress Level (elevated vs. not elevated [elevated = HADS anxiety or depression subscale ≥8]), and baseline value of the outcome of interest.
Abbreviations: BCPT, Breast Cancer Prevention Trial Checklist; beta, difference in adjusted mean score (STRIDE minus medication monitoring); CTSQ, Cancer Therapy Satisfaction Questionnaire; FACT, Functional Assessment of Cancer Therapy (Breast);
HADS, Hospital Anxiety and Depression Scale (A = Anxiety; D = Depression); MARS, Medication Adherence Rating Scale; MOCS-A, Measure of Current Status Part A; SESM-AET, Self-Efficacy for Managing Symptoms of Adjuvant Endocrine Therapy; STRIDE, Symptom-Targeted Randomized Intervention for Distress and Adherence to Adjuvant Endocrine Therapy.
+p < .1; *p < .05; **p < .01; ***p < .001.

to hot flashes (slope difference = −0.47; 95% CI. –0.84 to −0.10; p = .013), compared with those assigned to MedMon. Across the 24 weeks, patients assigned to STRIDE also reported significantly better QOL (slope difference = 4.66; 95% CI, 2.28–7.05; p < .001), increased ability to use stress coping skills (slope difference = 2.25; 95% CI, 0.83–3.67; p = .002), and reductions in anxiety symptoms (slope difference = −0.77; 95% CI, −1.44 to −0.10; p = .024), compared with those assigned to MedMon (Figs. 2A-2D). Compared with patients assigned to MedMon, those in STRIDE reported increases in self-management of symptoms (95% CI, −0.02 to 0.79) and reductions in depressed mood (95% CI, −0.92 to 0.04) that did not reach statistical significance. We did not observe group differences in self-reported adherence or satisfaction with AET across the 24 weeks.

Objective adherence outcome

As measured by MEMS caps, we observed significant decreases in monthly adherence scores in patients in both the STRIDE intervention (slope = −4.44%; 95% CI, −5.79 to −3.08%; p < .0001) and the MedMon control (slope = −3.78%; 95% CI, −5.15 to −2.41; p < .0001).

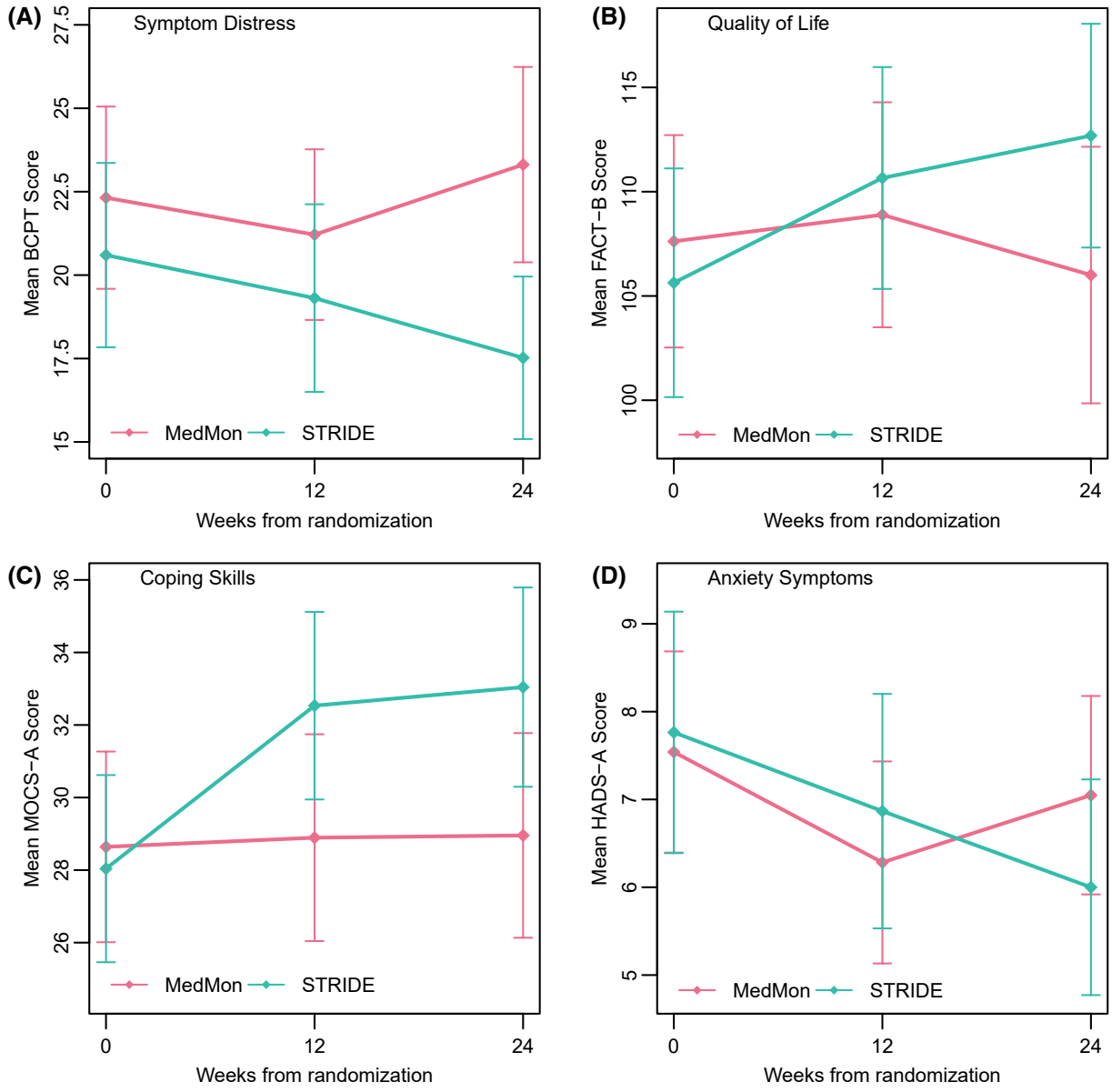

Figure 2. Study group differences in select patient-reported outcomes across 24 weeks. (A) Symptom distress (Breast Cancer Prevention Trial Symptom Scale). (B) Quality of life (Functional Assessment of Cancer Therapy-Breast Cancer). (C) Coping skills (Measure of Current Status-A). (D) Anxiety symptoms (Hospital Anxiety and Depression Scale-A).

However, there was no difference in the rate of change between the study groups (slope difference = −.066%; 95% CI, −2.59 to 1.27); $p = .504$); Figure 3. The weekly adherence scores followed a similar pattern.

DISCUSSION

This trial demonstrates that a brief, small-group telehealth intervention focused on symptom management, adherence, and distress is feasible and acceptable with promising efficacy for patients taking AET after breast cancer. More than two thirds of eligible patients enrolled in the study, with more than 90% completing the follow-up assessments and 86% completing all intervention sessions. Furthermore, STRIDE led to improvements in symptom distress, QOL, coping skills, anxiety symptoms, and self-efficacy for symptom management. However, we observed no differences in adherence or satisfaction with AET. These promising findings substantiate further investigation in a large-scale, fully powered efficacy trial.

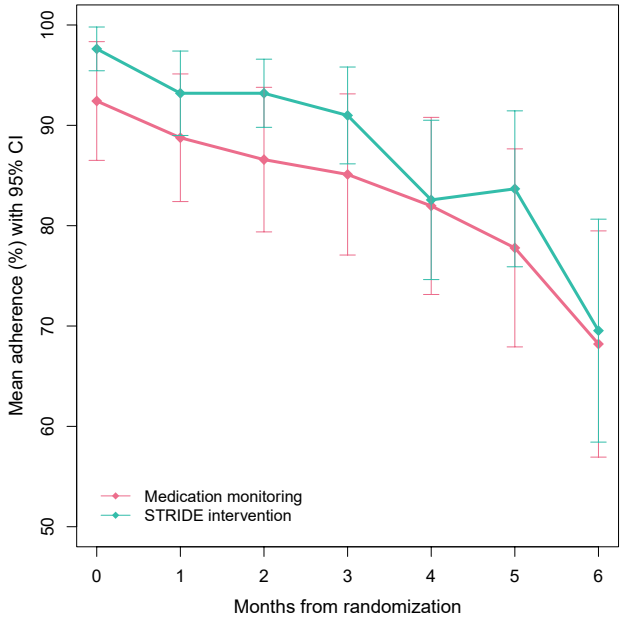

Figure 3. Study group differences in Medication Event Monitoring System Caps monthly adherence scores.

We demonstrated strong feasibility of the study design and intervention, with high rates of enrollment, retention, and session completion. Remarkably, we continued to accrue rapidly during the height of the COVID-19 pandemic, with only a short pause. Patients' high satisfaction and enthusiasm for the intervention material and support is notable. The high acceptability and homework completion scores indicate patients' willingness and desire to receive more formal support while on AET regimens that are disruptive to QOL, yet necessary for survival. No in-person study visits were required, which likely optimized attendance, engagement, and retention, especially for this population of patients adapting to life after breast cancer. The entirely virtual nature of the STRIDE intervention enhances the scalability and potential for dissemination across clinical care settings.

Similar to previous intervention studies,[44] we did not observe group differences in self-reported adherence or objective adherence scores on the MEMS Caps. Self-reported adherence on the MARS-5 was high in both groups, which may indicate a ceiling effect as well as the tendency for self-report methods to overestimate adherence.[21] Although there were differences in MEMS Caps adherence rates in the STRIDE vs. MedMon groups that may be clinically meaningful (e.g., 92.5% vs. 87.3% at month 2; 90.3% vs. 85.8% at month 3), the lack of statistical significance in these differences may be a result of low power as well as high variability in these scores. The absence of a gold standard and the inherent flaws in current adherence measurement continues to complicate our assessment of adherence optimizing interventions.[45] Our future work will entail tests of moderation to investigate whether certain subgroups of patients benefited from the intervention based on sociodemographic and/or clinical characteristics. For example, based on prior reviews, certain demographic or clinical characteristics, such as age, cancer stage, and number of concomitant medications, may be associated with adherence to oral anticancer therapies.[30] In addition, adherence may be different for patients taking tamoxifen vs. aromataste inhibitors given that these medications have slightly different side effect profiles.

In this pilot trial, we demonstrated preliminary efficacy of STRIDE for improving AET-related symptom distress, QOL, coping skills, and anxiety symptoms, with small to medium effect sizes. STRIDE led to more modest improvements in self-efficacy for symptom management and depressive symptoms that approached significance. These findings are notable given the length of time that patients take these medications, struggle with side effects, and experience deteriorations in QOL. These findings are also critical given that symptom distress, mood, and QOL are associated with adherence to oral anticancer treatment.[46] Among those with breast cancer, symptoms are the primary factor contributing to suboptimal adherence to AET.[5,13] Although evidence-based approaches for symptom management exist,[47] patients lack self-efficacy and skills to manage AET symptoms on their own[48] and receive no formal support to do so throughout the 5- to 10-year regimen.[49] Relatedly, a recent systematic review concluded that self-efficacy, a modifiable factor most consistently associated with adherence, should be a target for interventions to improve AET adherence.[50] Although this study was not powered to detect differences in adherence, future fully powered work should investigate patients' self-efficacy for managing and coping with AET symptoms as a path to reducing symptom distress, improving QOL and mood, and ultimately enhancing adherence.

Some limitations are worth noting, including the minimal socioeconomic and racial-ethnic diversity of the sample, as well as the large proportion of patients with stage I disease, which restricts the generalizability of these findings. Furthermore, all enrolled patients owned their own devices to access the virtual sessions, further illustrating the limited representation of our sample compared with the larger breast cancer population. In addition, study staff and participants were not blinded to randomization,

potentially introducing bias. Although most patients participated in pairs and reported benefitting from the group setting, some preferred individual sessions or were unable to be in a group because of scheduling conflicts. Flexibility in individual or group-based participation should be considered as a factor affecting implementation in a clinical setting. All therapists were clinical psychologists or psychology fellows; however, future work could examine the feasibility of training mental health clinicians from diverse disciplines.

In conclusion, a brief, small-group telehealth intervention for patients taking AET after breast cancer is highly feasible and acceptable, with promising benefits for improving symptom distress, QOL, coping skills, mood, and self-efficacy for symptom management. These findings warrant the efficacy testing of this intervention in a multisite trial while exploring potential mediators and moderators of intervention effects. Future trials will enroll patients from different geographic regions with greater racial, ethnic, and socioeconomic diversity that represents the socioeconomic and demographic makeup of the true breast cancer population. These trials will also use specific recruitment strategies (e.g., partnerships with community organizations, purposeful recruitment and enrollment monitoring, diverse representation in recruitment materials) to ensure enrollment of a diverse sample. Finally, using data from semistructured interviews with patients from a racial or ethnic minority background that completed the study, the intervention and telehealth approach will be culturally adapted to ensure cultural humility and relevance for patients from various sociodemographic backgrounds.

AUTHOR CONTRIBUTIONS

Jamie M. Jacobs: Conception and design, acquisition of data or analysis and interpretation of data, article draft, critical revision for important intellectual content, final manuscript approval, and accountability for all aspects of the work. **Kathryn Post:** Acquisition of data or analysis and interpretation of data, article draft, critical revision for important intellectual content, final manuscript approval, and accountability for all aspects of the work. **Katina Massad:** Acquisition of data, analysis and interpretation of data or analysis and interpretation of data, article draft or revision for important intellectual content, final manuscript approval, and accountability for all aspects of the work. **Nora K. Horick:** Conception and design, acquisition of data, analysis and interpretation of data, article draft or revision for important intellectual content, final approval of the manuscript and agree to be accountable for all aspects of the work. **Emily A. Walsh:** Concept and design, acquisition of data, analysis and interpretation of data, article draft or revision for important intellectual content, final manuscript approval, and accountability for all aspects of the work. **Julia Cohn:** Acquisition of data, analysis and interpretation of data, article draft or revision for important intellectual content, final manuscript approval, and accountability for all aspects of the work. **Chelsea S. Rapoport:** Acquisition of data, analysis and interpretation of data, article draft or revision for important intellectual content, final manuscript approval, and accountability for all aspects of the work. **Amy J. Clara:** Acquisition of data, analysis and interpretation of data, article draft or revision for important intellectual content, final manuscript approval, and accountability for all aspects of the work. **Michael H. Antoni:** Conception and design, acquisition of data, analysis and interpretation of data, article draft or revision for important intellectual content, final manuscript approval, and accountability for all aspects of the work. **Steven A. Safren:** Conception and design, acquisition of data, or analysis and interpretation of data, article draft or revision for important intellectual content, final manuscript approval, and accountability for all aspects of the work. **Ann H. Partridge:** Conception and design, acquisition of data, analysis and interpretation of data, article draft or revision for important intellectual content, final manuscript approval, and accountability for all aspects of the work. **Jeffrey M. Peppercorn:** Conception and design, acquisition of data, or analysis and interpretation of data, analysis and interpretation of data, article draft or revision for important intellectual content, final manuscript approval, and accountability for all aspects of the work. **Elyse R. Park:** Conception and design, acquisition of data, analysis and interpretation of data, article draft or revision for important intellectual content, final manuscript approval, and accountability for all aspects of the work. **Jennifer S. Temel:** Conception and design, acquisition of data, or analysis and interpretation of data, article draft or revision for important intellectual content, final manuscript approval, and accountability for all aspects of the work. **Joseph A. Greer:** Conception and design, acquisition of data, or analysis and interpretation of data, article draft or revision for important intellectual content, final manuscript approval, and accountability for all aspects of the work.

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CONFLICTS OF INTEREST

J.M.J. and J.A.G. are consultants for Blue Note Therapeutics.

REFERENCES

1. American Cancer Society. Cancer facts & figures 2021. Accessed July 29, 2022. https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2021/cancer-facts-and-figures-2021.pdf
2. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology; 2019. Accessed August 1, 2022. https://www.nccn.org/guidelines/guidelines-detail?category=1&id=1419
3. Burstein HJ, Temin S, Anderson H, et al. Adjuvant endocrine therapy for women with hormone receptor-positive breast cancer: American Society of Clinical Oncology clinical practice guideline focused update. *J Clin Oncol*. 2014;32(21):2255-2269.
4. Davies C, Godwin J, Gray R, et al. Relevance of breast cancer hormone receptors and other factors to the efficacy of adjuvant tamoxifen: patient-level meta-analysis of randomised trials. *Lancet*. 2011;378(9793):771-784.
5. Vaz-Luis I, Francis PA, Di Meglio A, Stearns V. Challenges in adjuvant therapy for premenopausal women diagnosed with luminal breast cancers. *Am Soc Clin Oncol Educ Book*. 2021;41:1-15.
6. Stanton AL, Petrie KJ, Partridge AH. Contributors to nonadherence and nonpersistence with endocrine therapy in breast cancer survivors recruited from an online research registry. *Breast Cancer Res Treat*. 2014;145(2):525-534.
7. Jacob Arriola KR, Mason TA, Bannon KA, et al. Modifiable risk factors for adherence to adjuvant endocrine therapy among breast cancer patients. *Patient Educ Couns*. 2014;95(1):98-103.
8. Moon Z, Moss-Morris R, Hunter MS, Carlisle S, Hughes LD. Barriers and facilitators of adjuvant hormone therapy adherence and persistence in women with breast cancer: a systematic review. *Patient Prefer Adherence*. 2017;11:305-322.
9. Ribi K, Luo W, Bernhard J, et al. Adjuvant tamoxifen plus ovarian function suppression versus tamoxifen alone in premenopausal women with early breast cancer: Patient-reported outcomes in the suppression of ovarian function trial. *J Clin Oncol*. 2016;34(14):1601-1610.

10. Yanez B, Gray RJ, Sparano JA, et al. Association of modifiable risk factors with early discontinuation of adjuvant endocrine therapy: a post hoc analysis of a randomized clinical trial. *JAMA Oncol*. 2021;7(8):1-7.
11. Accordino MK, Hershman DL. Disparities and challenges in adherence to oral antineoplastic agents. *Am Soc Clin Oncol Educ Book*. 2013;33:271-276.
12. Aiello Bowles EJ, Boudreau DM, Chubak J, et al. Patient-reported discontinuation of endocrine therapy and related adverse effects among women with early-stage breast cancer. *J Oncol Pract*. 2012;8(6):e149-e157.
13. Lambert LK, Balneaves LG, Howard AF, Gotay CC. Patient-reported factors associated with adherence to adjuvant endocrine therapy after breast cancer: an integrative review. *Breast Cancer Res Treat*. 2018;167(3):615-633.
14. Burstein HJ, Griggs JJ. Adjuvant hormonal therapy for early-stage breast cancer. *Surg Oncol Clin N Am*. 2010;19(3):639-647.
15. Murphy CC, Bartholomew LK, Carpentier MY, Bluethmann SM, Vernon SW. Adherence to adjuvant hormonal therapy among breast cancer survivors in clinical practice: a systematic review. *Breast Cancer Res Treatment*. 2012;134(2):459-478.
16. Partridge AH, Wang PS, Winer EP, Avorn J. Nonadherence to adjuvant tamoxifen therapy in women with primary breast cancer. *J Clin Oncol*. 2003;21(4):602-606.
17. Markkula A, Hietala M, Henningson M, Ingvar C, Rose C, Jernström H. Clinical profiles predict early nonadherence to adjuvant endocrine treatment in a prospective breast cancer cohort. *Cancer Prev Res (Phila)*. 2012;5(5):735-745.
18. Yood MU, Owusu C, Buist DS, et al. Mortality impact of less-than-standard therapy in older breast cancer patients. *J Am Coll Surg*. 2008;206(1):66-75.
19. Makubate B, Donnan PT, Dewar JA, Thompson AM, McCowan C. Cohort study of adherence to adjuvant endocrine therapy, breast cancer recurrence and mortality. *Br J Cancer*. 2013;108(7):1515-1524.
20. Hadji P, Blettner M, Harbeck N, et al. The patient's anastrozole compliance to therapy (pact) program: a randomized, in-practice study on the impact of a standardized information program on persistence and compliance to adjuvant endocrine therapy in postmenopausal women with early breast cancer. *Ann Oncol*. 2013;24(6):1505-1512.
21. Ziller V, Kyvernitakis I, Knöll D, Storch A, Hars O, Hadji P. Influence of a patient information program on adherence and persistence with an aromatase inhibitor in breast cancer treatment--the compas study. *BMC Cancer* 2013;13:407, Influence of a patient information program on adherence and persistence with an aromatase inhibitor in breast cancer treatment - the COMPAS study.
22. Neven P, Markopoulos C, Tanner M, et al. The impact of educational materials on compliance and persistence rates with adjuvant aromatase inhibitor treatment: first-year results from the compliance of aromatase inhibitors assessment in daily practice through educational approach (cariatide) study. *Breast*. 2014;23(4):393-399.
23. Onken LS, Carroll KM, Shoham V, Cuthbert BN, Riddle M. Reenvisioning clinical science: unifying the discipline to improve the public health. *Clin Psychol Sci*. 2014;2(1):22-34.
24. Jacobs JM, Walsh EA, Rapoport CS, et al. Development and refinement of a telehealth intervention for symptom management, distress, and adherence to adjuvant endocrine therapy after breast cancer. *J Clin Psychol Med Settings*. 2021;28(3):603-618.
25. Jacobs JM, Walsh EA, Park ER, et al. The patient's voice: adherence, symptoms, and distress related to adjuvant endocrine therapy after breast cancer. *Int J Behav Med*. 2020;27(6):687-697.
26. Jacobs JM, Rapoport CS, Horenstein A, et al. Study protocol for a randomised controlled feasibility trial of a virtual intervention (stride) for symptom management, distress and adherence to adjuvant endocrine therapy after breast cancer. *BMJ Open*. 2021;11(1):e041626.
27. Dabrowski M, Boucher K, Ward JH, et al. Clinical experience with the nccn distress thermometer in breast cancer patients. *J Natl Comprehensive Cancer Netw*. 2007;5(1):104-111.
28. Farmer KC. Methods for measuring and monitoring medication regimen adherence in clinical trials and clinical practice. *Clin Ther*. 1999;21(6):1074-1090.
29. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand*. 1983;67(6):361-370.
30. Greer JA, Amoyal N, Nisotel L, et al. A systematic review of adherence to oral antineoplastic therapies. *Oncologist*. 2016;21(3):354-376.
31. Safren SA, Bedoya CA, O'Cleirigh C, et al. Cognitive behavioural therapy for adherence and depression in patients with HIV: a three-arm randomised controlled trial. *Lancet HIV*. 2016;3(11):e529-e538.
32. Antoni MH, Smith R. Stress management intervention for women with breast cancer: participant's workbook. American Psychological Association; 2003:103.
33. Murray MD, Morrow DG, Weiner M, et al. A conceptual framework to study medication adherence in older adults. *Am J Geriatr Pharmacother*. 2004;2(1):36-43.
34. Hunter MS, Mann E. A cognitive model of menopausal hot flushes and night sweats. *J Psychosom Res*. 2010;69(5):491-501.
35. Attkisson CC, Zwick R. The client satisfaction questionnaire: psychometric properties and correlations with service utilization and psychotherapy outcome. *Eval Prog Planning*. 1982;5(3):233-237.
36. Horne R, Weinman J. Self-regulation and self-management in asthma: exploring the role of illness perceptions and treatment beliefs in explaining non-adherence to preventer medication. *Psychol Health*. 2002;17(1):17-32.
37. Abetz L, Coombs JH, Keininger DL, et al. Development of the cancer therapy satisfaction questionnaire: item generation and content validity testing. *Value Health*. 2005;8(suppl 1):S41-S53.
38. Cella D, Land SR, Chang CH, et al. Symptom measurement in the breast cancer prevention trial (bcpt) (p-1): psychometric properties of a new measure of symptoms for midlife women. *Breast Cancer Res Treat*. 2008;109(3):515-526.
39. Brady MJ, Cella DF, Mo F, et al. Reliability and validity of the functional assessment of cancer therapy-breast quality-of-life instrument. *J Clin Oncol*. 1997;15(3):974-986.
40. Antoni MH, Lechner SC, Kazi A, et al. How stress management improves quality of life after treatment for breast cancer. *J Consult Clin Psychol*. 2006;74(6):1143-1152.
41. Shelby RA, Edmond SN, Wren AA, et al. Self-efficacy for coping with symptoms moderates the relationship between physical symptoms and well-being in breast cancer survivors taking adjuvant endocrine therapy. *Support Care Cancer*. 2014;22(10):2851-2859.
42. Little RJ, D'Agostino R, Cohen ML, et al. The prevention and treatment of missing data in clinical trials. *N Engl J Med*. 2012;367(14):1355-1360.
43. Kahan BC, Morris TP. Improper analysis of trials randomised using stratified blocks or minimisation. *Stat Med*. 2012;31(4):328-340.
44. Ekinci E, Nathoo S, Korattyil T, et al. Interventions to improve endocrine therapy adherence in breast cancer survivors: what is the evidence? *J Cancer Survivorship*. 2018;12:1-9.
45. Stirratt MJ, Dunbar-Jacob J, Crane HM, et al. Self-report measures of medication adherence behavior: recommendations on optimal use. *Transl Behav Med*. 2015;5(4):470-482.
46. Jacobs JM, Pensak NA, Sporn NJ, et al. Treatment satisfaction and adherence to oral chemotherapy in patients with cancer. *J Oncol Pract*. 2017;13(5):e474-e485.
47. Franzoi MA, Agostinetto E, Perachino M, et al. Evidence-based approaches for the management of side-effects of adjuvant endocrine therapy in patients with breast cancer. *Lancet Oncol*. 2021;22(7):e303-e313.
48. Peate M, Saunders C, Cohen P, Hickey M. Who is managing menopausal symptoms, sexual problems, mood and sleep disturbance after breast cancer and is it working? Findings from a large community-based survey of breast cancer survivors. *Breast Cancer Res Treat*. 2021;187(2):427-435.
49. Berkowitz MJ, Thompson CK, Zibecchi LT, et al. How patients experience endocrine therapy for breast cancer: an online survey of side effects, adherence, and medical team support. *J Cancer Surviv*. 2021;15(1):29-39.
50. Toivonen KI, Williamson TM, Carlson LE, Walker LM, Campbell TS. Potentially modifiable factors associated with adherence to adjuvant endocrine therapy among breast cancer survivors: a systematic review. *Cancers (Basel)*. 2020;13(1):107.