

# Randomized Trial Comparing Telephone Versus In-Person Weight Loss Counseling on Body Composition and Circulating Biomarkers in Women Treated for Breast Cancer: The Lifestyle, Exercise, and Nutrition (LEAN) Study

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## ABSTRACT

### Purpose

Obesity is associated with a higher risk of breast cancer mortality. The gold standard approach to weight loss is in-person counseling, but telephone counseling may be more feasible. We examined the effect of in-person versus telephone weight loss counseling versus usual care on 6-month changes in body composition, physical activity, diet, and serum biomarkers.

### Methods

One hundred breast cancer survivors with a body mass index  $\geq 25$  kg/m<sup>2</sup> were randomly assigned to in-person counseling (n = 33), telephone counseling (n = 34), or usual care (UC) (n = 33). In-person and telephone counseling included 11 30-minute counseling sessions over 6 months. These focused on reducing caloric intake, increasing physical activity, and behavioral therapy. Body composition, physical activity, diet, and serum biomarkers were measured at baseline and 6 months.

### Results

The mean age of participants was  $59 \pm 7.5$  years old, with a mean BMI of  $33.1 \pm 6.6$  kg/m<sup>2</sup>, and the mean time from diagnosis was  $2.9 \pm 2.1$  years. Fifty-one percent of the participants had stage I breast cancer. Average 6-month weight loss was 6.4%, 5.4%, and 2.0% for in-person, telephone, and UC groups, respectively ( $P = .004$ ,  $P = .009$ , and  $P = .46$  comparing in-person with UC, telephone with UC, and in-person with telephone, respectively). A significant 30% decrease in C-reactive protein levels was observed among women randomly assigned to the combined weight loss intervention groups compared with a 1% decrease among women randomly assigned to UC ( $P = .05$ ).

### Conclusion

Both in-person and telephone counseling were effective weight loss strategies, with favorable effects on C-reactive protein levels. Our findings may help guide the incorporation of weight loss counseling into breast cancer treatment and care.

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## INTRODUCTION

Obesity has consistently been associated with worse overall and breast cancer-specific survival.<sup>1</sup> A recent meta-analysis estimated that compared with normal-weight women (body mass index [BMI] 18.5 to 24.9 kg/m<sup>2</sup>), those who were overweight (BMI 25.0 to 29.9 kg/m<sup>2</sup>) or obese (BMI  $\geq 30.0$  kg/m<sup>2</sup>) had statistically significant (11% and 35%, respectively) increased risks for breast cancer-specific mortality.<sup>1</sup>

The American Cancer Society recommends cancer survivors achieve and maintain a healthy weight; follow a dietary pattern high in vegetables, fruits, and whole grains; engage in 150 minutes per week of aerobic exercise plus two strength training sessions per week; and avoid physical inactivity.<sup>2</sup> Despite these recommendations, more than 65% of breast cancer survivors are overweight or obese, and fewer than 30% engage in recommended levels of physical activity.<sup>3,4</sup>

Recently, the American Society of Clinical Oncology published a position statement on

obesity and cancer, with a multipronged initiative to reduce the impact of obesity on cancer. One of the initiatives focused on determining best methods to help cancer survivors make effective changes in lifestyle behaviors.<sup>5</sup> The current “gold standard” method for effective weight loss involves behavioral treatment with in-person counseling.<sup>6</sup> The successful Diabetes Prevention Program weight loss program produced a 58% reduction in diabetes incidence, with an average weight loss of 8% within 3 months of treatment using individual in-person counseling.<sup>6</sup>

However, an obstacle to in-person weight loss counseling is time spent traveling to the counseling sessions, which potentially limits program participation. Telephone-based weight loss counseling may be a viable time-effective alternative to in-person visits. The telephone has increasingly been used to provide behavioral change interventions, and a recent study demonstrated its potential for delivering weight loss treatment to breast cancer survivors.<sup>7</sup> To our knowledge, only one pilot study in 35 breast cancer survivors has directly compared the effectiveness of telephone with in-person weight loss counseling.<sup>8</sup> The aim of our study was to compare 6-month changes in body weight by randomization group (in-person, telephone, or usual care) in 100 breast cancer survivors with a BMI  $\geq 25.0$  kg/m<sup>2</sup>. Secondary end points included examination of 6-month changes in waist and hip circumferences, body fat, lean body mass (LBM), bone mineral density (BMD), changes in physical activity, diet, serum biomarkers, and weight 6 months after completing the study, by randomization group.

## METHODS

The study was a three-arm (1:1:1) randomized trial comparing in-person versus telephone weight loss counseling versus usual care/control on baseline to 6-month changes in body composition, physical activity, diet, and serum biomarkers. The Yale School of Medicine Human Investigation Committee approved all procedures, including written informed consent.

### Participants and Recruitment

Eligible participants were breast cancer survivors with a BMI  $\geq 25.0$  kg/m<sup>2</sup>, diagnosed in the 5 years before enrollment with stage 0 to 3 breast cancer, who had completed chemotherapy and/or radiation therapy at least 3 months before enrollment. Women had to be physically able to exercise (ie, not be in a wheelchair or use a cane), agree to be randomly assigned, and give informed consent to participate in all study activities. They had to be accessible by telephone and English literate. Women were ineligible if they were pregnant or intending to become pregnant in the next year, had experienced a recent (past 6 months) stroke or myocardial infarction, or had severe uncontrolled mental illness.

Breast cancer survivors were recruited between June 1, 2011, and December 30, 2012, from five hospitals in Connecticut through the Rapid Case Ascertainment Shared Resource of the Yale Cancer Center, a field arm of the Connecticut Tumor Registry. Women self-referred via study brochures in the Breast Center at Smilow Cancer Hospital at Yale-New Haven and the Yale Cancer Center Survivorship Clinic.

### Primary Outcome Measure

Height (using a stadiometer) and weight were measured at baseline and 6 months. Participants were weighed and measured while wearing light indoor clothing, without shoes. Measurements were rounded up to the nearest 0.1 kg for weight and to the nearest 0.1 cm for height. All measurements, made by the same staff member, were performed and recorded twice in succession, then averaged for analyses.

### Secondary Outcome Measures

**Waist and hip circumference.** Measurements were taken at the smallest waist and largest hip circumference areas, rounding up to the nearest 0.1 cm. All measurements, made by the same staff member, were performed and recorded twice in succession, then averaged for analyses.

**Dual-energy x-ray absorptiometry scans.** Dual-energy x-ray absorptiometry scans were performed to assess body fat, LBM, and BMD at baseline and 6 months with a Hologic 4500 scanner. All scans were evaluated by a Radiologic Technician Certified in Bone Density who was blinded to randomization group.

**Physical activity.** At baseline and 6 months, participants completed an interview-administered physical activity questionnaire. The past 6 months of physical activity, including the type, frequency, and duration of 20 activities, were assessed.<sup>9</sup>

**Pedometers.** Yamax pedometers were used to measure number of steps walked per day for 7 days, at baseline and 6 months. Participants recorded the number of steps walked per day from waking until bedtime.

**Dietary intake.** Dietary change was assessed by mean group-level changes in daily caloric intake, on the basis of a 120-item food frequency questionnaire, which was developed for the Women's Health Initiative Study.<sup>10</sup> Food frequency questionnaires were administered at baseline and 6 months.

**Blood draw and serum biomarkers.** A fasting ( $\geq 12$  hours) blood draw was performed at baseline and 6 months. Serum samples were stored at  $-80^{\circ}\text{C}$  until assayed. Serum concentrations of insulin, leptin, and adiponectin were measured using radioimmunoassay kits; IL-6 and TNF- $\alpha$  were measured using high-sensitivity enzyme-linked immunosorbent assay kits; and C-reactive protein (CRP) and glucose were measured using an automated chemistry analyzer. Baseline and 6-month specimens were assayed simultaneously at the end of the study, and participants from all three groups were included in each batch of assays. Samples were measured in duplicate with coefficients of variation for all samples under 10%. Laboratory technicians were blinded to treatment assignment.

### Covariate Measures

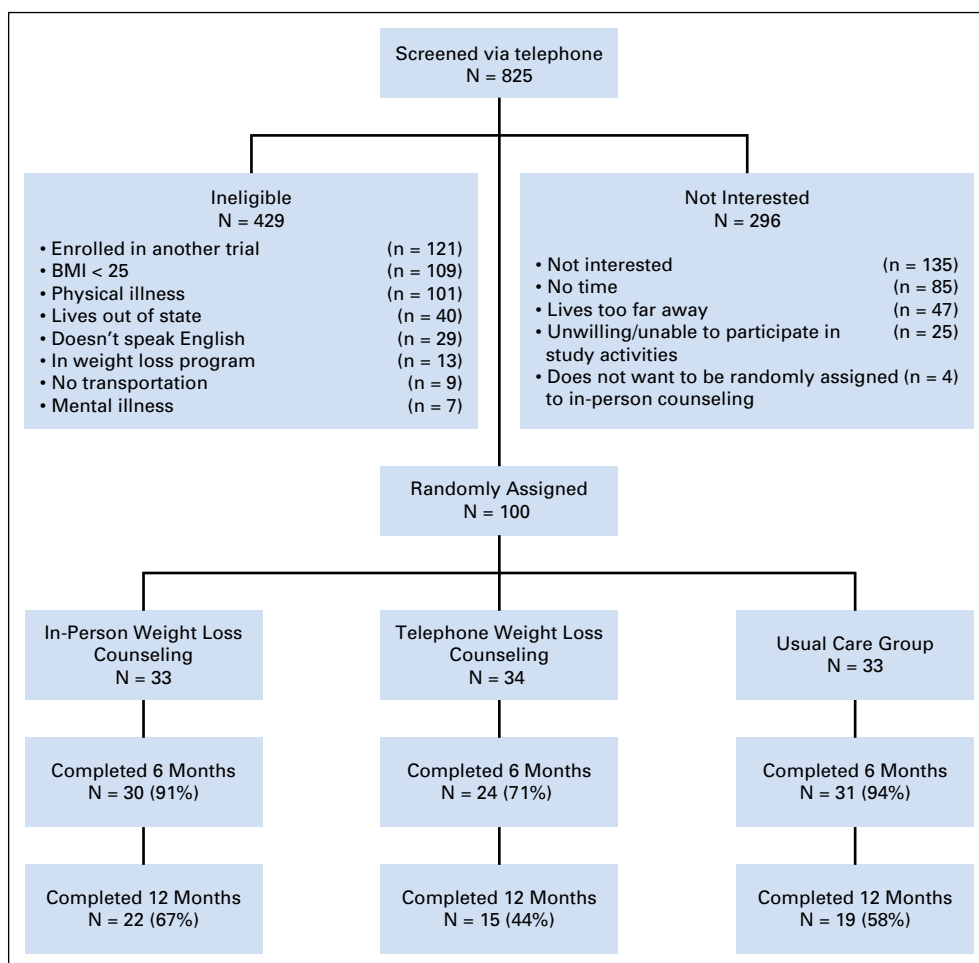
Medical record review and questionnaires were used to determine disease stage, surgery, adjuvant therapy, endocrine therapy, self-reported weight, and comorbidities at baseline, 6 months, and 12 months.

### Weight Loss Intervention

The weight loss intervention was adapted from the Diabetes Prevention Program,<sup>6</sup> updated with 2010 US Dietary Guidelines<sup>11</sup> and adapted to the breast cancer survivor population using the American Institute for Cancer Research/World Cancer Research Fund and American Cancer Society nutrition and physical activity guidelines.<sup>2</sup> A lifestyle intervention was designed using a combination of reduced caloric intake, increased physical activity, and behavioral therapy. Both the in-person and telephone groups received the same lifestyle intervention. All counseling was conducted by an experienced Registered Dietitian who was a Certified Specialist in Oncology Nutrition and trained in exercise physiology and behavior modification counseling.<sup>12</sup>

During the 6-month intervention, participants received individualized counseling sessions once per week (month 1), then every two weeks (months 2 and 3), and once per month (months 4, 5, and 6). The 11 sessions, 30 minutes each in duration, represented a core curriculum with specific information about nutrition, exercise, and behavior strategies on the basis of social-cognitive theory. To guide each session, we developed an 11-chapter LEAN book. On a daily basis, participants recorded in the LEAN Journal all food and beverage intake, minutes of physical activity, and pedometer steps. Women were provided with a scale (HoMedics), weighed themselves once per week, and recorded their weight in the LEAN Journal.

To achieve weight loss, participants were instructed to reduce energy intake to the range of 1,200 to 2,000 kcal/day based upon baseline weight and to incur an energy deficit of 500 kcal/day. The dietary fat goal



**Fig 1.** Flow of participants through the Lifestyle, Exercise, and Nutrition (LEAN) Study. BMI, body mass index.

was < 25% of total energy intake. The nutrition counseling promoted a predominantly plant-based diet, with education on portion sizes, tracking fat grams, reducing simple sugars, and increasing fiber. Mindful eating practices were taught, which included identification of hunger and fullness cues, and meal timing.

The physical activity program was home based, with a goal of 150 minutes per week of moderate-intensity activity, such as brisk walking. Women were given a pedometer and coached to increase their number of steps to 10,000 per day. Reducing sedentary behaviors was encouraged through activities of daily living.

**Usual Care Group**

The usual care group was provided with American Institute for Cancer Research nutrition and physical activity brochures and was also referred to the Yale Cancer Center Survivorship Clinic, which offers a two-session weight management program. At the completion of the study, usual care participants were offered the LEAN book and LEAN Journal, as well as an in-person counseling session.

**Statistical Analyses**

Sample size was estimated at the design stage to detect a difference in the primary end point, ie, change in body weight at 6 months. In our previous physical activity study in cancer survivors, we observed 6-month weight changes of -0.17 (standard deviation [SD] 3.51) kg in the control group.<sup>13</sup> Group sample sizes of 30 provide

93% power to detect a 3.5-kg difference in weight change between at least one intervention group and the control group, or a similar difference between two intervention groups at a two-sided significance level of 0.017, after simple Bonferroni correction for three-group comparisons. Such a difference corresponds to a standardized effect size of one. Participants were grouped according to the intention-to-treat principle. Permuted-block randomization with random block size was performed by the study biostatistician, with women randomly assigned into one of three study arms, by blinded study staff using unmarked envelopes. Intervention effects were evaluated by differences in mean changes at 6 months between the groups using a mixed-model repeated-measures analysis approach proposed by Fitzmaurice et al.<sup>14</sup>

The three study groups did not differ in participant characteristics at baseline. Post hoc analyses included stratifying analyses by baseline BMI, attendance to weight loss counseling sessions, and percentage of weight loss for biomarker analyses (ie, < 5% v ≥ 5% weight loss). Because there were 15 (15%) individuals who were missing body weight measurements at 6 months, multiple imputation with data augmentation under the multivariate normal model was conducted using SAS PROC MI, as described by Allison.<sup>15</sup> The final results were consistent with the results without multiple imputations. Similar analyses were performed for secondary end points. Analyses were performed using SAS version 9.3 (Cary, NC). Statistical significance was set at *P* < .05 using two-sided tests except for three pairwise group comparisons using *P* < .017.

**Table 1.** LEAN Study Participant Characteristics

Characteristic	Total N = 100	In Person n = 33	Telephone n = 34	Usual Care n = 33
Age, years, mean (SD)	59.0 (7.5)	58.9 (7.3)	60.0 (7.7)	58.0 (7.5)
Postmenopausal, n (%)	82 (82)	28 (85)	28 (82)	26 (79)
Non-Hispanic white, n (%)	91 (91)	32 (97)	29 (85)	30 (91)
Education, n (%)				
High school degree	8 (8)	2 (6)	2 (6)	4 (12)
Some college	26 (26)	11 (33)	8 (23)	7 (21)
College degree	29 (29)	12 (36)	11 (32)	6 (18)
Graduate degree	37 (37)	8 (24)	13 (38)	16 (48)
Time from diagnosis to LEAN enrollment, years, mean (SD)	2.9 (2.1)	3.1 (1.6)	2.7 (2.5)	2.8 (2.2)
Body weight, kg, mean (SD)	87.5 (18.0)	88.1 (18.3)	84.3 (15.3)	90.4 (20.3)
Baseline BMI, kg/m <sup>2</sup> , mean (SD)	33.1 (6.6)	33.5 (6.7)	31.8 (5.4)	34.0 (7.5)
BMI category, n (%)				
Overweight, BMI < 30	43 (43)	13 (39)	17 (50)	13 (39)
Obese, BMI ≥ 30	57 (57)	20 (61)	17 (50)	20 (61)
Disease stage, n (%)				
0	15 (15)	3 (9)	6 (18)	6 (18)
1	51 (51)	18 (55)	15 (44)	18 (55)
2	24 (24)	9 (27)	9 (26)	6 (18)
3	7 (7)	3 (9)	2 (6)	2 (6)
Unknown	3 (3)		2 (6)	1 (3)
Adjuvant treatment after surgery, n (%)				
None	15 (15)	3 (9)	5 (15)	7 (21)
Radiation only	36 (36)	11 (33)	12 (35)	13 (39)
Chemotherapy only	22 (22)	8 (24)	10 (29)	4 (12)
Radiation and chemotherapy	27 (27)	11 (33)	7 (21)	9 (27)
Current endocrine therapy, n (%)				
None	22 (22)	9 (27)	7 (21)	6 (18)
Tamoxifen	24 (24)	6 (18)	6 (18)	12 (36)
Aromatase inhibitors	54 (54)	18 (55)	21 (62)	15 (45)
Current smokers, n (%)	2 (2)	2 (6)	0 (0)	0 (0)

NOTE. No baseline differences between groups ( $P > .05$ ).

Abbreviations: BMI, body mass index; LEAN, Lifestyle, Exercise, and Nutrition; SD, standard deviation.

## RESULTS

A total of 825 breast cancer survivors were screened via telephone, with 744 women recruited via the tumor registry, 44 self-referred, and 37 recruited via additional physician referrals (Fig 1). Of these 825 women screened, 429 women were ineligible for LEAN, leaving 396 women who were eligible. A total of 100 women (25% of eligible women) then were randomly assigned into the LEAN Study. A total of 85 women returned for the 6-month clinic visit.

### Baseline Characteristics

Baseline characteristics were similar for women randomly assigned to the three groups (Table 1). Women were, on average,  $59.0 \pm 7.5$  (SD) years old, non-Hispanic white (91%),  $2.9 \pm 2.1$  years from diagnosis, with a BMI =  $33.1 \pm 6.6$  kg/m<sup>2</sup>. Women were diagnosed primarily with stage I breast cancer (51%).

### Changes in Body Composition

Average 6-month reductions in body weight were 5.6 kg (−6.4%), 4.8 kg (−5.4%), and 1.7 kg (−2.0%) for women randomly assigned to in-person, telephone, and usual care groups, respectively ( $P = .001$  comparing in-person to usual care;  $P = .009$  comparing telephone to usual care; and  $P = .46$  comparing in-

person to telephone) (Table 2). Baseline BMI did not modify the effect of the weight loss intervention on absolute body weight changes at 6 months ( $P = .74$ ).

The decline in waist and hip circumference at 6 months from baseline was significantly greater in women randomly assigned to in-person or telephone counseling compared with women randomly assigned to usual care ( $P < .017$ ). Similarly, patients randomly assigned to in-person counseling, but not telephone counseling, had a significantly greater reduction in percent body fat than those randomly assigned to usual care ( $P = .05$ ) (Table 2).

For all three randomization groups, change in self-reported weight from baseline to 12 months (ie, 6 months after completing the study) was similar to change in measured weight from baseline to 6 months, suggesting a maintenance of weight from 6 to 12 months (Table 2).

Baseline correlation between measured weight and self-reported weight was  $r = 0.99$ ,  $P < .001$ .

### Intervention Adherence

A total of 61% and 47% of women randomly assigned to in-person and telephone counseling, respectively, participated in all 11 counseling sessions. A total of 88% and 71% of women randomly assigned to in-person and telephone counseling, respectively,

**Table 2.** Comparison of 6- and 12-Month Changes in Outcomes Between Intervention and Usual Care Groups

Outcomes	Randomization Group			P of Overall Group Effect
	In Person	Telephone	Usual Care	
Measured weight (kg)				
Baseline*	88.1 (81.6 to 94.5)	84.3 (79.0 to 89.7)	90.4 (83.2 to 97.6)	.39
6-month change†	-5.6 (-7.1 to -4.1)	-4.8 (-6.5 to -3.1)	-1.7 (-3.2 to -0.3)	.001
% change‡	-6.4	-5.4	-2.0	
Intervention v usual care	P = .001	P = .009		
In-person v telephone	P = .46			
Waist circumference (cm)				
Baseline*	101.3 (96.8 to 105.9)	98.3 (94.4 to 102.2)	99.4 (93.9 to 104.8)	.64
6-month change†	-7.5 (-9.7 to -5.3)	-7.2 (-9.6 to -4.8)	-2.6 (-4.7 to -0.5)	.002
Intervention v usual care	P = .002	P = .005		
In-person v telephone	P = .87			
Hip circumference (cm)				
Baseline*	118.2 (113.5 to 122.9)	115.3 (111.2 to 119.4)	118.4 (112.6 to 124.2)	.60
6-month change†	-6.9 (-8.5 to -5.2)	-6.1 (-8.0 to -4.3)	-3.1 (-4.7 to -1.5)	.004
Intervention v usual care	P = .002	P = .01		
In-person v telephone	P = .55			
Percent body fat (%)				
Baseline*	43.3 (41.6 to 45.0)	43.3 (41.7 to 44.9)	42.7 (40.4 to 44.9)	.84
6-month change†	-3.3 (-4.4 to -2.1)	-2.4 (-3.7 to -1.2)	-1.7 (-2.8 to -0.5)	.15
Intervention v usual care	P = .05	P = .37		
In-person v telephone	P = .35			
LBM (kg)				
Baseline*	46.8 (43.8 to 49.7)	44.8 (42.3 to 47.2)	48.3 (45.4 to 51.3)	.20
6-month change†	-0.59 (-1.59 to 0.41)	-1.07 (-2.19 to 0.04)	0.04 (-0.97 to 1.03)	.33
Intervention v usual care	P = .37	P = .14		
In-person v telephone	P = .52			
BMD (g/cm <sup>-2</sup> )				
Baseline*	1.13 (1.09 to 1.16)	1.09 (1.05 to 1.14)	1.16 (1.11 to 1.20)	.09
6-month change†	-0.0003 (-0.013 to 0.012)	0.008 (-0.006 to 0.022)	0.0008 (-0.012 to 0.013)	.64
Intervention v usual care	P = .91	P = .44		
In-person v telephone	P = .38			
Self-reported weight (kg)				
Baseline*	89.1 (79.8 to 98.4)	81.5 (75.0 to 88.0)	88.9 (78.1 to 99.6)	
12-month change†	-5.6 (-8.0 to -3.3)	-6.3 (-9.9 to -2.6)	-3.8 (-5.6 to -1.9)	
% change‡	-6.3	-7.7	-4.2	
Intervention v usual care	P = .28	P = .19		
In-person v telephone	P = .72			

Abbreviations: BMD, bone mineral density; LBM, lean body mass.  
 \*Observed mean (95% CI).  
 †Least squares means from model.  
 ‡Calculated from model that forces baseline to be equal across groups.

attended at least 80% of the sessions. Weight loss was greater among women who attended all 11 weight loss counseling sessions (7.9% and 7.3% weight loss for women randomly assigned to in-person and telephone counseling, respectively), in contrast to 4.2% and 2.6% for those attending fewer than 11 sessions for the in-person ( $P = .024$ ) and telephone counseling groups ( $P = .022$ ), respectively.

**Changes in Physical Activity and Dietary Intake**

Women randomly assigned to in-person and telephone counseling increased their moderate- to vigorous-intensity physical activity by an average of  $114 \pm 130$  minutes per week and  $96 \pm 154$  minutes per week, respectively, compared with  $17 \pm 110$  minutes per week in the usual care group ( $P < .05$ ; Table 3). Baseline to 6-month changes in number of steps per day were  $1,847 \pm 2,758$ ,  $948 \pm 2,652$ , and  $-330 \pm 1,974$  steps per day for in-person counseling, telephone counseling, and usual care groups, respectively ( $P < .05$ ). Favorable changes were also seen in

percentage of energy from fat, fiber, added sugars, and fruit and vegetable intake in the intervention groups compared with the usual care group (Table 3).

**Changes in Serum Biomarkers**

Because similar weight losses were observed in the in-person and telephone counseling groups, biomarker results were compared between the two intervention groups combined versus the usual care group. Women randomly assigned to weight loss counseling experienced a 30% decrease in CRP levels compared with a 1% decrease in the usual care group ( $P = .05$ ) (Table 4). Changes in the other biomarkers measured did not differ between the intervention and usual care groups.

However, statistically significant decreases were observed for insulin, leptin, IL-6, and CRP when comparing women randomly assigned to weight loss counseling who lost  $\geq 5\%$  body weight compared with those who lost  $< 5\%$  body weight ( $P < .05$ ) (Table 5).

**Table 3.** Changes in Physical Activity and Diet

Outcomes	Randomization Group		
	In-Person	Telephone	Usual Care
Moderate- to vigorous-intensity physical activity (min/wk)			
Baseline	99 ± 127	111 ± 103	118 ± 133
6-month change	+114 ± 130*	+96 ± 154*	+17 ± 110
Pedometer (steps/day)			
Baseline	5,028 ± 2,895	6,055 ± 2,981	6,465 ± 3,558
6-month change	+1,847 ± 2,758*	+948 ± 2,652	-330 ± 1,974
Dietary intake from fat (%)			
Baseline	34.2 ± 7.4	29.9 ± 8.8	32.0 ± 6.9
6-month change	-5.1 ± 6.7*	-3.0 ± 6.2*	-1.1 ± 6.7
Fiber intake (gm/1,000 kcal)			
Baseline	11.9 ± 2.7	12.6 ± 4.9	12.6 ± 4.3
6-month change	+5.6 ± 4.1*	+3.9 ± 5.3*	1.3 ± 4.2
Fruit and vegetable (servings/day)			
Baseline	5.3 ± 2.7	4.6 ± 2.2	5.1 ± 2.8
6-month change	+1.2 ± 3.1*	+1.1 ± 2.9*	-0.3 ± 1.9
Added sugar (g/1,000 kcal)			
Baseline	31.0 ± 17.7	28.9 ± 12.3	32.8 ± 10.7
6-month change	-5.8 ± 14.1	-3.8 ± 16.2	-2.4 ± 9.4

NOTE. Values are expressed as the mean ± standard deviation.  
\**P* < .017 for in-person or telephone v usual care.

**Table 4.** Serum Cancer Biomarkers at Baseline and 6 Months for Weight Loss Intervention Groups (n = 64) Versus Usual Care (n = 33) Among Participants With Fasting Baseline Serum (N = 97)

Biomarker	Baseline, Mean (SE)	6 Months, Mean (SE)	Change Over 6 Months, Mean (SE)*	Change, %
Insulin (μU/mL)				
Control	19.04 (1.68)	18.31 (1.60)	-0.54 (0.85)	-2.84
Intervention	17.25 (1.41)	15.67 (1.36)	-1.68 (0.61)	-9.74
<i>P</i> †	.44	.24	.28	
Glucose (mg/dL)				
Control	101.88 (2.48)	102.39 (2.36)	0.52 (1.44)	0.51
Intervention	106.64 (2.62)	104.61 (2.93)	-2.03 (1.03)	-1.90
<i>P</i> †	.24	.62	.16	
CRP (mg/L)				
Control	4.77 (1.08)	4.38 (0.95)	-0.06 (0.41)	-1.26
Intervention	3.50 (0.54)	2.62 (0.33)	-1.05 (0.29)	-30.00
<i>P</i> †	.24	.04	.05	
Leptin (ng/mL)				
Control	31.00 (3.04)	28.49 (2.69)	-2.25 (1.72)	-7.26
Intervention	28.96 (2.05)	23.99 (2.16)	-5.10 (1.23)	-17.61
<i>P</i> †	.57	.21	.18	
Adiponectin (μg/mg)				
Control	13.75 (1.49)	14.10 (2.00)	0.28 (0.93)	2.04
Intervention	15.02 (0.83)	15.68 (0.82)	0.70 (0.67)	4.66
<i>P</i> †	.42	.39	.71	
IL-6 (pg/mL)‡				
Control	2.29 (0.33)	2.23 (0.34)	-0.02 (0.18)	-0.87
Intervention	1.89 (0.15)	2.16 (0.22)	0.14 (0.13)	7.41
<i>P</i> †	0.21	0.86	0.47	
TNF-α (pg/mg)				
Control	1.67 (0.08)	1.61 (0.08)	-0.06 (0.08)	-3.59
Intervention	1.86 (0.08)	1.80 (0.10)	-0.06 (0.05)	-3.17
<i>P</i> †	0.13	0.23	0.99	

NOTE. Baseline serum biomarker values were imputed for 16 participants with missing values at 6 months.

Abbreviations: CRP, C-reactive protein; IL, interleukin; TNF, tumor necrosis factor.

\*Adjusted for baseline biomarker values for biomarker of interest.

†*P* for *F* test comparing group means.

‡*n* = 96; one participant excluded due to a baseline IL-6 level that was below the lower limit of detection.

**Table 5.** Comparison of 6-Month Changes in Serum Cancer Biomarkers by Weight Loss Subgroups in the Intervention Groups, With Adjustment for Baseline Biomarker Level (N = 52)

Weight Loss (%) Over 6 Months	Δ Insulin, μU/mL, mean (SE)	Δ Glucose, mg/dL, mean (SE)	Δ CRP, mg/L, mean (SE)	Δ Leptin, ng/mL, mean (SE)	Δ Adiponectin, μg/mg, mean (SE)	Δ IL-6, pg/mL, mean (SE)*	Δ TNF-α, pg/mg, mean (SE)
< 5, n = 25	-0.59 (0.92)	-2.00 (1.70)	-0.54 (0.31)	-0.76 (2.19)	0.14 (0.95)	0.59 (0.24)	0.03 (0.11)
≥ 5, n = 27	-3.21 (0.89)	-2.96 (1.53)	-1.58 (0.30)	-11.08 (2.11)	1.44 (0.91)	-0.20 (0.24)	-0.17 (0.10)
P†	.05	.69	.02	.002	.33	.02	.19

NOTE. Twelve participants did not return for the 6-month clinic visit.

Abbreviations: CRP, C-reactive protein; IL, interleukin; TNF, tumor necrosis factor.

\*n = 51; one participant excluded due to a baseline IL-6 level that was below the lower limit of detection.

†P for F test comparing group means.

## Adverse Events

No adverse events were reported over the duration of the study.

## DISCUSSION

Both in-person and telephone weight loss counseling led to significant 6-month reductions in body weight that was maintained 6 months after completing the trial. The weight loss counseling also led to significant decreases in body fat, as well as waist and hip circumference measures. Weight loss was achieved via significant increases in physical activity and favorable changes in diet.

The average 6.4% weight loss from in-person counseling was slightly better but not statistically significantly different than the average 5.4% weight loss from telephone counseling; both exceeded clinically meaningful weight losses of 5%.<sup>16</sup> Similar findings were observed in a smaller pilot study in 35 breast cancer survivors, as well as in a larger study in 415 men and women without cancer, where telephone was as effective as in-person weight loss counseling.<sup>8,17</sup> In our study, we found a dose-response effect where weight loss was even greater for women who attended all 11 counseling sessions (7.9% and 7.3% for in-person and telephone counseling, respectively).

Interestingly, women randomly assigned to usual care experienced an average 2.0% measured weight loss at 6 months and an average self-reported 4.2% weight loss at 12 months. This weight loss may partially be explained by the fact that we referred these women to our Yale Cancer Center Survivorship Clinic, which offers a two-session weight management program. Also, upon finishing the 6-month study, they received the LEAN book, LEAN Journal, and a counseling session.

Biologic mechanisms hypothesized to mediate the relationship between obesity and breast cancer include insulin resistance and inflammation.<sup>18,19</sup> We observed a strong beneficial effect of the weight loss intervention on lowering of CRP levels. CRP is a nonspecific marker of inflammation that has been positively associated with an increased risk of death in women with breast cancer.<sup>20</sup> A weight loss of 5% or more was also associated with significant decreases in insulin, leptin, and IL-6 levels, all of which are related to breast cancer risk and mortality.<sup>18</sup>

Only a small number of randomly assigned weight loss trials have been conducted in breast cancer survivors.<sup>7,21-25</sup> However, given that weight management programs carry tremendous

potential to improve both the length and quality of survival, and to prevent or control morbidities associated with breast cancer or its treatment, oncologists and primary care physicians should be encouraged to refer their patients to weight management programs.

Strengths of our study include the randomly assigned design, valid measures, and a weight loss intervention adapted from the Diabetes Prevention Program (further adapted specifically for breast cancer survivors). Weight loss counseling was also conducted by a registered dietitian with specialized certification in oncology nutrition and training in exercise physiology. Although our study was statistically powered, the sample size may be small for subgroup analyses. Another limitation of our study was that compliance was lower for the telephone counseling group, primarily due to significant life events for some of the telephone participants (ie, family caregiving needs and new employment), and probably not due to randomization to that particular group.

An additional limitation is that we used pedometer and self-reported physical activity, which may be less accurate than supervised exercise or blank screen accelerometry. Also, our study findings are generalizable to primarily non-Hispanic white breast cancer survivors. Lastly, there is a potential for recruitment bias, given that various recruitment approaches were used.

In summary, our findings support telephone weight loss counseling as a potentially more time-effective alternative to in-person weight loss counseling. Our findings may help guide the incorporation of weight loss counseling into breast cancer treatment and care.

## AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at [www.jco.org](http://www.jco.org).

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**AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST**

**Randomized Trial Comparing Telephone Versus In-Person Weight Loss Counseling on Body Composition and Circulating Biomarkers in Women Treated for Breast Cancer: The Lifestyle, Exercise, and Nutrition (LEAN) Study**

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