

# Results of a Diet/Exercise Feasibility Trial to Prevent Adverse Body Composition Change in Breast Cancer Patients on Adjuvant Chemotherapy

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## Abstract

**Purpose:** Patients with breast cancer on adjuvant chemotherapy can experience weight gain and concurrent losses in muscle mass. Exercise interventions can prevent these changes, but time and travel pose barriers to participation. The Survivor Training for Enhancing Total Health (STRENGTH) trial assessed the feasibility and impact of 2 home-based interventions. **Patients and Methods:** Ninety premenopausal patients with breast cancer on adjuvant chemotherapy were randomized to a calcium-rich diet (CA) intervention (attention control) or to 2 experimental arms: a CA + exercise (EX) arm or a CA + EX and high fruit and vegetable, low-fat diet (FVLF) arm. Exercise arms included aerobic and strength-training exercises. Body composition, weight status, waist circumference, dietary intake, physical activity, quality of life, anxiety, depression, serum lipids, sex-hormone binding globulin, insulin, proinsulin, C-reactive protein, interleukin-1B, and tumor-necrosis factor receptor-II were measured at baseline and at 6-month follow-up. **Results:** Accrual targets were achieved and modest attrition was observed (8.8%). Self-reports suggest increased calcium intakes in all arms, and higher fruit and vegetable and lower fat intake in the CA + EX + FVLF arm; no differences in physical activity were observed. While measures of adiposity were generally lower in the CA + EX + FVLF arm, the only significant difference was in percentage of body fat (arms and legs); change in scores (mean  $\pm$  standard deviation) were  $+0.7\% \pm 2.3\%$  (CA);  $+1.2\% \pm 2.7\%$  (CA + EX); and  $+0.1\% \pm 2\%$  (CA + EX + FVLF;  $P = .047$ ). Lean body mass was largely preserved, even in the control arm (net gain of  $452 \text{ g} \pm 2395 \text{ g}$ ). No differences were observed in other endpoints. **Conclusion:** Diet and exercise interventions can prevent weight gain and adverse body composition changes, but more research is needed to determine optimally effective interventions that can be implemented during active treatment and that promote adherence.

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**Key words:** Dual-energy x-ray absorptiometry, Epirubicin, Metabolic equivalent task, Sarcopenia

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## Introduction

Weight gain commonly occurs after the diagnosis of breast cancer.<sup>1,2</sup> Weight gain is associated with decreased quality of life (QOL) and increased risk for several comorbid conditions, such as cardiovascular disease and diabetes.<sup>3</sup> Recently, Kroenke et al found that patients with breast cancer who gained modest amounts of weight (increases in body mass index [BMI]  $\geq 0.5 \text{ kg/m}^2$ ) were significantly more likely to experience disease recurrence and die from breast cancer and other causes than those who were weight stable.<sup>4</sup> Recent reports suggest that mean weight gain during chemotherapy ranges from 1-5 kg; however, roughly 20% of women gain 10-20 kg.<sup>1,2,5,6</sup> Weight gain is most prevalent



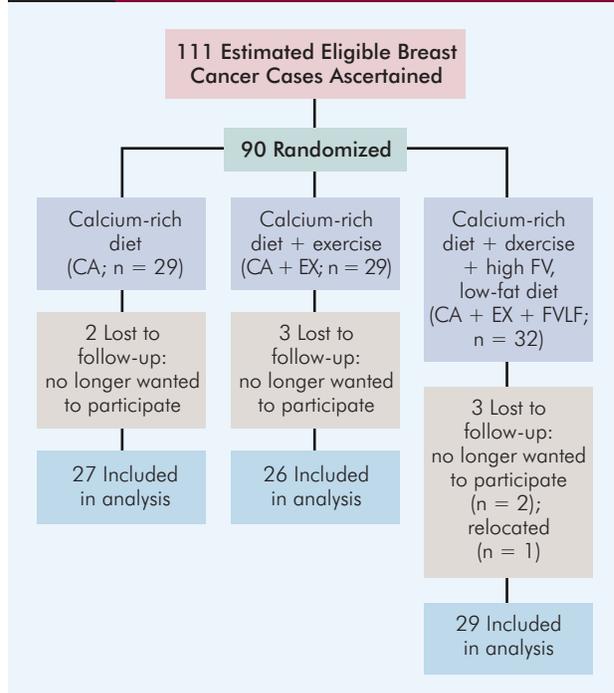
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among premenopausal patients receiving adjuvant chemotherapy<sup>1,2</sup> and can vary by treatment regimen. A 2004 study by Ingram and Brown of 76 premenopausal patients found mean weight gains of 1 kg, 1.5 kg, and 5 kg among patients on cyclophosphamide/doxorubicin (AC), cyclophosphamide/epirubicin/5-fluorouracil (5-FU; CEF), and cyclophosphamide/methotrexate/5-FU (CMF), respectively.<sup>5</sup>

In addition, two thirds of the studies that have assessed body composition change in relation to weight gain in this patient population observe no net gain in muscle mass or loss in muscle mass as body weight and adipose tissue increase.<sup>5,7-14</sup> This unique pattern of weight gain is termed sarcopenic obesity and calls for interventions that promote exercise, especially strength training.<sup>15</sup>

To date, exercise interventions that target survivors of breast cancer have largely focused on aerobic exercise; however, there have been a few studies that have explored the effects of strength training on body composition.<sup>16,17</sup> Recent studies by Cheema et al (n = 31),<sup>18</sup> Ohira et al (n = 86),<sup>19</sup> and Schmitz et al (n = 85)<sup>20</sup> found significant reductions in adiposity and gains in lean body mass with strength-training interventions. All of these studies, however, were conducted among survivors of breast cancer who had completed their therapy, and most were  $\geq 18$  months after diagnosis. Thus, these studies were not aimed at preventing adverse body composition changes, but rather at correcting for changes after they occurred. One of the few reported studies that has implemented a strength training intervention among newly diagnosed patients with breast cancer actively receiving chemotherapy was conducted by our group.<sup>21</sup> Data from this pilot study (n = 10) suggested that a combined program of strength training, aerobic exercise, and a high fruit and vegetable and low-fat (FV; LF) diet was successful in preventing adverse body composition changes (change in percentage of body fat of  $-1.3\%$  vs.  $+1.8\%$  among historical controls;  $P = .002$ ). The generalizability of those findings, however, is limited because this study was not well controlled, and it also accrued a sample that was exclusively white and largely upper socioeconomic, considered physically active and of normal weight. Given that 83% of refusals listed time and travel as barriers to participation, we adapted this intervention to a home-based program that: (1) relied on select strength training exercises that utilized body weight and portable equipment for training loads;<sup>22</sup> (2) used pace tapes and heart rate monitors to promote aerobic exercise at moderate-to-high intensity; (3) was delivered exclusively via mailed materials and telephone counseling; and (4) promoted exercise alone or in combination with a FVLF diet (as in our clinic-based study). The intervention, entitled Survivor Training for Enhancing Total Health (STRENGTH), was unique because, although telephone counseling and mailed material interventions have been used successfully to promote improvement in physical activity and dietary behaviors among cancer survivors, none have attempted programs that target strength training and none have been implemented among patients with cancer actively receiving

**Figure 1** STRENGTH Trial Schema



treatment.<sup>23-26</sup> Given its novelty, the primary aim of this investigation was to assess feasibility and begin to document the effects achievable with such an intervention.

## Patients and Methods

### Patients

Potential study subjects were identified through the Breast Oncology Clinic at Duke University Medical Center and sites affiliated with the Comprehensive Cancer Center of Wake Forest Community Clinical Oncology Program, August 2001-January 2004. Women with newly diagnosed stage I-III breast cancer were screened based on the following eligibility criteria: (1) scheduled for adjuvant chemotherapy and able to perform baseline measures before the second cycle of treatment; (2) premenopausal (< 4 months since previous menstrual period and/or follicle-stimulating hormone in the premenopausal range); (3) no serious medical conditions precluding unsupervised exercise or a diet rich in calcium or FV (eg, calcium-based renal calculi, pharmacologic warfarin use, osteoarthritis, abnormal stress tests, or multi-gated acquisition scans); (4) English-speaking and writing with telephone access; (5) mentally competent; (6) not planning reconstructive surgery within 6 months; and (7) agreement to be randomized and participate in the assigned intervention. Medical oncologists and/or clinic staff introduced the study to patients, and study staff followed up with participants in person during clinic visits or via telephone within a few days after clinic visits. Written informed consent was obtained from all participants. The protocol was approved by the Institutional Review Boards at Duke University Medical Center, Wake Forest University, and each of the referring sites.

**Table 1** Study Sample Characteristics

Characteristics (Percentage of Sample Unless Otherwise Specified)	All (N = 90)	CA (n = 29)	CA + EX (n = 29)	CA + EX + FVLF (n = 32)
Mean Age (SD; Range, 25-53 Years)	41.8 (5.6)	41.1 (5.8)	41.9 (4.8)	42.3(6.2)
<b>Ethnicity</b>				
White	85	90	79	84
Black	12	10	14	13
Other	3	0	7	3
Mean BMI, kg/m <sup>2</sup> (SD)	25.8 (6.1)	26.4 (7.2)	25.4 (5.2)	25.6 (5.9)
<b>Stage</b>				
I	33	31	34	34
IIA	38	38	45	31
IIB	21	24	7	31
IIIA	8	7	14	3
<b>Nodes Dissected</b>				
0	3	3	0	7
1-4	29	28	28	31
5-15	29	31	24	31
> 15	36	35	48	28
Unknown	2	3	0	3
<b>Node Positivity*</b>	47	48	45	47
<b>Chemotherapy Regimen†</b>				
AC	81	83	72	88
Cyclophosphamide/doxorubicin/5-FU	6	17	0	0
CEF	12	0	28	9
Other	1	0	0	3
<b>Treatment with Taxanes</b>	48	41	38	62
<b>Tamoxifen/Other Hormonal Treatment</b>	50	59	55	38
<b>Radiation Therapy During Study Period</b>	33	38	38	25
<b>Antiemetic Use During Study Period</b>				
Serotonin	49	48	55	44
Phenothiazides‡	44	45	62	25
Diazonines	46	45	59	34
Corticosteroids	46	45	52	41
<b>Routine Exercise Prediagnosis</b>	49	45	52	50

\*Unknown n = 4.

†CEF therapy was significantly more prevalent in the CA + EX arm ( $P < .05$ ).

‡Phenothiazide use was significantly higher in the CA + EX arm ( $P < .05$ ).

### Baseline Measures

Enrolled participants were asked to complete the Diet History Questionnaire, a 144-item food frequency questionnaire that uses cognitive cues to ascertain information on foods consumed and portion size; the Diet History Questionnaire has proven reliability and validity for, fat, FV consumption, and calcium.<sup>27,28-30</sup> The Longitudinal Study Physical Activity Questionnaire (LSPAQ) was also administered; this instrument includes standard physical

activity items and items on strength training (including exercubes) and has proven reliability and validity (Spearman's rho = 0.4-0.61) against activity records for up to 10 years.<sup>31,32</sup>

In addition, participants were asked to complete the Hospital Anxiety and Depression Scale (HADS)<sup>33</sup>; the Functional Assessment of Cancer Therapy–Breast Cancer (FACT-B) QOL Instrument<sup>34</sup>; and to respond to items regarding confidence (self-efficacy) in making changes in

**Table 2** Completion Rates for Telephone Counseling and Self-Monitoring and Reported Behaviors Through Self-Monitored Record Keeping

Adherence Measure	CA (n = 29)	CA + EX (n = 29)	CA + EX + FVLF (n = 32)
Telephone Counseling Sessions Completed (14 Max)* Mean (SD)	12 (3) <sup>†</sup>	10.2 (4.7) <sup>†,‡</sup>	11.2 (3.5) <sup>‡</sup>
Self-Monitoring Logs Submitted (13 Max)* Mean (SD)	10.3 (3.2) <sup>§</sup>	8.3 (5.2) <sup>§</sup>	9.0 (3.6)
Self-Monitored Calcium Intake Estimates Mean (SD) Percentage reporting intakes ≥ 1200 mg per day	1432 (284) 82	1352 (217) 87	1357 (278) 74
Self-Monitored Aerobic Frequency (Sessions per Week) Mean (SD)		3.2 (1.1)	2.9 (1.2)
Self-Monitored Aerobic Duration (Minutes per Session) Mean (SD) Percentage who exercised at least thrice weekly ≥ 30 minutes per session		35 (11) 43	32 (11) 26
Self-Monitored Strength Training (Percent of 7 Exercises) Mean (SD) Percentage who completed all 7 exercises		63 (24) 8	72 (23) 10
Self-Monitored Fat Intake (g per Day) Mean (SD) Percentage reporting intakes ≤ 30% fat			37.1 (8.3) 16
Self-Monitored Intake of FV (Servings per Day) Mean (SD) Percentage reporting intakes of ≥ 5 servings per day			4.7 (1.1) 39

\* $P < .05$ .

<sup>†</sup>Significant differences were observed between the CA and CA + EX arms ( $P = .0076$ ).

<sup>‡</sup>Borderline differences were observed between the CA + EX and CA + EX + FVLF arms ( $P = .0708$ ).

<sup>§</sup>Significant differences were observed between the CA and CA + EX arms ( $P = .0087$ ).

their dietary or exercise practices.<sup>35</sup> They reported for the baseline assessment after a 12-hour fast, whereupon dual-energy x-ray absorptiometry (DXA) whole-body and bone density scanning was performed on daily calibrated densitometers; height, weight, and waist circumference were measured; and 10 mL of blood was drawn via venipuncture. Serum was separated and stored at  $-80^{\circ}\text{C}$  until completion of the study, whereupon it was batch analyzed using enzyme-linked immunosorbent assays for insulin, proinsulin, sex hormone binding globulin (SHBG), C-reactive protein (CRP), insulin-like growth factor-1 (IGF-1), interleukin-1B (IL-1B), and tumor necrosis factor receptor-II (TNFR2). Sera was also analyzed for total low density lipoprotein (LDL) and high density lipoprotein levels (HDL) cholesterol. Additionally, participants recorded their physical activity consecutively for 3 days using blank-screen accelerometers.

### Randomization

Participants were stratified by ethnicity (white vs. non-white), BMI ( $< 25 \text{ kg/m}^2$  vs.  $\geq 25 \text{ kg/m}^2$ ) and self-reported history of vigorous exercise ( $< 30$  minutes in duration,  $\geq 3$  times weekly [yes vs. no]) and assigned to 1 of 3 study arms using permuted block randomization within strata (Figure 1). Interventions consisted of a calcium-rich diet (CA; attention control arm), a calcium-rich diet plus exercise (CA + EX), or a calcium-rich diet plus exercise plus a high FVLF (CA + EX + FVLF).

### Interventions

Despite differing content, all 3 interventions shared the following elements: (1) identical incentives (\$50 after completing each follow-up); (2) identical schedules for telephone counseling (14 contacts of 10-30 minutes each/once weekly for the first month and semiweekly for the remaining 5 months); (3) written and verbal instruction based on Social Cognitive Theory (key concepts of promoting self-efficacy and behavioral monitoring);<sup>35</sup> and (4) a study tote and workbook that provided the rationale and instructions for dietary and/or exercise regimens. Additionally, all participants received the attention control intervention of written and verbal instruction on a calcium-rich diet (intakes of 1200-1500 mg), based on the rationale that osteoporosis is a key health concern in this population.<sup>1</sup> The intervention was delivered exclusively through mailed materials and telephone counseling, and all counseling calls were placed by one prepared Master's counselor with dual degrees in nutrition and kinesiology.

**Calcium-Rich Diet with Exercise.** Participants in the CA + EX arm were encouraged to pursue aerobic exercise  $\geq 30$  minutes per day  $\geq 3$  times weekly and to perform strength-training exercises every other day. These goals were based on exercise prescriptions used in previous studies of cancer survivors<sup>36</sup> as well as prevailing guidelines for strength training.<sup>37</sup> Figure 2 illustrates the equipment provided to support these exercises, including a headset, pace tapes, a heart rate

**Table 3** Dietary Intake and Levels of Physical Activity over Time and Between Arms\*

Activity/Intake Measure	CA	CA + EX	CA + EX + FVLF
<b>Physical Activity</b>			
MET hours per week from LSPAQ			
Baseline mean (SD)	19.5 (20.9)	29 (28.3)	17 (14)
3-Month mean (SD)	20.1 (27.4)	24.6 (19.6)	21.5 (18.7)
6-Month mean (SD)	21.5 (23.7)	26.5 (22)	23.1 (16.9)
Weekly exercise-induced sweating			
Baseline mean (SD)	2.5 (1.9)	2.8 (2.6)	2.3 (1.8)
3-Month mean (SD)	2.5 (2.1)	2.9 (2.1)	2.7 (2.1)
6-Month mean (SD)	3.3 (3.3)	2.7 (2.2)	3.1 (2.1)
Accelerometer output (kcal per day)			
Baseline mean (SD)	459 (210)	423 (143)	397 (164)
3-Month mean (SD)	405 (146)	461 (155)	452 (209)
6-Month mean (SD)	456 (205)	498 (166)	426 (166)
<b>Dietary Intake</b>			
Energy (kcal per day)			
Baseline mean (SD)	1866 (808)	2148 (1083)	2031 (875)
3-Month mean (SD)	1784 (685)	1841 (617)	1881 (664)
6-Month mean (SD)	1809 (840)	1809 (639)	1839 (766)
Calcium (mg per day) <sup>†,‡</sup>			
Baseline mean (SD)	847 (489)	845 (418)	834 (373)
3-Month mean (SD)	1026 (534)	943 (461)	1024 (518)
6-Month mean (SD)	1019 (702)	996 (946)	937 (427)
Calories from fat (%)			
Baseline mean (SD)	34.1 (6.5)	34 (8.1)	33.9 (6.3)
3-Month mean (SD)	34.8 (7)	32.2 (6.7)	29.6 (5) <sup>§,  </sup>
6-Month mean (SD)	35.6 (5.9)	33.2 (7.2)	28.7 (4.1) <sup>§,‡</sup>
Calories from saturated fat (%)			
Baseline mean (SD)	11.2 (2.5)	10.9 (3.1)	10.6 (2.2)
3-Month mean (SD)	11.9 (2.6)	10.3 (2.3)	9.4 (1.9) <sup>§,¶</sup>
6-Month mean (SD)	11.9 (2.3)	11.3 (4.1)	8.8 (2) <sup>§,‡</sup>
Fruit & vegetables (servings per day)			
Baseline mean (SD)	6.1 (4)	7.2 (5.3)	7 (3.7)
3-Month mean (SD)	5.7 (2.5)	6.5 (3.4)	8.6 (4.4) <sup>§,  </sup>
6-Month mean (SD)	6.2 (2.9)	6.7 (3.4)	8.7 (4.6) <sup>§,  </sup>

\*Sample sizes for each measure largely reflect those featured in Figure 1, ie, at baseline a total of 90 participants distributed as follows: CA (n = 29), CA + EX (n = 29), and CA + EX + FVLF (n = 32); and at follow-up a total of 82 participants distributed as follows: CA (n = 27), CA + EX (n = 26), and CA + EX + FVLF (n = 29).

<sup>†</sup>Significant differences from baseline.

<sup>‡</sup>P < .001.

<sup>§</sup>Significant differences were observed between the CA + EX + FVLF arm and both the CA and CA + EX arms.

<sup>||</sup>P < .05.

<sup>¶</sup>P < .10.

monitor (to promote aerobic exercise of adequate duration and intensity) and an exercise ball, resistance bands, and water-fillable ankle weights (to promote strength-training). The workbook and videotape provided detailed instruction regarding use of the equipment and exercises, which included 2 sets of stretches (to avoid injury) and 7 strength exercises that were adapted from our previous clinic-based intervention that focused exclusively on the lower body and which utilized body weight, therabands, or ankle weights as training loads.<sup>22</sup>

**Calcium-Rich, Low-Fat, High Fruit and Vegetable Diet with Exercise.** Participants in the CA + EX + FVLF arm received the CA + EX intervention and were also encouraged to maintain an FVLF diet to reduce the energy density of

the diet.<sup>38</sup> Goal levels of ≤ 20% of energy from fat and ≥ 5 servings of FV per day were selected based on preliminary studies associated with the Women's Intervention Nutrition Study<sup>39,40</sup> and the US Dietary Guidelines during that time.<sup>41</sup>

### Follow-up

During each counseling session, participants were asked to report any changes in health and whether health events were attributable to the intervention. At 3 months of follow-up, all written surveys conducted at baseline were repeated, and women were asked to wear activity monitors again during an identical weekday period as performed at baseline. At 6 months of follow-up, all written surveys and activity monitor measures were repeated, as were DXA scans and bloodwork. In addition, participants were debriefed on the feasibility of the intervention using a 5-point rating scale, eg, "How likely do you feel it is for a young woman with breast cancer to follow the intervention promoted in this program, with 1 being very likely and 5 being very unlikely?"

### Statistical Analysis

This pilot study was designed to assess the feasibility of a home-based diet and exercise intervention program, to provide estimates of outcome variability for use in designing a larger efficacy trial, and to estimate the change in the percentage of body fat within each arm and the difference in that outcome between arms. Accrual of 30 women per arm would allow us to estimate the dropout rate in

each arm to within ± 0.16 (assuming attrition was < 20%), estimate the percentage of body fat change within each arm to within ± 1.1%, and estimate the difference in percentage of body fat change among arms to within ± 1.5%, each with 95% confidence, assuming that the standard deviation (SD) for percentage of body fat change in this home-based intervention would be 2.7%.<sup>19</sup> Proportions, means, and SDs were used to describe the patient characteristics and outcome measures separately for each arm. Note that percentage of body fat was obtained in 2 ways from whole-body DXA scans; the first used values from the entire scan and the second used values from only the legs and arms (minus the trunk). This alternate approach was employed to avoid error associated with body composition changes occurring with healing of the mastectomy/lumpectomy site,

re-excision, and unscheduled reconstructive surgery or associated procedures (tissue expanders, etc). Furthermore, metabolic equivalent task (MET)-hour data from exercise items on the LSPAQ were capped at 70 MET-hours per week to reduce effects of over-reporting or outliers. Confidence intervals for percentage of body fat were obtained using normal approximations. Pearson Correlation Coefficients were generated between physical activity measures (ie, MET data derived from the LSPAQ exercise items and weekly sweating frequency to vigorous exercise of the same questionnaire, and kcal expenditure from the activity monitors).<sup>21</sup> Analysis of covariance (ANCOVA) was used to assess differences in postrandomization outcomes among arms (adjusting for prerandomization values of the outcome measure and other factors including age, BMI, baseline exercise level, and stage of disease). Participants who dropped out of the study before their follow-up visit (n = 8) were excluded from these analyses.

## Results

### Accrual and Retention

The recruitment index for this feasibility study was approximately 10 days for each randomized participant.<sup>42</sup> Sixty percent of participants were recruited from Duke University Medical Center, and because only the Duke Institutional Review Board allowed collection of de-identified data on study refusals, we extrapolate these data in an effort to better describe our study sample (Figure 1). Most women (81%) approached for study agreed to participate. The leading reason for nonparticipation was no time/competing commitments (46% of refusals); lesser concerns (< 8% of refusals) were travel (for baseline and 6-month assessments), and lack of a desire for additional tests, to fast (for bloodwork), to be randomized, to exercise, or to follow a special diet. Refusals did not differ from participants on BMI, age, stage, marital status, education, smoking status, or exercise history; however, they were significantly more likely to be black patients ( $P < .0001$ ). Characteristics of the study sample are reported in Table 1. Most participants had stage II breast cancer (staged via axillary node dissection and treated with docetaxel and cyclophosphamide). A majority of participants had at least some college education (78%), had children in the home (69%), were married (70%), non-smoking (84%), and were nonminority (85%). Additionally, roughly half were overweight and did not regularly exercise

**Table 4** Body Composition, Anthropometric, and Quality of Life Indices over Time and Between Arms\*

Measurement	CA	CA + EX	CA + EX + FVLF
<b>Body Fat (%)</b>			
Baseline mean (SD)	35.3 (8.3)	35.4 (6.6)	34.7 (8.4)
6-Month mean (SD)	36.6 (8.7)	37.6 (8.4)	35.3 (8.4)
<b>Body Fat Without Trunk (%)</b>			
Baseline mean (SD)	38.9 (7.2)	39.7 (5.4)	38.8 (7.2)
6-Month mean (SD)	40. (7.1)	41.4 (6.8)	39 (7.6) <sup>†‡</sup>
<b>Total Fat Mass (kg)</b>			
Baseline mean (SD)	26.28 (12.81)	24.50 (8.5)	25.05 (12.34)
6-Month mean (SD)	28.14 (13.12)	27.03 (10.89)	25.48 (12.4)
<b>Total Lean Mass (kg)</b>			
Baseline mean (SD)	42.51 (6.61)	41.06 (7.08)	41.57 (5.68)
6-Month mean (SD)	43.2 (7.42)	40.62 (7.08)	41.28 (7.04)
<b>Bone Density, Spine (t-Score)</b>			
Baseline mean (SD)	-0.1 (1)	-0.1 (1.4)	0.2 (1.6)
6-Month mean (SD)	-0.5 (0.9)	-0.6 (1.3)	-0.1 (1.6)
<b>Bone Density, Hip (t-Score)</b>			
Baseline mean (SD)	-0.1 (1.1)	-0.1 (1.1)	0.2 (1.1)
6-Month mean (SD)	-0.3 (1.1)	-0.4 (1)	-0.1 (1.1)
<b>Body Weight (kg)</b>			
Baseline mean (SD)	71.6 (18.5)	68.0 (14)	69.2 (17.2)
6-Month mean (SD)	73.3 (19.1)	70.3 (15.8)	69.5 (18.6)
<b>BMI (kg/m<sup>2</sup>)</b>			
Baseline mean (SD)	26.4 (7.2)	25.4 (5.2)	25.6 (5.9)
6-Month mean (SD)	27 (7.4)	26.3 (5.6)	25.7 (6.3)
<b>Waist Circumference (cm)</b>			
Baseline mean (SD)	83.8 (15.3)	81 (11.8)	80.2 (14.8)
6-Month mean (SD)	84 (15.5)	82.2 (13.2)	79.3 (15.9)
<b>Quality of Life (FACT-G)</b>			
Baseline mean (SD)	82.2 (15.5)	78.5 (16.5)	79.2 (12.7)
3-Month mean (SD)	79.6 (17.6)	78.1 (18.6)	79.5 (17.5)
6-Month mean (SD)	88.3 (16.5)	82.9 (16.9)	82.4 (13.7)
<b>Anxiety &amp; Depression (HADS)</b>			
Baseline mean (SD)	9.8 (6.3)	11.9 (6.9)	10.3 (6)
3-Month mean (SD)	9.5 (5.9)	12.5 (7.7)	10.2 (7.2)
6-Month mean (SD)	7.5 (5.4)	11 (7.9)	8.7 (6.3)

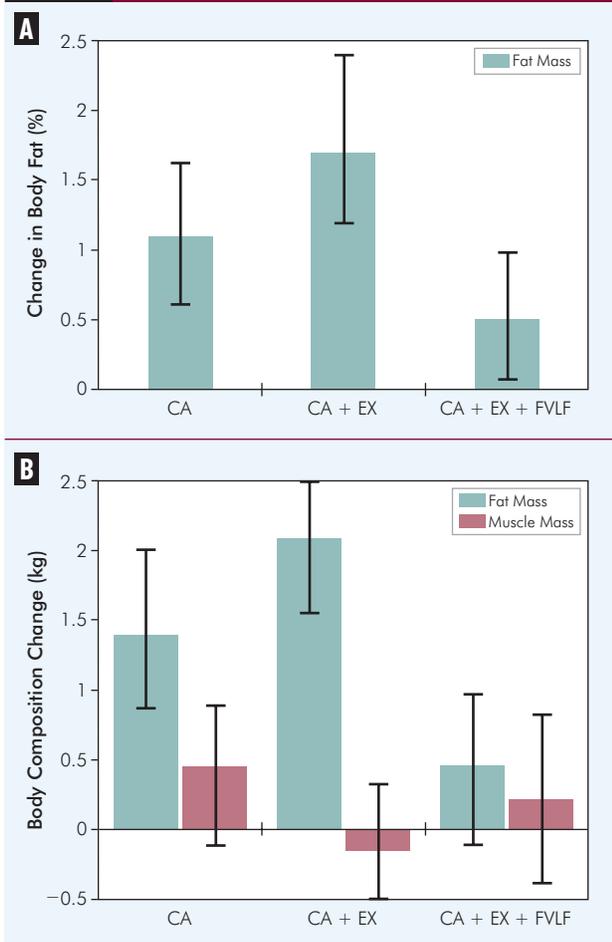
\*Sample sizes for each measure largely reflect those featured in Figure 1, ie, at baseline a total of 90 participants distributed as follows: CA (n = 29), CA + EX (n = 29), and CA + EX + FVLF (n = 32); and at follow-up a total of 82 participants distributed as follows: CA (n = 27), CA + EX (n = 26), and CA + EX + FVLF (n = 29).

<sup>†</sup>Significant difference was observed between the CA + EX + FVLF arm and the CA + EX arm.

<sup>‡</sup>P < .05.

before diagnosis, and one third (34%) took antidepressants. The only significant differences noted among study arms were CEF chemotherapy and phenothiazide use, which were greater in the CA + EX arm ( $P$  values, < .05). Within the sample, there were 20 women who had undergone hysterectomy (ovaries intact); however, of those who were menstruating at study entry, 88% experienced cessation of menses by 6-month follow-up. No differences were observed among study arms.

No adverse events related to the intervention were reported during the study period and no differences between arms were observed for other health events. An 8.8% rate of attrition was observed (see Figure 1 for distribution among arms); 7 of 8 patients who dropped out reported that they “just didn’t want to be in the study anymore,” and 1 patient relocated out-of-state.

**Figure 3** Change in Pre- and Postintervention Body Composition

(A) Changes (SD) in percent body fat, and (B) fat and muscle mass in the CA, CA + EX, and CA + EX + FVLF arms over the 6-month study period.

Patients who dropped out were significantly younger than those who completed study (37.4 years [SD, 4.8] vs. 42.3 [SD, 5.5] years;  $P = .0194$ ), and did not differ with regard to race, randomization status, education, stage, marital status, BMI, smoking status, or exercise history.

### Adherence

Table 2 features data regarding counseling call and self-monitoring log completion and self-reported estimates of behavior. Significant differences, adjusted for baseline covariates, were noted among arms for counseling call and log completion, with the CA + EX arm exhibiting poorer overall adherence, especially when compared with the CA arm. Regression models consistently suggest that advanced cancer stage and sedentary baseline behavior were significantly associated with lower completion rates (calls and self-monitoring logs), and advanced stage also was associated with reduced logged exercise frequency ( $P$  values,  $< .05$ ). Significant inverse associations were observed between age and completion of counseling calls and adherence to dietary fat restriction ( $P$  values,  $< .05$ ).

### Outcomes

Diet and physical activity data are featured in Table 3, and anthropometric and QOL outcomes are presented in Table 4 and Figure 3.  $P$  values reported in these tables were obtained from the ANCOVA models. Results of serological testing are included in Table 5.

**Physical Activity.** Modest yet significant correlations were observed between exercise MET-hours per week and frequency of exercise-induced sweating ( $\rho = 0.38$ ;  $P = .0005$ ) and accelerometer caloric expenditure ( $\rho = 0.24$ ;  $P = .034$ ), thus suggesting concordance among various self-reported and objective exercise measures. However, none of the measures of physical activity changed significantly over time or differed among arms in crude or adjusted analysis. In contrast to the lack of a significant association found between change in physical activity and arm assignment, baseline MET-hours per week of physical activity was consistently found to be significantly and positively associated with future levels of physical activity ( $P < .0001$ ).

**Diet.** Mean calcium intakes significantly increased over time ( $P = .02$ ; baseline vs. 3 months and 6 months) and no differences were noted among arms. In contrast, significant differences were noted among arms for FV consumption and percentage of kcal from fat and saturated fat, with the CA + EX + FVLF arm exhibiting higher FV intakes and lower fat intakes at 3-month and 6-month follow-up. No differences in energy intake were observed among arms.

**Body Composition.** Consistent increases for all measures of adiposity were observed over time and among all groups (Table 4 and Figure 3), with the exception of waist circumference, which decreased in the CA + EX + FVLF arm. At 6 months of follow-up, the CA + EX + FVLF arm also had significantly lower scores for percentage of body fat (minus the trunk). Follow-up measures of adiposity were significantly and positively associated with baseline levels ( $P < .0001$ ), and negatively associated with age ( $P = .14$ ) and history of vigorous physical activity ( $P = .05$ ). Overall, lean body mass was largely preserved, and no significant changes were detected over time or among arms.

**Bone Density.** Spine and hip t-scores were slightly lower at 6 months of follow-up than at baseline for all arms with no significant differences detected among arms.

**Serologic Biomarkers.** No significant differences were observed among arms over time for serum insulin, proinsulin, IGF-1, CRP, cholesterol (total, LDL, and HDL), SHBG, IL-1B, and TNFR2 (Table 5).

**Quality of Life, Anxiety, and Depression.** Significant improvements in QOL were observed over time among all groups with no differences observed. No differences over time or among groups were noted in depression or anxiety.

**Feasibility.** The CA diet received the highest feasibility scores ranging from 1.3 to 1.5 (“very likely” to “likely”) with no differences noted among arms. In contrast, the CA + EX + FVLf arm rated other dietary modifications less favorably; scores for the FVLf diet were 1.8 (“likely” to “very likely”) and 2.0 (“likely”), respectively. Differences were noted between the CA + EX and CA + EX + FVLf arms with regard to the feasibility of aerobic exercise (1.9 [SD, 1] vs. 2.5 [SD, 0.95];  $P = .035$ ), and to a lesser extent strength-training exercise (2.0 [SD, 0.88] vs. 2.4 [SD, 0.90];  $P = .065$ ).

## Discussion

STRENGTH is the first home-based diet and exercise intervention evaluated in women actively receiving adjuvant chemotherapy for breast cancer. Although this pilot study is modest in size, it provides valuable data on the feasibility, variability, and effect sizes achievable with this multi-component, distance, medicine-based intervention.

First and foremost, the intervention appeared safe and was not associated with any adverse events. Further, the high acceptance rate and the low rate of attrition, as compared with other diet-exercise interventions,<sup>43</sup> also suggests that the intervention was well received. However, although the trial was able to accrue a sample that was relatively diverse in terms of BMI and exercise practices, like most diet and exercise trials, it accrued a sample that was primarily of white ethnicity and of higher socioeconomic standing.<sup>43</sup>

Compared with our previous clinic-based intervention, where significant decreases in percentage of body fat and fat mass were observed, all women regardless of study arm experienced increases in adiposity. Because of the pilot nature of this study, we did not necessarily expect to see significant differences among groups; however, we did anticipate that both exercise arms would experience lower indices of adiposity and less loss in lean body mass than the control group. There could be several reasons why these patterns did not emerge. First, the calisthenic-type exercises which relied solely on exercise bands, aquatic weights, and body weight as sources of resistance might have been unable to reproduce the intensity of strength training afforded by weight machines. Indeed, a recent study on 35 middle-aged women by Tsourlou et al found that, while compared with controls, women assigned to formal weight training significantly reduced their percentage of body fat, whereas those assigned to a program of “light weight training” calisthenics showed

**Table 5** Serologic Indices over Time and Between Arms\*

Measurement	CA	CA + EX	CA + EX + FVLf
<b>SHBG (nmol/L)</b>			
Baseline mean (SD)	56.4 (27.6)	75.3 (46.3)	64.3 (37.5)
6-Month mean (SD)	79.7 (47.1)	74.2 (43.3)	69.1 (37.6)
<b>Insulin (<math>\mu</math>U/mL)</b>			
Baseline mean (SD)	18.7 (23.2)	37.7 (106.2)	44.3 (95.9)
6-Month mean (SD)	27.9 (81.6)	33.5 (94.4)	21.5 (62.3)
<b>Pro-insulin (pmol/L)</b>			
Baseline mean (SD)	12.6 (17.5)	15.3 (36.5)	9.9 (8.9)
6-Month mean (SD)	15 (17)	7.7 (5.6)	11 (13)
<b>IGF-1 (ng/mL)</b>			
Baseline mean (SD)	118.9 (53.1)	105.5 (60.2)	106.3 (44.1)
6-Month mean (SD)	105.6 (56.2)	98.6 (52.8)	107.9 (55.5)
<b>Total Cholesterol (mg/dL)</b>			
Baseline mean (SD)	192.4 (36.8)	188.5 (34.6)	206.5 (40.1)
6-Month mean (SD)	203.8 (39.6)	201.1 (38.4)	210.6 (35.5)
<b>LDL Cholesterol (mg/dL)</b>			
Baseline mean (SD)	120.3 (32)	108.8 (28.1)	127.4 (30.5)
6-Month mean (SD)	124.1 (36.8)	118.6 (33.5)	131.8 (31.4)
<b>HDL Cholesterol (mg/dL)</b>			
Baseline mean (SD)	59 (14.4)	65.1 (25.1)	55.3 (14.1)
6-Month mean (SD)	61.6 (14)	67.4 (24.7)	54.5 (13.4)
<b>C-Reactive Protein (ng/mL)</b>			
Baseline mean (SD)	1.6 (2.6)	1.6 (1.8)	1.7 (3.2)
6-Month mean (SD)	2.6 (7.2)	0.8 (0.7)	2 (5.6)
<b>IL-1B (pg/mL)</b>			
Baseline mean (SD)	0.3 (1.2)	1.4 (3.2)	1.5 (3.2)
6-Month mean (SD)	0.2 (0.6)	0.7 (2.3)	0.5 (1.4)
<b>TNFR2 (pg/mL)</b>			
Baseline mean (SD)	3126 (1347)	4506 (3757)	3797 (2019)
6-Month mean (SD)	3363 (2241)	3831 (2388)	1504 (3487)

\*Sample sizes for each measure largely reflect those featured in Figure 1, ie, at baseline a total of 90 participants distributed as follows: CA (n = 29), CA + EX (n = 29), and CA + EX + FVLf (n = 32); and at follow-up a total of 82 participants distributed as follows: CA (n = 27), CA + EX (n = 26) and CA + EX + FVLf (n = 29). All results were nonsignificant.

“dubious” change.<sup>44</sup> Therefore, future efforts aimed at preventing adverse body composition change among patients with breast cancer receiving active treatment might need to refer participants to local gyms or continue with clinic-based interventions with the realization that such programs might attract a self-select population.

Another possible reason for unexpected findings is nonadherence, which was a particular issue in the CA + EX arm. Undoubtedly, there are a host of challenges for exercise interventions that target populations where substantial numbers are sedentary; however, this challenge is only heightened if the intervention is timed during a period when patients are saddled with competing time constraints and when their emotional and physical energies are being drained.

Two studies by Courneya et al illustrate this point by showing adherence and attrition rates of 98.5% and 1.9%, respectively, for an exercise trial conducted after active treatment, as compared with rates of 68%-72% and 7.9% achieved with an intervention timed during active treatment.<sup>45,46</sup> Thus, although it can be argued that interventions can incur optimal benefit if timed during treatment, it

must be recognized that there are a host of barriers that can impede adherence during this point in time and that robust strategies are needed to enhance adherence to exercise prescriptions. Data from this study suggest that this need is heightened even more so among patients with breast cancer who have been physically inactive.

Based on data from self-report, it appears that better adherence was achieved with dietary regimens as compared with exercise regimens. Calcium intakes significantly increased among all arms, and the FVLF arm significantly increased their intake of FVs and decreased their fat consumption. Participants also rated the feasibility of dietary interventions far more favorably.

Furthermore, even though the dietary changes in the CA + EX + FVLF arm were fairly modest, this arm generally experienced lesser increases in adiposity and had significant lower gains in percentage of body fat in peripheral zones. These data are similar to findings of the Women's Intervention Nutrition Study (WINS) which found a mean weight loss of 6 pounds over 60 months with a low-fat diet, though the magnitude of dietary fat restriction was more rigorous in WINS than STRENGTH (15% vs. 20% of total energy).<sup>39</sup> Thus, multi-component interventions that include diet and exercise might yield more promise for weight management than interventions based solely on exercise alone. Such interventions, which incur reductions in dietary fat intake to 25%-35% of total calories, also might exhibit cardioprotective effects, though disappointingly, no changes in lipids were noted in the CA + EX + FVLF arm of this study.<sup>47</sup>

Curiously, our overall study sample did not experience the losses in muscle mass (CA =  $+0.5 \pm 2.4$  kg; CA + EX =  $-0.1 \pm 2.2$  kg; CA + EX + FVLF =  $+0.2 \pm 3.3$  kg) and the degree of sarcopenic obesity reported among historic controls ( $-0.3 \pm 3$  kg). Unfortunately, it is not known whether this attenuation is attributable to newer chemotherapeutic regimens or to the potential effects of dietary calcium which have been shown to preserve muscle and reduce adiposity.<sup>48</sup> Duly noted, we did not observe significant associations between calcium intake and any measure of body composition; however, calcium intakes within our sample were fairly high and nonvariable. Thus, this issue requires further study.

Overall, the limitations of this study are associated with its pilot/feasibility nature, reliance on self-reported measures, and modest sample size. This study was not designed to detect differences among arms with regard to body composition and secondary endpoints. The use of a calcium-rich diet as our attention control also introduced confounding for which we were unable to control.

The benefit of the CA control, however, was that it provided a solid yardstick on which to gauge QOL, which was found to increase over time among all study arms. Given that almost all exercise interventions have used wait-list controls, such findings call into question whether increases in QOL noted in previous studies are indeed a product of exercise, or are an inherent benefit of interventions.

## Conclusion

In conclusion, this pilot study provides evidence that, although behavioral interventions are safe and generally well-received, more research is necessary to develop interventions that effectively reduce the sarcopenic obesity that occurs with adjuvant chemotherapy. Data suggest that a calcium-rich, low-fat diet that includes ample amounts of FVs can be helpful in curbing gains in fat and losses in muscle mass. More work, however, appears necessary to engender adherence to exercise interventions, which might be of particular need with home-based approaches and/or with interventions implemented during active treatment.

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## References

1. Rock CL, Demark-Wahnefried W. Nutrition and survival after the diagnosis of breast cancer: a review of the evidence. *J Clin Oncol* 2002; 20:3302-16.
2. Harvie MN, Campbell IT, Baidam A, et al. Energy balance in early breast cancer patients receiving adjuvant chemotherapy. *Breast Cancer Res Treat* 2004; 83:201-10.
3. Chlebowski RT, Aiello E, McTiernan A. Weight loss in breast cancer patient management. *J Clin Oncol* 2002; 20:1128-43.
4. Kroenke CH, Chen WY, Rosner B, et al. Weight, weight gain, and survival after breast cancer diagnosis. *J Clin Oncol* 2005; 23:1370-8.
5. Ingram C, Brown JK. Patterns of weight and body composition change in premenopausal women with early stage breast cancer: has weight gain been overestimated? *Cancer Nurs* 2004; 27:483-90.
6. Irwin ML, McTiernan A, Baumgartner RN, et al. Changes in body fat and weight after a breast cancer diagnosis: influence of demographic, prognostic, and lifestyle factors. *J Clin Oncol* 2005; 23:774-82.
7. Aslani A, Smith RC, Allen BJ, et al. Changes in body composition during breast cancer chemotherapy with the CMF-regimen. *Breast Cancer Res Treat* 1999; 57:285-90.
8. Cheney CL, Mahloch J, Freeny P. Computerized tomography assessment of women with weight changes associated with adjuvant treatment for breast cancer. *Am J Clin Nutr* 1997; 66:141-6.
9. Del Rio G, Zironi S, Valeriani L, et al. Weight gain in women with breast cancer treated with adjuvant cyclophosphamide, methotrexate and 5-fluorouracil. Analysis of resting energy expenditure and body composition. *Breast Cancer Res Treat* 2002; 73:267-73.
10. Demark-Wahnefried W, Hars V, Conaway MR, et al. Reduced rates of metabolism and decreased physical activity in breast cancer patients receiving adjuvant chemotherapy. *Am J Clin Nutr* 1997; 65:1495-1501.
11. Demark-Wahnefried W, Peterson BL, Winer EP, et al. Changes in

- weight, body composition, and factors influencing energy balance among premenopausal breast cancer patients receiving adjuvant chemotherapy. *J Clin Oncol* 2001; 19:2381-9.
12. Freedman RJ, Aziz N, Albanes D, et al. Weight and body composition changes during and after adjuvant chemotherapy in women with breast cancer. *J Clin Endocrinol Metab* 2004; 89:2248-53.
  13. Kutynec CL, McCargar L, Barr SI, et al. Energy balance in women with breast cancer during adjuvant treatment. *J Am Diet Assoc* 1999; 99:1222-7.
  14. Campbell KL, Lane K, Martin AD, et al. Resting energy expenditure and body mass changes in women during adjuvant chemotherapy for breast cancer. *Cancer Nurs* 2007; 30:95-100.
  15. Heber D, Ingles S, Ashley JM, et al. Clinical detection of sarcopenic obesity by bioelectrical impedance analysis. *Am J Clin Nutr* 1996; 64(3 suppl):472s-7s.
  16. Jones LW, Demark-Wahnefried W. Diet, exercise, and complementary therapies after primary treatment for cancer. *Lancet Oncol* 2006; 7:1017-26.
  17. Markes M, Brokaw T, Resch KL. Exercise for women receiving adjuvant chemotherapy for breast cancer. *Cochrane Database of Systematic Reviews* 2006; 4(CD005001).
  18. Cheema BS, Gaul CA. Full-body exercise training improves fitness and quality of life in survivors of breast cancer. *J Strength Condition Res* 2006; 20:14-21.
  19. Ohira T, Schmitz KH, Ahmed RL, et al. Effects of weight training on quality of life in recent breast cancer survivors: the Weight Training for Breast Cancer Survivors (WTBS) study. *Cancer* 2006; 106:2076-83.
  20. Schmitz KH, Ahmed RL, Hannan PJ, et al. Safety and efficacy of weight training in recent breast cancer survivors to alter body composition, insulin, and insulin-like growth factor axis proteins. *Cancer Epidemiol Biomarkers Prev* 2005; 14:1672-80.
  21. Demark-Wahnefried W, Kenyon AJ, Eberle P, et al. Preventing sarcopenic obesity among breast cancer patients who receive adjuvant chemotherapy: results of a feasibility study. *Clin Exerc Physiol* 2002; 4:44-9.
  22. Bird SP, Tarpenning KM, Marino FE. Designing resistance training programmes to enhance muscular fitness: a review of the acute programme variables. *Sports Med* 2005; 35:841-51.
  23. Bennett JA, Lyons KS, Winters-Stone K, et al. Motivational interviewing to increase physical activity in long-term cancer survivors: a randomized controlled trial. *Nurs Res* 2007; 56:18-27.
  24. Castro CM, King AC, Castro CM, et al. Telephone-assisted counseling for physical activity. *Exerc Sport Sci Rev* 2002; 30:64-8.
  25. Demark-Wahnefried W, Clipp EC, Morey MC, et al. Lifestyle intervention development study to improve physical function in older adults with cancer: outcomes from Project LEAD. *J Clin Oncol* 2006; 24:3465-73.
  26. Pinto BM, Frierson GM, Rabin C, et al. Home-based physical activity intervention for breast cancer patients. *J Clin Oncol* 2005; 23:3577-87.
  27. Subar AF, Thompson FE, Kipnis V, et al. Comparative validation of the Block, Willett, and National Cancer Institute food frequency questionnaires: the Eating at America's Table Study. *Am J Epidemiol* 2001; 154:1089-99.
  28. Thompson FE, Subar AF, Brown CC, et al. Cognitive research enhances accuracy of food frequency questionnaire reports: results of an experimental validation study. *J Am Diet Assoc* 2002; 102:212-25.
  29. Millen AE, Midthune D, Thompson FE, et al. The National Cancer Institute diet history questionnaire: validation of pyramid food servings. *Am J Epidemiol* 2006; 163:279-88.
  30. Sebring NG, Denkinger BI, Menzie CM, et al. Validation of three food frequency questionnaires to assess dietary calcium intake in adults. *J Am Diet Assoc* 2007; 107:752-59.
  31. Kohl HW, Blair SN, Paffenbarger RS, Jr, et al. A mail survey of physical activity habits as related to measured physical fitness. *Am J Epidemiol* 1988; 127:1228-39.
  32. Bowles HR, FitzGerald SJ, Morrow JR, Jr, et al. Construct validity of self-reported historical physical activity. *Am J Epidemiol* 2004; 160:279-86.
  33. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psych Scand* 1983; 67:361-70.
  34. 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; 15:974-86.
  35. Bandura A. Self-efficacy: toward a unifying theory of behavioral change. *Psychol Rev* 1977; 84:191-215.
  36. Courneya KS, Friedenreich CM. Physical exercise and quality of life following cancer diagnosis: a literature review. *Ann Behav Med* 1999; 21:171-9.
  37. Abernethy PJ, Jurimae J, Logan PA, et al. Acute and chronic response of skeletal muscle to resistance exercise. *Sports Med* 1994; 17:22-38.
  38. Ledikwe JH, Blanck HM, Khan LK, et al. Low-energy-density diets are associated with high diet quality in adults in the United States. *J Am Diet Assoc* 2006; 106:1172-80.
  39. Chlebowski RT, Blackburn GL, Buzzard IM, et al. Adherence to a dietary fat intake reduction program in postmenopausal women receiving therapy for early breast cancer. The Women's Intervention Nutrition Study. *J Clin Oncol* 1993; 11:2072-80.
  40. Heber D, Ashley JM, McCarthy WJ, et al. Assessment of adherence to a low-fat diet for breast cancer prevention. *Prev Med* 1992; 21:218-27.
  41. 1995 Dietary Guidelines for Americans. Available at: <http://www.nal.usda.gov/fnic/dga/dguide95.html>. Accessed: August 10, 2007.
  42. Rojavin MA. Recruitment index as a measure of patient recruitment activity in clinical trials. *Contemp Clin Trials*. 2005; 26:552-6.
  43. Stull VB, Snyder DC, Demark-Wahnefried W. Lifestyle interventions in cancer survivors: designing programs that meet the needs of this vulnerable and growing population. *J Nutr* 2007; 137(1 suppl):243s-8s.
  44. Tsourlou T, Gerodimos V, Kellis E, et al. The effects of a calisthenics and a light strength training program on lower limb muscle strength and body composition in mature women. *J Strength Condition Res* 2003; 17:590-8.
  45. Courneya KS, Mackey JR, Bell GJ, et al. Randomized controlled trial of exercise training in postmenopausal breast cancer survivors: cardiopulmonary and quality of life outcomes.[see comment]. *J Clin Oncol* 2003; 21:1660-8.
  46. Courneya KS, Segal R, Mackey JR, et al. Effects of aerobic and resistance exercise in breast cancer patients receiving adjuvant chemotherapy: A multicenter randomized controlled trial. *J Clin Oncol* 2007. In press.
  47. Pasternak R. Adult Treatment Panel II versus Adult Treatment Panel III: what has changed and why? *Am J Cardiol* 2002; 89(5A):3C-7C.
  48. Zemel MB. Role of calcium and dairy products in energy partitioning and weight management. *Am J Clin Nutr* 2004; 79:907s-912s.