Effect of Exercise on Serum Estrogens in Postmenopausal Women: A 12-Month Randomized Clinical Trial

Anne McTiernan,1,2,3 Shelley S. Tworoger,1,2 Cornelia M. Ulrich,1,2 Yutaka Yasui,1 Melinda L. Irwin,4 Kumar B. Rajan,1,2 Bess Sorensen,1,2 Rebecca E. Rudolph,1,3 Deborah Bowen,1 Frank Z. Stanczyk,6 John D. Potter,1,2 and Robert S. Schwartz5

1Cancer Prevention Research Program, The Fred Hutchinson Cancer Research Center, Seattle, Washington; 2Department of Epidemiology, School of Public Health and Community Medicine, University of Washington, Seattle, Washington; 3Department of Medicine, School of Medicine, University of Washington, Seattle, Washington; 4Yale University School of Medicine, Department of Epidemiology and Public Health, New Haven, Connecticut; 5University of Colorado Health Sciences Center, Department of Internal Medicine, Division of Geriatric Medicine, Denver, Colorado; and 6School of Medicine, University of Southern California, Los Angeles, California

ABSTRACT

Elevated circulating estrogens and a sedentary lifestyle increase risk for breast cancer. The effect of exercise on circulating estrogens in sedentary postmenopausal women is unknown. The objective of this study was to examine the effects of a 12-month moderate-intensity exercise intervention on serum estrogens. We randomly assigned 173 sedentary, overweight (body mass index > 24.0 kg/m2, body fat > 33%), postmenopausal women, ages 50–75 years, not using hormone therapy, living in the Seattle, Washington, area for the next year, and willing to be randomly assigned to an exercise intervention or stretching control group. The exercise intervention included facility and home-based exercise (45 min, 5 days/week moderate intensity sports/recreational exercise). A total of 170 (98.3%) women completed the study with exercisers averaging 171 min/week of exercise. After 3 months, exercisers experienced declines in estrone, estradiol, and free estradiol of 3.8, 7.7, and 8.2%, respectively, versus no change or increased concentrations in controls (P = 0.03, 0.07, and 0.02, respectively). At 12 months, the direction of effect remained the same, although the differences were no longer statistically significant. The effect was limited to women who lost body fat: women whose percentage of body fat [by dual energy x-ray absorptiometry (DEXA)] decreased by ≥2% had statistically significant (comparing exercisers versus controls) decreases at 12 months of 11.9, 13.7, and 16.7% for serum estrone, estradiol, and free estradiol, respectively. We concluded that a 12-month moderate-intensity exercise intervention in postmenopausal women resulted in significant decreases in serum estrogens. The association between increased physical activity and reduced risk for postmenopausal breast cancer may be partly explained by effects on serum estrogens.

INTRODUCTION

Despite considerable efforts, few modifiable risk factors for breast cancer have been identified (1). Sedentary behavior is modifiable, although the effect of increasing physical activity on breast cancer biomarkers is unknown. Overweight, obese, and sedentary postmenopausal women have elevated concentrations of circulating estrogens and lower concentrations of sex hormone binding globulin (SHBG; Refs. 2–4), which puts them at a 2-fold increased risk for breast and endometrial cancers (5, 6). The increased estrogen concentrations in overweight and breast cancer patients may explain their reduced prognosis compared with lighter-weight women (7). Postmenopausal women who engage in regular (≥3 h/week) physical activity have a reduced risk for breast cancer compared with inactive women (8, 9). Although not proven, a reasonable hypothesis is that reduction of circulating postmenopausal estrogen concentrations would lower breast cancer risk.

We conducted a randomized clinical trial to examine the effect of a 12-month moderate-intensity exercise intervention on serum estrone, estradiol, free estradiol, and SHBG in sedentary, overweight/obese postmenopausal women not taking hormone therapy. We previously reported that this program significantly decreases body fat in postmenopausal women (10) and hypothesized that it would therefore lower serum estrogens because adipose tissue is a major source of estrogens in postmenopausal women (11). In secondary analyses planned before initiation of the study, we assessed the effect of exercise on serum estrogens and SHBG by change in adiposity and, among exercisers, by amount of exercise and change in fitness.

MATERIALS AND METHODS

The study was a randomized clinical trial comparing the effect of a 12-month moderate-intensity aerobic exercise intervention versus stretching control program on hormones measured at baseline and 3 and 12 months (12). All study procedures, including written informed consent, were reviewed and approved by the Fred Hutchinson Cancer Research Center Institutional Review Board.

Participants. Participants were women ages 50–75 years, from the greater Seattle area, sedentary (<60 min/week of moderate- or vigorous-intensity recreational activity and a maximal oxygen consumption (VO2max) < 25.0 ml/kg/min), with a body mass index (BMI) > 25.0 kg/m2 (or a BMI between 24.0 and 25.0 kg/m2 if percent body fat measured by bioelectrical impedance was >33.0%), not taking hormone therapy in any form in the past 6 months, without serious comorbidities including diabetes, and nonsmokers. We defined postmenopausal as having no menstrual periods for the previous 12 months and for women ages 50–54 years, a serum follicle stimulating hormone > 30 mIU/ml.

We recruited women through a combination of mass mailings and media placements (13). After extensive screening (Fig. 1), we randomly assigned 173 women to an exercise intervention (n = 87) or a control group (n = 86), stratified by BMI (<27.5 versus ≥27.5 kg/m2). Randomization was performed by random number generation, and group assignment was placed in a sealed envelope, which was opened by the study coordinator at the time of randomization.

Exercise Intervention. The exercise prescription consisted of at least 45 min of moderate-intensity exercise, 5 days/week for 12 months. Participants were required to attend the three offered supervised sessions/week at a study facility (University of Washington or a commercial gym) during months 1–3, and to exercise on 2 days/week at home. For months 4–12, they were required to attend at least one of the three offered sessions/week at a study facility and to exercise 4 days/week either at home or at the facility. The training program started at 40% of observed maximal heart rate for 16 min/session and gradually increased to 60–75% of maximal heart rate for 45 min/session by week 8. Participants wore Polar heart rate monitors during exercise sessions and primarily engaged in treadmill and outdoor walking and stationary bicycling (10).

Control participants attended one weekly 45-min stretching session for the

Received 10/29/03; revised 2/2/04; accepted 2/6/04.

Grant support: National Cancer Institute Research Grant R01-69334, National Cancer Institute Cancer Prevention Training Grant T32 CA09661 (M. L. Irwin), and National Institutes of Environmental Health Sciences Training Grant T32EF07262 (S. S. Tworoger). A portion of this work was conducted through the Clinical Research Center Facility at the University of Washington and supported by NIH Grants M01-RR-00037 and AG10941.

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked advertisement in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

Requests for reprints: Anne McTiernan, Fred Hutchinson Cancer Research Center, P.O. Box 19024, MP-900, Seattle, WA 98109-1024. Phone: (206) 667-7979; Fax: (206) 667-7850; E-mail: amctiern@fhcrc.org.
12 months and were asked not to change other exercise habits. Exercisers and control participants were asked to maintain their usual diet.

We used several measures of exercise adherence. We assessed baseline and 12-month VO_{2}max in all participants using a maximal-graded treadmill test, with heart rate and oxygen uptake monitored by an automated metabolic cart (Medgraphics, St. Paul, MN; Ref. 10). Exercisers and controls also completed Physical Activity Questionnaires every 3 months (see below). In addition, exercise intervention participants kept daily activity logs (facility attendance logs and home activity logs) of all sports or recreational activities of exercise intervention participants kept daily activity logs (facility attendance logs and home activity logs) of all sports or recreational activities of exercise adherence using the facility and home exercise log data and strategized for interventions to improve and maintain adherence in the exercisers. We also used these data for a measure of exercise adherence. We added together the total minutes of aerobic exercise from the facility attendance logs, plus daily minutes/week of sports and recreational data from home logs, and calculated average number of minutes/week of exercise.

**Study Measures.** At baseline and 3 and 12 months, we collected demographic information, medical history, health habits, medication use, reproductive and body weight history, total energy intake over the previous 3 months via a 120-item self-administered food frequency questionnaire (15), and frequency, duration, and intensity of physical activity over the previous 3 months with a self-administered adaptation of the Minnesota Physical Activity Questionnaire (16). Baseline, 3-, and 12-month weight and height (to the nearest 0.1 kg and 0.1 cm, respectively) were obtained using a balance beam scale and wall-mounted stadiometer. Waist (standing, smallest circumference between abdomen and chest) and hip (standing, largest circumference between waist and thigh) circumferences were measured in a standardized manner to the nearest 0.1 cm using an anthropometric fiberglass tape measure. All measurements were taken in duplicate and averaged.

We assessed total body fat and percent body fat using a dual energy x-ray absorptiometry (DEXA) whole-body scanner (Hologic QDR 1500; Hologic, Inc., Waltham, MA) and intra-abdominal and s.c. fat with computed tomography (CT) (General Electric model CT 9800 scanner; General Electric, Waukesha, WI) at baseline and 12 months. The CT scan was performed at the umbilicus (L4-L5 space; at 125 kV and with a slice thickness of 8 mm). A technician who was blinded to group assignment measured the s.c. and intra-abdominal fat areas using a computerized image analysis that identifies and measures each of the areas of interest by tracing lines around them and computing the circumscribed areas (17). Coefficients of variation for repeat measurement of the CT images of s.c. and intra-abdominal fat were 1.2 and 1.5%, respectively. At baseline and 3 and 12 months, participants provided a 12-h fasting 50-ml sample of blood. Blood was processed within 1 h of collection, and serum was aliquoted into 1.8-ml tubes and stored at −70°C.

**Hormone Assays.** Laboratory assays were performed at the Reproductive Endocrine Research Laboratory (University of Southern California). Samples were placed into batches such that, within each batch, all samples from a participant were included, the numbers of exercise and control participants were approximately equal, the randomization dates of participants were similar, and the sample order was random. Two specimens of a quality control pooled sample were placed in each batch as well as a 10% random sample of repeat blood draws. Laboratory personnel were blinded to sample identity.

Estrone and estradiol were quantified by radioimmunoassays after organic solvent extraction and Celite column partition chromatography (18, 19). Chromatographic separation of the steroids was achieved by use of different concentrations of toluene in isooctane and ethyl acetate in isooctane. We quantified SHBG via an immunometric assay using the Immulite Analyzer (Diagnostic Products Corporation, Los Angeles, CA). The assay used monoclonal murine anti-SHBG attached to a bead and a polyclonal rabbit anti-SHBG conjugated to alkaline phosphatase; both antibodies were highly specific for SHBG. Free estradiol was calculated using the measured values for estradiol and SHBG and an assumed constant for albumin (20–22). The intra-assay, inter-assay, and within-person coefficients of variation were as follows: estrone (12.4, 17.6, 14.2); estradiol (12.4, 15.8, 22.0); and SHBG (6.7, 10.0, 21.1). No woman had undetectable levels of any of the hormones or SHBG.

**Statistical Analyses.** We first assessed the baseline correlations between body composition and hormone variables using Spearman correlation coeffi-
The analysis considered log-transformed hormone measures at baseline, 3
and 12 months as repeated measures and assessed the intervention
effect of exercise on hormone concentrations varied with degree of change in
regression model (23). For secondary analyses, we examined whether the
analysis were done on log-transformed values. The primary trial analysis
assessed the intervention effect based on assigned treatment at the time of
dynamic characteristics, body composition, mean daily
caloric intake, fitness levels, and hormone concentrations (Tables 1
and 2). Participants on average were 61 years old, obese, highly
educated, and with a low level of fitness. Less than one-third of the
participants worked full-time; 86% were non-Hispanic white, 4%
were African American, and 6% were Asian American.

**Exercise Adherence.** On average over the 12 months, the exercisers
participated in moderate-intensity sports/recreational activity for a
mean 3.7 ± 1.4 days/week for a total of 171 ± 87.9 min/week (versus
goal 225 min/week); these data were taken from the participants’ daily
exercise logs. Exercise adherence was significantly higher during
months 1–3 of the intervention than during months 4–12 (10). The
exercisers attended an average of 98% of the required exercise ses-
sions (i.e., 4.0 ± 1.2 sessions) in the first 3 months and 73% of the
required exercise sessions (i.e., 3.6 ± 1.9 sessions) in months 4–12.
Six (8%) exercisers dropped out of the intervention (all after 3
months). However, 3 provided 12-month blood and are included in the
analyses. Among the control participants, 6 (7%) reported an increase
of at least 225 min/week of moderate-vigorous sports/recreational
activity on the 12-month Physical Activity Questionnaire. The control
participants attended an average 49.9 ± 27.1% of the 52 offered
stretching sessions over the 12 months. Using data from the Physical
Activity Questionnaire, exercisers increased from an average 25 ± 49
min/week of moderate/vigorous activity at baseline to 126 ± 98
min/week at 12 months. In contrast, controls increased from an
average baseline 28 ± 56 to 53 ± 77 min/week at 12 months. On
average, VO₂max increased in exercisers by 12.7% and in controls by
0.8% (P < 0.0001).

### Table 1 Baseline characteristics of randomized participants (n = 173) a

<table>
<thead>
<tr>
<th></th>
<th>Exercisers</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>87 (90)</td>
<td>86 (90)</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>60.7 ± 6.7</td>
<td>60.6 ± 6.8</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>30.4 ± 4.1</td>
<td>30.5 ± 3.7</td>
</tr>
<tr>
<td>Percent body fat (DEXA)</td>
<td>47.4 ± 4.8</td>
<td>47.3 ± 4.6</td>
</tr>
<tr>
<td>VO₂max (ml/kg - min)</td>
<td>20.0 ± 3.5</td>
<td>20.4 ± 3.0</td>
</tr>
<tr>
<td>Alcohol (g/day)</td>
<td>4.0 ± 1.8</td>
<td>4.6 ± 1.7</td>
</tr>
<tr>
<td>Total calories (kcal/day)</td>
<td>1635 ± 792.2</td>
<td>1722 ± 671.8</td>
</tr>
<tr>
<td>Min moderate/vigorous</td>
<td>25 ± 49</td>
<td>28 ± 56</td>
</tr>
<tr>
<td>race (from physical activity questionnaire)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n (%)</td>
<td>25 (29)</td>
<td>25 (29)</td>
</tr>
<tr>
<td>Full-time employment</td>
<td>10 (12)</td>
<td>9 (10)</td>
</tr>
<tr>
<td>Education (%)</td>
<td>36 (41)</td>
<td>35 (41)</td>
</tr>
<tr>
<td>College graduate</td>
<td>5 (6)</td>
<td>10 (12)</td>
</tr>
<tr>
<td>Graduate degrees</td>
<td>36 (41)</td>
<td>32 (37)</td>
</tr>
<tr>
<td>Ethnicity (%)</td>
<td>74 (86)</td>
<td>75 (87)</td>
</tr>
<tr>
<td>American white</td>
<td>4 (5)</td>
<td>3 (4)</td>
</tr>
<tr>
<td>Hispanic/Latino</td>
<td>14 (16)</td>
<td>16 (19)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (2)</td>
<td>1 (1)</td>
</tr>
</tbody>
</table>

**RESULTS**

**Study Subjects.** Blood was available for 173 women at 3 months and
170 at 12 months. One woman used vaginal estrogen cream after
randomization, which resulted in estradiol concentrations comparable
with premenopausal levels at 3 and 12 months (67 and 46 pg/ml,
respectively); her data were deleted from the entire analysis. One
woman had an extremely high estradiol concentration at 3 months (98
pg/ml); her data were deleted from the 3-month dataset. This left 171
subjects for 3-month and 169 for 12-month analyses.

At baseline, the intervention and control groups were similar with
regards to demographic characteristics, body composition, mean daily
caloric intake, fitness levels, and hormone concentrations (Tables 1
and 2). Participants on average were 61 years old, obese, highly
educated, and with a low level of fitness. Less than one-third of the
participants worked full-time; 86% were non-Hispanic white, 4%
were African American, and 6% were Asian American.

**Hormone concentrations at baseline and 3 and 12 months in exercise intervention and control participants**

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>3 months</th>
<th>12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Geometric mean (95% confidence interval)</td>
<td>44.2 (40.7–47.9)</td>
<td>42.5 (39.3–45.8)</td>
<td>43.4 (40.2–46.8)</td>
</tr>
<tr>
<td>Exercisers</td>
<td>43.9 (41.2–46.8)</td>
<td>45.4 (42.2–48.8)</td>
<td>45.6 (42.7–48.7)</td>
</tr>
<tr>
<td>Controls</td>
<td>18.3 (17.0–19.7)</td>
<td>16.9 (15.7–18.2)</td>
<td>17.5 (16.3–18.7)</td>
</tr>
<tr>
<td>Estradiol (pg/ml)</td>
<td>17.9 (16.7–19.1)</td>
<td>17.8 (16.8–19.0)</td>
<td>17.8 (16.7–19.0)</td>
</tr>
<tr>
<td>Exercisers</td>
<td>35.2 (32.3–38.4)</td>
<td>37.2 (34.0–40.8)</td>
<td>38.3 (35.2–41.8)</td>
</tr>
<tr>
<td>Controls</td>
<td>35.8 (32.3–39.8)</td>
<td>35.6 (32.1–39.6)</td>
<td>36.7 (32.8–40.9)</td>
</tr>
<tr>
<td>Sex hormone binding globulin (nmol/l)</td>
<td>0.49 (0.45–0.54)</td>
<td>0.45 (0.41–0.49)</td>
<td>0.46 (0.42–0.50)</td>
</tr>
<tr>
<td>Exercisers</td>
<td>0.47 (0.44–0.52)</td>
<td>0.47 (0.43–0.51)</td>
<td>0.47 (0.43–0.51)</td>
</tr>
<tr>
<td>Controls</td>
<td>0.45 (0.31–0.61)</td>
<td>0.45 (0.31–0.61)</td>
<td>0.45 (0.31–0.61)</td>
</tr>
</tbody>
</table>

**a** There were no statistically significant differences at baseline between intervention and control groups for these variables.

**References.**

- EXERCISE AND ESTROGENS IN POSTMENOPAUSAL WOMEN
- SAS software (version 8.2; SAS Institute, Inc., Cary, NC).

**Table 2 Hormone concentrations at baseline and 3 and 12 months in exercise intervention and control participants**

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>3 months</th>
<th>12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Geometric mean (95% confidence interval)</td>
<td>44.2 (40.7–47.9)</td>
<td>42.5 (39.3–45.8)</td>
<td>43.4 (40.2–46.8)</td>
</tr>
<tr>
<td>Exercisers</td>
<td>43.9 (41.2–46.8)</td>
<td>45.4 (42.2–48.8)</td>
<td>45.6 (42.7–48.7)</td>
</tr>
<tr>
<td>Controls</td>
<td>18.3 (17.0–19.7)</td>
<td>16.9 (15.7–18.2)</td>
<td>17.5 (16.3–18.7)</td>
</tr>
<tr>
<td>Estradiol (pg/ml)</td>
<td>17.9 (16.7–19.1)</td>
<td>17.8 (16.8–19.0)</td>
<td>17.8 (16.7–19.0)</td>
</tr>
<tr>
<td>Exercisers</td>
<td>35.2 (32.3–38.4)</td>
<td>37.2 (34.0–40.8)</td>
<td>38.3 (35.2–41.8)</td>
</tr>
<tr>
<td>Controls</td>
<td>35.8 (32.3–39.8)</td>
<td>35.6 (32.1–39.6)</td>
<td>36.7 (32.8–40.9)</td>
</tr>
<tr>
<td>Sex hormone binding globulin (nmol/l)</td>
<td>0.49 (0.45–0.54)</td>
<td>0.45 (0.41–0.49)</td>
<td>0.46 (0.42–0.50)</td>
</tr>
<tr>
<td>Exercisers</td>
<td>0.47 (0.44–0.52)</td>
<td>0.47 (0.43–0.51)</td>
<td>0.47 (0.43–0.51)</td>
</tr>
<tr>
<td>Controls</td>
<td>0.45 (0.31–0.61)</td>
<td>0.45 (0.31–0.61)</td>
<td>0.45 (0.31–0.61)</td>
</tr>
</tbody>
</table>

**a** Difference in hormone change from baseline to 3 months in exercisers versus controls.

**b** Difference in hormone change from baseline to 12 months in exercisers versus controls.
Baseline Associations between Adiposity and Serum Hormones.

The correlation between BMI and percent body fat was +0.69 ($P < 0.0001$). Correlations between percent body fat and estrone, estradiol, free estradiol, and SHBG at baseline were +0.34 ($P < 0.0001$), +0.26 ($P = 0.001$), +0.28 ($P = 0.0003$), and −0.11 ($P = 0.17$), respectively. Similar correlations were observed for BMI. CT-measured intra-abdominal fat was significantly associated with estrone (+0.17, $P = 0.03$), free estradiol (+0.22, $P = 0.006$), and SHBG (−0.43, $P < 0.0001$).

**Intervention Effects.** At 3 and 12 months, women in the exercise group experienced 3.8 and 1.8% declines in estrone, respectively, compared with increases of 3.4 and 3.9% in controls ($P = 0.03$ and $P = 0.13$; Table 2). Exercisers experienced a 7.7% decline in estradiol at 3 months, compared with a decline of just 0.6% in controls ($P = 0.07$); at 12 months, the decline in exercisers was present but attenuated. SHBG increased from baseline to 3 and 12 months in exercisers to a larger degree than controls, but the differences were of only marginal statistical significance. Exercisers had an 8.2% decrease in free estradiol from baseline to 3 months, compared with no change in controls ($P = 0.02$). At 12 months, the decline in estradiol in exercisers was slightly less than at 3 months.

As we have previously reported, fat mass decreased in exercisers by 1.4 kg after 12 months versus a decrease of 0.1 kg in controls ($P = 0.001$; Ref. 10). Daily median alcohol intake increased by 0.1 g in exercisers and 0 g in controls. Mean energy intake decreased in exercisers and controls by 15 and 114 kcal/day, respectively ($P = 0.34$). Medication use did not change differently in exercisers versus controls (data not shown).

At 3 and 12 months, the concentrations of estrone, estradiol, and free estradiol decreased only among exercisers who lost at least 0.5% body fat (Table 3). The amount of hormone decrease was larger for those who lost the greatest percent body fat, and the results were statistically significant comparing exercisers versus controls, at a specific fat change category versus fat gain, for most of these comparisons. Among the exercisers who lost >2% body fat, concentrations of estrone, estradiol, and free estradiol decreased by 11.9, 13.7, and 16.7%, respectively, and SHBG increased by 13.1% at 12 months. In contrast, among the controls who lost body fat, concentrations of estradiol and free estradiol increased, whereas estrone decreased by just 3.6%. SHBG increased in controls who lost body fat to a similar degree to that seen in exercisers.

Adjustment for change in mean kcal energy intake in exercisers and controls.
controls did not change the results. Results observed according to changes in BMI and waist and hip circumferences, and s.c. abdominal fat were consistent with these findings (data not shown). Conversely, change in intra-abdominal fat did not modify the effect of the exercise intervention on hormone concentrations (data not shown).

The change in estrogen concentrations from baseline to 12 months was not consistently related to change in VO\textsubscript{2} max, although exercisers whose fitness increased had almost twice the relative increase in SHBG compared with exercisers whose fitness levels did not increase (Table 4). Hormone changes were not greater for women participating in more (i.e., more minutes/week) exercise (data not shown).

**DISCUSSION**

The results of this randomized clinical trial suggest that exercise can lower levels of circulating estrogens and increase levels of SHBG in previously sedentary, overweight/obese postmenopausal women. The study had excellent retention and adherence, which decreases the chance of biased results and increases study power. The data indicate that loss of body fat in conjunction with exercise is needed to achieve these hormone changes but that exercise need not be of vigorous intensity. This is the first randomized clinical trial to test an exercise intervention so that the long-term biological effect of exercise can more readily be determined. We did not test the effect of dietary change and so cannot address the overall issue of energy balance and serum hormone effects. The study included mostly non-Hispanic white women, so it is not clear if the results can be generalized to other groups. Furthermore, the study was limited to overweight and obese women; it is therefore not clear if the same effect would be observed in lighter-weight women. However, most women in Western countries in the age group studied (50–75 years) are overweight or obese.

Women who change exercise behaviors might also change other behaviors. However, we observed no differences between exercisers and controls with respect to changes in factors that could affect hormone levels, including alcohol use, energy intake, or medication use.

One potential adverse effect of lowering estrogens in postmenopausal women might be a decrease in bone density. Whole-body bone density from DEXA scans, however, showed no decrease in bone density in exercisers from baseline to 12 months ($P = 0.20$) and no difference in changes in a year between exercisers and controls ($P = 0.60$).

The exercise intervention in this study was specifically designed to be acceptable and achievable by postmenopausal, previously sedentary women and may be a useful low-risk regimen for reducing risk of breast cancer.

**ACKNOWLEDGMENTS**

We thank Lilly Chang, M.D., for her technical assistance of hormone determinations and the participants in the Physical Activity for Total Health Study for their dedication to the study.

**REFERENCES**

Effect of Exercise on Serum Estrogens in Postmenopausal Women: A 12-Month Randomized Clinical Trial

Anne McTiernan, Shelley S. Tworoger, Cornelia M. Ulrich, et al.