Exercise Dose and Quality of Life

A Randomized Controlled Trial

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Background: Improved quality of life (QOL) is a purported benefit of exercise, but few randomized controlled trials and no dose-response trials have been conducted to examine this assertion.

Methods: The effect of 50%, 100%, and 150% of the physical activity recommendation on QOL was examined in a 6-month randomized controlled trial. Participants were 430 sedentary postmenopausal women (body mass index range, 25.0-43.0 [calculated as weight in kilograms divided by height in meters squared]) with elevated systolic blood pressure randomized to a nonexercise control group (n=92) or 1 of 3 exercise groups: exercise energy expenditure of 4 (n=147), 8 (n=96), or 12 (n=95) kilocalories per kilogram of body weight per week. Eight aspects of physical and mental QOL were measured at baseline and month 6 with the use of the Medical Outcomes Study 36-Item Short Form Health Survey.

Results: Change in all mental and physical aspects of QOL, except bodily pain, was dose dependent (trend analyses were significant, and exercise dose was a significant predictor of QOL change; $P<.05$). Higher doses of exercise were associated with larger improvements in mental and physical aspects of QOL. Controlling for weight change did not attenuate the exercise-QOL association.

Conclusion: Exercise-induced QOL improvements were dose dependent and independent of weight change.

Trial Registration: clinicaltrials.gov Identifier: NCT00011193

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A SEDENTARY LIFESTYLE IS A risk factor for many chronic conditions, including diabetes mellitus, heart disease, stroke, and certain types of cancers.[1-6] Regular physical activity and higher levels of cardiorespiratory fitness are associated with lower risk for premature mortality, and exercise training has been demonstrated to improve a number of important risk factors, such as cardiorespiratory fitness,[7] weight, high-density lipoprotein cholesterol level, and fasting insulin level.[8] Although mood, level of functioning, energy level, and other measures of quality of life (QOL) are purported to be improved by regular exercise, this claim is largely unsubstantiated in populations without significant morbidities. There is strong evidence that regular exercise substantially improves QOL in populations with serious diseases, such as cancer[9] or chronic obstructive pulmonary disease,[10] but the data are not as supportive in populations without disease. Although many, but not all, epidemiological studies have found an association between exercise and QOL, the available data from intervention trials fail to consistently find a strong effect of exercise training on QOL.[11,12] Furthermore, the data from intervention trials are difficult to interpret because of small sample sizes, inadequate control groups, and poor exercise compliance. In addition, many studies include a weight loss component, making it difficult to separate the benefits of weight loss from the benefits of increased exercise.

To our knowledge, there are no well-controlled, properly powered, randomized controlled trials (RCTs) examining the role of exercise in improving QOL among individuals without significant comorbidities. The Dose-Response to Exercise in postmenopausal Women (DREW) study was designed to examine the health benefits of 50%, 100%, and 150% of the National Institutes of Health Consensus Development Panel[13] physical activity recommendation among 464 sedentary, overweight or obese postmenopausal women with elevated blood pressure. The primary outcomes of cardiorespiratory fitness and blood pressure have been reported,[7] but data on a number of important secondary outcomes also were included a priori in the study design, in-

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cluding a QOL survey.[14] Given the relatively large sample size, very high compliance with a tightly controlled exercise intervention, and high participant retention rate, the DREW study provides an excellent opportunity to examine the effects of exercise on QOL. Identifying a dose-response relationship between exercise and QOL could not only help determine minimum exercise thresholds for promoting QOL but also increase assurance that the exercise-induced benefits are not spurious or the result of chance alone. Therefore, the primary aim of this study was to examine changes in QOL across different doses of supervised exercise. We hypothesized that 6 months of structured, moderate-intensity exercise would significantly improve QOL in a dose-dependent manner.

METHODS

STUDY DESIGN

A complete description of the DREW study design and methods has been published elsewhere.[7,14] In brief, the study was a randomized dose-response exercise trial with a nonexercise control group and 3 exercise groups assigned to incrementally higher doses of energy expenditure. Participants in the nonexercise control group were asked to maintain their baseline level of activity during the 6-month study period. The research protocol was reviewed and approved annually by The Cooper Institute Institutional Review Board. Written informed consent was obtained from all participants.

STUDY PARTICIPANTS

Thorough descriptions of the recruiting and screening processes, as well as the methods, have been previously published.[7,14] Briefly, the study was limited to postmenopausal women aged 45 to 75 years who were sedentary (not exercising more than 20 minutes on 3 or more days a week and taking fewer than 8000 steps per day, assessed for 1 week), overweight or obese (body mass index [BMI] range, 25.0-43.0 [calculated as weight in kilograms divided by height in meters squared]), and had systolic blood pressure of 120.0 to 159.9 mm Hg. Exclusion criteria included history of stroke, heart attack, diabetes mellitus, or any medical condition that prevented participants from adhering to the protocol or exercising safely. Women with a score of 10 or more on the Center for Epidemiological Studies Depression scale[15] were excluded based on data from our laboratory indicating that these women have a greater probability of attrition and from other studies demonstrating that depressed mood is associated with attrition from exercise programs as part of weight loss programs[16] and cardiac rehabilitation.[17] Participants were recruited from the Dallas, Texas, area from April 2001 to June 2005.

OUTCOMES

Change in QOL was measured with the use of the Medical Outcomes 36-Item Short Form Health Survey (SF-36).[18,19] The SF-36 is a self-administered 36-item questionnaire that measures physical and mental QOL. Physical QOL is measured with the following 4 scales: physical functioning, role limitations because of physical problems, bodily pain, and general health perception. Mental QOL also is measured with the use of 4 scales: role limitations because of emotional problems, social functioning, vitality, and mental health. The validity and reliability of the SF-36 have been established, and there are standardized norms available for comparative purposes.[18,19] Participants' raw scores were converted into scale scores ranging from 0 to 100, with higher scores representing better QOL or higher functioning for all scales.

OTHER MEASURES

Maximal fitness testing was conducted using an Excalibur Sport cycle ergometer (Lode Medical Technology, Groningen, the Netherlands), and respiratory gases were measured using a metabolic measurement system (True Max 2400; ParvoMedics, Sandy, Utah). Weight was measured on an electronic scale (Siemens Medical Solutions, Malvern, Pennsylvania), and height was measured using a stadiometer. Smoking history, medical history, and medication use were assessed by responses on detailed medical history questionnaires. Blood pressure was measured using an automated blood pressure unit (model STBP-780; Colin Medical Instruments, San Antonio, Texas) with participants in the recumbent position. Detailed descriptions of the testing procedures are provided elsewhere.[7,14]

EXERCISE TRAINING

Women were assigned to either a nonexercise control group or to groups that expended 4, 8, or 12 kilocalories per kilogram of body weight per week (KKW), which corresponds to 50%, 100%, and 150%, respectively, of current public health physical activity recommendations.[13] Smaller changes in study endpoints were expected in the 4-KKW group; therefore, randomization procedures were created to assign more participants to that group based on the recommendation of the study biostatistician. Exercising women participated in 3 or 4 training sessions each week for 6 months with training intensity at the heart rate associated with 50% of each woman's peak volume of oxygen consumed ($\dot{V}O_2$). All exercise sessions were performed under observation and supervision in an exercise laboratory with standardized prescriptions for exercise dose and strict monitoring of the amount of exercise completed in each session. Participants were weighed each week, and their weight was multiplied by their exercise dosage to determine the number of calories to be expended for the week. Women in the exercise groups alternated training sessions on semirecumbent cycle ergometers and treadmills. Adherence to exercise training during the entire 6-month period was calculated for each individual by dividing the number of kilocalories expended during the exercise training by the number of kilocalories prescribed for the training period multiplied by 100.

PARTICIPANT RETENTION, ADHERENCE, BLINDED ASSESSMENT, AND RANDOMIZATION

A detailed description of procedures for participant retention, adherence, blinded assessment, and random assignment are provided elsewhere.[7,14] To facilitate retention and adherence, participants completed a 2-week prerandomization run-in period and signed behavioral contracts in which they agreed to adhere to the study protocol. Participants were compensated a total of $150, $75 for completion of the baseline assessment and $75 for follow-up. An additional $350 in incentives was available based on adherence. Assessment personnel were blinded to treatment assignment, although blinded assessment was not possible for intervention personnel. Participants were reminded not to discuss their group assignment with the assessment team. Randomization assignment was computer generated and conducted by the statistician.

STATISTICAL ANALYSIS

Descriptive baseline characteristics of groups were tabulated as means and standard deviations or as percentages. Differences in baseline SF-36 scale scores among specific subgroups (ethnicity/race, age, smoking status, marital status, antidepressant use, employment status, and BMI range) were evaluated using analysis of variance, with post hoc tests when appropriate.

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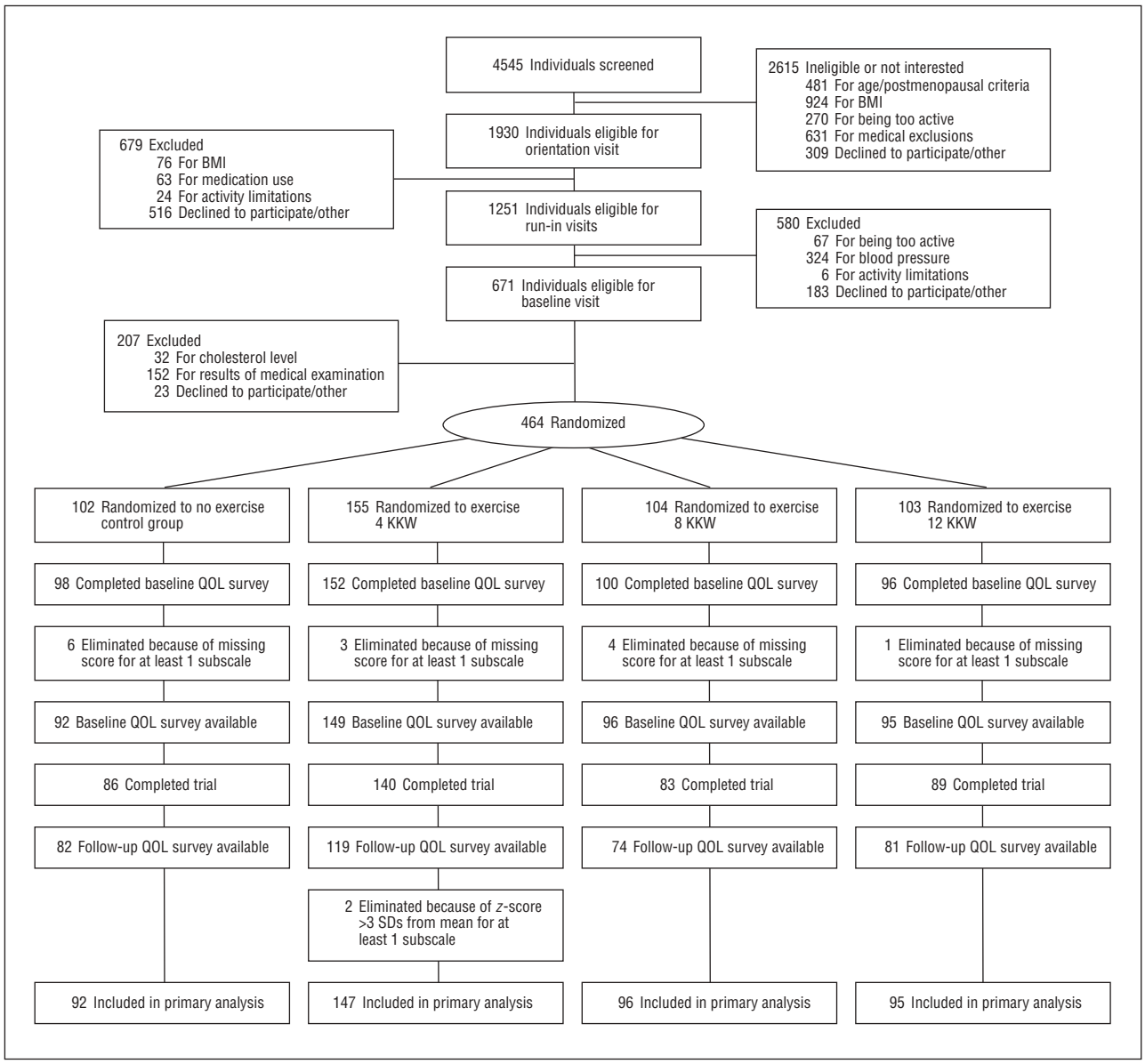

Figure 1. Consolidated Standards of Reporting Trials (CONSORT) diagram describing recruitment and retention of participants. If follow-up quality of life (QOL) scores were missing, baseline values were carried forward. BMI indicates body mass index (calculated as weight in kilograms divided by height in meters squared); KKW, kilocalories per kilogram of body weight per week.

Dose-response effects were evaluated with regression analysis to test for trends in QOL change across groups with adjustment for prespecified covariates identified during the subgroup analysis. Differences in QOL change across groups were tested by analysis of covariance with adjustment. For statistically significant analyses of covariance ($P<.05$), pairwise comparisons between exercise groups and the control group were made using the Bonferroni correction for multiple testing. An α level of .0167 (.05/3) was used because it was our a priori intention to compare only the differences between the exercise groups and the control group; hence, *P* values were multiplied by 3. Results are presented as adjusted least-squares means with 95% confidence intervals.

Analyses were limited to participants with baseline data. If the outcome value was missing for the participant, we inserted the baseline value for that outcome (ie, last observation carried forward). Any QOL values greater than 3 SDs from the mean were defined as outliers and eliminated. For exploratory purposes, all QOL outcomes were tested using only available data, without using baseline values carried forward for missing follow-up data. The results from these analyses did not differ substantially from the analyses with baseline values carried forward (the primary analyses); therefore, only the primary analyses are presented. All reported *P* values are 2-sided. All analyses were performed using SAS statistical software, version 9.1 (SAS Inc, Cary, North Carolina).

RESULTS

A total of 4545 telephone screening calls were conducted. Based on exclusion and inclusion criteria, 4081 potential participants (89.8%) were ineligible (**Figure 1**). After giving informed consent, 464 (10.2%) were randomized, of whom 432 (93.1%) had complete QOL data at baseline and 398 (85.8%) completed the study with 356 usable follow-up QOL surveys (76.7%). Baseline val-

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Table 1. Baseline Characteristics[a]

Characteristic	All Participants (N=430)	Control Group (n=92)	Exercise Groups		
			4 KKW (n=147)	8 KKW (n=96)	12 KKW (n=95)
Demographics					
Age, y	57.4 (6.5)	57.1 (6.0)	57.9 (6.6)	57.7 (6.6)	56.5 (6.7)
Educational level, No. (%), y					
<12	12 (2.8)	3 (3.3)	4 (2.7)	3 (3.1)	2 (2.1)
12-16	295 (68.6)	66 (71.7)	103 (70.1)	63 (65.6)	63 (66.3)
>16	123 (28.6)	23 (25.0)	40 (27.2)	30 (31.3)	30 (31.6)
Married, No. (%)	393 (91.4)	86 (93.5)	138 (93.9)	85 (88.5)	84 (88.4)
Ethnicity, No. (%)					
White	280 (65.1)	62 (67.4)	90 (61.2)	60 (62.5)	68 (71.6)
African American	122 (28.4)	20 (21.7)	48 (32.7)	30 (31.3)	24 (25.3)
Hispanic/other	28 (6.5)	10 (10.9)	9 (6.1)	6 (6.2)	3 (3.2)
Employed, No. (%)	329 (76.5)	68 (73.9)	109 (74.2)	75 (78.1)	77 (81.1)
Cigarette smoker, No. (%)	19 (4.4)	3 (3.3)	8 (5.4)	2 (2.1)	6 (6.3)
History of depression, No. (%)	128 (29.8)	27 (29.3)	41 (27.9)	24 (25.0)	36 (37.9)
Antidepressant medication use, No. (%)	78 (18.1)	17 (18.5)	27 (18.4)	18 (18.8)	16 (16.8)
Thyroid medication use, No. (%)	65 (15.1)	13 (14.1)	18 (12.2)	16 (16.7)	18 (18.9)
Hormone therapy use, No. (%)	196 (45.6)	48 (52.2)	62 (42.2)	42 (43.8)	44 (46.3)
Cardiovascular Disease Factors					
Cholesterol level, mg/dL					
LDL	118.4 (26.4)	118.3 (26.4)	117.6 (27.2)	118.2 (25.3)	120.2 (26.7)
HDL	57.4 (14.3)	56.4 (13.3)	58.1 (14.5)	57.0 (15.2)	57.8 (14.0)
Triglycerides level, mg/dL	129.2 (64.0)	133.9 (67.7)	130.0 (60.1)	127.8 (58.2)	124.9 (71.8)
Fasting glucose level, mg/dL	94.7 (9.6)	95.1 (13.2)	94.4 (8.6)	94.6 (8.3)	95.1 (8.3)
Blood pressure, mm Hg					
Systolic	139.8 (13.0)	141.6 (12.2)	139.4 (13.2)	140.2 (13.5)	138.2 (12.9)
Diastolic	81.0 (8.5)	80.9 (7.8)	80.9 (9.0)	80.9 (8.0)	81.0 (8.9)
Anthropometric Measurements					
Weight, kg	84.6 (6.5)	86.4 (12.3)	83.4 (11.5)	85.2 (12.8)	84.3 (11.2)
BMI	31.8 (3.8)	31.4 (3.6)	32.1 (4.1)	31.5 (3.7)	32.4 (3.9)
QOL (SF-36 Score)					
Physical					
Physical functioning	78.2 (18.6)	78.9 (16.6)	78.0 (19.3)	75.4 (21.0)	80.8 (16.6)
Role limitations because of physical problems	75.5 (34.1)	78.8 (31.2)	72.8 (37.0)	77.6 (33.5)	74.5 (32.8)
Bodily pain	70.7 (19.5)	69.8 (17.0)	71.4 (20.3)	72.0 (20.9)	69.2 (19.2)
General health	72.0 (16.2)	70.9 (16.2)	72.9 (16.1)	70.5 (17.3)	73.3 (16.4)
Mental					
Role limitations because of emotional problems	78.3 (33.9)	77.2 (36.3)	78.2 (34.6)	84.0 (29.8)	73.7 (34.0)
Social functioning	84.8 (19.4)	83.4 (20.3)	85.7 (18.4)	87.6 (16.3)	81.8 (22.4)
Vitality	54.2 (20.3)	52.7 (19.7)	54.5 (21.0)	56.3 (20.1)	53.1 (20.3)
Mental health	77.7 (13.8)	76.6 (14.6)	78.1 (13.5)	78.5 (13.1)	77.3 (14.3)

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); HDL, high-density lipoprotein; KKW, kilocalories per kilogram of body weight per week; LDL, low-density lipoprotein; QOL, quality of life; SF-36, Medical Outcomes Study 36-Item Short Form Health Survey.

SI conversion factors: to convert LDL and HDL to millimoles per liter, multiply by 0.0259; to convert triglycerides to millimoles per liter, multiply by 0.0113; to convert glucose to millimoles per liter, multiply by 0.0555.

[a] Data presented as mean (standard deviation) unless otherwise indicated.

ues were carried forward for missing data or dropouts, so data from 430 of 464 participants (92.7%) were included in the primary analyses. In the 4-KKW group, 2 participants' data were eliminated due to being outliers.

The study population had a mean (SD) age of 57.4 (6.5) years and a mean BMI of 31.8 (3.8); 34.9% were nonwhite (**Table 1**). Almost 30% of the study population reported a history of depression, and 18.1% were taking antidepressant medication at baseline. Only 4.4% of participants were current smokers, and 76.5% were employed. Almost half the participants were using hormone therapy, and 15.1% were taking thyroid medication. With the exception of blood pressure, cardiovascular risk factors were within normal ranges. The mean baseline peak $\dot{V}O_2$ was very low (15.4 [2.9] mL/kg/min) (**Table 2**). Adherence to exercise was 95.4%, 88.1%, and 93.7% for the 4-, 8-, and 12-KKW groups, respectively, and each group spent 73.9, 138.3, and 183.6 min/wk exercising (Table 2).

The mean baseline QOL scale scores for the total population and by group are presented in Table 1. At baseline, the DREW study sample had scores similar to the US population (**Figure 2**).[21] The mean QOL scores for the DREW study sample differed from the national mean by only 0.02 to 0.22 SD units, which are considered differences of small magnitude.[20] The mean baseline scores

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Table 2. Exercise-Related Variables at Baseline and After Exercise Training[a]

Exercise-Related Variable	All Participants (N=430)	Control Group (n=92)	Exercise Groups		
			4 KKW (n=147)	8 KKW (n=96)	12 KKW (n=95)
Peak relative $\dot{V}O_2$, mL/kg/min					
Baseline	15.4 (2.9)	15.5 (3.1)	15.5 (3.0)	14.7 (2.5)	15.7 (3.0)
Change	0.78 (1.9)	–0.30 (1.9)	0.65 (1.9)	1.33 (1.6)	1.52 (1.80)
6-mo Adherence, %[b]	92.8 (20.4)	NA	95.4 (15.5)	88.1 (26.4)	93.7 (19.5)
Sessions per week, mean	2.9	NA	2.7	2.9	3.1
Time spent exercising, min/wk[c]	113.8 (61.3)	NA	73.9 (15.5)	138.3 (25.3)	183.6 (43.3)

Abbreviations: KKW, kilocalories per kilogram of body weight per week; NA, not applicable; $\dot{V}O_2$, volume of oxygen consumed.
[a] Data are given as mean (standard deviation) unless otherwise indicated.
[b] Adherence was calculated for each individual by dividing the number of kilocalories expended during the 6-month exercise training by the number of kilocalories prescribed for the training period times 100.
[c] Among individuals who completed the intervention. Data are for the exercise training period but excluding the initial ramping period, which represents 6 months of data for the 4-KKW group, 5 months for the 8-KKW group, and 4 months for the 12-KKW group.

for QOL scales across specific subgroups are presented in **Table 3**, and, although some comparisons had small sample sizes, these data demonstrate that we observed many of the expected QOL differences among groups. For example, QOL at baseline was lower on all scales among participants taking antidepressant medication compared with participants not taking such medication. In addition, employed participants reported better QOL on the physical functioning, role limitations because of physical problems, and bodily pain scales.

Figure 3 summarizes the mean changes in SF-36 measures in the control and exercise groups. The positive linear trend across groups was statistically significant for all physical and mental QOL scales (all $P<.001$), and exercise dose was a significant independent predictor of change for all QOL scales ($P<.001$ to .04), except bodily pain ($P=.19$). Therefore, a dose-response effect of exercise on QOL was noted for all aspects of QOL except bodily pain. The analyses of covariance indicated that for all physical and mental QOL scales except bodily pain ($P=.32$), the 12-KKW group had significantly improved QOL compared with the control group ($P<.001$ to .04). In addition, the 4-KKW group had significantly improved general health perception, vitality, and mental health compared with the control group ($P=.01$ to .04). All 3 exercise groups had significantly improved social functioning compared with the control group ($P<.001$ to .03). The analyses were conducted without the aforementioned covariates, and the results were virtually identical.

The mean changes in weight across the control, 4-KKW, 8-KKW, and 12-KKW groups were –0.94 (4.0), –1.34 (3.5), –1.86 (3.4), and –1.34 (2.9) kg, respectively, with no between-group differences. To examine the effect of weight loss on improvement in SF-36 measures, all analyses were repeated with additional adjustment for change in body weight. Weight change was a significant covariate in only 2 of 8 comparisons, and inclusion of this covariate did not have a meaningful effect on any of the mean values, significance, or trends across exercise groups. To further assure that weight loss was not responsible for the observed results, change in SF-36 scores across the exercise groups was examined with participants divided into those who lost weight and those who maintained or gained

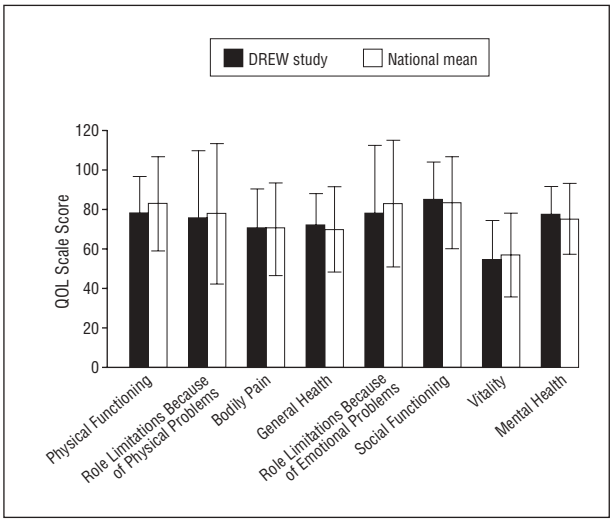

Figure 2. Mean (standard deviation) baseline Medical Outcomes Study 36-Item Short Form Health Survey (SF-36) scores for the DREW (Dose-Response to Exercise in postmenopausal Women) study sample at baseline and the national mean for the United States. The mean quality of life (QOL) scores for the DREW sample differed from the national mean by only 0.02 to 0.22 SD units, which are considered differences of small magnitude.[20]

weight. **Figure 4** summarizes the change in SF-36 scores across exercise groups for these subgroups. The *P* values for the treatment × subgroup interactions for the SF-36 scales ranged from 0.07 to 0.95. These nonsignificant interactions indicate that the pattern of change in each of the SF-36 measures across the exercise groups was similar for those who did and did not lose weight.

All analyses were repeated with change in fitness as a covariate, and the conclusions from these analyses were not meaningfully affected. Change in fitness was also correlated with change in QOL, and only 2 of 8 correlation coefficients differed significantly from 0 and the size of the coefficients was small (physical functioning, $r=0.11$ and $P=.02$; role limitations owing to physical problems, $r=0.12$ and $P=.02$). These findings suggest that changes in fitness are not necessary to improve QOL when individuals increase physical activity.

To explore the effect of antidepressant use on the results, participants were grouped by antidepressant use

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Table 3. Baseline Quality of Life (SF-36) Scores by Subgroup[a]

Baseline Category	No. of Participants	Physical Health Measures				Mental Health Measures			
		Physical Functioning	Role Limitations Because of Physical Problems	Bodily Pain	General Health	Role Limitations Because of Emotional Problems	Social Functioning	Vitality	Mental Health
Ethnicity/race									
White	280	76.4 (18.6)[b]	74.7 (33.7)	70.3 (18.9)	72.3 (15.6)	78.0 (33.4)	84.9 (19.5)	52.3 (19.7)[b]	77.4 (13.4)
African American	122	81.5 (18.9)[c]	77.5 (35.0)	71.3 (20.7)	70.8 (17.3)	77.9 (35.5)	83.3 (20.3)	57.9 (21.0)[c]	77.8 (14.9)
Hispanic/other	28	83.1 (15.1)[b,c]	75.0 (35.4)	72.0 (20.9)	74.5 (17.7)	83.3 (32.1)	89.7 (12.3)	57.1 (21.4)[b,c]	79.6 (12.5)
Age, y									
45-54	175	81.6 (17.2)[b]	79.3 (31.2)	71.6 (19.5)	69.1 (17.1)[b]	77.7 (33.0)	81.8 (20.8)[b]	54.3 (21.0)	76.3 (14.0)
55-64	195	77.8 (18.7)[b]	74.7 (34.6)	70.0 (19.6)	73.2 (15.0)[c]	78.1 (34.8)	87.2 (17.3)[c]	54.1 (20.0)	78.2 (13.5)
≥65	60	70.0 (19.8)[c]	67.1 (39.2)	70.4 (19.3)	76.7 (16.1)[c]	80.6 (33.8)	85.8 (20.5)[b,c]	54.1 (19.7)	79.6 (13.7)
Smoker									
Never	307	78.0 (19.3)	76.0 (33.4)	70.6 (19.4)[b,c]	71.7 (16.0)	77.6 (34.7)	85.1 (19.6)	54.1 (20.7)	77.7 (14.1)
Former	104	79.9 (16.1)	76.4 (35.0)	73.1 (18.2)[b]	73.9 (16.6)	79.2 (32.6)	84.2 (19.2)	55.0 (20.0)	78.6 (12.5)
Current	19	72.9 (19.2)	63.1 (40.3)	59.7 (24.9)[c]	66.6 (18.0)	84.2 (28.0)	82.9 (17.3)	50.8 (17.3)	72.0 (14.0)
Marital status									
Not married	37	81.9 (14.3)	81.8 (30.4)	74.6 (18.7)	68.9 (17.7)	75.7 (32.1)	78.4 (22.6)	48.1 (23.4)	75.5 (16.2)
Married	393	77.9 (18.9)	74.9 (34.4)	70.3 (19.6)	72.3 (16.1)	78.5 (34.1)	85.4 (19.0)	54.8 (20.0)	77.9 (13.5)
Antidepressant use									
No	351	79.1 (18.0)[b]	77.2 (33.0)[b]	71.7 (18.9)[b]	73.4 (15.9)[b]	80.8 (32.2)[b]	86.1 (18.9)[b]	56.4 (20.0)[b]	78.6 (13.7)[b]
Yes	78	74.6 (20.7)[c]	67.9 (38.0)[c]	66.4 (21.5)[c]	65.7 (16.3)[c]	67.1 (38.9)[c]	78.8 (20.7)[c]	44.4 (19.2)[c]	73.3 (13.3)[c]
Employed									
No	101	72.8 (21.5)[b]	67.8 (40.5)[b]	65.2 (20.9)[b]	71.9 (16.4)	76.2 (38.4)	84.0 (20.8)	54.1 (21.1)	76.8 (14.2)
Yes	329	79.9 (17.3)[c]	77.9 (31.6)[c]	72.4 (18.8)[c]	72.1 (16.2)	78.9 (32.4)	85.0 (18.9)	54.2 (20.1)	77.9 (13.6)
BMI range									
Overweight (25.0-29.9)	151	83.1 (16.3)[b]	79.0 (31.6)[b]	72.3 (19.5)[b]	75.1 (15.6)[b]	75.1 (35.9)	86.8 (18.6)	55.8 (20.6)	77.3 (15.3)
Obese class I (30.0-34.9)	177	77.8 (18.4)[c]	77.1 (33.2)[b,c]	72.0 (19.2)[b,c]	71.1 (16.0)[b,c]	82.3 (30.4)	84.6 (20.5)	54.5 (20.8)	78.3 (12.5)
Obese class II (35.0-39.9)	102	71.9 (20.2)[d]	67.6 (38.1)[c]	66.1 (19.6)[c]	69.1 (16.9)[c]	76.1 (36.1)	82.2 (18.4)	51.2 (18.9)	77.0 (13.6)

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); SF-36, Medical Outcomes Study 36-Item Short Form Health Survey.

[a] Data are given as unadjusted fitted mean (standard deviation) unless otherwise indicated. *P* values for group differences were assessed by analysis of variance using Bonferroni correction. For pairwise comparisons within subgroups and SF-36 scales, means that differ significantly ($P < .05$) are noted with different superscripts (b, c, and d). For example, employed participants reported significantly better physical functioning, role limitations because of physical problems, and bodily pain aspects of quality of life at baseline compared with participants who were not working. Employed participants did not differ significantly from participants who were not working on any other SF-36 scales.

(yes/no), and change in QOL among exercise groups was tested with an exercise group × antidepressant use interaction. The interaction term was not significant for all 4 physical measures of QOL ($P > .11$), but it was significant for the role limitations because of emotional problems, social functioning, and vitality scales (mental health scale, $P = .06$). These findings and examination of group means indicated that participants in the nonexercise control group who took antidepressant medication experienced no increase in QOL during the trial, and for some mental health measures they experienced decreased QOL. Conversely, control participants who were not taking antidepressant medication experienced small increases in QOL during the trial.

COMMENT

The primary finding from this randomized controlled exercise trial was a significant, positive dose-response relationship between the amount of exercise performed and improvements in physical and mental QOL measures. Although improved QOL is routinely cited as a benefit of regular exercise, data to support this claim are limited to conflicting epidemiological reports or studies whose participants were diagnosed as having major chronic diseases, such as cancer. Although not observed for all measures, it is of interest that even 4 KKW of exercise (approximately 74 min/wk) was associated with a significant improvement in QOL for several scales compared with the nonexercise control group. The improvements in QOL occurred at a modest training intensity (heart rate at 50% peak $\dot{V}O_2$) and, as demonstrated by our low dropout rate and excellent adherence in all exercise groups to the 6-month caloric expenditure target, the exercise prescriptions were well tolerated by participants. As a consequence of randomizing more participants to the 4-KKW group, statistical power was sufficient to detect differences in QOL change between the control and 4-KKW group, but not the control and 8-KKW group, despite very similar effect sizes. However, the significant trend (regression) analyses confirm the dose-response effect.

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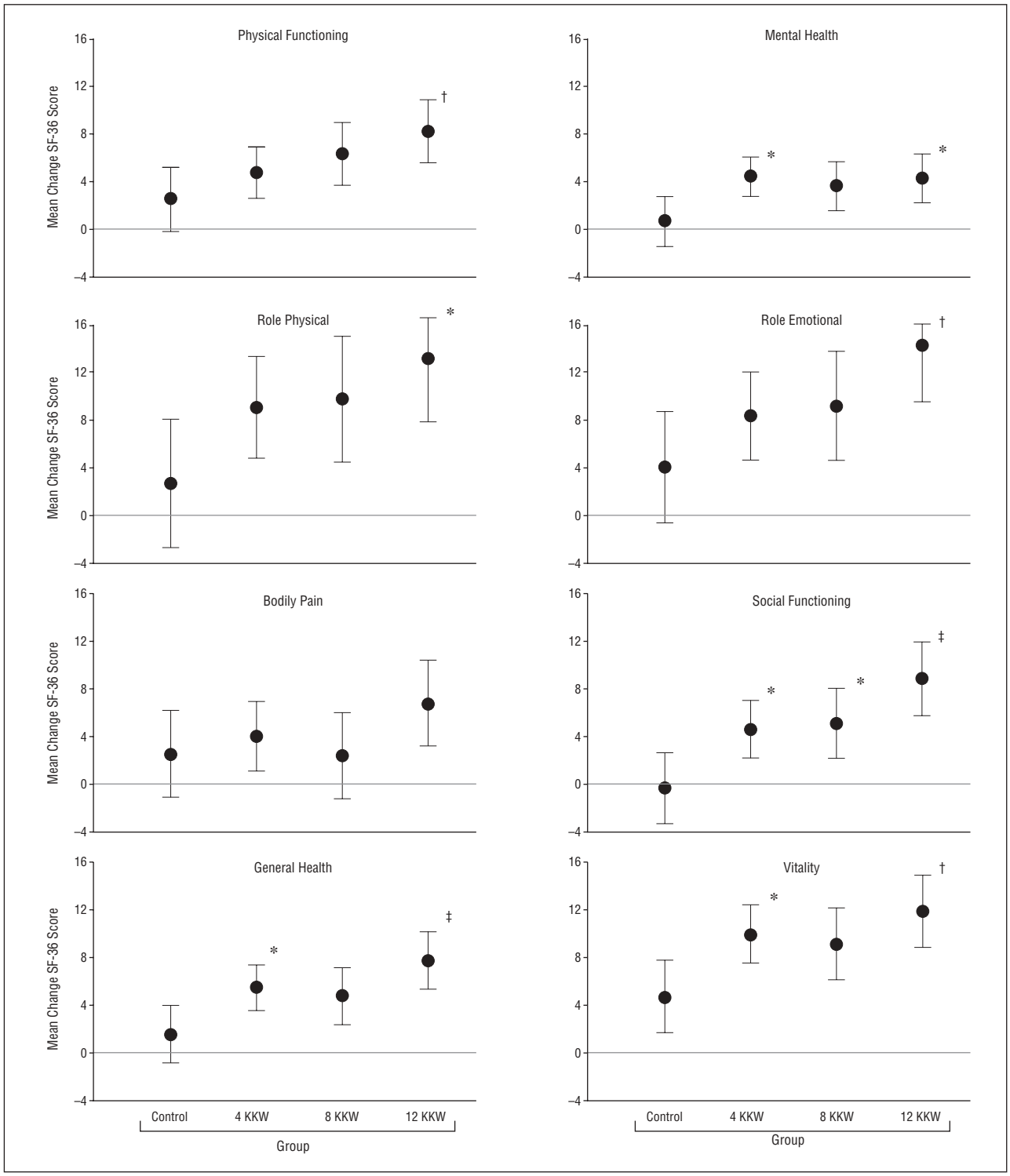

Figure 3. Mean change (least-squares [LS] means±95% confidence interval [CI]) in Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) scores for the control and exercise groups. The dose-response relationships between exercise dose and change in quality of life (QOL) were evaluated with regression analysis to test for trends across groups. Significant trends were found for all QOL scales (all $P<.001$), with exercise dose being an independent predictor of change in physical functioning (PF) ($t_1=3.19$; $P=.002$); role physical problems (RP) ($t_1=2.62$; $P=.009$); general health perception (GH) ($t_1=3.21$; $P=.001$); mental health (MH) ($t_1=2.03$; $P=.04$); role emotional problems (RE) ($t_1=3.00$; $P=.003$); social functioning (SF) ($t_1=4.17$; $P<.001$); and vitality (VT) ($t_1=2.88$; $P=.004$); but not bodily pain (BP) ($t_1=1.31$; $P=.19$). Differences in QOL change across groups were tested by analysis of covariance (ANCOVA) with adjustment for prespecified covariates (age, antidepressant use, body mass index, employment status, ethnicity, marital status, and smoking status at baseline). Significant ANCOVAs ($P<.05$) were followed by pairwise comparisons to test whether exercise groups differed significantly from the control group. The α level was set at .0167 (.05/3), and all P values were multiplied by 3; hence, the following notation depicted statistical significance: * $P<.05$; †, $P<.01$; and ‡, $P<.001$. For significant comparisons, the LS mean differences (95% CI) between the 12 kilocalories per kilogram of body weight per week (KKW)–and control groups were: PF, 5.7 (1.2-10.2); RP, 10.4 (1.3-19.5); GH, 6.2 (2.1-10.4); MH, 3.6 (0.2-7.1); RE, 10.4 (2.3-18.4); SF, 9.1 (4.1-14.2); and VT, 7.1 (1.9-12.2). Similarly, significant LS mean differences (95% CI) between the 4-KKW and control groups were: GH, 3.9 (0.2-7.6); VT, 5.2 (0.5-9.9); SF, 4.9 (0.3-9.4); and MH, 3.8 (0.7-6.9). The 8-KKW group had significantly improved social functioning compared with the control group: 5.4 (0.4-10.4).

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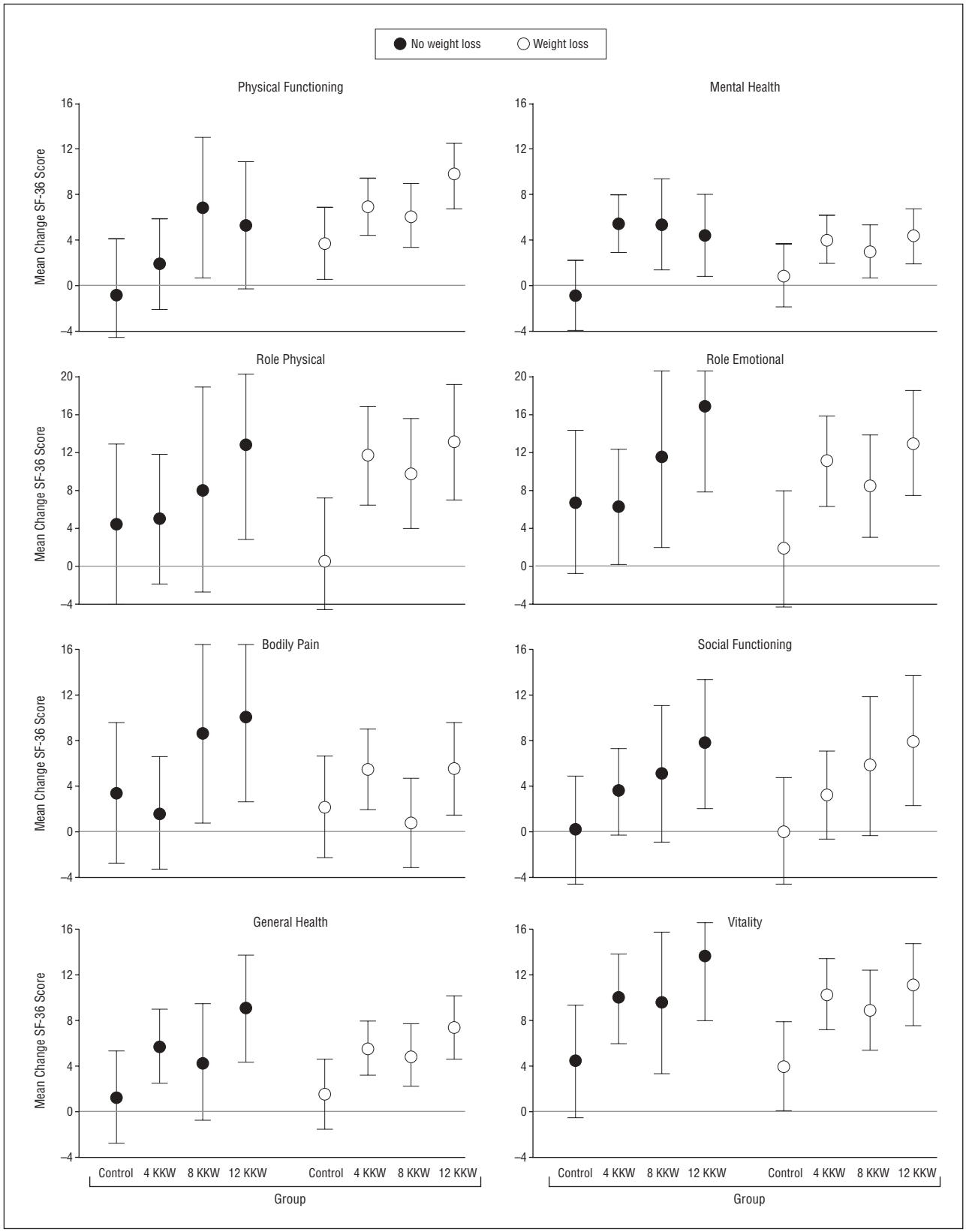

Figure 4. Mean change (least-squares means ±95% confidence interval) in Medical Outcomes Study 36-Item Short Form Health Survey (SF-36) scores across the exercise groups was examined for 2 subgroups, those who lost weight vs those who maintained or gained weight, using analysis of covariance (ANCOVA) with baseline age, antidepressant use, employment status, ethnicity, marital status, and smoking status as covariates. The results from the ANCOVAs were: physical functioning, $F_{3,416}=0.12$, $P=.95$; role limitations because of physical problems (role physical), $F_{3,416}=1.00$, $P=.39$; bodily pain, $F_{3,416}=1.41$, $P=.24$; general health perception, $F_{3,416}=0.28$, $P=.84$; mental health, $F_{3,416}=0.18$, $P=.91$; role limitations because of emotional problems (role emotional), $F_{3,416}=2.41$, $P=.07$; social functioning, $F_{3,416}=0.87$, $P=.46$; and vitality, $F_{3,416}=0.11$, $P=.95$. These nonsignificant interactions indicate that the pattern of change in each of the SF-36 measures across the exercise groups was similar for those who did and did not lose weight. KKW indicates kilocalories per kilogram of body weight per week.

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Most cross-sectional studies have observed that higher levels of activity are associated with higher QOL scores,[12] particularly for physical aspects of QOL.[22] However, in one cross-sectional study, extended bouts of exercise were associated with poor QOL.[23] Prospective observational studies suggest that people who report higher levels of exercise also report higher QOL scores, at least among women.[24] Nevertheless, as in all observational studies, these findings do not imply causation, and it is easy to hypothesize that people with a higher perceived QOL are more like to be physically active or more likely to increase their level of exercise. To our knowledge, we are the first to demonstrate in an RCT that instituting a regular exercise program results in significant improvements in mental and physical QOL and that these improvements are sensitive to exercise dose, ie, dose dependent. The robust effect of exercise on mental QOL in the present study is of interest because cross-sectional studies find an association primarily between physical aspects of QOL and exercise. It is also of interest that physical activity–induced changes in QOL were independent of changes in fitness, suggesting that changes in fitness are not required for physical activity–induced improvements in QOL.

In an uncontrolled weight loss study that included exercise, weight loss and/or exercise were associated with improved QOL,[25] and a prospective observational study supports the hypothesis that weight loss among overweight women is associated with improved QOL.[26] The findings from the DREW study provide insight into the relative importance of weight loss in exercise-induced changes in QOL because weight loss in the DREW sample was small and did not differ significantly among groups. Moreover, exercise-induced improvements in QOL were independent of weight loss, and the magnitude of change in QOL was similar among those who did and did not lose weight. These results support the hypothesis that exercise in the absence of substantial weight loss can significantly improve physical and mental QOL.

The public health implications of our findings are significant. We are in the midst of a large shift in the demographic characteristics of the United States, and the proportion of Americans older than 65 years will grow dramatically during the next few decades. Although maximizing longevity is of great importance, maximizing QOL should also be a priority. Our findings suggest that increasing physical activity is an effective tool to improve QOL. Increasing exercise, particularly as individuals age, has many health benefits, such as a reduction in cardiovascular disease risk factors.[7,8] Our results indicate that improved QOL can be added to the list of exercise benefits and that these improvements are dose dependent and independent of weight loss, at least among people similar to this study's sample.

The study has limitations because the sample included only sedentary, overweight or obese postmenopausal women at risk for cardiovascular disease. Therefore, we do not know whether the results will apply to other women or men. Nevertheless, the study sample was a group that would likely benefit from exercise training and represents a sizeable proportion, probably a majority, of US women aged 45 to 75 years. Furthermore, although baseline SF-36 scores were similar to the national mean, baseline QOL scores were high, yet we were able to detect significant improvements in QOL. Because participants assigned to incrementally higher doses of exercise spent more time exercising at the center, they had more contact with study personnel, and this contact could have influenced QOL. However, in the only other RCTs testing whether exercise affects QOL,[11] the amount of contact between study personnel and participants varied systematically among the study groups yet no consistent effect of exercise on QOL was found, suggesting that contact with study personnel has little effect on QOL. Last, the DREW study was not designed specifically to evaluate the effect of exercise on QOL. However, QOL measures were preplanned secondary outcomes, and this RCT provides compelling evidence of the dose-response relationship between exercise and improved QOL.

The study does have many strengths. It is an RCT that studied 3 different exercise doses, and all exercise was completed in the laboratory. Our study had a large proportion of nonwhite participants, primarily African Americans, and exercise energy expenditure, heart rate, and steps taken during exercise on the treadmill were extensively monitored. Exercise adherence was excellent, the dropout rate was low, and baseline SF-36 values were similar to the national mean for the United States. In addition, expected differences on baseline QOL scores were observed among subgroups, including BMI category and employment status. The exercise doses are easily obtainable and were well tolerated by sedentary women, resulting in confidence that the exercise doses used in this study can be achieved by women in the community.

CONCLUSIONS

In this study of previously sedentary, overweight or obese postmenopausal women, exercise improved physical and mental QOL in a dose-dependent fashion, and the improvements in QOL were independent of weight loss.

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cational, and lay groups. During the past 5 years, Dr Martin has provided consultation to Pfizer Inc, Zephyr Sciences, and BAROnova, and he received a research grant from Abbott Laboratories and Sunny Health Co, Ltd. Dr Church is a consultant for Trestle Tree, Inc and has a book in publication from which he will receive royalties. Ms Thompson receives honoraria for lectures from scientific and educational groups. In addition to the aforementioned, Dr Blair receives book royalties (<$5000 per year) from Human Kinetics and honoraria for services on the medical advisory boards for Matria Health Care and Jenny Craig. He also is paid as an executive lecturer by the University of North Texas. He gives these fees to the University of South Carolina Educational Foundation or to other nonprofit groups. During the past 5 years, he has received a research grant from Jenny Craig and currently has a research grant from BodyMedia.

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