

ONLINE FIRST

Trial of Prevention and Reduction of Obesity Through Active Living in Clinical Settings

A Randomized Controlled Trial

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Background: The efficacy of physical activity with a healthful diet to reduce obesity is established; however, little is known about the translation of effective lifestyle strategies for obesity reduction in primary care settings.

Methods: We assessed the effectiveness of a 2-year behaviorally based physical activity and diet program implemented entirely within clinical practices to reduce obesity. A total of 490 sedentary, obese adults were randomized to usual care (n=241) or to the behavioral intervention (n=249). The usual care group received advice from their physicians about lifestyle as a strategy for obesity reduction. The behavioral intervention included individual counseling from health educators to promote physical activity with a healthful diet. The primary outcome was change in waist circumference (WC).

Results: A total of 396 participants completed the trial (80.8%). A significant main effect was observed for WC change within the intervention compared with usual care ($P < .001$) that was sustained at 24 months (mean [SE],

-0.9 [0.4] vs 0.2 [0.4] cm; $P = .05$). Secondary analyses revealed significant main effects for change in WC in men ($P = .009$) and women ($P = .02$). In men, the mean (SE) reduction in WC at 24 months was greater with behavioral intervention compared with usual care (-1.6 [0.6] vs 0.1 [0.6] cm; $P = .049$). In women, the behavioral intervention was associated with differences in WC compared with usual care at 6 and 12 months ($P \leq .01$) but not at 24 months ($P = .10$).

Conclusions: Behavioral intervention in clinical settings is associated with modest reductions in WC during a 2-year study in obese patients. However, the effectiveness of the intervention is restricted to men.

Trial Registration: clinicaltrials.gov Identifier: NCT00665158

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OBESITY INCREASES THE RISK of numerous chronic diseases, resulting in a decline in the quality and duration of life.^{1,2} Despite widespread awareness of the importance of reducing obesity and promoting healthy lifestyles, most primary care clinicians fail to counsel obese patients adequately.³ Commonly cited barriers include limited time, counseling expertise, and staff support and a lack of effective treatments.^{4,5} These limitations are reinforced by the recommendation that clinicians screen adults for obesity and offer intensive counseling and behavioral interventions for weight management.^{1,6} The US Preventive Services Task Force recommends intensive counseling (defined as >1 visit per month for 6 months) because evidence does not support the use of low- or moderate-intensity counseling (3-6 visits

during 1-2 years) by primary care physicians alone as an effective strategy for achieving weight loss.^{6,7} The time and expense required for primary care practitioners to provide high-intensity behavioral counseling as recommended is unlikely given the absence of adequate reimbursement and the routine demands of office practice.

We acknowledged these limitations and proposed in response that effective obesity reduction at the primary care level requires that the clinician work in close concert with a specially trained health educator. Insertion of the health educator into the clinical practice would provide these professionals with direct and immediate access to patients and extensive opportunities to interact with physicians and other clinical staff. Inclusion of the health educator as an integral component of the primary care team would op-

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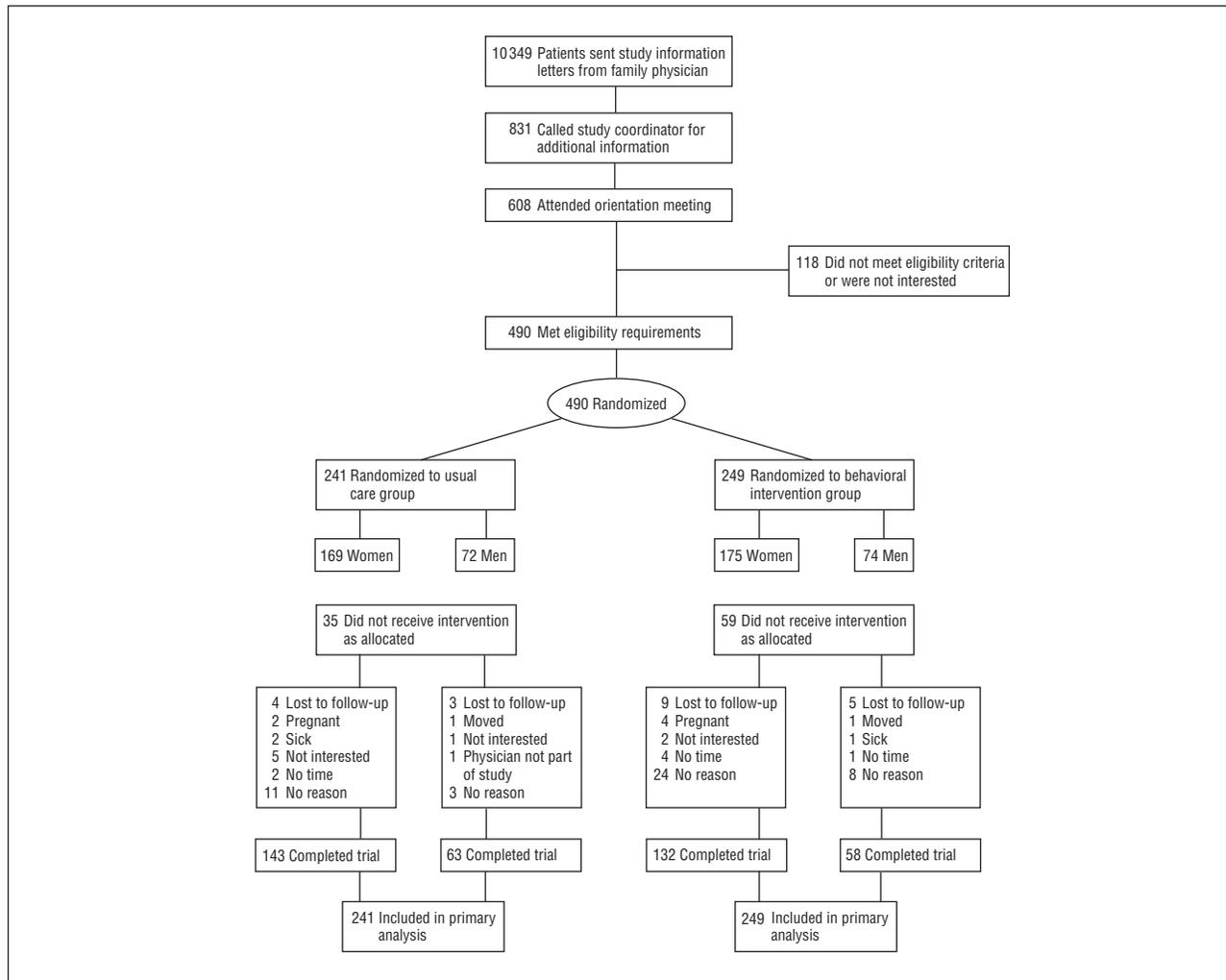


Figure 1. Participant flow diagram.

optimize the physician's contribution to the intervention and underscore the perceived value of obesity reduction to the patient. The feasibility and/or effectiveness of placing a health educator within the primary care practice to deliver the lifestyle intervention and the willingness of patients to participate in a long-term obesity reduction trial in a clinical setting is unknown.

The Prevention and Reduction of Obesity Through Active Living (PROACTIVE) trial was specifically designed to assess the effectiveness of a 24-month behaviorally based physical activity and diet program aimed at reducing obesity and related metabolic risk factors in abdominally obese adults in primary care settings. We hypothesized that a pragmatic individualized education and behavior counseling program delivered to patients by a health educator would result in a reduction in waist circumference (WC) compared with usual care.

METHODS

DESIGN

Details of the PROACTIVE trial's design and methods have been published elsewhere.⁸ PROACTIVE was a 24-month random-

ized, controlled trial with 2 arms: a usual care control condition and a lifestyle-based behavioral intervention. The study was approved by the Queen's University Faculty of Health Sciences Research Ethics Board. Participants provided written informed consent before participation.

Approximately 36 physicians from 3 family medicine clinics participated in the trial. Physicians supplied their patient list to the project coordinator, who subsequently created an information letter for each participant. Participant flow throughout the trial is illustrated in **Figure 1**.

PARTICIPANTS

A total of 10 349 patients received personalized recruitment/information letters from December 1, 2004, through January 31, 2008. In all, 490 sedentary (planned activity ≤ 1 time/wk), overweight (body mass index [BMI; calculated as weight in kilograms divided by height in meters squared], 27-39), and abdominally obese (WC, ≥ 102 cm in men or ≥ 88 cm in women) adults were randomly assigned to the intervention or to the usual care arm. Patients with dyslipidemia, type 2 diabetes mellitus, or hypertension were not excluded from participation. Exclusion criteria included serious medical conditions that prevented participants from increasing daily physical activity.

INTERVENTIONS

Usual Care

Participants randomized to usual care received advice from their physicians regarding lifestyle as a strategy for obesity reduction and continued to meet with their physician according to their usual schedule. Physicians were asked not to change their routine counseling approach for obese PROACTIVE patients.

Behavioral Intervention

Details of the behavioral intervention are published elsewhere.⁸ The 2-year, multiphase intervention was designed to promote physical activity concurrent with the consumption of a balanced diet. The intervention included individually tailored counseling based on the transtheoretical model and social cognitive theory.⁹⁻¹¹ Counseling was delivered by health educators who had degrees in kinesiology and who received behavioral counseling training from a clinical psychologist. Each health educator was assigned to 1 of 3 family medicine clinics and delivered all counseling sessions on site within a private office. Motivational interviewing served as the counseling model.⁹ During phase 1 of the intervention (months 0-6, 15 sessions), the health educator worked one on one with participants to provide knowledge and skills to increase daily physical activity and consume a healthful diet. Phase 2 (months 7-12, 6 sessions) started at session 16 and encouraged the participants to maintain their current program (45-60 minutes of activity per day and healthy eating patterns). During phase 3 (months 13-24, 12 sessions), contact with health educators continued, but the session duration was determined according to each participant's WC value and physical activity level.

RANDOMIZATION

Eligible participants were randomized on the basis of a computer-automated randomization sequence after the acquisition of primary outcome data. Randomization was stratified by sex, age, and WC measurement. It was not possible to conceal the group assignment from the patients or the physicians. Strategies to decrease the likelihood of contamination and bias included the following: (1) baseline data were collected before randomization; (2) participants were asked not to disclose their group assignment to measurement staff at subsequent visits; (3) measurements used to determine the presence of the metabolic syndrome included automated blood pressure and laboratory tests (fasting glucose, triglyceride, and high-density lipoprotein cholesterol levels) that are unlikely to be affected by human bias; and (4) physicians were explicitly informed of the importance of not making changes to their usual approach to lifestyle counseling during the study.

Follow-up data collection occurred within a laboratory removed from the participating medical clinics at 6-month intervals after randomization. Primary outcome data and physical activity data based on the 7-day Physical Activity Recall interview¹² were obtained at all visits. Information on adverse events and medication use was also obtained by self-report at each visit.

OUTCOME MEASURES

The primary outcome variable was WC measured at the superior edge of the iliac crest.¹³ Secondary outcomes included common metabolic risk factors, body fat percentage measured using bioelectrical impedance (BCA-418; Tanita Corporation of America, Inc), and the metabolic syndrome identified using the

consensus-harmonized definition and a WC threshold of at least 102 cm in men and at least 88 cm in women.¹⁴ All metabolic measurements were performed in the morning after an overnight fast using standard procedures.⁸

SAMPLE SIZE AND STATISTICAL POWER

Sample size and power calculations were computed for WC and the metabolic syndrome. Given that WC is a continuous variable and the metabolic syndrome is a dichotomous variable, the sample size derivation was based on the metabolic syndrome. Assuming an α level of .05, a β level of .20, and a study population metabolic syndrome prevalence of 55%, 174 subjects were required in each study arm to identify a 15% reduction in the metabolic syndrome prevalence. The sample size achieved was 490, including 241 (169 women and 72 men) in the usual care arm and 249 (175 women and 74 men) in the intervention arm. This sample size provided a power of more than 99% to detect a 5% (5.3 cm with an SD of 11 cm) difference in WC and a power of more than 88% to detect a 3% (3.2-cm) difference in WC. For the subset analysis in men, we had a power of more than 82% to detect a 5% (5.3-cm) difference in WC.

STATISTICAL ANALYSIS

Analyses were performed on an intent-to-treat basis.¹⁵ All randomized subjects were included. All analyses were performed using commercially available software (SAS, version 9.2; SAS Institute, Inc). An α value of .05 was used to determine statistical significance. Differences in continuous and categorical variables between dropouts and participants who completed the study were examined using a 2-tailed *t* test and a χ^2 test, respectively. For WC, a linear mixed model for repeated measures over time was applied separately for men and women. The model included the following fixed effects: intervention, time, and their 2-factor interactions, with age and medical clinic as covariates. For the metabolic syndrome, a generalized linear mixed model with a logit link was applied using the same modeling approach used for WC. An unstructured covariance matrix was imposed for these models. Estimated within-group changes in WC between baseline and 6 to 24 months were estimated and compared using contrasts within the mixed models. Baseline outcome was further included in the mixed models as a covariate to determine the change in outcome from baseline.

RESULTS

Of the 490 participants, 396 (80.8%) returned for follow-up testing at 24 months. Return for follow-up within the usual care and intervention groups was 85.5% and 76.3%, respectively, and for men and women, 82.9% and 79.9%, respectively (Figure 1). There were no significant baseline differences between participants who completed vs those who dropped out of the trial (data not shown). Adherence to the intervention, defined as the percentage of sessions attended with the health educator, averaged 73.5% (73.4% in men and 73.9% in women) and ranged from 0% (n=3) to 100% (n=35); 127 participants attended at least 90% of the expected sessions.

As summarized in **Table 1**, the mean (SD) age of the participants in the usual care and intervention groups was 52.4 (11.8) and 51.3 (11.0) years, respectively. The mean (SD) WC level in the groups was 105.9 (10.8) and 107.2

Table 1. Participant Characteristics^a

Characteristic	All		Men		Women	
	Usual Care (n = 241)	Intervention (n = 249)	Usual Care (n = 72)	Intervention (n = 74)	Usual Care (n = 169)	Intervention (n = 175)
Age, y	52.4 (11.8)	51.3 (11.0)	55.7 (11.5)	53.2 (10.7)	50.9 (11.7)	50.5 (11.1)
Anthropometric variables						
WC, cm	105.9 (10.8)	107.2 (11.0)	113.1 (9.4)	113.9 (9.7)	102.8 (9.8)	104.3 (10.3)
Weight, kg	89.2 (14.1)	91.2 (14.1)	98.2 (13.5)	101.4 (13.2)	85.3 (12.5)	86.9 (12.1)
BMI	32.0 (4.2)	32.6 (4.1)	32.0 (4.0)	32.4 (3.7)	32.0 (4.3)	32.7 (4.3)
Body fat, %	39.8 (7.0)	40.1 (7.3)	31.3 (4.1)	31.2 (4.8)	43.5 (4.2)	43.8 (4.4)
Cardiometabolic variables						
Total cholesterol level, mg/dL	196.2 (40.3)	201.5 (41.9)	184.4 (43.6)	192.0 (41.7)	201.3 (37.8)	205.6 (41.4)
LDL-C level, mg/dL	112.4 (34.5)	115.6 (36.0)	106.9 (38.0)	109.3 (36.4)	114.7 (32.7)	118.3 (35.6)
HDL-C level, mg/dL	56.2 (15.5)	56.1 (14.1)	46.5 (11.2)	48.2 (11.9)	60.2 (15.2)	59.4 (13.7)
Triglyceride level, mg/dL	139.2 (69.3)	151.2 (86.3)	157.5 (73.4)	174.3 (98.4)	131.3 (66.0)	141.4 (78.9)
Fasting glucose level, mg/dL	92.9 (19.5)	94.1 (24.2)	98.0 (22.4)	98.4 (28.2)	90.7 (17.8)	92.3 (22.2)
Blood pressure, mm Hg						
Systolic	119.6 (14.8)	119.3 (13.7)	123.2 (13.2)	120.1 (13.5)	118.1 (15.2)	119.0 (13.7)
Diastolic	75.9 (8.6)	75.6 (8.7)	78.6 (7.6)	78.8 (9.0)	74.8 (8.8)	74.2 (8.2)
Metabolic syndrome prevalence, No. (%)	87 (36.1)	96 (38.6)	39 (54.2)	40 (54.1)	48 (28.4)	56 (32.0)
Indication for medication use, No. (%)						
Control blood pressure	80 (33.2)	64 (25.7)	32 (44.4)	23 (31.1)	48 (28.4)	41 (23.4)
Control lipid/cholesterol levels	5 (2.1)	8 (3.2)	5 (6.9)	7 (9.5)	0	1 (0.6)
Control glucose levels	18 (7.5)	22 (8.8)	10 (13.9)	13 (17.6)	8 (4.7)	9 (5.1)
Physical activity, kcal/kg/d	33.3 (2.5)	34.3 (3.3)	34.9 (3.4)	35.6 (4.5)	33.5 (1.9)	33.7 (2.4)

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; WC, waist circumference.

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

^aUnless otherwise indicated, data are presented as mean (SD).

Table 2. WC During and After Intervention^a

	Baseline WC, cm	Within-Group Changes in WC, cm				P Value ^b
		6 mo	12 mo	18 mo	24 mo	
All						
Usual care	108.0 (0.7)	-1.1 (0.3)	-0.9 (0.4)	-0.4 (0.4)	0.2 (0.4)	
Intervention	109.1 (0.7)	-3.1 (0.3)	-2.5 (0.4)	-1.8 (0.4)	-0.9 (0.4)	
P value ^c		<.001	.001	.01	.05	<.001
Men						
Usual care	113.0 (1.1)	-1.0 (0.5)	-1.3 (0.5)	-0.5 (0.6)	0.1 (0.6)	
Intervention	113.9 (1.1)	-3.2 (0.4)	-2.9 (0.6)	-2.2 (0.6)	-1.6 (0.6) ^d	
P value ^c		<.001	.04	.04	.049	.009
Women						
Usual care	102.8 (0.8)	-1.2 (0.3)	-0.8 (0.4)	-0.4 (0.5)	0.3 (0.5)	
Intervention	104.4 (0.8)	-3.0 (0.3)	-2.4 (0.4)	-1.6 (0.5)	-0.6 (0.5)	
P value ^c		<.001	.01	.10	.24	.02
		No. of Participants				
All						
Usual care	241	213	208	203	206	
Intervention	249	225	207	201	190	
Men						
Usual care	72	65	63	62	63	
Intervention	74	67	61	60	58	
Women						
Usual care	169	148	145	141	143	
Intervention	175	158	146	141	132	

Abbreviation: WC, waist circumference.

^aValues are expressed as estimated means (SE) and mean changes (SE) from sex-specific mixed-effects models adjusted for age and family medicine clinic.

^bIndicates overall P value for the main effect of group.

^cIndicates group comparison at each time point.

^dP < .001 for within-group comparison of 24-month value compared with baseline.

(11.0) cm, respectively. Rates of medication use for blood pressure and lipid and glucose levels were not different between groups.

Table 2 presents the primary outcome measure. A significant main effect was observed for change in WC

in response to the intervention compared with usual care (P < .001). The mean reduction in WC was greater in the intervention group than in the usual care group at each follow-up visit and remained statistically different at 24 months (mean [SE], -0.9 [0.4])

Table 3. Anthropometric and Body Composition Variables During and After Intervention^a

Variable	Baseline, Mean (SE)	Within-Group Changes, Mean (SE)				P Value ^b
		6 mo	12 mo	18 mo	24 mo	
Weight, kg						
All						
Usual care	92.29 (0.87)	-0.66 (0.25)	-0.85 (0.36)	-0.73 (0.41)	-0.60 (0.41)	
Intervention	94.22 (0.86)	-2.37 (0.25)	-2.41 (0.34)	-1.70 (0.42)	-1.18 (0.42) ^c	
P value ^d		<.001	.002	.08	.33	.007
Men						
Usual care	98.67 (1.56)	-0.43 (0.43)	-0.77 (0.57)	0.11 (0.62)	0.39 (0.61)	
Intervention	101.26 (1.57)	-2.49 (0.42)	-2.34 (0.58)	-1.59 (0.63)	-1.48 (0.63)	
P value ^d		<.001	.05	.06	.03	.01
Women						
Usual care	85.47 (0.92)	-0.81 (0.31)	-0.94 (0.43)	-1.38 (0.50)	-1.24 (0.53) ^e	
Intervention	86.87 (0.91)	-2.37 (0.30)	-2.49 (0.42)	-2.02 (0.50)	-1.24 (0.53) ^e	
P value ^d		<.001	.01	.36	.99	.09
BMI						
All						
Usual care	32.12 (0.29)	-0.23 (0.09)	-0.27 (0.13)	-0.25 (0.15)	-0.23 (0.15)	
Intervention	32.57 (0.29)	-0.82 (0.09)	-0.84 (0.13)	-0.59 (0.15)	-0.46 (0.16) ^c	
P value ^d		<.001	.001	.10	.26	.007
Men						
Usual care	32.15 (0.44)	-0.12 (0.14)	-0.23 (0.18)	0.04 (0.19)	0.12 (0.20)	
Intervention	32.34 (0.44)	-0.76 (0.14)	-0.72 (0.18)	-0.50 (0.20)	-0.56 (0.21) ^c	
P value ^d		<.001	.06	.05	.02	.01
Women						
Usual care	32.02 (0.33)	-0.34 (0.12)	-0.34 (0.12)	-0.49 (0.18)	-0.45 (0.19) ^e	
Intervention	32.70 (0.32)	-0.90 (0.11)	-0.93 (0.14)	-0.73 (0.18)	-0.50 (0.19) ^c	
P value ^d		<.001	.01	.35	.88	.08
Body Fat, %						
All						
Usual care	37.52 (0.30)	-0.39 (0.15)	-0.28 (0.20)	-0.35 (0.23)	-0.19 (0.21)	
Intervention	37.62 (0.30)	-1.14 (0.15)	-1.16 (0.20)	-0.70 (0.23)	-0.66 (0.21) ^c	
P value ^d		<.001	.001	.13	.10	.008
Men						
Usual care	31.23 (0.52)	-0.22 (0.26)	-0.22 (0.33)	-0.21 (0.39)	0.22 (0.34)	
Intervention	31.33 (0.52)	-1.32 (0.26)	-1.05 (0.34)	-0.61 (0.40)	-0.75 (0.35) ^e	
P value ^d		.003	.08	.47	.05	.04
Women						
Usual care	43.53 (0.33)	-0.48 (0.18)	-0.35 (0.23)	-0.46 (0.26)	-0.45 (0.24)	
Intervention	43.88 (0.32)	-1.06 (0.17)	-1.26 (0.23)	-0.77 (0.26)	-0.69 (0.25) ^c	
P value ^d		.02	.01	.39	.48	.07

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared).

^a Results are estimated means (SE) and mean changes (SE) from sex-specific mixed-effects models, and all are adjusted for age and family medicine clinic.

^b Indicates overall P value for the main effect of group.

^c P < .01 for within-group comparison of 24-month value compared with baseline.

^d Group comparison of mean changes at each time point.

^e P < .05 for within-group comparison of 24-month value compared with baseline.

vs 0.2 [0.4] cm; P=.05). Secondary analyses revealed significant main effects for a change in WC in men (P=.009) and women (P=.02; Table 2). In men, the reduction in WC was greater within the intervention than usual care groups at each follow-up visit and remained statistically different at 24 months (P=.049). In women, the reduction in WC was greater in the intervention group compared with the usual care group at 6 and 12 months (P≤.01) but was not sustained at 24 months.

Table 3 and **Table 4** present the secondary outcome measures. A significant main effect was observed for change in body weight, BMI, and body fat percentage in response to the intervention compared with usual care (P<.05 for all). The mean reduction for all 3 vari-

ables was greater in the intervention group compared with the usual care group at 6 and 12 months (P≤.005 for all) but was not sustained at 24 months (P≥.10 for all). For all 3 variables, significant within-group reductions were for the intervention alone (P<.01). For men, significant main effects for change in body weight (P=.01), BMI (P=.01), and body fat percentage (P=.04) were observed in the intervention group compared with the usual care group at 24 months. For women, no significant differences between treatment groups were observed for any anthropometric variable at 24 months (P>.05 for all).

No differences between groups were observed for any of the cardiometabolic risk factors or the metabolic syndrome at 24 months (P>.05); however, there were reductions within groups over time for several cardiometabolic

Table 4. Metabolic Risk Factors During and After Intervention^a

Variable	Baseline, Mean (SE)	Within-Group Changes, Mean (SE)				P Value ^b
		6 mo	12 mo	18 mo	24 mo	
Triglyceride Level, mg/dL						
All						
Usual care	144.93 (5.40)	-11.50 (3.85)	-11.37 (4.12)	-14.81 (4.08)	-18.62 (4.63) ^c	
Intervention	155.93 (5.33)	-15.37 (3.78)	-22.58 (4.12)	-21.99 (4.09)	-22.06 (4.55) ^c	
P value ^d		.45	.04	.19	.58	.17
Men						
Usual care	157.36 (10.31)	-11.84 (7.70)	-13.61 (7.89)	-11.12 (8.17)	-18.04 (9.53) ^e	
Intervention	171.46 (10.29)	-23.73 (7.61)	-33.39 (7.95)	-33.77 (8.24)	-30.55 (9.72) ^c	
P value ^d		.27	.09	.05	.36	.09
Women						
Usual care	131.05 (5.62)	-9.15 (4.09)	-6.76 (4.52)	-14.02 (4.32)	-16.57 (4.70) ^c	
Intervention	141.54 (5.52)	-9.39 (3.98)	-14.86 (4.49)	-14.75 (4.35)	-16.68 (4.77) ^c	
P value ^d		.96	.20	.90	.99	.66
HDL-C Level, mg/dL						
All						
Usual care	52.65 (0.95)	-2.24 (0.55)	-3.75 (0.62)	-5.89 (0.64)	-8.49 (0.66) ^c	
Intervention	53.59 (0.94)	-2.01 (0.54)	-3.96 (0.62)	-5.64 (0.64)	-9.19 (0.68) ^c	
P value ^d		.76	.80	.78	.44	.87
Men						
Usual care	45.75 (1.34)	-2.17 (0.91)	-2.74 (0.95)	-5.03 (1.01)	-7.46 (1.03) ^c	
Intervention	48.10 (1.34)	0.35 (0.90)	-2.27 (0.96)	-3.64 (1.02)	-7.83 (1.06) ^c	
P value ^d		.05	.73	.34	.80	.37
Women						
Usual care	60.10 (1.11)	-3.02 (0.65)	-4.95 (0.75)	-7.12 (0.76)	-9.65 (0.80) ^c	
Intervention	59.44 (1.09)	-3.78 (0.63)	-5.50 (0.74)	-7.39 (0.76)	-10.50 (0.81) ^c	
P value ^d		.40	.63	.82	.46	.049
Fasting Glucose Level, mg/dL						
All						
Usual care	94.97 (1.50)	0.65 (0.81)	1.67 (0.95)	3.14 (1.04)	3.97 (1.12) ^c	
Intervention	95.96 (1.48)	0.55 (0.80)	-1.55 (0.95)	2.00 (1.04)	1.49 (1.14)	
P value ^d		.93	.01	.42	.11	.10
Men						
Usual care	98.48 (2.96)	1.56 (1.62)	2.00 (1.52)	0.98 (1.84)	4.20 (2.38)	
Intervention	99.39 (2.95)	0.51 (1.61)	-2.19 (1.54)	4.82 (1.86)	1.17 (2.41)	
P value ^d		.64	.06	0.14	.37	.57
Women						
Usual care	91.39 (1.51)	0.01 (0.87)	1.70 (1.12)	3.94 (1.17)	3.89 (1.10) ^c	
Intervention	92.90 (1.48)	0.34 (0.84)	-0.99 (1.11)	0.84 (1.16)	1.58 (1.12)	
P value ^d		.79	.08	.06	.14	.11
Systolic Blood Pressure, mm Hg						
All						
Usual care	120.41 (0.94)	-1.50 (0.83)	-2.35 (0.82)	-2.08 (0.85)	-0.72 (0.91)	
Intervention	119.78 (0.93)	-2.59 (0.81)	-2.87 (0.82)	-0.84 (0.85)	-0.66 (0.93)	
P value ^d		.33	.64	.28	.96	.94
Men						
Usual care	123.00 (1.58)	-2.84 (1.30)	-3.46 (1.38)	-1.06 (1.40)	-0.31 (1.52)	
Intervention	120.01 (1.58)	-1.83 (1.28)	-2.92 (1.40)	-0.99 (1.42)	-1.69 (1.56)	
P value ^d		.58	.78	.97	.53	.96
Women						
Usual care	118.47 (1.03)	-0.65 (0.98)	-1.43 (0.94)	-2.67 (0.99)	-0.70 (1.06)	
Intervention	119.59 (1.01)	-2.64 (0.96)	-2.39 (0.93)	-0.89 (0.98)	-0.01 (1.07)	
P value ^d		.15	.47	.20	.65	.91

(continued)

bolic variables ($P < .05$; Table 4). No differences between groups for men or women were observed for any of the cardiometabolic risk factors at 24 months ($P > .05$). However, the proportion of men with the metabolic syndrome at 24 months was reduced in response to the intervention compared with usual care ($P = .03$). At no point during follow-up was the prevalence of the metabolic syndrome different for women in the intervention compared with usual care.

Although no differences between groups were observed for physical activity levels at 24 months (data not shown), the reduction in WC was greater among men

and women in the intervention group in the highest vs the lowest tertiles of change in physical activity (**Figure 2**; $P = .04$).

The participants' physicians did not change the prescription of medication for control of blood pressure and levels of glucose, low- and high-density lipoprotein cholesterol, and triglycerides in response to the intervention (**Table 5**). Cardiovascular events and resulting physician visits and hospitalizations were less common in the intervention group compared with the usual care group (**Table 6**). Rates of musculoskeletal injuries were similar between groups.

Table 4. Metabolic Risk Factors During and After Intervention^a (continued)

Variable	Baseline, Mean (SE)	Within-Group Changes, Mean (SE)				P Value ^b
		6 mo	12 mo	18 mo	24 mo	
Diastolic Blood Pressure, mm Hg						
All						
Usual care	76.77 (0.59)	-1.19 (0.47)	-1.76 (0.47)	-2.03 (0.52)	-0.88 (0.53)	
Intervention	76.57 (0.59)	-2.51 (0.47)	-2.34 (0.47)	-1.62 (0.52)	-1.36 (0.54) ^e	
P value ^d		.04	.37	.55	.51	.37
Men						
Usual care	78.50 (0.99)	-1.75 (0.83)	-2.53 (0.82)	-2.27 (0.87)	-0.88 (0.88)	
Intervention	78.59 (0.99)	-2.91 (0.82)	-2.98 (0.83)	-1.81 (0.88)	-2.26 (0.90) ^e	
P value ^d		.33	.70	.71	.28	.53
Women						
Usual care	74.89 (0.66)	-0.65 (0.54)	-1.02 (0.54)	-1.77 (0.60)	-0.61 (0.62)	
Intervention	74.29 (0.65)	-2.05 (0.53)	-1.63 (0.54)	-1.32 (0.60)	-0.71 (0.63)	
P value ^d		.06	.43	.60	.91	.53
Total Cholesterol Level, mg/dL						
All						
Usual care	191.33 (2.83)	-4.79 (1.83)	-3.59 (1.92)	-4.33 (2.08)	-10.55 (2.09) ^c	
Intervention	198.62 (2.79)	-6.04 (1.79)	-8.39 (1.92)	-8.43 (2.09)	-12.27 (2.13) ^c	
P value ^d		.61	.06	.15	.55	.17
Men						
Usual care	183.80 (5.08)	-6.06 (3.15)	-4.91 (3.32)	-3.76 (3.61)	-9.13 (4.24) ^e	
Intervention	189.88 (5.09)	-4.48 (3.12)	-3.00 (3.35)	-5.34 (3.64)	-11.04 (4.35) ^e	
P value ^d		.72	.68	.76	.76	.99
Women						
Usual care	201.04 (3.00)	-4.46 (2.11)	-4.21 (2.20)	-5.55 (2.39)	-11.63 (2.19) ^c	
Intervention	206.00 (2.92)	-7.70 (3.09)	11.91 (2.17)	-10.73 (2.38)	13.46 (2.23) ^c	
P value ^d		.40	.01	.13	.56	.09
LDL-C Level, mg/dL						
All						
Usual care	110.02 (2.46)	-0.65 (1.59)	2.34 (1.70)	4.25 (1.81)	1.55 (1.77)	
Intervention	114.17 (2.45)	-1.06 (1.57)	-0.22 (1.70)	1.43 (1.82)	1.48 (1.81)	
P value ^d		.85	.27	.25	.98	.44
Men						
Usual care	107.25 (4.39)	-2.26 (2.74)	-0.17 (2.82)	2.62 (3.03)	1.25 (3.47)	
Intervention	108.16 (4.44)	-0.19 (2.73)	5.77 (2.84)	4.95 (3.04)	2.96 (3.55)	
P value ^d		.59	.14	.59	.73	.40
Women						
Usual care	114.79 (2.61)	0.23 (1.83)	2.51 (1.97)	4.45 (2.10)	1.44 (1.88)	
Intervention	118.28 (2.56)	-1.21 (1.79)	-3.70 (1.96)	-0.50 (2.10)	0.64 (1.92)	
P value ^d		.58	.03	.10	.77	.13
Metabolic Syndrome^f						
All						
Usual care	39.91 (3.55)	0.0 (3.2)	2.2 (3.3)	8.8 (3.3)	15.0 (3.5) ^c	
Intervention	42.85 (3.47)	-3.9 (3.1)	-1.7 (3.2)	5.3 (3.2)	9.9 (3.6) ^e	
P value ^d		.39	.40	.45	.32	.28
Men						
Usual care	55.06 (6.02)	-1.6 (5.5)	-2.8 (6.5)	8.7 (5.9)	18.8 (6.4) ^c	
Intervention	55.74 (5.95)	-8.3 (5.4)	-6.1 (6.4)	-1.5 (6.1)	-1.8 (7.0)	
P value ^d		.39	.72	.23	.03	.13
Women						
Usual care	28.76 (3.55)	1.7 (3.5)	6.0 (3.4)	9.6 (3.6)	13.2 (3.8) ^c	
Intervention	32.84 (3.62)	-1.0 (3.4)	2.5 (3.5)	9.7 (3.6)	16.5 (4.0) ^c	
P value ^d		.58	.45	.93	.66	.78

Abbreviations: HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol. SI conversion factors: To convert cholesterol to millimoles per liter, multiply by 0.0259; triglycerides to millimoles per liter, multiply by 0.0113; and glucose to millimoles per liter, multiply by 0.0555.

^aResults are estimated means (SE) and mean changes (SE) from sex-specific mixed-effects models, and all are adjusted for age and family medicine clinic.

^bIndicates overall P value for the main effect of group.

^cP < .001 for within-group comparison of 24-month value compared with baseline.

^dGroup comparison of mean changes at each time point.

^eP < .05 for within-group comparison of 24-month value compared with baseline.

^fExpressed as estimated prevalence (SE) (percentage of subjects with the metabolic syndrome) and changes of prevalence (SE) of the metabolic syndrome derived from sex-specific, generalized, linear mixed models adjusted for age and family medicine clinic.

COMMENT

The primary finding of this trial is that a lifestyle-based intervention delivered by a trained health educator within the primary care setting was associated with significant

reductions in abdominal obesity compared with usual care. However, the magnitude of the reduction in WC was modest and the effectiveness of the intervention was restricted to men, suggesting that behavioral interventions designed to reduce obesity may be sex dependent.

Our finding that WC in response to an intensive behavioral intervention was reduced at 24 months contrasts with previous studies in which attempts by primary care physicians alone to provide low- to moderate-intensity counseling failed to achieve or sustain weight loss.^{6,16} Our findings also contrast with those of Logue et al,¹⁷ who conducted a 2-year randomized clinical trial with 665 overweight and obese adults from 15 primary care sites. In that study, the combination of mailed patient materials and monthly telephone calls aimed at increasing physical activity and consumption of a balanced diet failed to achieve a reduction in WC. The reductions we observed in abdominal obesity are similar to those reported in response to a more intensive lifestyle modification program implemented in primary care that included on-site supervised aerobic and resistance exercise.¹⁸ Our principal finding also differs from the recent findings of the Practice-Based Opportunities for Weight Reduction Trial at the University of Pennsylvania (POWER-UP trial), in which obese patients in primary care randomized to a 2-year lifestyle intervention provided by the combination of the primary care provider (quarterly visits) and lifestyle coaches (monthly visits) did not reduce body weight compared with usual care by the primary care provider alone.¹⁹ However, in the POWER-UP trial, an enhanced counseling strategy that combined the behavioral intervention with meal replacement or pharmacological (orlistat or sibutramine hydrochloride) intervention achieved significant weight loss at 2 years compared with usual care.

Although the reduction in WC we observed was maintained at 2 years in men, the magnitude of the reduction was modest, and the major improvement occurred in the first 6 months with a general erosion of benefit during the remaining 18 months. This pattern of attenuated benefit over time is not uncommon to lifestyle-based interventions regardless of setting. Similar to our finding with WC, the weight reduction in response to the enhanced lifestyle intervention compared with usual care in the POWER-UP trial at 12 months was substantially reduced in the second year,¹⁹ suggesting that in both studies the benefit may have been abolished with longer follow-up. These findings confirm that much of the benefit in response to lifestyle intervention in primary care settings regardless of the counseling model used occurs early during the intensive phase, with a general erosion of benefit during the maintenance phase characterized by a tapering of contact with the patient. Whether increasing the frequency of contact face-to-face or electronically (eg, booster sessions) would facilitate adherence to healthy behaviors and associated obesity reduction in a cost-effective manner remains to be demonstrated.

The principal finding from our study and others also reinforces the challenges inherent to the sustained adoption of healthy behaviors in today's environment and suggests that the prevention of weight gain combined with modest reduction in WC during the 2-year study may reflect a more realistic expectation. Even a modest reduction in WC has benefits because, for a given BMI, increases in WC are positively associated with increased risk of mortality²⁰ and cardiovascular disease.²¹

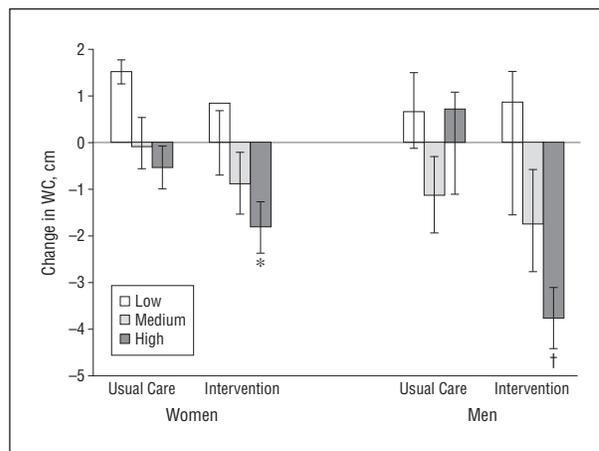


Figure 2. Changes in waist circumference (WC) during the 24-month study by tertile of change (low, medium, and high) in physical activity. * $P < .05$ compared with low tertile. † $P < .01$ compared with low tertile.

It is suggested that men show greater weight loss than women in response to diet and exercise.²² We confirmed that, for WC and the metabolic syndrome, men in the intervention group responded favorably compared with the usual care group, whereas women did not. Reasons for the observed sex difference are unclear. Our intervention was delivered by female health educators to all participants, and adherence throughout the intervention was similar, with men and women both attending 73.5% of the planned sessions. Although men sustained reductions in WC throughout the 2-year intervention, the women in the intervention group responded well in the first year but showed notable recidivism in the second year. The intervention provided fewer person-to-person contacts in the second year. The reduced contact frequency in the second year may be effective for men to maintain behaviors that result in favorable changes in WC and metabolic risk factors but may have negatively affected behavioral adherence in women. Alternatively, our finding is consistent with other reports that women are more resistant than men to a change in body weight or body composition consequent to lifestyle intervention alone.^{22,23} Whether resistance to weight loss and/or a failure to achieve one's WC or weight loss expectations affects women's adherence to treatment differently than men's is unclear.²⁴

That our behavioral intervention was not associated with improvement in the cardiometabolic risk factors is consistent with other reports in which modest reductions in WC were observed consequent to prolonged^{16,18} or short-term follow-up.²⁵ It is possible that the reduction in WC or body weight observed is below the threshold required for reduction in cardiometabolic risk. Alternatively, the lack of treatment effect may be explained by the observation that about 40% of our participants were taking medications to lower lipid levels or blood pressure, and baseline values were well within the clinically acceptable range. That our behavioral intervention was not associated with a reduction in the proportion of participants with the metabolic syndrome contrasts with shorter-term (12-month) trials that report a lowering of metabolic syndrome prevalence in response to diet and/or

Table 5. Changes in Medication Use During Intervention^a

Indication for Medication Use	Self-reported Medication Use, No. (%) of Participants by Study Group ^b					
	All		Men		Women	
	Usual Care (n = 206)	Intervention (n = 190)	Usual Care (n = 63)	Intervention (n = 58)	Usual Care (n = 143)	Intervention (n = 132)
Control blood pressure						
No change	199 (96.6)	184 (96.8)	60 (95.2)	57 (98.3)	139 (97.2)	127 (96.2)
Started	5 (2.4)	5 (2.6)	1 (1.6)	1 (1.7)	4 (2.8)	4 (3.0)
Discontinued	2 (1.0)	1 (0.5)	2 (3.2)	0	0	1 (0.8)
Control LDL-C level						
No change	196 (95.1)	184 (96.8)	60 (95.2)	54 (93.1)	136 (95.1)	130 (98.5)
Started	8 (3.9)	5 (2.6)	2 (3.2)	3 (5.2)	6 (4.2)	2 (1.5)
Discontinued	2 (1.0)	1 (0.5)	1 (1.6)	1 (1.7)	1 (0.7)	0
Control HDL-C and triglyceride levels						
No change	205 (99.5)	187 (98.4)	62 (98.4)	57 (98.3)	143 (100)	130 (98.5)
Started	0	3 (1.6)	0	1 (1.7)	0	2 (1.5)
Discontinued	1 (0.5)	0	1 (1.6)	0	0	0
Control glucose level						
No change	203 (98.5)	186 (97.9)	63 (100)	57 (98.3)	140 (97.9)	129 (97.7)
Started	3 (1.5)	4 (2.1)	0	1 (1.7)	3 (2.1)	3 (2.3)
Discontinued	0	0	0	0	0	0

Abbreviations: HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

^aComparison of groups for change in medication use determined with the Fisher exact test revealed no significant differences ($P > .10$).

^bPercentages have been rounded and might not total 100.

Table 6. Adverse Events Reported by Participants as Occurring During 24 Months of Intervention and Usual Care

	No. (%) by Study Group					
	Intervention			Usual Care		
	Men (n = 74)	Women (n = 175)	All Group (n = 249)	Men (n = 72)	Women (n = 169)	All Group (n = 241)
Musculoskeletal event during or after exercise ^a						
Any	96 (129.7)	204 (116.6)	300 (120.5)	96 (133.3)	215 (127)	311 (129.0)
Requiring a physician visit	51 (68.9)	124 (70.9)	175 (70.3)	50 (69.4)	110 (65.1)	160 (66.4)
Requiring hospitalization	2 (2.7)	3 (1.7)	5 (2.0)	2 (2.8)	10 (5.9)	12 (5.0)
Potential cardiovascular event ^b						
Any	46 (62.2)	69 (39.4)	115 (46.2)	39 (54.2)	98 (58.0)	137 (56.8)
Requiring a physician visit	36 (48.6)	40 (22.9)	76 (30.5)	29 (40.3)	54 (32.0)	83 (34.4)
Requiring hospitalization	7 (9.5)	2 (1.1)	9 (3.6)	9 (12.5)	9 (5.3)	18 (7.5)

^aIncludes pain or cramping in leg, knee, or foot; strained muscle, tendon, or ligament; and broken bone.

^bIncludes chest pain, difficulty breathing, and dizziness or loss of consciousness.

exercise compared with control arms in obese adults.^{26,27} In those studies, the reduction in the prevalence of the metabolic syndrome was removed after statistical control for weight loss²⁶ or body fat loss.²⁷ Our sex-based analyses support this observation because, in contrast to women, men within the intervention group reduced body weight, WC, and total adiposity. Concurrently, the proportion of men in the intervention group with the metabolic syndrome was reduced by approximately 20% at 2 years compared with men in the usual care group.

Strengths of the PROACTIVE trial include excellent adherence during the intervention and a favorable retention rate compared with obesity-related pharmacological trials that routinely report loss to follow-up of 40% to 50%.^{28,29} The intervention was delivered entirely within the primary care setting, facilitating direct communica-

tion between the physician and the health educator without disturbing the flow of patients or the regular practice of the physicians. That both men and women attended 73.5% of the planned counseling sessions confirms the willingness of patients to participate in long-term interventions located in primary care settings. The intervention was completed with no increase in musculoskeletal injuries and fewer cardiovascular complications. Our sample was diverse in age, sex, and medication use, making our findings generalizable; however, the participants were abdominally obese and predominantly white. Lack of objective measures for physical activity may have limited our ability to detect small differences between groups. Our study was not designed to test the relative contributions of dietary changes, increased physical activity, and weight loss to the reduction in WC or the meta-

bolic syndrome; thus, the independent effects of these components remain to be determined. However, that changes in WC were positively associated with increases in physical activity in a dose-response manner (Figure 2) is consistent with established observations.³⁰ Whether incorporating health educators into primary care settings is cost-effective remains to be determined.

Given the high prevalence of obesity and related medical complications, primary care providers will continue to encounter obese patients at exceedingly high rates. Our primary finding that intensive behavioral counseling delivered by trained experts in collaboration with the primary care physician can effectively achieve even modest reduction in abdominal obesity is encouraging. However, our findings also suggest that effective translation of obesity-reduction strategies in primary care settings may be sex dependent.

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