Annals of Internal Medicine ORIGINAL RESEARCH

Effects of Exercise Amount and Intensity on Abdominal Obesity and Glucose Tolerance in Obese Adults

A Randomized Trial

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Background: Exercise reduces obesity and related glucose tolerance, but whether increasing exercise intensity offers additional benefit at fixed exercise amounts is unknown.

Objective: To determine the separate effects of exercise amount and intensity on abdominal obesity and glucose tolerance.

Design: 24-week, single-center, parallel-group trial from 2009 to 2013. (ClinicalTrials.gov: NCT00955071)

Setting: Kingston, Ontario, Canada.

Participants: 300 abdominally obese adults.

Intervention: Control (no exercise) (n = 75) or 5 weekly sessions of low-amount, low-intensity exercise (LALI) (180 and 300 kcal/session for women and men, respectively, at 50% of maximum oxygen consumption [$\dot{V}O_2$peak]) (n = 73); high-amount, low-intensity exercise (HALI) (360 and 600 kcal/session, respectively, at 50% of $\dot{V}O_2$peak) (n = 76); or high-amount, high-intensity exercise (HAHI) (360 and 600 kcal/session, respectively, at 75% of $\dot{V}O_2$peak) (n = 76). Daily unsupervised physical activity and sedentary time were measured by accelerometer.

Measurements: Waist circumference and 2-hour glucose level (primary outcomes) and cardiorespiratory fitness and measures of insulin action (secondary measurements).

Results: 217 participants (72.3%) completed the intervention. Mean exercise time in minutes per session was 31 (SD, 4.4) for LALI, 58 (SD, 7.6) for HALI, and 40 (SD, 6.2) for HAHI. Daily unsupervised physical activity and sedentary time did not change in any exercise group versus control (P > 0.33). After adjustment for age and sex in a linear mixed model, reductions in waist circumference were greater in the LALI (−3.9 cm [95% CI, −5.6 to −2.3 cm]; P < 0.001), HALI (−4.6 cm [CI, −6.2 to −3.0 cm]; P < 0.001), and HAHI (−4.6 cm [CI, −6.3 to −2.9 cm]; P < 0.001) groups than the control group but did not differ among the exercise groups (P > 0.43). After adjustment for covariates, reductions in 2-hour glucose level were greater in the HAHI group (−0.7 mmol/L [−12.5 mg/dL] [CI, −1.3 to −0.1 mmol/L {−23.5 to −1.5 mg/dL}]; P = 0.027) than the control group but did not differ for the LALI or HALI group versus the control group (P > 0.159). Weight loss was greater in all exercise groups than the control group (P < 0.001); however, reduction in body weight did not differ among the exercise groups (P > 0.182).

Limitation: The clinical importance of reducing 2-hour glucose level in nondiabetic adults remains undetermined.

Conclusion: Fixed amounts of exercise independent of exercise intensity resulted in similar reductions in abdominal obesity. Reduction in 2-hour glucose level was restricted to high-intensity exercise.

Primary Funding Source: Canadian Institutes of Health Research.

Ann Intern Med. 2015;162:325-334. doi:10.7326/M14-1189 **www.annals.org**
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The high prevalence of obesity and associated type 2 diabetes mellitus among adults presents a major public health challenge (1). Physical inactivity is a significant determinant of obesity, and most adults in the United States are inactive (2). Although progress has been made to elucidate the effects of exercise as a strategy for reducing obesity and related glucose tolerance, the specific exercise exposures required to achieve optimal benefit continue to be the source of considerable uncertainty and debate.

Implicit within current guidelines for physical activity and health is the observation that 75 minutes of weekly high-intensity exercise is equivalent to 150 minutes of weekly lower-intensity exercise (3, 4). Therefore, guidelines suggest that there are no added health benefits of high-intensity exercise other than the shorter time frame needed to expend the appropriate amount of energy. Thus, the benefits of engaging in high-intensity exercise are attributed to the greater amount of energy expenditure per unit of time and do not relate to intensity per se (3). The scientific committee report from which current guidelines were developed recognized that many unanswered issues exist in response to the question of how much of what type of activity is appropriate for a given health outcome, and acknowledged that future investigations need to evaluate the effects of exercise intensity at fixed amounts of energy expenditure.

We therefore performed a randomized clinical trial to investigate the separate effects of habitual exercise differing in amount and intensity on abdominal obesity and glucose tolerance. We studied abdominally obese adults because they are at substantially increased risk for morbidity (5) and mortality (6) and because it is estimated that 60% of men and 45% of women between the ages of 35 and 65 years in the United States are abdominally obese (7).

See also:

Editorial comment 385
Summary for Patients I-19

EDITORS' NOTES

Context

Whether there is added benefit from performing the same amount of exercise at a higher intensity is unclear.

Contribution

In this 24-week study, participants randomly assigned to complete the same total amount of exercise at higher or lower intensities had similar reductions in waist circumference and weight. High-intensity exercise alone improved 2-hour glucose tolerance and led to the greatest increase in cardiorespiratory fitness.

Caution

The importance of improved 2-hour glucose tolerance in participants without diabetes is unclear.

Implication

For the same amount of exercise, higher-intensity exercise may not result in greater reduction in waist circumference or weight but may provide benefits in glucose tolerance and cardiorespiratory fitness.

METHODS

Setting and Participants

Details of the trial design and methods are published (8). We conducted a 24-week, single-center, parallel-group, randomized, controlled trial between 2009 to 2013. Potential participants were excluded if they reported a history of heart disease, stroke, or any condition that would prevent them from engaging in exercise; were already engaging in 2 or more planned exercise sessions per week; or were diabetic.

All participants provided informed consent before participation. The study was approved by the Queen's University Health Sciences Research Ethics Board, Kingston, Ontario, Canada.

Interventions

Participants were randomly assigned to 1 of the following groups: control (no exercise) or 5 sessions per week of low-amount, low-intensity exercise (LALI) (180 and 300 kcal/session for women and men, respectively, at 50% of maximum oxygen consumption [$\dot{V}O_2$peak]); high-amount, low-intensity exercise (HALI) (360 and 600 kcal/session for women and men, respectively, at 50% of $\dot{V}O_2$peak); or high-amount, high-intensity exercise (HAHI) (360 and 600 kcal/session for women and men, respectively, at 75% of $\dot{V}O_2$peak).

Exercise Interventions

All participants performed walk/jog exercise consistent with consensus recommendations on a treadmill for the time required to achieve the desired amount of exercise (energy expenditure in kilocalories per session, relative to $\dot{V}O_2$peak) 5 times per week for 24 weeks. Using the heart rate and $\dot{V}O_2$ data obtained from the baseline exercise test, we assigned the target heart rate associated with a $\dot{V}O_2$peak of approximately 50% (LALI and HALI) and approximately 75% (HAHI) for each participant. At these exercise intensities, the energy expenditure targets (exercise amount) for women and men, respectively, were 180 and 300 kcal for the LALI group and 360 and 600 kcal for the HALI and HAHI groups. Follow-up exercise tests to measure $\dot{V}O_2$peak were performed at weeks 4, 8, and 16 to verify the relationship between heart rate and $\dot{V}O_2$. Continual adjustment of the heart rate–$\dot{V}O_2$ relationship accounted for improvement in cardiorespiratory fitness (CRF), which alters the time required to achieve the prescribed exercise amount (for example, energy expenditure). Heart rate was monitored continuously for all exercise participants at every session to ensure adherence to the prescribed exercise intensity. All exercise sessions were supervised, and all exercise participants were asked not to engage in any structured exercise outside of the supervised sessions.

Nonexercise Control Group

Participants in the control group were asked to maintain their level of physical activity throughout the trial and received diet composition advice similar to that received in the exercise groups.

Daily Physical Activity

Unsupervised physical activity was monitored using ActiGraph GT3X accelerometers for 1-week periods at baseline and at 8, 16, and 25 weeks. Participants were required to wear the accelerometer for at least 4 days each period. Established accelerometer cut points were used to estimate physical activity and sedentary time (9).

Dietary Regimen

During a 1-week baseline period, participants were instructed to maintain baseline body weight by monitoring their calorie intake and recording their daily consumption of self-selected foods. During the intervention, participants were instructed to maintain the calorie intake targets measured during baseline. All participants were prescribed a balanced diet and were asked to submit daily dietary intake records during the intervention. Two weeks of records for all groups were analyzed using a computerized program to assess the accuracy of self-reported records.

Outcomes and Follow-up

Primary outcome variables were waist circumference (WC), which was measured at the superior edge of the iliac crest (10) at baseline and at 8 (exercise groups only), 16, and 24 weeks, and 2-hour glucose level, which was measured in response to a 2-hour, 75-g oral glucose tolerance test between 36 and 48 hours after the last exercise session at baseline and at 16 and 24 weeks (8). Secondary outcomes included CRF ($\dot{V}O_2$peak) assessed by using standard open-circuit spirometry techniques with a mass flow sensor (SensorMedics) during a graded exercise test in which participants walked on a treadmill at a self-selected speed at 0 elevation for 3 minutes, after which the incline was increased every 2 minutes until the participant stopped

voluntarily. Levels of glucose, triglycerides, high- and low-density lipoprotein cholesterol, and insulin and blood pressure were measured using established procedures (8). The Matsuda index (an indication of insulin sensitivity) was calculated as follows: (10 000/[{fasting glucose level × fasting insulin level} × {mean glucose level × mean insulin level during the oral glucose tolerance test}]$^{1/2}$) (11). There were separate assessment and intervention personnel, and all assessment personnel were blinded to participant randomization assignment.

Sample Size and Power

Sample size was determined for WC and 2-hour glucose level on the basis of reduction after treatment. Previous trials suggested that exercise-induced weight loss of approximately 6% was associated with WC reductions of 6.9 cm (SD, 2.6) in men (12) and 6.5 cm (SD, 2.6) in women (13). For 2-hour glucose level, mean reductions of 0.70 mmol/L (SD, 1.9) (12.6 mg/dL [SD, 34.2]) and 0.94 mmol/L (SD, 0.7) (16.9 mg/dL [SD, 12.6]) were seen in men and women, respectively (12, 13). The sample size calculation incorporated the larger SDs for WC and 2-hour glucose level.

The sample-size formula (equation 13 of Overall and Doyle [14]) relevant to the repeated-measures analysis of variance design was applied. The formula is based on a simple 2-group comparison of the pretreatment and posttreatment outcome changes, and it accounts for the correlation between the pretreatment and posttreatment outcome variables. With a correlation of 0.7 between pretreatment and posttreatment glucose tolerance and WC, and allowance for a dropout rate of 30%, a sample of 40 men or women with 28 completers in each treatment group gives more than 85% power to detect a mean difference of 2 cm in WC and a mean difference of 1.9 mmol/L (34.2 mg/dL) in glucose tolerance between any 2 treatment groups.

Randomization

Participants were randomly assigned to the 4 groups using the method of permuted blocks, with random block sizes of 4, 8, or 12 within strata. Randomization was stratified by sex and age, with a fifth stratum for the few couples participating to ensure that they were randomly assigned to the same treatment. The computer-generated randomization list was maintained by an independent statistician otherwise uninvolved in the study and was concealed from study personnel until the time of randomization. After baseline data collection, the study coordinator contacted the statistician by e-mail to obtain treatment assignment.

Statistical Analysis

Analyses were done on an intention-to-treat basis (15). All randomly assigned participants were included in the analyses. Differences in continuous and categorical variables between dropouts and participants who completed the study were examined by using a 2-tailed *t* test and a chi-square test, respectively. For WC, 2-hour glucose level, and all secondary outcomes, a linear mixed model for repeated measures over time was applied. The final mixed model included intervention group, time, and their 2-factor interactions; sex and its interaction with time; and age as a covariate. The mixed model was extended to include the 2-way interaction of sex by group and 3-way interaction of sex by group by time to verify that the effect of treatment did not vary by sex. An unstructured covariance matrix was imposed for these mixed models. Within-group changes in WC and 2-hour glucose level between baseline and 16 and 24 weeks were estimated and compared by using contrasts constructed from the 2-way interaction of group by time within the mixed models. In particular, the PROC MIXED procedure was used to fit mixed models. A 2-sided α of 0.05 was used to determine statistical significance, and no adjustment was made for multiple comparisons. All analyses were done by using SAS, version 9.2 (SAS Institute).

To examine the possible effect of missing data on the main outcomes, we applied a sensitivity analysis using the pattern-mixture model (16, 17). These models extend the final mixed models by including an indicator that describes the main patterns of missing data as a main effect and an interaction with other variables (group, time, sex, group by time, and sex by time). Significant interactions with the missing data indicator on the main variables suggest that its effects differ across missing data patterns and that missing data may not be missing at random. In our study, we defined 2 missing data patterns by an indicator of noncompleters (those who did not have 24-week data) versus completers. Because the focus of our study is to compare groups by their 16- and 24-week changes from baseline, which are derived from the group-by-time interaction, the 3-way interaction (group by time by noncompleter) in the pattern-mixture model would allow us to investigate the differential changes across time between intervention groups to see if they vary from completers to noncompleters. Therefore, this 3-way interaction is of particular interest in this pattern-mixture model.

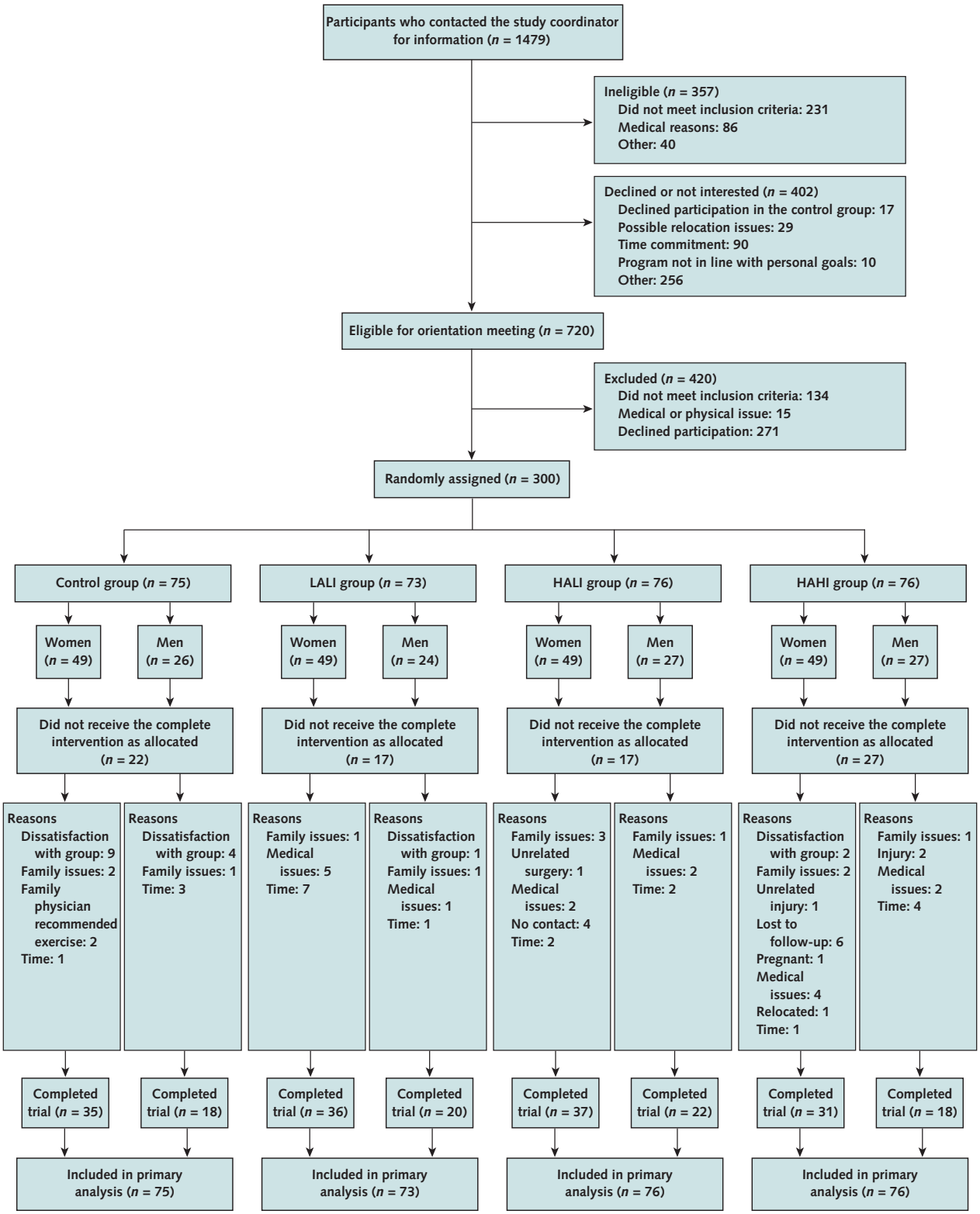
Role of the Funding Source

The funding source had no role in the design, protocol development, or conduct of the trial; data collection, management, or analysis; interpretation, preparation, review, or approval of the manuscript; or the decision to submit the manuscript for publication.

RESULTS

A total of 1479 persons responded to media advertisements seeking obese adults to participate in an exercise study (**Figure 1**). In all, 300 sedentary, abdominally obese adults were randomly assigned to 1 of 4 groups: control (no exercise) (n = 75), LALI (n = 73), HALI (n = 76), or HAHI (n = 76). Of the 300 participants randomly assigned, 217 (72.3%) returned for follow-up testing at 24 weeks. Return rates for follow-up at 24 weeks were 70.6%, 76.7%, 78.9%, and 63.0% within the control, LALI, HALI, and HAHI groups, respectively (**Figure 1**). Retention did not differ among groups (chi-square = 5.66). Baseline anthropometric variables did

Figure 1. Study flow diagram.



HAHI = high-amount, high-intensity exercise; HALI = high-amount, low-intensity exercise; LALI = low-amount, low-intensity exercise.

Table 1. Participant Characteristics*

Characteristic	Total (*n* = 300)	Control (*n* = 75)	LALI (*n* = 73)	HALI (*n* = 76)	HAHI (*n* = 76)
Age, *y*	51.4 (8.1)	52.2 (8.2)	52.1 (7.4)	50.9 (8.6)	50.3 (8.1)
Anthropometric					
WC, *cm*	110.6 (11.2)	109.5 (10.5)	110.7 (11.3)	111.1 (11.2)	111.3 (12.1)
Weight, *kg*	95.3 (16.6)	94.2 (17.1)	94.0 (15.2)	95.8 (17.9)	97.0 (16.4)
BMI, *kg/m²*	33.4 (4.5)	33.1 (4.6)	33.7 (4.4)	33.5 (4.9)	33.4 (4.3)
Metabolic					
2-h glucose level, *mmol/L*	7.3 (1.6)	7.5 (1.8)	7.3 (1.8)	7.4 (1.5)	7.1 (1.6)
Total cholesterol level, *mmol/L*	5.2 (1.0)	5.3 (1.1)	5.3 (0.9)	5.3 (0.9)	5.1 (1.1)
LDL cholesterol level, *mmol/L*†	3.3 (0.9)	3.3 (1.0)	3.4 (0.8)	3.4 (0.8)	3.1 (1.0)
HDL cholesterol level, *mmol/L*	1.22 (0.34)	1.21 (0.30)	1.22 (0.30)	1.20 (0.35)	1.23 (0.43)
Non-HDL cholesterol level, *mmol/L*	4.0 (1.0)	4.1 (1.0)	4.1 (0.9)	4.1 (0.9)	3.8 (1.0)
Triglyceride level, *mmol/L*	1.6 (0.9)	1.9 (1.0)	1.5 (1.0)	1.6 (0.8)	1.5 (0.7)
Fasting glucose level, *mmol/L*	5.4 (0.5)	5.5 (0.7)	5.5 (0.6)	5.4 (0.6)	5.4 (0.5)
Glucose AUC, *mmol/L*	33.0 (5.8)	33.8 (6.4)	32.7 (5.1)	33.4 (6.0)	32.1 (5.4)
Fasting insulin level, *pmol/L*	67.5 (37.5)	67.6 (34.8)	76.0 (51.0)	64.3 (36.4)	65.0 (31.8)
2-h insulin level, *pmol/L*	510.3 (412.2)	486.0 (354.8)	541.9 (428.6)	523.0 (460.9)	491.3 (402.8)
Insulin AUC, *pmol/L*†	2058.9 (1203.2)	1956.1 (972.4)	2235.1 (1334.8)	2041.3 (1280.2)	2010.6 (1204.4)
HOMA-IR score‡	2.4 (1.4)	2.4 (1.3)	2.7 (2.0)	2.3 (1.4)	2.3 (1.2)
Matsuda index score†§	4.6 (2.8)	4.5 (2.6)	4.2 (2.3)	4.7 (2.8)	4.9 (3.2)
Blood pressure, *mm Hg*‖					
Systolic	120.9 (13.3)	120.9 (12.9)	120.8 (10.9)	121.6 (13.0)	120.3 (16.1)
Diastolic	79.4 (8.3)	78.7 (7.8)	79.7 (7.8)	79.3 (8.6)	79.7 (8.9)
CRF¶					
$\dot{V}O_2$peak					
L/min	2.7 (0.7)	2.7 (0.8)	2.6 (0.7)	2.7 (0.7)	2.7 (0.7)
mL/kg/min	28.2 (5.4)	28.5 (5.9)	28.1 (5.4)	28.3 (4.8)	28.1 (5.6)
Total physical activity, *min***	308 (94)	296 (91)	308 (77)	319 (112)	307 (94)

AUC = area under the curve; BMI = body mass index; CRF = cardiorespiratory fitness; HAHI = high-amount, high-intensity exercise; HALI = high-amount, low-intensity exercise; HDL = high-density lipoprotein; HOMA-IR = Homeostasis Assessment of Insulin Resistance; LALI = low-amount, low-intensity exercise; LDL = low-density lipoprotein; $\dot{V}O_2$peak = maximum oxygen consumption; WC = waist circumference.
* Values are means (SDs). Sample sizes are as shown unless otherwise indicated.
† Total (*n* = 298), LALI (*n* = 72), and HALI (*n* = 75).
‡ This index has no normal score. Higher scores indicate more insulin resistance.
§ This index has no normal score. Higher scores indicate more insulin sensitivity.
‖ Total (*n* = 294), control (*n* = 73), LALI (*n* = 71), HALI (*n* = 75), and HAHI (*n* = 75).
¶ Total (*n* = 299) and control (*n* = 74).
** Total (*n* = 271), control (*n* = 66), LALI (*n* = 68), HALI (*n* = 68), and HAHI (*n* = 69).

not significantly differ between completers and noncompleters. Most of the study sample (96%) was white, and 20% and 10% were receiving antihypertensive and lipid-lowering medications, respectively. Incidence of medication use was not different between groups. No participant reported taking any glucose-lowering medication.

Participant characteristics are summarized in Table 1 and Appendix Table 1 (available at www.annals.org). Men and women within the same treatment group did not differ significantly in response to exercise for any primary or secondary variable. Therefore, all exercise-induced changes are shown collapsed across sex.

Table 2 presents the exercise adherence and 24-week follow-up data. Adherence to exercise intervention, defined as the percentage of exercise sessions attended, was 87.3%, 90.7%, and 84.4% for the LALI, HALI, and HAHI groups, respectively. The mean exercise times were 31.2 (SD, 4.4), 58.4 (SD, 7.6), and 40.0 (SD, 6.2) minutes per session for the LALI, HALI, and HAHI groups, respectively.

Table 3 presents the primary and secondary outcome measures. Reductions in WC at 24 weeks were greater in the LALI (adjusted mean difference, −3.9 cm [95% CI, −5.6 to −2.3 cm]; $P < 0.001$), HALI (−4.6 cm [CI, −6.2 to −3.0 cm]; $P < 0.001$), and HAHI (−4.6 cm [CI, −6.3 to −2.9 cm]; $P < 0.001$) groups than the control group but did not differ among the exercise groups ($P > 0.43$) (Figure 2). Reductions in 2-hour glucose level at 24 weeks were greater in the HAHI group (−0.7 mmol/L [CI, −1.3 to −0.1 mmol/L]; $P = 0.027$) than the control and LALI groups (−0.7 mmol/L [CI, −1.3 to −0.1 mmol/L]; $P = 0.030$). No significant changes in 2-hour glucose level were seen for LALI or HALI groups compared with the control group ($P > 0.159$).

Results of the pattern-mixture model indicate no significant interaction of noncompleters with group and time for WC ($F = 1.65$; $P = 0.174$) and 2-hour glucose level ($F = 2.29$; $P = 0.113$), which suggests that the missing data do not invalidate the intervention effect for either outcome (Appendix Table 2, available at www.annals.org).

Table 2. Exercise Intervention Descriptive Data for Study Completers

Variable	Completers			Noncompleters*		
	LALI (*n* = 56)	HALI (*n* = 59)	HAHI (*n* = 49)	LALI	HALI	HAHI
Adherence						
Sessions prescribed, *n*	120	120	120	120	120	120
Mean sessions attended (SD), *n*	104.8 (22.3)	108.8 (21.8)	101.3 (27.1)	36.1 (24.8)	49.9 (26.7)	29.2 (26.5)
Mean attendance (SD), %†	87.3 (18.6)	90.7 (18.2)	84.4 (22.6)	30.1 (20.7)	41.6 (22.3)	24.3 (22.1)
Adherence						
Prescribed energy expended, *kcal/session*						
Women	180	360	360	180	360	360
Men	300	600	600	300	600	600
Mean actual energy expended (SD), *kcal/session*						
Women	183.7 (5.0)	362.0 (9.1)	359.6 (17.8)	183.3 (13.4)	359.1 (7.4)	340.9 (42.7)
Men	304.9 (6.7)	610.7 (7.4)	598.5 (23.7)	303.6 (6.8)	572.6 (61.9)	525.1 (85.4)
Prescribed intensity, *% of* $\dot{V}O_2$peak	50	50	75	50	50	75
Mean actual intensity (SD)						
% of $\dot{V}O_2$peak	50.6 (2.0)	51.2 (3.1)	74.6 (1.8)	50.2 (1.5)	51.0 (1.5)	67.8 (13.4)
MET‡	4.4 (0.8)	4.7 (0.8)	7.0 (1.3)	5.9 (1.3)	6.0 (1.1)	6.1 (1.6)
Mean exercise time (SD), *min/session*	31.2 (4.4)	58.4 (7.6)	40.0 (6.2)	31.3 (3.5)	61.8 (7.6)	42.4 (4.9)

HAHI = high-amount, high-intensity exercise; HALI = high-amount, low-intensity exercise; LALI = low-amount, low-intensity exercise; MET = metabolic equivalent; $\dot{V}O_2$peak = maximum oxygen consumption.
* Participants who were randomly assigned to exercise but did not start the intervention (HAHI [*n* = 2], HALI [*n* = 3], and LALI [*n* = 2]).
† Attendance did not differ among groups as determined by 1-way analysis of variance (*P* = 0.26).
‡ Derived using the oxygen cost of prescribed exercise during the intervention.

Glucose area under the curve did not change in any exercise group compared with the control group. Reductions in the area under the curve for insulin level were greater for the HALI (−431.5 pmol/L [CI, −701.0 to −162.0 pmol/L]; *P* = 0.002) and HAHI (−464.1 pmol/L [−745.8 to −182.3 pmol/L]; *P* = 0.001) groups than the control group but did not differ from each other (*P* > 0.82). The change for the LALI group did not differ from that for the control group (*P* > 0.065). The increase in the Matsuda index was greater for the HALI (*P* = 0.004) and HAHI groups (*P* = 0.001) than the control group. The change for the LALI group did not differ from the control group (*P* = 0.189) (**Appendix Table 3**, available at www.annals.org).

Reductions in body weight were greater in all exercise groups than in the control group (*P* < 0.001). Reduction in body weight did not differ among the exercise groups (*P* > 0.182) (**Appendix Table 3**).

The increases in CRF for the LALI (0.2 L/min [CI, 0.1 to 0.3 L/min]; *P* < 0. 001), HALI (0.4 L/min [CI, 0.3 to 0.5 L/min]; *P* < 0.001), and HAHI (0.5 L/min [CI, 0.4 to 0.6 L/min]; *P* < 0.001) groups were greater than in the con-

Table 3. Change in Primary and Secondary Outcomes During and After the Intervention*

Outcome	Between-Group Differences From Baseline to 24 wk†					
	LALI vs. Control		HALI vs. Control		HAHI vs. Control	
	Value	*P* Value	Value	*P* Value	Value	*P* Value
Primary						
WC, *cm*						
16 wk	−3.1 (−4.6 to −1.7)	<0.001	−3.6 (−5.1 to −2.2)	<0.001	−3.6 (−5.0 to −2.1)	<0.001
24 wk	−3.9 (−5.6 to −2.3)	<0.001	−4.6 (−6.2 to −3.0)	<0.001	−4.6 (−6.3 to −2.9)	<0.001
2-h glucose level, *mmol/L*						
16 wk	−0.08 (−0.70 to 0.60)	0.81	−0.5 (−1.1 to 0.2)	0.147	−0.60 (−1.30 to 0.05)	0.070
24 wk	−0.02 (−0.60 to 0.60)	0.94	−0.4 (−1.0 to 0.2)	0.159	−0.7 (−1.3 to −0.1)	0.026
Secondary						
Glucose AUC, *mmol/L*‡						
24 wk	0.3 (−1.2 to 1.9)	0.70	−1.0 (−2.6 to 0.5)	0.190	−1.3 (−2.9 to 0.3)	0.105
Insulin AUC, *pmol/L*‡						
24 wk	−260.0 (−535.4 to 15.5)	0.065	−431.5 (−701.0 to −162.0)	0.002	−464.1 (−745.8 to −182.3)	0.001
Matsuda index score§						
24 wk	0.7 (−0.3 to 1.8)	0.189	1.5 (0.5 to 2.6)	0.004	1.9 (0.8 to 3.0)	0.001

AUC = area under the curve; HAHI = high-amount, high-intensity exercise; HALI = high-amount, low-intensity exercise; LALI = low-amount, low-intensity exercise; WC = waist circumference.
* Values are least-squares estimated means (95% CIs) adjusted for age and sex.
† Pairwise comparisons.
‡ Obtained from the 2-h oral glucose tolerance test.
§ Positive changes in the Matsuda index indicate improvement in insulin sensitivity.

trol group ($P < 0.001$) (**Appendix Figure**, available at www.annals.org). Improvement in CRF at 24 weeks was greater for the HALI group than for the LALI group (0.2 L/min [CI, 0.1 to 0.3 L/min]; $P = 0.001$). The increase in CRF at 24 weeks was greater for the HAHI group than for both the LALI (0.3 L/min [CI, 0.2 to 0.4 L/min]; $P < 0.001$) and HALI (0.1 L/min [CI, 0.0 to 0.2 L/min]; $P = 0.033$]) groups.

Table 4 presents the data on unsupervised physical activity and sedentary time. After adjustment for covariates, unsupervised physical activity and sedentary time did not change at 24 weeks in any exercise group compared with the control group ($P > 0.33$). No differences were seen among the exercise groups for total caloric intake or dietary fat intake ($P > 0.53$) (**Appendix Table 4**, available at www.annals.org).

The number of adverse events reported was generally low across groups, and the incidence of adverse events overall and of musculoskeletal injuries was highest in the HAHI group (**Appendix Table 5**, available at www.annals.org).

DISCUSSION

Physical activity guidelines suggest that there are no added health benefits of high-intensity exercise other than the shorter time frame needed to expend the appropriate amount of energy (3). The findings of this randomized, controlled trial provide only partial support for current guidelines and suggest that increasing exercise intensity provides additional benefit depending on the targeted health outcome. Exercise that is consistent with current guidelines is associated with substantial reduction in abdominal obesity independent of exercise intensity. For reducing 2-hour glucose level, however, benefit was restricted to the high-intensity group. Despite similar reductions in WC and body weight, moderate-intensity exercise consistent with guidelines was not associated with benefit. When combined with the observation that improvement in CRF—a strong marker of morbidity and mortality (18)—was greatest in the high-intensity group, exercise intensity seems to be a clinically relevant consideration.

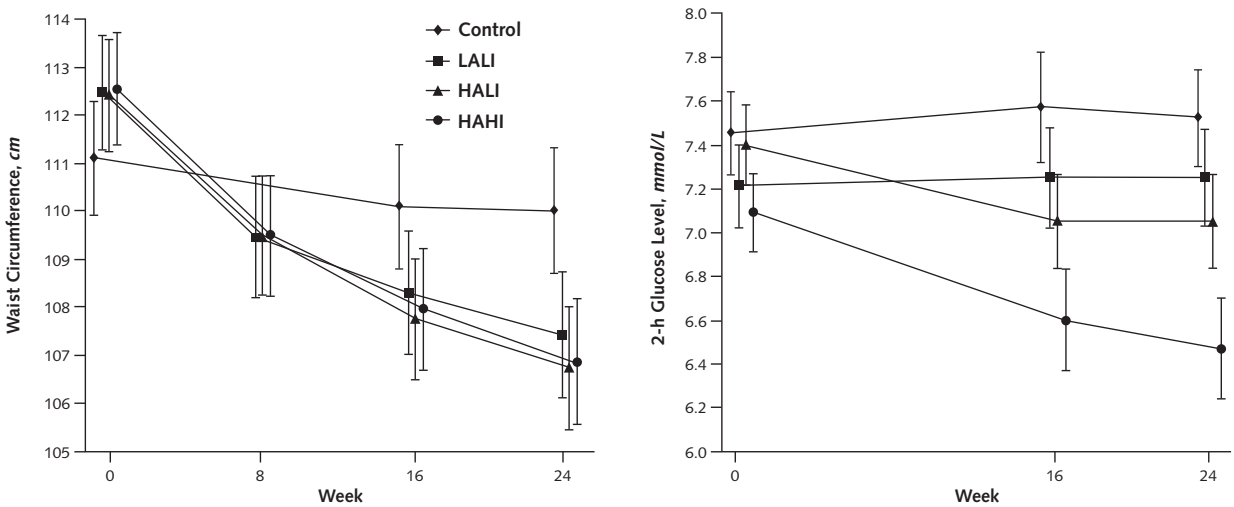
In agreement with current guidelines, our findings provide evidence showing that exercise consistent with consensus recommendations is associated with substantial (approximately 4.5 cm) reduction in WC independent of exercise intensity. Of note, the reduction in WC is the same when the same amount of energy is expended by exercising for 300 minutes per week at moderate intensity (routine walking at 50% intensity) or 200 minutes per week at vigorous intensity (brisk walking or light jogging at 75% intensity). Combined with the observation that a 5-cm reduction in WC is associated with a 9% lower risk for death in healthy middle-aged adults (19), our findings are encouraging and provide treatment options for clinicians who seek lifestyle-based strategies for reducing abdominal obesity in adults at increased health risk.

Perhaps the most important finding was that benefit with respect to reduction of 2-hour glucose level was restricted to the higher-intensity exercise group. That 200 minutes per week of vigorous exercise was associated with a 9% improvement in glucose tolerance is reinforced by our finding that 2-hour insulin level, insulin area under the curve, and the Matsuda index were also improved compared with the control group. These observations agree with a prior, cross-sectional study suggesting that vigorous physical activity had a greater

Table 3–Continued

Between-Group Differences From Baseline to 24 wk†					
HALI vs. LALI		HAHI vs. LALI		HALI vs. HAHI	
Value	*P* Value	Value	*P* Value	Value	*P* Value
−0.5 (−1.8 to 0.8)	0.47	−0.4 (−1.8 to 1.0)	0.56	0.1 (−1.3 to 1.4)	0.91
−0.6 (−2.2 to 1.0)	0.43	−0.6 (−2.3 to 1.0)	0.45	0.0 (−1.6 to 1.6)	1.00
−0.4 (−1.0 to 0.2)	0.200	−0.5 (−1.2 to 0.1)	0.094	−0.1 (−0.7 to 0.5)	0.65
−0.4 (−1.0 to 0.2)	0.200	−0.7 (−1.3 to −0.1)	0.030	−0.3 (−0.9 to 0.3)	0.40
−1.3 (−2.8 to 0.2)	0.084	−1.6 (−3.2 to −0.1)	0.043	−0.3 (−1.9 to 1.3)	0.70
−171.5 (−438.7 to 96.7)	0.21	−204.1 (−483.7 to 75.6)	0.154	−32.6 (−306.3 to 241.2)	0.82
0.8 (−0.2 to 1.8)	0.111	1.2 (0.1 to 2.3)	0.034	0.3 (−0.7 to 1.4)	0.52

Figure 2. Waist circumference and 2-h glucose level during the 24-wk study.



Participants with waist circumference and 2-h glucose data at each time point, *n*

Control	75	–	37	53	75	38	53
LALI	73	58	52	56	73	52	56
HALI	76	64	59	59	76	59	60
HAHI	76	55	48	49	76	49	48

Data represent least-square means and were adjusted for age and sex; errors bars indicate 95% CIs. Analyses were done by using all randomly assigned participants. At baseline, waist circumference or 2-hour glucose level did no differ among groups. HAHI = high-amount, high-intensity exercise; HALI = high-amount, low-intensity exercise; LALI = low-amount, low-intensity exercise. **Left.** Waist circumference. At weeks 16 and 24, the reductions were greater in all exercise groups than in the control group ($P < 0.001$) but did not differ from each other ($P > 0.10$). **Right.** 2-hour glucose level. At week 16, there were no differences between the LALI or HALI and control groups ($P > 0.10$) or the HAHI and control groups ($P = 0.07$). At week 24, the decrease was greater in the HAHI group than the control ($P = 0.03$) and LALI ($P = 0.04$) groups. No significant changes were seen for the LALI or HALI groups compared with the control group ($P > 0.10$).

influence on cardiometabolic risk factors than an equivalent amount of moderate intensity physical activity (20). However, despite evidence establishing an association between incremental increases in 2-hour glucose level and cardiovascular disease (21, 22), the clinical importance of reducing 2-hour glucose level by the magnitude reported here remains unknown.

Our finding that 150 minutes per week of low-intensity exercise was not associated with improvement in 2-hour glucose level or any measure of insulin action

Table 4. Absolute and Relative Change in Total Unstructured Physical Activity and Sedentary Time Over the 24-wk Intervention*

Variable	Control (*n* = 75)	LALI (*n* = 73)	HALI (*n* = 76)	HAHI (*n* = 76)
Total unstructured physical activity				
Baseline, *min/d*	285 (263 to 307)	298 (276 to 320)	304 (282 to 325)	296 (275 to 318)
Wake time, %	30 (29 to 32)	32 (30 to 34)	31 (29 to 33)	33 (30 to 34)
Change at 25 wk, *min/d*†	−2 (−25 to 21)	−3 (−24 to 18)	4 (−15 to 24)	11 (−11 to 33)
Wake time, %	1 (−1 to 3)	−0.1 (−2.0 to 2.0)	−1.0 (−0.5 to 3.0)	1 (−1 to 3)
Sedentary time				
Baseline, *min/d*	635 (614 to 656)	613 (592 to 634)	645 (624 to 665)	620 (600 to 641)
Wake time, %	67 (65 to 69)	66 (64 to 68)	67 (65 to 69)	67 (65 to 69)
Change at 25 wk, *min/d*†	−31 (−65 to 4)	−15 (−47 to 16)	−38 (−69 to −8)	−22 (−56 to 11)
Wake time, %	0.2 (−3 to 3)	−2 (−4 to 1)	−2 (−4 to 1)	−4 (−7 to −1)
Adherence				
Participants who completed the study and wore the accelerometer at 25 wk/completed the study, *n/N (%)*‡	42/53 (79)	48/56 (86)	52/59 (88)	41/49 (84)

HAHI = high-amount, high-intensity exercise; HALI = high-amount, low-intensity exercise; LALI = low-amount, low-intensity exercise.
* Values are differences between least-squares estimated means (95% CIs) adjusted for age and sex unless otherwise indicated.
† Compared with control ($P > 0.33$).
‡ Accelerometry data were obtained the week immediately after completion of the intervention.

counters the consensus statement of the American Diabetes Association, which suggests that lifestyle modification therapy for reducing 2-hour glucose level should emphasize modest weight loss (5% to 10%) and 150 minutes per week of low-intensity exercise (23). In our study, the reduction in body weight approximated 5% to 6%, thus reinforcing the independent contribution of exercise intensity per se and consequently, that low-intensity exercise for 150 minutes per week in association with a 5% to 6% weight loss may not be sufficient to improve glucose tolerance.

A novel finding of this trial was that for a fixed amount of exercise, improvement in CRF was also intensity-dependent because the increase in CRF was greater in the high-intensity group (19.6% [2.2 metabolic equivalents]) than in both low-intensity groups. However, our findings also show that improvement in CRF is volume-dependent because the greater amount (approximately 300 minutes per week) of exercise was associated with a greater increase in CRF compared with 150 minutes per week; they confirm other studies in which a graded increase in CRF across exercise groups differed in exercise volume but not intensity (21, 24). The improvement in CRF has clinical relevance because an increase in CRF of 1 metabolic equivalent is associated with a 15% to 20% decrease in risk for death from cardiovascular disease (25). The risk reduction for the high-intensity group (30% to 40%) was twice that of the low-intensity group that exercised for 150 minutes per week.

Finally, increasing exercise amount or intensity was not associated with change in daily physical activity, which suggests that obese adults who perform exercise consistent with current guidelines do not compensate for energy expended during exercise regardless of intensity (20, 26). It is also clinically relevant that sedentary time was unaltered independent of exercise amount or intensity as sedentary time is positively associated with glucose tolerance independent of moderate to vigorous exercise.

Strengths of our study include excellent adherence and compliance to the exercise regimens. Additional strengths include the tight control of all exercise sessions performed under supervision with automated monitoring of heart rate during each exercise session. Monitoring of daily dietary intake combined with objective measures of unsupervised physical activity levels helped to isolate the effects of exercise.

Limitations include a homogeneous sample of abdominally obese white adults. Because approximately 45% and 60% of adult women and men are abdominally obese and at greater risk for diabetes, however, a sizeable proportion of the adult population would probably benefit from the exercise strategies studied. Our study was conducted under ideal circumstances with motivated adults who were supervised during all exercise sessions and encouraged to strictly follow their diet regimen. The loss to follow-up may limit the generalizability of our findings. The relatively high incidence of dropout in the high-intensity group suggests that high-intensity exercise may not be a clinical intervention with high adherence for some adults. Our interpretation is based on group data, and whether variation in interindividual responses to standardized exercise differs depending on exercise intensity is unknown.

In summary, significant reduction in abdominal obesity was seen in response to fixed amounts of exercise independent of exercise intensity. Reduction in 2-hour glucose level was restricted to the high-intensity group, the clinical importance of which remains to be determined.

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Grant Support: By the Canadian Institutes of Health Research (grant OHN-63277).

Disclosures: Authors have disclosed no conflicts of interest. Forms can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M14-1189.

Reproducible Research Statement: *Study protocol*: Published elsewhere (8). *Statistical code*: Available from Dr. Ross (e-mail, rossr@queensu.ca). *Data set*: Not available.

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Obtaining of funding: R. Ross, R. Hudson, M. Lam.
Administrative, technical, or logistic support: R. Hudson, P.J. Stotz.
Collection and assembly of data: P.J. Stotz.

Appendix Table 1. Participant Characteristics, by Sex*

Characteristic	Men				Women			
	Control (*n* = 26)	LALI (*n* = 24)	HALI (*n* = 27)	HAHI (*n* = 27)	Control (*n* = 49)	LALI (*n* = 49)	HALI (*n* = 49)	HAHI (*n* = 49)
Age, *y*	53.8 (8.3)	53.8 (7.8)	52.1 (9.3)	51.4 (8.4)	51.4 (8.1)	51.3 (7.2)	50.2 (8.3)	49.7 (7.9)
Anthropometric								
WC, *cm*	116.5 (9.3)	117.4 (9.8)	117.8 (10.2)	117.2 (8.7)	105.8 (9.1)	107.4 (10.5)	107.4 (10.0)	108.1 (12.6)
Weight, *kg*	107.2 (14.3)	104.9 (15.3)	108.5 (18.2)	107.5 (14.1)	87.4 (14.3)	88.7 (12.0)	88.8 (13.4)	91.1 (14.7)
BMI, kg/m^2	33.9 (3.8)	33.4 (4.1)	34.0 (4.7)	33.3 (3.5)	32.7 (5.0)	33.9 (4.5)	33.3 (5.1)	33.4 (4.7)
Metabolic								
2-h glucose level, *mmol/L*	7.5 (1.7)	7.1 (1.6)	7.9 (1.6)	6.8 (1.9)	7.4 (1.8)	7.2 (1.5)	7.1 (1.3)	7.2 (1.5)
Total cholesterol level, *mmol/L*	4.7 (0.9)	5.1 (1.0)	5.1 (0.6)	5.1 (1.1)	5.6 (1.1)	5.3 (0.9)	5.4 (1.0)	5.1 (1.1)
LDL cholesterol level, *mmol/L*†	2.8 (0.7)	3.4 (0.8)	3.3 (0.6)	3.2 (1.1)	3.5 (1.0)	3.4 (0.8)	3.4 (0.9)	3.2 (0.8)
HDL cholesterol level, *mmol/L*	0.98 (0.18)	1.08 (0.28)	0.96 (0.21)	1.03 (0.26)	1.33 (0.28)	1.29 (0.29)	1.34 (0.33)	1.38 (0.41)
Non-HDL cholesterol level, *mmol/L*	3.8 (0.9)	4.1 (0.9)	4.2 (0.6)	4.1 (1.1)	4.3 (1.1)	4.0 (0.9)	4.1 (1.0)	3.7 (0.9)
Triglyceride level, *mmol/L*	2.0 (1.0)	1.5 (0.8)	1.9 (1.1)	1.8 (0.8)	1.7 (0.9)	1.5 (1.1)	1.4 (0.7)	1.2 (0.6)
Fasting glucose level, *mmol/L*	5.6 (0.6)	5.6 (0.4)	5.6 (0.6)	5.7 (0.5)	5.3 (0.5)	5.4 (0.6)	5.3 (0.4)	5.3 (0.5)
Glucose AUC, *mmol/L*	36.0 (6.7)	34.3 (3.3)	36.2 (6.4)	32.8 (6.0)	32.6 (5.9)	32.0 (5.6)	31.9 (5.2)	31.6 (5.1)
Fasting insulin level, *pmol/L*	82.1 (34.9)	73.0 (49.8)	79.3 (35.7)	69.7 (27.8)	59.0 (30.0)	74.5 (47.0)	56.1 (34.5)	62.4 (33.8)
2-h insulin level, *pmol/L*	521.9 (414.1)	520.8 (374.6)	598.8 (473.9)	463.3 (351.6)	467.0 (322.0)	552.2 (456.0)	481.3 (453.1)	506.8 (431.1)
Insulin AUC, *pmol/L*‡	2177.6 (1010.3)	2332.3 (1342.5)	2262.3 (1088.5)	2202.0 (971.4)	1838.6 (941.0)	2186.5 (1342.6)	1919.5 (1369.8)	1902.9 (1314.8)
HOMA-IR score§	3.0 (1.3)	2.6 (1.9)	2.9 (1.4)	2.6 (1.1)	2.1 (1.1)	2.6 (1.8)	1.9 (1.2)	2.1 (1.2)
Matsuda index score‡‖	3.4 (1.6)	4.1 (2.7)	3.6 (2.1)	3.7 (1.3)	5.1 (2.8)	4.2 (2.1)	5.3 (3.0)	5.6 (3.8)
Blood pressure, *mm Hg*¶								
Systolic	122.0 (12.2)	119.1 (9.5)	123.7 (11.1)	125.1 (18.6)	120.3 (13.3)	121.6 (11.5)	120.4 (13.9)	117.6 (14.0)
Diastolic	81.8 (6.9)	81.0 (7.0)	84.0 (8.0)	82.7 (8.6)	77.0 (7.8)	79.1 (8.1)	76.6 (7.8)	78.0 (8.6)
CRF**								
$\dot{V}O_2$peak								
L/min	3.5 (0.7)	3.4 (0.7)	3.4 (0.6)	3.4 (0.6)	2.3 (0.4)	2.3 (0.4)	2.3 (0.3)	2.3 (0.4)
mL/kg/min	32.7 (5.6)	32.9 (4.6)	31.7 (4.7)	32.0 (5.1)	26.2 (4.7)	25.7 (4.0)	26.4 (3.7)	26.0 (4.6)
Total physical activity, *min*††	283 (91)	298 (77)	324 (156)	303 (113)	303 (91)	314 (78)	316 (79)	309 (83)

AUC = area under the curve; BMI = body mass index; CRF = cardiorespiratory fitness; HAHI = high-amount, high-intensity exercise; HALI = high-amount, low-intensity exercise; HDL = high-density lipoprotein; HOMA-IR = Homeostasis Assessment of Insulin Resistance; LALI = low-amount, low-intensity exercise; LDL = low-density lipoprotein; $\dot{V}O_2$peak = maximum oxygen consumption; WC = waist circumference.

* Values are means (SDs). Sample sizes are as shown unless otherwise indicated.

† For men, HALI (*n* = 26); for women, LALI (*n* = 48).

‡ For women, LALI (*n* = 48) and HAHI (*n* = 48).

§ This index has no normal score. Higher scores indicate more insulin resistance.

‖ This index has no normal score. Higher scores indicate more insulin sensitivity.

¶ For men, LALI (*n* = 23). For women, control (*n* = 47), LALI (*n* = 48), HALI (*n* = 48), and HAHI (*n* = 48).

** For women, control (*n* = 48).

†† For men, control (*n* = 23), HALI (*n* = 25), and HAHI (*n* = 24). For women, control (*n* = 43), LALI (*n* = 44), HALI (*n* = 43), and HAHI (*n* = 45).

Appendix Table 2. Sensitivity Analysis: Mixed-Effects Pattern-Mixture Logistic Regression Results (n = 300)*

Parameter	Mixed Model		Pattern Mixture					
			Completers†		Noncompleters‡		Averaged Results	
	Parameter Estimate (±SE)	*P* Value	Parameter Estimate (±SE)	*P* Value	Parameter Estimate (±SE)	*P* Value	Parameter Estimate (±SE)	*P* Value
WC								
Intercept	123.40 ± 4.15	<0.001	126.3 ± 4.86	<0.001	112.0 ± 8.09	<0.001	122.4 ± 4.17	<0.001
Group								
LALI vs. control	1.36 ± 1.66	0.41	1.47 ± 1.91	0.44	2.16 ± 3.28	0.51	1.66 ± 1.65	0.31
HALI vs. control	1.30 ± 1.64	0.43	1.14 ± 1.89	0.54	3.23 ± 3.30	0.33	1.72 ± 1.64	0.29
HAHI vs. control	1.44 ± 1.65	0.38	2.04 ± 1.98	0.30	0.47 ± 2.90	0.87	1.60 ± 1.64	0.33
Time								
16 wk vs. baseline	−1.76 ± 0.65	0.007	−1.95 ± 0.65	0.003	1.58 ± 3.65	0.67	−0.97 ± 1.11	0.39
24 wk vs. baseline	−1.94 ± 0.72	0.008	−2.10 ± 0.73	0.004	–		–	
Group × time								
LALI vs. control: 16 wk	−3.15 ± 0.75	<0.001	−3.11 ± 0.74	<0.001	−4.36 ± 5.25	0.41	−3.45 ± 1.55	0.027
LALI vs. control: 24 wk	−3.94 ± 0.84	<0.001	−3.93 ± 0.84	<0.001	–		–	
HALI vs. control: 16 wk	−3.65 ± 0.73	<0.001	−3.93 ± 0.73	<0.001	−2.71 ± 4.19	0.52	−3.59 ± 1.28	0.005
HALI vs. control: 24 wk	−4.58 ± 0.82	<0.001	−4.86 ± 0.83	<0.001	–		–	
HAHI vs. control: 16 wk	−3.57 ± 0.75	<0.001	−3.59 ± 0.76	<0.001	−7.03 ± 4.36	0.108	−4.54 ± 1.33	0.001
HAHI vs. control: 24 wk	−4.58 ± 0.86	<0.001	−4.65 ± 0.87	<0.001	–		–	
2-h glucose level								
Intercept	7.33 ± 0.60	<0.001	7.65 ± 0.69	<0.001	6.33 ± 1.23	<0.001	7.29 ± 0.60	<0.001
Group								
LALI vs. control	−0.24 ± 0.26	0.36	−0.49 ± 0.30	0.110	0.43 ± 0.52	0.40	−0.23 ± 0.26	0.38
HALI vs. control	−0.05 ± 0.26	0.85	−0.26 ± 0.30	0.39	0.51 ± 0.53	0.34	−0.04 ± 0.26	0.87
HAHI vs. control	−0.36 ± 0.26	0.170	−0.66 ± 0.31	0.040	0.32 ± 0.46	0.49	−0.39 ± 0.26	0.137
Time								
16 wk vs. baseline	0.06 ± 0.29	0.83	−0.02 ± 0.29	0.94	0.39 ± 1.19	0.75	0.09 ± 0.39	0.82
24 wk vs. baseline	−0.18 ± 0.26	0.50	−0.27 ± 0.27	0.32	–		–	
Group x time								
LALI vs. control: 16 wk	−0.08 ± 0.33	0.82	−0.04 ± 0.34	0.90	3.76 ± 1.74§	0.031§	1.01 ± 0.54	0.063
LALI vs. control: 24 wk	−0.02 ± 0.30	0.94	0.05 ± 0.31	0.87	–		–	
HALI vs. control: 16 wk	−0.47 ± 0.32	0.147	−0.39 ± 0.33	0.24	−0.49 ± 1.27	0.70	−0.42 ± 0.43	0.33
HALI vs. control: 24 wk	−0.42 ± 0.30	0.159	−0.33 ± 0.31	0.28	–		–	
HAHI vs. control: 16 wk	−0.61 ± 0.34	0.070	−0.53 ± 0.35	0.126	NA‖		NA‖	
HAHI vs. control: 24 wk	−0.69 ± 0.31	0.026	−0.59 ± 0.32	0.069	–		–	

HAHI = high-amount, high-intensity exercise; HALI = high-amount, low-intensity exercise; LALI = low-amount, low-intensity exercise; NA = not available; WC = waist circumference.

* Beneficial group effects are reflected in the group-by-time interaction by negative coefficients. Sex, sex-by-time interaction, and age were also included in the analysis (data not shown).

† Those who had data at 24 wk (n = 217).

‡ Those missing data at 24 wk (n = 83).

§ Data are based on a single noncompleter having data at 16 wk.

‖ Noncompleter data are unavailable because all noncompleters in the HAHI group did not complete blood work before 16 wk.

Appendix Table 3. Change in Secondary Outcomes After 24-wk Intervention*

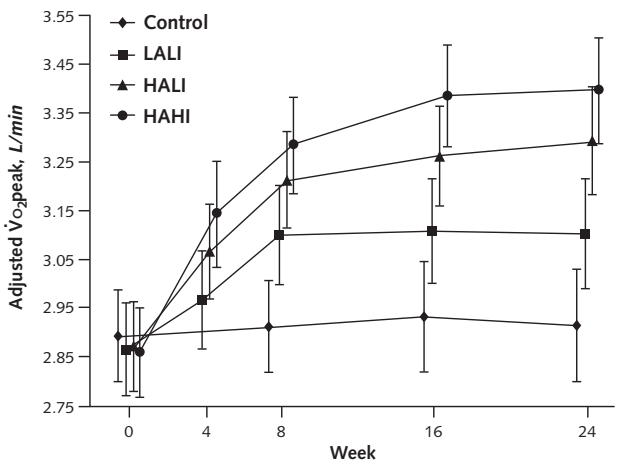
Outcome	Between-Group Differences From Baseline to 24 wk†					
	LALI vs. Control		HALI vs. Control		HAHI vs. Control	
	Value	*P* Value	Value	*P* Value	Value	*P* Value
Anthropometric						
Weight, *kg*	−3.8 (−5.5 to −2.1)	<0.001	−4.9 (−6.5 to −3.3)	<0.001	−4.6 (−6.3 to −2.9)	<0.001
BMI, kg/m^2	1.5 (−2.0 to −0.9)	<0.001	−1.9 (−2.4 to −1.3)	<0.001	−1.6 (−2.2 to −1.0)	<0.001
Metabolic						
Total cholesterol level, *mmol/L*	−0.1 (−0.3 to 0.2)	0.57	−0.05 (−0.3 to 0.2)	0.69	−0.1 (−0.3 to 0.2)	0.62
LDL cholesterol level, *mmol/L*	−0.1 (−0.4 to 0.1)	0.165	−0.1 (−0.3 to 0.1)	0.192	−0.2 (−0.4 to 0.0)	0.081
HDL cholesterol level, *mmol/L*	0.04 (−0.02 to 1.0)	0.22	0.1 (0.01 to 0.1)	0.021	0.05 (−0.02 to 0.1)	0.159
Non-HDL cholesterol level, *mmol/L*	−0.1 (−0.3 to 0.1)	0.32	−0.1 (−0.3 to 0.1)	0.26	−0.1 (−0.3 to 0.1)	0.30
Triglyceride level, *mmol/L*	0.1 (−0.5 to 0.7)	0.77	0.004 (−0.6 to 0.6)	0.99	0.4 (−0.2 to 1.0)	0.148
Fasting glucose level, *mmol/L*	−0.1 (−0.2 to 0.1)	0.30	−0.1 (−0.2 to 0.1)	0.39	−0.03 (−0.2 to 0.1)	0.67
Fasting insulin level, *pmol/L*	−9.7 (−18.5 to −0.9)	0.031	−10.7 (−19.3 to −2.0)	0.016	−8.4 (−17.5 to 0.6)	0.068
2-h insulin level, *pmol/L*	−87.4 (−197.9 to 23.1)	0.122	−186.4 (−295.1 to −77.6)	<0.001	−213.5 (−326.7 to −100.3)	<0.001
HOMA-IR score‡	−0.4 (−0.7 to 0.03)	0.035	−0.4 (−0.7 to −0.05)	0.022	−0.3 (−0.6 to 0.05)	0.094
Blood pressure, *mm Hg*						
Systolic	−0.8 (−4.8 to 3.3)	0.71	−4.6 (−8.6 to −0.6)	0.023	−3.2 (−7.3 to 1.0)	0.139
Diastolic	−0.6 (−3.3 to 2.1)	0.65	−3.6 (−6.2 to −0.9)	0.008	−2.0 (−4.8 to 0.7)	0.152

BMI = body mass index; HAHI = high-amount, high-intensity exercise; HALI = high-amount, low-intensity exercise; HDL = high-density lipoprotein; HOMA-IR = Homeostasis Assessment of Insulin Resistance; LALI = low-amount, low-intensity exercise; LDL = low-density lipoprotein.
* Values are least-squares estimated means (95% CIs) adjusted for age and sex.
† Pairwise comparisons.
‡ Negative changes in the HOMA-IR score indicate improvement in insulin resistance.

Appendix Table 3–Continued

Between-Group Differences From Baseline to 24 wk†					
HALI vs. LALI		HAHI vs. LALI		HALI vs. HAHI	
Value	*P* Value	Value	*P* Value	Value	*P* Value
−1.1 (−2.7 to 0.5)	0.20	−0.8 (−2.4 to 0.9)	0.36	0.3 (−1.3 to 1.9)	0.71
−0.4 (−1.0 to 0.2)	0.160	−0.2 (−0.8 to 0.4)	0.54	0.2 (−0.3 to 0.8)	0.45
0.02 (−0.2 to 0.3)	0.86	0.01 (−0.2 to 0.3)	0.95	−0.01 (−0.3 to 0.2)	0.91
0.01 (−0.2 to 0.2)	0.91	−0.04 (−0.3 to 0.2)	0.70	−0.1 (−0.3 to 0.2)	0.61
0.03 (−0.03 to 0.09)	0.29	0.01 (−0.06 to 0.07)	0.82	−0.03 (−0.09 to 0.04)	0.42
−0.01 (−0.2 to 0.2)	0.92	−0.01 (−0.2 to 0.2)	0.96	0.005 (−0.2 to 0.2)	0.97
−0.1 (−0.6 to 0.5)	0.77	0.3 (−0.2 to 0.9)	0.24	0.4 (−0.1 to 1.0)	0.144
0.01 (−0.1 to 0.2)	0.84	0.05 (−0.1 to 0.2)	0.55	0.03 (−0.1 to 0.2)	0.68
−1.0 (−9.5 to 7.6)	0.83	1.3 (−7.7 to 10.2)	0.78	2.2 (−6.6 to 11.0)	0.62
−99.0 (−206.4 to 8.5)	0.072	−126.1 (−238.0 to −14.2)	0.028	−27.1 (−137.3 to 83.1)	0.63
−0.02 (−0.3 to 0.3)	0.86	0.1 (−0.3 to 0.4)	0.58	0.1 (−0.2 to 0.4)	0.46
−3.8 (−7.8 to 0.1)	0.055	−2.4 (−6.5 to 1.7)	0.25	1.5 (−2.6 to 5.5)	0.48
−3.0 (−5.6 to −0.3)	0.028	−1.4 (−4.2 to 1.3)	0.31	1.5 (−1.2 to 4.2)	0.27

Appendix Figure. Cardiorespiratory fitness during the 24-wk study.



Participants with cardiorespiratory fitness data, *n*

Control	74	–	–	24	44
LALI	73	62	55	52	53
HALI	76	67	63	60	56
HAHI	76	59	51	46	42

Data represent least-square means and were adjusted for age and sex; errors bars indicate 95% CIs. Analyses were done on an intention-to-treat basis. At baseline, there were no differences between groups. At weeks 4, 8, 16, and 24, the increase in $\dot{V}O_2$peak was greater for the HAHI group than the LALI ($P < 0.001$) and control ($P < 0.001$) groups. At weeks 16 and 24, the increase in $\dot{V}O_2$peak was greater for the HALI group than the control ($P < 0.001$) and LALI ($P < 0.001$) groups. The increase in $\dot{V}O_2$peak for the HAHI group was greater than the HALI group at 8, 16, and 24 weeks ($P = 0.03$, 0.002, and 0.03, respectively), with intention-to-treat. The number of participants at each time point is indicated. At weeks 4 and 8, participant data in the control group were not collected. HAHI = high-amount, high-intensity exercise; HALI = high-amount, low-intensity exercise; LALI = low-amount, low-intensity exercise; $\dot{V}O_2$peak = maximum oxygen consumption.

Appendix Table 4. Analysis of Dietary Intake*

Group	Self-Reported Dietary Intake†		Computerized Analysis of Diet Records‡	
	Caloric Intake, *kcal/d*	Fat Intake, *% of total*	Caloric Intake, *kcal/d*	Fat Intake, *% of total*
Control (*n* = 44)	1773 (389)	31.6 (5.4)	1818 (444)	32.0 (4.0)
LALI (*n* = 70)	1836 (346)	30.3 (4.3)	1782 (554)	30.1 (3.6)
HALI (*n* = 72)	1882 (462)	30.4 (4.2)	1924 (508)	30.3 (5.2)
HAHI (*n* = 67)	1836 (478)	30.9 (4.2)	2052 (603)	28.5 (5.5)

HAHI = high-amount, high-intensity exercise; HALI = high-amount, low-intensity exercise; LALI = low-amount, low-intensity exercise.
* Values are means (SDs). Mean caloric or fat intake did not differ among groups as determined by 1-way analysis of variance ($P > 0.53$). Self-reported dietary intake and computerized analysis of diet records did not differ as determined by paired *t* tests ($P > 0.147$). Sample sizes are as shown unless otherwise indicated.
† 1–24 wk.
‡ 6 and 20 wk. Subset of computerized analysis sample sizes are control (*n* = 18), LALI (*n* = 10), HALI (*n* = 11), and HAHI (*n* = 10).

Appendix Table 5. Adverse Responses

Variable	Control (*n* = 75)	LALI (*n* = 73)	HALI (*n* = 76)	HAHI (*n* = 76)
Musculoskeletal events during or after exercise, *n**				
Any event	2	8	5	12
Events requiring a physician visit	1	1	2	4
Events requiring hospitalization	–	–	–	–
Events resulting in dropout	–	–	–	3
Potential cardiovascular events, *n*†				
Any event	1	2	1	4
Events requiring a physician visit	1	1	1	1
Events requiring hospitalization	–	–	–	1
Events resulting in dropout	–	–	–	–
Other events, *n*‡	10	8	16	11
Other events resulting in dropout‡	0	6	4	6
Total events reported, *n (%)*	13 (17.3)	18 (24.7)	22 (28.9)	27 (35.5)
Total musculoskeletal events, *n (%)*	2 (2.7)	8 (11.0)	5 (6.6)	12 (15.8)
Total cardiovascular events, *n (%)*	1 (1.3)	2 (2.7)	1 (1.3)	4 (5.3)
Total participants who had an adverse event, *n (%)*	12 (16.0)	16 (21.9)	18 (23.7)	25 (32.9)
Total participants who discontinued the intervention because of an adverse event, *n (%)*	0 (0.0)	6 (8.2)	4 (5.3)	9 (11.8)

HAHI = high-amount, high-intensity exercise; HALI = high-amount, low-intensity exercise; LALI = low-amount, low-intensity exercise.
* Includes pain or cramping in the leg, knee, or foot; strained muscle, tendon, or ligament; and broken bone.
† Includes chest pain, difficulty breathing, and dizziness or loss of consciousness.
‡ Medical issues other than musculoskeletal or cardiovascular events, such as chronic pain, diabetes, depression, or fatigue.