

Effects of Aerobic Training, Resistance Training, or Both on Glycemic Control in Type 2 Diabetes

A Randomized Trial

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Background: Previous trials have evaluated the effects of aerobic training alone and of resistance training alone on glycemic control in type 2 diabetes, as assessed by hemoglobin A_{1c} values. However, none could assess incremental effects of combined aerobic and resistance training compared with either type of exercise alone.

Objective: To determine the effects of aerobic training alone, resistance training alone, and combined exercise training on hemoglobin A_{1c} values in patients with type 2 diabetes.

Design: Randomized, controlled trial.

Setting: 8 community-based facilities.

Patients: 251 adults age 39 to 70 years with type 2 diabetes. A negative result on a stress test or clearance by a cardiologist, and adherence to exercise during a 4-week run-in period, were required before randomization.

Interventions: Aerobic training, resistance training, or both types of exercise (combined exercise training). A sedentary control group was included. Exercise training was performed 3 times weekly for 22 weeks (weeks 5 to 26 of the study).

Measurements: The primary outcome was the change in hemoglobin A_{1c} value at 6 months. Secondary outcomes were changes in body composition, plasma lipid values, and blood pressure.

Results: The absolute change in the hemoglobin A_{1c} value in the combined exercise training group compared with the control group was −0.51 percentage point (95% CI, −0.87 to −0.14) in the aerobic training group and −0.38 percentage point (CI, −0.72 to −0.22) in the resistance training group. Combined exercise training resulted in an additional change in the hemoglobin A_{1c} value of −0.46 percentage point (CI, −0.83 to −0.09) compared with aerobic training alone and −0.59 percentage point (CI, −0.95 to −0.23) compared with resistance training alone. Changes in blood pressure and lipid values did not statistically significantly differ among groups. Adverse events were more common in the exercise groups.

Limitations: The generalizability of the results to patients who are less adherent to exercise programs is uncertain. The participants were not blinded, and the total duration of exercise was greater in the combined exercise training group than in the aerobic and resistance training groups.

Conclusion: Either aerobic or resistance training alone improves glycemic control in type 2 diabetes, but the improvements are greatest with combined aerobic and resistance training.

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Physical activity is important in the management of type 2 diabetes mellitus. Systematic reviews (1–4) found that structured aerobic exercise (walking, jogging, or cycling) or resistance exercise (weightlifting) reduced the absolute hemoglobin A_{1c} value by about 0.6%. The hemoglobin A_{1c} value reflects the mean plasma glucose concentration over the previous 2 to 3 months. A 1% absolute decrease in the hemoglobin A_{1c} value is associated with a 15% to 20% decrease in major cardiovascular events (5) and a 37% reduction in microvascular complications (6). The only study that compared combined aerobic and resistance training with aerobic training alone found no differences in hemoglobin A_{1c} values between the groups, but the low average baseline hemoglobin A_{1c} value (6.7%) and small sample (9 to 10 persons per group) limited the power to detect a difference (7).

We designed the DARE (Diabetes Aerobic and Resistance Exercise) clinical trial to determine the effects of aerobic and resistance training alone versus a sedentary control group, and the incremental effects of doing both types of exercise (combined exercise training) versus aerobic or resistance training alone, on glycemic control and other risk factors for cardiovascular disease. We report our results

for the primary outcome (change in hemoglobin A_{1c} value from baseline to the end of the intervention) and for the secondary outcomes of plasma lipid levels, blood pressure, and body composition. We hypothesized that the decrease in hemoglobin A_{1c} value would be greater in the aerobic and resistance training groups than the control group and would be even greater in the combined exercise training group than the aerobic or resistance training group.

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Context

The benefits of exercise in improving glycemic control in patients with type 2 diabetes are well documented. Previous studies have examined aerobic or resistance exercise alone but not in combination.

Contribution

This randomized, controlled trial showed better reduction in hemoglobin A_{1c} values in patients who followed a combined aerobic exercise and resistance training program 3 times weekly than in patients who followed a program of either exercise type alone.

Caution

Patients in the combined exercise group had a longer duration of exercise than those in the other exercise groups; the study thus does not permit definitive conclusions about whether the benefits were due to longer exercise duration or to the combined exercise training.

—The Editors

METHODS**Design**

We conducted a 26-week, single-center, randomized, controlled trial with a parallel-group design. After a 4-week run-in phase, previously inactive persons with type 2 diabetes were randomly assigned to 1 of 4 groups: aerobic training, resistance training, combined aerobic and resistance training, or a control group that reverted to prestudy exercise levels. Participants and trainers could not feasibly be blinded to group assignment after randomization, but the main study outcomes were measured by blinded technologists using objective methods. The study was approved by the Ottawa Hospital Research Ethics Board, and all participants gave informed consent.

Setting

The exercise intervention took place at 8 community-based exercise facilities in the Ottawa–Gatineau, Canada, region. Exercise was supervised by personal trainers.

Participants

Previously inactive patients with type 2 diabetes who were 39 to 70 years of age were recruited through advertising, physicians, and word of mouth. Inclusion criteria included type 2 diabetes (as defined by the American Diabetes Association [8]) for more than 6 months and a baseline hemoglobin A_{1c} value of 6.6% to 9.9% (normal range, 4.0% to 6.0%). Exclusion criteria were current insulin therapy; participation in exercise 2 or more times weekly for 20 minutes or longer per session or in any resistance training during the previous 6 months; changes during the previous 2 months in oral hypoglycemic, antihypertensive, or lipid-lowering agents or body weight ($\geq 5\%$); serum creatinine level of 200 $\mu\text{mol/L}$ or greater ($\geq 2.26 \text{ mg/dL}$); proteinuria greater than 1 g/d; blood pressure greater than

160/95 mm Hg; restrictions in physical activity because of disease; or presence of other medical conditions that made participation inadvisable.

After initial screening by telephone, requisitions for hemoglobin A_{1c} testing were mailed to potentially eligible individuals. Those with a screening hemoglobin A_{1c} value of 6.6% to 9.9% were invited for in-person assessment, where informed consent was obtained, followed by a history and physical examination. Participants returned on a separate day for maximal exercise stress testing with electrocardiographic monitoring by using a ramp protocol on a treadmill. Persons with abnormalities on this test were allowed to proceed in the trial only if cleared by a cardiologist.

Run-in Phase

Before randomization, all participants entered a 4-week run-in phase to assess adherence. Participants performed 15 to 20 minutes of aerobic exercise and 1 or 2 sets of 8 resistance exercises, at moderate intensity and with supervision. Only persons who attended 10 or more of the scheduled 12 run-in sessions were eligible for randomization.

Randomization

Participants were randomly allocated in equal numbers to the aerobic training, resistance training, combined exercise training, and control groups and were stratified by sex and age (39 to 54 years or 55 to 70 years). Central randomization was used, with allocation concealment before randomization, and block sizes varied randomly between 4 and 8. To permit blinding of the research coordinator, the personal trainer rather than the research coordinator handled the randomization visit.

Intervention

All exercise group participants were provided with a 6-month membership at the exercise facility; the membership fees were covered by study funding to remove economic barriers to participation. Individual exercise supervision was provided weekly for the first 4 weeks after randomization and biweekly thereafter. Attendance was verified through direct observation, exercise logs, and electronic scanning of membership cards. Exercise group participants exercised 3 times weekly, and training progressed gradually in duration and intensity. The aerobic training group exercised on treadmills or bicycle ergometers. Heart rate monitors (Polar Electro Oy, Kempele, Finland) were used to adjust workload to achieve the target heart rate. Participants progressed from 15 to 20 minutes per session at 60% of the maximum heart rate to 45 minutes per session at 75% of the maximum heart rate, as determined by using a maximal treadmill exercise test. The resistance training group performed 7 different exercises on weight machines each session, progressing to 2 to 3 sets of each exercise at the maximum weight that could be lifted 7 to 9 times. The combined exercise training group did the full aerobic training program plus the full resistance training program to ensure an adequate dose of each type of exercise. The frequency of direct supervision by trainers was

the same in all exercise groups. Control participants were asked to revert to prestudy activity levels. The A (available at www.annals.org) shows details of the exercise training programs.

Background physical activity was assessed in all participants by using pedometers (Yamax DIGIWALKER SW-700, Yamax Corporation, Tokyo, Japan). Participants wore pedometers for 1 full week at baseline, week 13, and week 26, except when showering or sleeping. Background activity was defined as the mean daily total step count for the days on which the pedometer was worn, excluding steps during scheduled exercise sessions.

We recommended a diet to all participants that would not cause weight loss to minimize dietary variability among groups. Dietary counseling was based on Canadian Diabetes Association guidelines (9). The dietitian interviewed each participant at baseline, 3 months, and 6 months and reviewed a 3-day food diary. Food diaries were coded by using Nutribase software, version 4 (Cybersoft, Phoenix, Arizona). Prescribed energy intake was 90% or more of estimated weight maintenance requirements (10).

We took steps to minimize dietary and medication co-intervention. Letters were sent to participants' physicians asking that therapy with antihypertensive, lipid-altering, or glucose-lowering medications not be initiated or altered during the 6-month intervention unless it was medically necessary. When medication changes were deemed necessary, we asked physicians and participants to inform us of these. If the hemoglobin A_{1c} value increased at 3 months to 10.5% or greater, we increased oral hypoglycemic therapy in a stepwise manner. If frequent hypoglycemia occurred, we decreased oral hypoglycemic medication in a stepwise manner. We did not initiate changes in antihypertensive or lipid-lowering agents between enrollment and 6 months.

Control participants had the same dietary intervention and spent the same time with the research coordinator and dietitian as did participants in the exercise groups. Control participants and exercise group participants who completed 70% or more of the prescribed sessions received free YMCA memberships for 6 months after the end of the intervention. No other compensation was provided to the participants. Control participants were offered the exercise program of their choice after we obtained measurements at 6 months. This minimized the likelihood of contamination during the intervention and provided an incentive to participate in the study. After the end of the intervention, participants who exercised previously received exercise supervision only at their request, and restrictions on exercise method or medication changes were lifted for all groups.

Outcomes and Measurements

The primary outcome was the absolute change in hemoglobin A_{1c} value between baseline and the end of the 6-month supervised exercise period. Secondary outcomes were plasma lipid values, blood pressure, and body com-

position. Hemoglobin A_{1c} was measured by using turbidimetric immunoinhibition, and total cholesterol, high-density lipoprotein (HDL) cholesterol, and triglyceride levels were measured by using enzymatic methods on a Beckman-Coulter LX20 analyzer (Beckman Instruments, Brea, California). Low-density lipoprotein (LDL) cholesterol levels were calculated by using the Friedewald equation (11). Impedance and reactance were obtained by using a bioelectrical impedance analyzer (101A Analyzer, RJL Systems, Clinton, Michigan), and fat-free mass was calculated by using the equation of Kyle and colleagues (12). Fat mass was calculated by subtracting fat-free mass from body weight. Percentage of body fat was calculated by dividing fat mass by body weight. Blood pressure was measured after 10 minutes at rest; the mean of 2 readings obtained 2 minutes apart was used in statistical analysis.

On separate days at least 48 hours apart, participants underwent strength testing and computed tomography (CT). Strength testing involved determination of the maximum weight that could be lifted 8 times while maintaining proper form. The CT protocol included a scout radiograph, a transverse cut at L4 to L5 to measure abdominal visceral and subcutaneous fat (13, 14), and a mid-thigh cut midway between the inguinal crease and the proximal border of the patella to assess muscle cross-sectional area (15). The images were downloaded as digital files and analyzed by using Slice-O-Matic software, version 4 (Tomovision, Montréal, Québec, Canada), as described elsewhere (7).

All participants were reassessed as described at 3 and 6 months (the end of the intervention), except that CT was performed only at baseline and 6 months. Participants were instructed not to exercise for 48 hours or more before each visit.

Adverse Events

We used a standard form to log each adverse event. Participants were questioned on adverse events by the research coordinator at the 3- and 6-month visits and by the exercise specialist if a scheduled exercise session was missed. In addition, adverse event forms were completed if a participant spontaneously reported an adverse event to any research staff.

Statistical Analysis

We calculated that a sample size of 216 persons (54 per group) was needed to have 80% power to detect a moderate 0.65-SD difference for each of 4 comparisons tested simultaneously, with an overall α value of 0.05: aerobic training versus control, resistance training versus control, combined exercise training versus aerobic training (incremental effect of resistance training beyond that of aerobic training), and combined exercise training versus resistance training (incremental effect of aerobic training beyond that of resistance training). We exceeded this sample size to allow for withdrawals. Previous studies of the effect of aerobic training alone (1) and resistance training alone (16–18) suggested that results of each type of exer-

cise would be comparable. Therefore, the study was not powered to compare aerobic training with resistance training, which would have required a much larger sample.

We performed analyses on an intention-to-treat basis and included all randomly allocated persons (including those who later withdrew). We used SAS, version 9 (SAS Institute, Cary, North Carolina), for all analyses of continuous variables.

For the primary analysis, we used a linear mixed-effects model for repeated measures over time, with hemoglobin A_{1c} as the dependent variable and effects for time, study group, and time-by-group interaction; covariates were age, sex, body mass index, use of oral hypoglycemic medication, and specific exercise facility, with an unstructured covariance matrix. Within the mixed model, we estimated 95% CIs and *P* values for the 4 prespecified intergroup contrasts (combined exercise training versus aerobic training, combined exercise training versus resistance training, aerobic training versus control, and resistance training versus control) for change in hemoglobin A_{1c} value between baseline and 6 months and over time within each group.

To test whether changes in the hemoglobin A_{1c} value differed according to the baseline hemoglobin A_{1c} value, we reran the model with the addition of a term for hemoglobin A_{1c} values at or above the median and a term for the interaction between hemoglobin A_{1c} values at or above the median and time. In a prespecified secondary analysis, we repeated the primary analysis separately for participants with baseline hemoglobin A_{1c} values at or above the median and for those with values below the median. In a sensitivity analysis, we repeated the primary analysis, excluding participants with changes in oral hypoglycemic medication.

For continuous secondary outcomes (anthropometric variables, body composition, lipid values, blood pressure), we used the same procedure as in the primary analysis. Models for lipid values and blood pressure used the same covariates as the hemoglobin A_{1c} models. Models for body composition used the same covariates except for body mass index. For blood pressure, we also performed a sensitivity analysis that excluded participants who had changes to their antihypertensive medication regimen, and for lipid values, we performed a sensitivity analysis that excluded participants who had changes to their lipid medication regimen. For all linear mixed-model analyses, we examined the distributions of residuals and used transformations to achieve normality when necessary.

For discrete secondary outcomes, such as starting or increasing the dose of hypoglycemic medication and discontinuing or decreasing the dose of hypoglycemic medication, we used the Fisher exact test (available at www.graphpad.com/quickcalcs/contingency1.cfm) for the 4 prespecified intergroup comparisons. Changes in antihypertensive and lipid-altering drugs were analyzed separately by using the same procedure as for changes in oral

hypoglycemic drugs. In a post hoc analysis, we used the Fisher exact test to compare the numbers of participants with adverse events in all exercise groups combined versus those in the control group.

Role of the Funding Sources

The DARE trial was supported by grants from the Canadian Institutes of Health Research (MCT-44155) and the Canadian Diabetes Association (The Lillian Hollefriend Grant). The funding sources had no role in design, conduct, or reporting of the study.

RESULTS

Between October 1999 and December 2003, 2282 people were screened. The **Flowchart** shows the flow of participants from recruitment to follow-up. The most common reasons for medical exclusion were musculoskeletal problems limiting exercise (33%), undiagnosed diabetes (24%), and current insulin therapy (13%). Follow-up for the final participant was completed in May 2005. Of the 258 people who entered the run-in phase, 251 (97.3%) were randomly assigned. Of the 7 people who were not randomly assigned, 4 had inadequate adherence and 3 chose not to proceed because of aggravation of arthritis.

Table 1 shows the participants' baseline characteristics. The groups were similar in age, sex, ethnicity, duration of diabetes, and medication use.

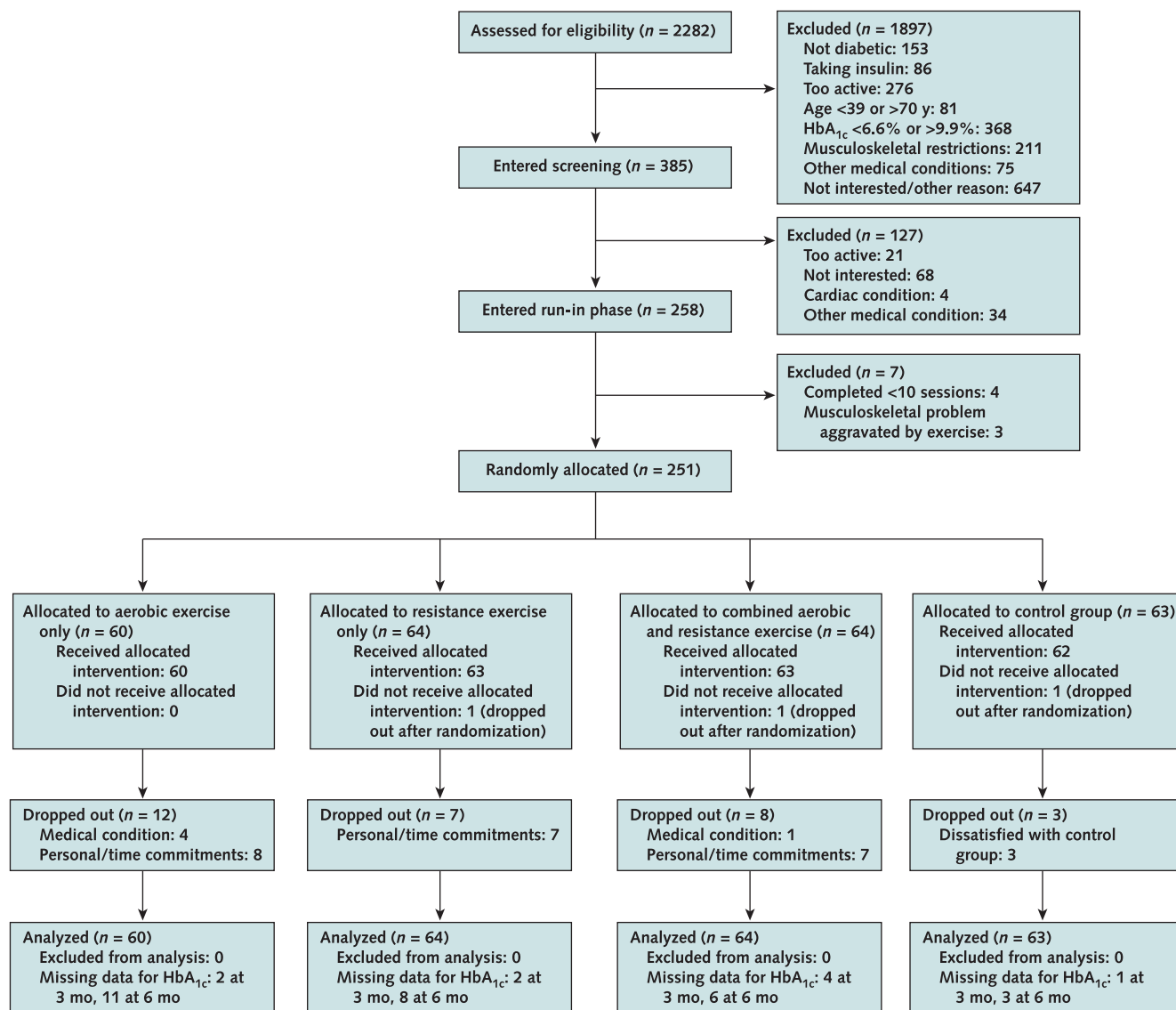
Adherence to Exercise Training

From baseline to 26 weeks, the median exercise training attendance was 86% (interquartile range, 74% to 92%) in the combined exercise training group, 80% (interquartile range, 46% to 93%) in the aerobic training group, and 85% (interquartile range, 72% to 91%) in the resistance training group. Thirty (12%) persons withdrew between randomization and 6 months: 8 (13%) combined exercise training participants, 12 (20%) aerobic training participants, 7 (11%) resistance training participants, and 3 (5%) control participants. The 4 persons who withdrew for medical reasons were all in the aerobic training group. The remaining persons in the exercise groups who withdrew cited a lack of time or loss of interest. Three individuals assigned to the control group withdrew because they were dissatisfied with allocation to this group. Only 1 person assigned to aerobic training reported participating in resistance training, and no one assigned to resistance training reported engaging in aerobic activity beyond prestudy levels. Outside of DARE exercise sessions, background physical activity recorded with pedometers did not change materially over time in any group.

Glycemic Control

Table 2 shows overall results, and **Appendix Table 1** (available at www.annals.org) provides details on within-group changes and subgroup analyses. Adjusted absolute hemoglobin A_{1c} values decreased significantly in the aero-

Figure. Study flow diagram.



HbA_{1c} = hemoglobin A_{1c}.

bic training group compared with the control group (change, -0.51 percentage point; $P = 0.007$) and in the resistance training group compared with the control group (change, -0.38 percentage point; $P = 0.038$). In the combined exercise training group, hemoglobin A_{1c} values changed by an additional -0.46 percentage point compared with the aerobic training group ($P = 0.014$) and -0.59 percentage point compared with the resistance training group ($P = 0.001$). Among participants with a baseline hemoglobin A_{1c} value at or above the median of 7.5%, decreases in hemoglobin A_{1c} value were greater than in those with values less than the median ($P < 0.001$ for interaction of group, time, and hemoglobin A_{1c} value), whereas among participants with baseline hemoglobin A_{1c}

values less than 7.5%, significant decreases occurred only in the combined exercise training group. In a sensitivity analysis, we excluded persons with any changes in oral hypoglycemic medications, and results were similar to those of the overall study sample.

Four combined exercise training participants, 5 resistance training participants, 5 aerobic training participants, and 9 control participants had increases in the dose or initiation of oral hypoglycemic therapy; 4, 5, 6, and 3 participants, respectively, had a decrease in dose or discontinuation of therapy; and 2, 0, 1, and 1 participant, respectively, had both increases and decreases in dose. No significant intergroup differences were observed for any of these changes (A T 2, available at www.annals.org).

Table 1. Baseline Characteristics

Characteristic	Combined Exercise Training Group (n = 64)	Aerobic Training Group (n = 60)	Resistance Training Group (n = 64)	Control Group (n = 63)
Men/women, n/n	40/24	39/21	40/24	41/22
Mean age (SD), y	53.5 (7.3)	53.9 (6.6)	54.7 (7.5)	54.8 (7.2)
Non-Hispanic white race/other race, n/n	55/9	59/1	55/9	61/2
Mean duration of diabetes (SD), y	5.2 (4.8)	5.1 (3.5)	6.1 (4.7)	5.0 (4.5)
Mean hemoglobin A _{1c} value (SD), %	7.67 (0.91)	7.68 (0.85)	7.71 (0.86)	7.66 (0.89)
Medications, n (%)				
Oral hypoglycemic agents				
Total	43 (67)	49 (82)	48 (75)	50 (83)
Metformin	36 (56)	42 (70)	41 (64)	43 (68)
Sulfonylurea	23 (36)	33 (55)	28 (44)	32 (51)
Meglitinide	1 (2)	2 (3)	4 (6)	4 (6)
α -Glucosidase inhibitor	1 (2)	1 (2)	2 (3)	1 (2)
Thiazolidinedione	14 (22)	13 (22)	15 (23)	7 (11)
Antihypertensive agents				
Total	35 (55)	32 (53)	36 (56)	35 (56)
Angiotensin-converting enzyme inhibitor	28 (44)	20 (33)	28 (44)	27 (43)
Diuretic	8 (13)	9 (15)	8 (13)	10 (17)
β -Blocker	2 (3)	4 (7)	9 (14)	6 (10)
Angiotensin-receptor blocker	3 (5)	4 (7)	3 (5)	4 (10)
Calcium-channel blocker	9 (14)	6 (10)	6 (9)	7 (11)
Other	1 (2)	3 (5)	0 (0)	3 (5)
Lipid-lowering agents				
Total	25 (39)	24 (40)	26 (41)	27 (43)
Statin	22 (34)	17 (28)	26 (41)	24 (38)
Fibrate	7 (11)	9 (15)	1 (2)	6 (10)
Other	1 (2)	2 (3)	0 (0)	0 (0)
Antidepressant	4 (6)	11 (18)	9 (14)	6 (10)
Antiplatelet agent	17 (27)	10 (17)	14 (22)	15 (24)
Antiobesity agent	0 (0)	0 (0)	1 (2)	0 (0)

Blood Pressure and Lipid Values

The distribution of residuals was found to be positively skewed for HDL cholesterol and triglycerides. These variables were therefore transformed to the logarithm for analyses, resulting in normal distributions of residuals. Changes in blood pressure; total cholesterol, HDL cholesterol, LDL cholesterol, and triglyceride levels; and the total cholesterol–HDL cholesterol ratio did not statistically significantly differ among groups (Table 2). Six combined exercise training participants, 10 aerobic training participants, 5 resistance training participants, and 4 control participants had increases in the dose or initiation of oral antihypertensive therapy; 4, 1, 0, and 2 participants, respectively, had a decrease in dose or discontinuation of therapy; and 1, 1, 0, and 3 participants, respectively, had both increases and decreases in dose. Nine combined exercise training participants, 6 aerobic training participants, 4 resistance training participants, and 7 control participants had an increase in dose or initiation of lipid-lowering medication; 4, 1, 0, and 2 participants, respectively, had a decrease in dose or discontinuation of therapy; and 0, 1, 1, and 0 participants, respectively, had both increases and decreases in dose. These changes were initiated by the participants' regular physicians or the participants themselves, not by DARE investigators, and did not differ in frequency among groups. No statistically significant intergroup dif-

ferences were observed in any of these changes (Appendix Table 2, available at www.annals.org).

Body Composition

Table 3 shows changes in body composition. Changes in the combined exercise training group did not differ from those in the aerobic training or resistance training groups. Body weight and body mass index decreased more in the aerobic training group than in the control group ($P = 0.008$ and $P = 0.009$, respectively). Waist circumference decreased more in the aerobic training and resistance training groups than in the control group ($P = 0.030$ and $P = 0.054$, respectively), as did abdominal subcutaneous fat ($P = 0.035$ and $P = 0.020$, respectively). Intergroup differences in change in abdominal visceral fat were not statistically significant. Increases in mid-thigh muscle cross-sectional area were significantly greater in the aerobic training and resistance training groups than in the control group ($P = 0.003$ and $P < 0.001$, respectively).

Dietary Intake

All groups had similar slight decreases in overall caloric intake over time. No statistically significant intergroup differences in macronutrient composition were observed (Appendix Table 3, available at www.annals.org).

Table 2. Changes in Hemoglobin A_{1c}, Blood Pressure, and Lipid Values*

Variable	Mean (SD) Value			Difference in Change from Baseline to 6 Months (95% CI)	P Value
	Baseline	3 mo	6 mo		
Hemoglobin A_{1c} [patients], % [n]†					
Combined exercise group	7.46 (1.48) [64]	6.99 (1.56) [60]	6.56 (1.55) [58]	–	–
Aerobic training group	7.41 (1.50) [60]	7.00 (1.59) [58]	6.98 (1.50) [49]	–	–
Resistance training group	7.48 (1.47) [64]	7.35 (1.57) [62]	7.18 (1.52) [56]	–	–
Control group	7.44 (1.38) [63]	7.33 (1.49) [62]	7.51 (1.47) [59]	–	–
Intergroup comparisons					
Aerobic training vs. control	–	–	–	–0.51 (–0.87 to –0.14)	0.007
Resistance training vs. control	–	–	–	–0.38 (–0.72 to –0.22)	0.038
Combined exercise vs. aerobic training	–	–	–	–0.46 (–0.83 to –0.09)	0.014
Combined exercise vs. resistance training	–	–	–	–0.59 (–0.95 to –0.23)	0.001
Systolic blood pressure, mm Hg					
Combined exercise group	131 (22)	133 (26)	129 (23)	–	–
Aerobic training group	134 (22)	131 (26)	131 (23)	–	–
Resistance training group	136 (22)	129 (26)	131 (23)	–	–
Control group	133 (20)	131 (24)	129 (21)	–	–
Intergroup comparisons					
Aerobic training vs. control	–	–	–	1.0 (–3.6 to 5.7)	0.66
Resistance training vs. control	–	–	–	–0.9 (–5.4 to 3.7)	0.71
Combined exercise vs. aerobic training	–	–	–	1.3 (–3.4 to 6.0)	0.59
Combined exercise vs. resistance training	–	–	–	3.2 (–1.4 to 7.8)	0.168
Diastolic blood pressure, mm Hg					
Combined exercise group	79 (13)	78 (14)	79 (14)	–	–
Aerobic training group	82 (14)	79 (14)	79 (14)	–	–
Resistance training group	80 (13)	78 (14)	78 (14)	–	–
Control group	80 (12)	81 (13)	79 (13)	–	–
Intergroup comparisons					
Aerobic training vs. control	–	–	–	–1.5 (–4.7 to 1.7)	0.36
Resistance training vs. control	–	–	–	–1.4 (–4.6 to 1.7)	0.37
Combined exercise vs. aerobic training	–	–	–	1.7 (–1.5 to 5.0)	0.30
Combined exercise vs. resistance training	–	–	–	1.7 (–1.5 to 4.9)	0.30
HDL cholesterol level‡					
Combined exercise group					
mmol/L	1.11 (0.40)	1.13 (0.40)	1.15 (0.40)	–	–
mg/dL	42.7 (15.2)	43.8 (16.0)	44.4 (16.8)	–	–
Aerobic training group					
mmol/L	1.09 (0.39)	1.11 (0.39)	1.10 (0.39)	–	–
mg/dL	42.1 (15.5)	42.8 (15.5)	42.6 (16.3)	–	–
Resistance training group					
mmol/L	1.11 (0.40)	1.11 (0.40)	1.11 (0.40)	–	–
mg/dL	42.7 (15.2)	42.9 (15.2)	42.8 (16.0)	–	–
Control group					
mmol/L	1.06 (0.32)	1.08 (0.40)	1.06 (0.40)	–	–
mg/dL	41.0 (13.5)	41.5 (13.5)	41.1 (14.3)	–	–
Intergroup comparisons					
Aerobic training vs. control					0.78
mmol/L	–	–	–	0.01 (–0.06 to 0.08)	
mg/dL	–	–	–	0.4 (–2.2 to 2.9)	
Resistance training vs. control					0.95
mmol/L	–	–	–	0.00 (–0.07 to 0.06)	
mg/dL	–	–	–	–0.1 (–2.6 to 2.4)	
Combined exercise vs. aerobic training					0.35
mmol/L	–	–	–	0.03 (–0.04 to 0.10)	
mg/dL	–	–	–	1.2 (–1.4 to 3.8)	
Combined exercise vs. resistance training					0.194
mmol/L	–	–	–	0.04 (–0.02 to 0.11)	
mg/dL	–	–	–	1.7 (–0.8 to 4.2)	
LDL cholesterol level§					
Combined exercise group					
mmol/L	3.09 (1.44)	3.01 (1.52)	2.98 (1.44)	–	–
mg/dL	119.2 (56.0)	116.3 (57.6)	115.0 (56.0)	–	–

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Table 2—Continued

Variable	Mean (SD) Value			Difference in Change from Baseline to 6 Months (95% CI)	P Value
	Baseline	3 mo	6 mo		
Aerobic training group					
mmol/L	3.24 (1.46)	3.13 (1.54)	3.08 (1.46)	—	—
mg/dL	124.9 (56.8)	121.0 (58.4)	119.0 (56.8)	—	—
Resistance training group					
mmol/L	3.03 (1.43)	2.93 (1.51)	3.01 (1.43)	—	—
mg/dL	117.0 (55.6)	113.2 (57.1)	116.2 (56.4)	—	—
Control group					
mmol/L	2.99 (1.34)	3.11 (1.42)	2.97 (1.34)	—	—
mg/dL	115.5 (52.8)	119.9 (54.3)	114.5 (52.8)	—	—
Intergroup comparisons					
Aerobic training vs. control					0.33
mmol/L	—	—	—	−0.13 (−0.38 to 0.13)	
mg/dL	—	—	—	−4.9 (−14.8 to 4.9)	
Resistance training vs. control					0.97
mmol/L	—	—	—	0.00 (−0.24 to 0.25)	
mg/dL	—	—	—	0.2 (−9.3 to 9.6)	
Combined exercise vs. aerobic training					0.74
mmol/L	—	—	—	0.04 (−0.21 to 0.30)	
mg/dL	—	—	—	1.6 (−8.2 to 11.5)	
Combined exercise vs. resistance training					0.47
mmol/L	—	—	—	−0.09 (−0.33 to 0.16)	
mg/dL	—	—	—	−3.4 (−12.9 to 6.0)	
Non-HDL cholesterol level					
Combined exercise group					
mmol/L	3.92 (1.68)	3.70 (1.68)	3.66 (1.68)	—	—
mg/dL	151.2 (63.2)	143.0 (66.4)	141.1 (67.4)	—	—
Aerobic training group					
mmol/L	4.07 (1.70)	3.93 (1.70)	4.00 (1.78)	—	—
mg/dL	157.1 (64.3)	151.8 (66.6)	154.3 (67.4)	—	—
Resistance training group					
mmol/L	3.97 (1.60)	3.85 (1.68)	3.85 (1.68)	—	—
mg/dL	153.1 (63.2)	148.7 (65.6)	148.6 (65.6)	—	—
Control group					
mmol/L	3.98 (1.51)	4.09 (1.59)	3.94 (1.59)	—	—
mg/dL	153.7 (58.7)	157.7 (61.9)	151.9 (61.1)	—	—
Intergroup comparisons					
Aerobic training vs. control					0.87
mmol/L	—	—	—	−0.03 (−0.34 to 0.29)	
mg/dL	—	—	—	−1.0 (−13.3 to 11.2)	
Resistance training vs. control					0.65
mmol/L	—	—	—	−0.07 (−0.38 to 0.24)	
mg/dL	—	—	—	−2.7 (−14.6 to 9.1)	
Combined exercise vs. aerobic training					0.25
mmol/L	—	—	—	−0.19 (−0.51 to 0.13)	
mg/dL	—	—	—	−7.2 (−19.5 to 5.1)	
Combined exercise vs. resistance training					0.36
mmol/L	—	—	—	−0.14 (−0.44 to 0.17)	
mg/dL	—	—	—	−5.5 (−17.5 to 6.4)	
Triglyceride level†					
Combined exercise group					
mmol/L	1.61 (1.36)	1.36 (1.20)	1.35 (1.20)	—	—
mg/dL	142.4 (124.0)	120.4 (104.8)	119.2 (136.3)	—	—
Aerobic training group					
mmol/L	1.78 (1.55)	1.64 (1.47)	1.69 (1.55)	—	—
mg/dL	157.2 (137.9)	145.0 (127.0)	149.7 (136.3)	—	—
Resistance training group					
mmol/L	1.83 (1.52)	1.79 (1.52)	1.62 (1.44)	—	—
mg/dL	161.5 (139.2)	158.7 (136.8)	143.6 (128.0)	—	—
Control group					
mmol/L	1.88 (1.51)	1.82 (1.43)	1.89 (1.59)	—	—
mg/dL	166.5 (134.1)	161.0 (129.4)	167.0 (138.9)	—	—

Table 2—Continued

Variable	Mean (SD) Value			Difference in Change from Baseline to 6 Months (95% CI)	P Value
	Baseline	3 mo	6 mo		
Intergroup comparisons					
Aerobic training vs. control					0.48
mmol/L	—	—	—	−0.09 (−0.35 to 0.16)	
mg/dL	—	—	—	−8.1 (−30.6 to 14.3)	
Resistance training vs. control					0.089
mmol/L	—	—	—	−0.21 (−0.46 to 0.03)	
mg/dL	—	—	—	−18.9 (−40.6 to 2.9)	
Combined exercise vs. aerobic training					0.078
mmol/L	—	—	—	−0.23 (−0.48 to 0.03)	
mg/dL	—	—	—	−20.3 (−42.9 to 2.3)	
Combined exercise vs. resistance training					0.39
mmol/L	—	—	—	−0.11 (−0.36 to 0.14)	
mg/dL	—	—	—	−9.6 (−31.5 to 12.4)	
Total cholesterol–HDL cholesterol ratio					
Combined exercise group	4.67 (2.08)	4.37 (2.08)	4.28 (2.24)	—	—
Aerobic training group	4.78 (2.09)	4.63 (2.09)	4.79 (2.25)	—	—
Resistance training group	4.73 (2.08)	4.62 (2.08)	4.64 (2.16)	—	—
Control group	4.82 (1.90)	4.85 (1.90)	4.86 (2.06)	—	—
Intergroup comparisons					
Aerobic training vs. control	—	—	—	−0.02 (−0.46 to 0.42)	0.92
Resistance training vs. control	—	—	—	−0.13 (−0.56 to 0.29)	0.54
Combined exercise vs. aerobic training	—	—	—	−0.40 (−0.84 to 0.04)	0.076
Combined exercise vs. resistance training	—	—	—	−0.29 (−0.72 to 0.14)	0.18

* Results are estimated means from linear mixed-effects models, adjusted for age, sex, exercise training site, body mass index, and use or nonuse of oral hypoglycemic medication. Unless otherwise indicated, the sample for analysis was 64 combined exercise training participants, 60 aerobic training participants, 64 resistance training participants, and 63 control participants. HDL = high-density lipoprotein; LDL = low-density lipoprotein.

† Values in brackets are numbers of patients with complete data.

‡ Values were transformed to the logarithm for analysis and then exponentiated.

§ The sample for analysis was 64 combined exercise training participants, 59 aerobic training participants, 63 resistance training participants, and 62 control participants. Plasma triglyceride levels were too high in 3 participants to use the Friedewald equation to calculate the LDL cholesterol level.

Adverse Events

Table 4 shows details of adverse events. Four individuals, all in the aerobic training group, withdrew because of adverse events: worsening osteoarthritis (2 persons), angina (1 person), and newly diagnosed spinal stenosis (1 person). Overall, adverse events occurred in 71 of the 188 (38%) exercise group participants and 10 of the 63 (14%) control participants ($P = 0.001$, Fisher exact test for control group versus exercise groups). Musculoskeletal injury or discomfort requiring modification of the exercise program or temporary restriction of activity occurred in 49 of the 188 (26%) exercise group participants and 9 of the 63 (14%) control participants ($P = 0.059$ for control group versus exercise groups). No episode of hypoglycemia was severe enough to require assistance. Two combined exercise training participants, 4 aerobic training participants, 4 resistance training participants, and 1 control participant reported mild hypoglycemia. Doses of hypoglycemic medications were subsequently reduced in 9 of these 12 participants, and dietary carbohydrate intake was adjusted in the remaining 3 (1 resistance training participant and 2 aerobic training participants).

DISCUSSION

Our primary findings were that aerobic training and resistance training each improved glycemic control, and that the combination of these 2 forms of exercise was su-

perior to either type of exercise alone. Exercise-induced improvements in glycemic control were greater among persons with higher baseline hemoglobin A_{1c} values. Among persons with lower baseline hemoglobin A_{1c} values, only combined aerobic and resistance training improved values; aerobic or resistance training alone did not. Therefore, individuals with good glycemic control who wish to further improve their hemoglobin A_{1c} through lifestyle measures would be well advised to do both aerobic and resistance exercise. If glycemic control is poor, either aerobic or resistance training alone would also improve the hemoglobin A_{1c} value, but the combination of these forms of exercise would be better.

We chose to have the combined exercise training group perform the full aerobic training program plus the full resistance training program, rather than keeping total exercise time constant across groups by abbreviating the aerobic and resistance training programs in this group. This ensured that participants received an adequate dose of each type of exercise, and the programs for each type of exercise were similar to those of proven hemoglobin A_{1c}-lowering efficacy in previous trials. Our trial was not designed to study effects of exercise volume or duration per se, and the superior effect of combined aerobic and resistance training may reflect the greater amount of exercise

Table 3. Changes in Body Composition*

Variable	Mean Value (SD)			Difference in Change from Baseline to 6 Months (95% CI)	P Value
	Baseline	3 mo	6 mo		
Body weight, kg					
Combined exercise group	101.9 (30.4)	100.2 (30.4)	99.3 (30.4)	–	–
Aerobic training group	103.5 (31.0)	101.8 (30.2)	100.9 (30.2)	–	–
Resistance training group	99.1 (30.4)	98.1 (30.4)	98.0 (30.4)	–	–
Control group	101.3 (28.6)	100.5 (27.8)	101.0 (27.8)	–	–
Intergroup comparisons					
Aerobic training vs. control	–	–	–	–2.2 (–3.9 to –0.6)	0.008
Resistance training vs. control	–	–	–	–0.7 (–2.4 to 0.9)	0.36
Combined exercise vs. aerobic training	–	–	–	0.0 (–1.6 to 1.7)	0.98
Combined exercise vs. resistance training	–	–	–	–1.5 (–3.1 to 0.1)	0.075
Body mass index, kg/m²					
Combined exercise group	35.0 (9.6)	34.5 (9.6)	34.2 (9.6)	–	–
Aerobic training group	35.6 (10.1)	35.1 (10.1)	34.8 (10.1)	–	–
Resistance training group	34.1 (9.6)	33.8 (9.6)	33.7 (9.6)	–	–
Control group	35.0 (9.5)	34.8 (8.7)	34.9 (8.7)	–	–
Intergroup comparisons					
Aerobic training vs. control	–	–	–	–0.74 (–1.29 to –0.18)	0.009
Resistance training vs. control	–	–	–	–0.26 (–0.80 to 0.28)	0.35
Combined exercise vs. aerobic training	–	–	–	0.03 (–0.58 to 0.53)	0.93
Combined exercise vs. resistance training	–	–	–	–0.50 (–1.05 to 0.04)	0.069
Waist circumference, cm					
Combined exercise group	112 (24)	109 (24)	108 (24)	–	–
Aerobic training group	113 (23)	110 (23)	110 (23)	–	–
Resistance training group	110 (24)	108 (24)	107 (24)	–	–
Control group	112 (24)	110 (24)	111 (24)	–	–
Intergroup comparisons					
Aerobic training vs. control	–	–	–	–2.1 (–4.1 to –0.2)	0.030
Resistance training vs. control	–	–	–	–1.8 (–3.7 to 0.03)	0.054
Combined exercise vs. aerobic training	–	–	–	0.1 (–1.8 to 2.0)	0.91
Combined exercise vs. resistance training	–	–	–	–0.2 (–2.1 to 1.7)	0.85
Lean body mass, kg†					
Combined exercise group	63.9 (13.6)	63.5 (13.6)	63.2 (13.6)	–	–
Aerobic training group	64.0 (13.9)	63.1 (13.9)	63.0 (13.9)	–	–
Resistance training group	62.3 (13.6)	61.9 (13.6)	62.5 (13.6)	–	–
Control group	63.0 (12.7)	62.5 (12.7)	62.5 (12.7)	–	–
Intergroup comparisons					
Aerobic training vs. control	–	–	–	–0.47 (–1.96 to 1.03)	0.54
Resistance training vs. control	–	–	–	0.75 (–0.70 to 2.20)	0.31
Combined exercise vs. aerobic training	–	–	–	0.31 (–1.20 to 1.81)	0.69
Combined exercise vs. resistance training	–	–	–	–0.91 (–2.37 to 0.55)	0.22
Fat mass, kg†					
Combined exercise group	37.6 (19.2)	36.3 (19.2)	35.7 (19.2)	–	–
Aerobic training group	39.2 (19.4)	38.3 (19.4)	37.6 (19.4)	–	–
Resistance training group	36.5 (19.2)	35.9 (18.4)	35.2 (19.2)	–	–
Control group	38.0 (17.5)	37.7 (17.5)	38.2 (17.5)	–	–
Intergroup comparisons					
Aerobic training vs. control	–	–	–	–1.84 (–3.63 to –0.05)	0.044
Resistance training vs. control	–	–	–	–1.54 (–3.29 to 0.20)	0.082
Combined exercise vs. aerobic training	–	–	–	–0.23 (–2.03 to 1.57)	0.80
Combined exercise vs. resistance training	–	–	–	–0.53 (–2.28 to 1.23)	0.56
Body fat, %†					
Combined exercise group	36.0 (9.6)	35.2 (9.6)	35.0 (9.6)	–	–
Aerobic training group	37.0 (9.3)	36.8 (9.3)	36.3 (9.3)	–	–
Resistance training group	35.9 (9.6)	35.8 (9.6)	35.0 (9.6)	–	–
Control group	36.6 (8.7)	36.7 (8.7)	36.9 (9.5)	–	–
Intergroup comparisons					
Aerobic training vs. control	–	–	–	–1.0 (–2.6 to 0.6)	0.23
Resistance training vs. control	–	–	–	–1.2 (–2.7 to 0.4)	0.130
Combined exercise vs. aerobic training	–	–	–	–0.4 (–2.0 to 1.2)	0.66
Combined exercise vs. resistance training	–	–	–	–0.1 (–1.7 to 1.4)	0.87

Table 3—Continued

Variable	Mean Value (SD)			Difference in Change from Baseline to 6 Months (95% CI)	P Value
	Baseline	3 mo	6 mo		
Abdominal subcutaneous fat, cm²±§					
Combined exercise group	416 (230)	ND	389 (230)	–	–
Aerobic training group	448 (230)	ND	431 (230)	–	–
Resistance training group	412 (227)	ND	394 (227)	–	–
Control group	420 (209)	ND	416 (209)	–	–
Intergroup comparisons					
Aerobic training vs. control	–	–	–	–13.5 (–25.8 to –1.0)	0.035
Resistance training vs. control	–	–	–	–14.3 (–26.3 to –2.2)	0.020
Combined exercise vs. aerobic training	–	–	–	–9.5 (–21.9 to 2.9)	0.133
Combined exercise vs. resistance training	–	–	–	–8.6 (–20.6 to 3.4)	0.160
Abdominal visceral fat, cm²±§					
Combined exercise group	246 (159)	ND	224 (159)	–	–
Aerobic training group	257 (161)	ND	244 (161)	–	–
Resistance training group	228 (156)	ND	218 (156)	–	–
Control group	252 (147)	ND	250 (147)	–	–
Intergroup comparisons					
Aerobic training vs. control	–	–	–	–11.4 (–27.2 to 4.4)	0.157
Resistance training vs. control	–	–	–	–8.0 (–23.3 to 7.3)	0.30
Combined exercise vs. aerobic training	–	–	–	–8.6 (–24.4 to 7.1)	0.28
Combined exercise vs. resistance training	–	–	–	–12.0 (–27.3 to 3.3)	0.124
Mid-thigh muscle cross-sectional area, cm²±					
Combined exercise group	309 (71)	ND	317 (71)	–	–
Aerobic training group	309 (67)	ND	314 (67)	–	–
Resistance training group	302 (69)	ND	308 (69)	–	–
Control group	314 (62)	ND	311 (62)	–	–
Intergroup comparisons					
Aerobic training vs. control	–	–	–	7.2 (2.5 to 11.8)	0.003
Resistance training vs. control	–	–	–	8.0 (3.5 to 12.5)	<0.001
Combined exercise vs. aerobic training	–	–	–	3.3 (–1.4 to 7.9)	0.168
Combined exercise vs. resistance training	–	–	–	2.4 (–2.1 to 6.9)	0.30

* Results are estimated means from linear mixed-effects models, adjusted for age, sex, exercise training site, and use or nonuse of oral hypoglycemic medication. Unless otherwise indicated, the sample for analysis was 64 combined exercise training participants, 60 aerobic training participants, 64 resistance training participants, and 63 control participants. ND = not done.

† Estimated from bioelectrical impedance analysis.

‡ Derived by using computed tomography. Computed tomography was performed only at baseline and 6 months.

§ The sample for analysis included 63 combined exercise training participants, 59 aerobic training participants, 61 resistance training participants, and 60 control participants. Computed tomography could not be performed in the remaining individuals because they were too large for the scanner.

|| The sample for analysis included 62 combined exercise training participants, 56 aerobic training participants, 59 resistance training participants, and 60 control participants. Computed tomography could not be performed in the remaining individuals because they were too large for the scanner.

performed by the combined exercise training group. However, because the physiologic effects of aerobic training (19) differ from those of resistance training (20, 21), we cannot assume that our results reflect only additional exercise time. Aerobic training involves continuous activity of multiple large muscle groups, whereas resistance training involves isolated, brief activity of single muscle groups. Because of the need to rest between sets due to anaerobic metabolism in resistance training, less than half the time of each resistance exercise session involves active muscle contraction, whereas aerobic exercise is continuous. If our findings simply reflected duration of active exercise, we would expect that the effect of resistance training on hemoglobin A_{1c} would be less than half that of aerobic training, and that the effects of combined exercise training would be less than 1.5 times that of aerobic training. Instead, the effects of aerobic training and resistance training

on hemoglobin A_{1c} were approximately equal, and those of combined exercise training were twice those of aerobic exercise. Even if we assumed that our findings were solely an effect of greater exercise duration in the combined exercise training group, the combined aerobic and resistance program is likely to be more sustainable, because many people would find doing 90 minutes of only 1 type of exercise monotonous. The effects of aerobic and resistance exercise on fitness are complementary: Aerobic exercise increases cardiorespiratory fitness, whereas resistance training increases muscle strength and endurance.

The effect of resistance training on hemoglobin A_{1c} values that we observed was less than that in trials by Dunstan and associates (17) and Castaneda and colleagues (16). There are several possible reasons for this discrepancy. Our participants were younger on average than participants in those 2 trials. Older persons may benefit more from resis-

Table 4. Adverse Events*

Adverse Event	Combined Exercise Training Group (n = 64)	Aerobic Training Group (n = 60)	Resistance Training Group (n = 64)	Control Group (n = 63)†
Serious adverse events‡	0 (0)	4 (7)	0 (0)	0 (0)
Hospitalizations	0 (0)	2 (3)	0 (0)	0 (0)
Any injury or musculoskeletal discomfort	17 (27)	18 (30)	21 (33)	9 (14)
Injury requiring modification of exercise program or restriction of activity	15 (23)	16 (27)	18 (28)	9 (14)
Withdrawal for medical reasons	1 (2)	4 (7)	0 (0)	0 (0)
All participants with an adverse event	22 (34)	24 (40)	25 (39)	10 (16)
Physical adverse events				
Shoulder pain	6 (9)	2 (3)	7 (11)	2 (3)
Aggravation of preexisting arthritis	0 (0)	2 (3)	0 (0)	0 (0)
Tendonitis/epicondylitis/fasciitis	2 (3)	3 (5)	4 (6)	0 (0)
Back pain	2 (3)	3 (5)	2 (3)	0 (0)
Shin splints	1 (2)	1 (2)	0 (0)	0 (0)
Heel spurs	0 (0)	2 (3)	0 (0)	0 (0)
Torn ligament or tendon	1 (2)	0 (0)	1 (2)	0 (0)
Pinched nerve (sciatic, femoral, or cervical)	0 (0)	2 (3)	2 (3)	2 (3)
Musculoskeletal injury due to accident while exercising (dropped weight)	0 (0)	0 (0)	2 (3)	0 (0)
Musculoskeletal injury due to accident outside of exercise program	5 (8)	2 (3)	1 (2)	0 (0)
Other musculoskeletal discomfort	3 (5)	4 (7)	4 (6)	5 (8)
Medical adverse events				
Hypoglycemia	2 (3)	4 (7)	4 (6)	1 (2)
Other medical events§	0 (0)	4 (7)	0 (0)	0 (0)

* Data are the number (percentage) of participants. Percentages are rounded to the nearest 1%. Some individuals had more than 1 type of adverse event—for example, back pain and shoulder pain.

† Injuries in the control group were not related to the study exercise program.

‡ Serious adverse events (hospitalization or lasting disability) were 2 hospitalizations (1 for elective hysterectomy and 1 for elective hernia repair), 1 case of newly diagnosed spinal stenosis, and 1 case of worsening angina.

§ Includes 1 case each of spinal stenosis, elective hysterectomy, temporomandibular joint pain, and inguinal hernia.

tance training than do younger persons, because often they have lost more muscle mass through disuse (22, 23). Mean hemoglobin A_{1c} values at the start of the other 2 studies were higher than those in the DARE trial, and we found greater improvements in participants with higher baseline hemoglobin A_{1c} values. Dunstan and associates (17) did not perform an intention-to-treat analysis, which would bias toward overestimation of intervention effectiveness.

None of our exercise programs had a significant effect on blood pressure compared with the control group, and the effects of exercise training on plasma lipid levels were likewise modest. A recent meta-analysis also did not find significant exercise-induced changes in these variables (4). To achieve greater changes, higher volumes or intensities of exercise might be necessary (24).

The number of adverse events was larger than we expected and than other investigators have reported, possibly because we made a more systematic effort to seek out and document such events. The fact that exercise group participants were more frequently questioned about adverse events may have contributed to the higher number of adverse events reported in these groups compared with the control group. No exercise-induced event led to lasting disability, no severe hypoglycemic episodes occurred, a substantial proportion of control participants had adverse events, and the risk for adverse events was no greater in the combined exercise training or resistance training group than in the aerobic exercise group.

Our study participants were probably more adherent to exercise and healthier on average than the general population with type 2 diabetes. Our findings cannot be generalized to patients who cannot or do not wish to undertake exercise programs, just as findings of medication trials cannot be generalized to people who do not wish to take medications or are intolerant of them. However, the number of individuals participating in our trial far exceeded the numbers recruited locally for any pharmaceutical trial, indicating that there is considerable interest in lifestyle interventions. We excluded patients who were receiving insulin or who had advanced diabetes complications; therefore, our findings cannot necessarily be generalized to such patients. Moreover, our findings cannot necessarily be generalized to unsupervised exercise programs. The monthly cost of our intervention (exercise facility membership fee plus trainer time) averaged \$130 (Canadian) per participant in the aerobic or resistance training groups and \$197 in the combined exercise training group. These costs would decrease over time as the frequency of sessions with a personal trainer decreased.

In summary, aerobic training and resistance training alone each led to improvements in glycemic control, and combined aerobic and resistance training had effects that were greater than those of either method alone. These effects were more powerful among individuals with poor glycemic control at baseline. The combined aerobic and resistance training program was not associated with reduced

adherence compared with the programs featuring just 1 type of exercise, and the number of adverse events was no greater in the combined exercise training group than in the aerobic or resistance training groups alone. Therefore, persons with type 2 diabetes who wish to improve their metabolic control through physical activity should be encouraged to perform both aerobic and resistance training.

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APPENDIX: THE DARE TRIAL EXERCISE INTERVENTION PROGRAMS

An exercise specialist was present for a minimum of 3 scheduled sessions weekly at each site and supervised all exercise programs. After randomization, the exercise specialist met each participant individually at least weekly for 4 weeks, every 2 weeks for the subsequent 2 months, and monthly for the remainder of the program to ensure appropriate progression through the program. If a participant missed a scheduled session, the exercise specialist contacted him or her to ascertain what had happened and whether any specific problems could be addressed. After the initial 2 weeks of the postrandomization period (weeks 5 to 6 of the study), participants were free to attend at the times that were most convenient for them, but they were required to come at

least once weekly during hours when the exercise specialist was present.

The exercise specialist monitored attendance and completion of exercise logs. Attendance was verified by the exercise logs and by electronic scanning of the membership card each time a participant came to the gym.

Every exercise session began with a 5- to 10-minute warm-up consisting of very light exercises, which was designed to allow a gradual warming of the muscles before engaging in vigorous exercise, and ended with a cool-down (5 to 10 minutes of light exercises and stretching).

Aerobic Training

Aerobic training was divided into a prerandomization run-in phase (weeks 1 to 4) and a postrandomization intervention phase (weeks 5 to 26). The aim of the run-in phase was to permit the body to gradually adapt to exercise and to avoid soreness, injury, and discouragement.

All aerobic activities were performed on a cycle ergometer or treadmill. Participants were free to vary the machine used from one visit to the next. Exercise intensity was standardized by using heart rate monitors (Polar Electro Oy) that displayed the participant's heart rate and emitted a warning signal when the heart rate was outside the prescribed training zone, thus guiding the participant in adjusting the workload up or down to achieve the desired intensity. During the run-in phase, participants exercised at a target intensity of 60% of maximum heart rate (defined by maximum heart rate achieved during the maximal treadmill exercise test performed at baseline). This corresponded to a moderate exercise intensity of about 50% of the maximum oxygen consumption. Progression during the intervention phase was more rapid than during the run-in phase. The intensity and duration of exercise were increased on a weekly basis (**Appendix Table 4**).

Resistance Training

Resistance training was divided into a prerandomization run-in phase (weeks 1 to 4) and a postrandomization intervention phase (weeks 5 to 26). The aim of the run-in phase was to build strength gradually without developing undue muscular soreness or injury. This was accomplished by use of light weights and a high number of repetitions.

Resistance exercises were performed on weight machines. Throughout the resistance training program, participants alternated between the exercises of group A and those of group B shown in **Appendix Table 5**. Participants were instructed to exhale while lifting a weight and inhale while lowering it, to minimize blood pressure excursions, and to rest for 2 to 3 minutes between sets. Warm-up and cool-down were the same as for aerobic training.

During the run-in phase, participants performed 1 set per resistance exercise twice weekly for the first 2 weeks and 2 sets of each resistance exercise twice weekly during weeks 3 and 4. Weight or resistance was increased by 5 to 10 pounds when the participant could perform more than 15 repetitions while maintaining proper form. The third weekly session of the run-in phase involved only aerobic exercise, not resistance exercise. The tran-

Appendix Table 1. Changes in Hemoglobin A_{1c} Value*

Group	Mean (SD) Hemoglobin A _{1c} Value [Patients], % [n] [†]			Absolute Change in Hemoglobin A _{1c} Value from Baseline to 6 Months (95% CI), percentage points	P Value	Adjusted Change in Hemoglobin A _{1c} Value from Baseline to 6 Months (95% CI), percentage points	P Value
	Baseline	3 mo	6 mo				
Overall							
Combined exercise group	7.46 (1.48) [64]	6.99 (1.56) [60]	6.56 (1.55) [58]	−0.90 (−1.15 to −0.64)	<0.001	—	—
Aerobic training group	7.41 (1.50) [60]	7.00 (1.59) [58]	6.98 (1.50) [49]	−0.43 (−0.70 to −0.17)	0.002	—	—
Resistance training group	7.48 (1.47) [64]	7.35 (1.57) [62]	7.18 (1.52) [56]	−0.30 (−0.56 to −0.05)	0.018	—	—
Control group	7.44 (1.38) [63]	7.33 (1.49) [62]	7.51 (1.47) [59]	0.07 (−0.18 to 0.32)	0.57	—	—
Combined exercise vs. aerobic training	—	—	—	—	—	−0.46 (−0.83 to −0.09)	0.014
Combined exercise vs. resistance training	—	—	—	—	—	−0.59 (−0.95 to −0.23)	0.001
Aerobic training vs. control	—	—	—	—	—	−0.51 (−0.87 to −0.14)	0.007
Resistance training vs. control	—	—	—	—	—	−0.38 (−0.72 to −0.22)	0.038
Baseline hemoglobin A _{1c} value ≥7.5%							
Combined exercise group	8.44 (1.04) [30]	7.64 (1.32) [28]	7.02 (1.35) [27]	−1.42 (−1.83 to −1.01)	<0.001	—	—
Aerobic training group	8.31 (1.16) [28]	7.51 (1.45) [27]	7.47 (1.33) [21]	−0.83 (−1.28 to −0.38)	<0.001	—	—
Resistance training group	8.29 (1.14) [36]	8.06 (1.48) [35]	7.80 (1.42) [30]	−0.49 (−0.87 to −0.10)	0.013	—	—
Control group	8.30 (1.03) [33]	8.06 (1.38) [33]	8.28 (1.39) [31]	−0.02 (−0.40 to 0.36)	0.90	—	—
Combined exercise vs. aerobic training	—	—	—	—	—	−0.59 (−1.20 to 0.02)	0.058
Combined exercise vs. resistance training	—	—	—	—	—	−0.93 (−1.49 to −0.37)	0.001
Aerobic training vs. control	—	—	—	—	—	−0.81 (−1.40 to −0.21)	0.008
Resistance training vs. control	—	—	—	—	—	−0.46 (−1.00 to 0.08)	0.094
Baseline hemoglobin A _{1c} value <7.5%							
Combined exercise group	6.93 (0.41) [34]	6.76 (0.79) [32]	6.48 (0.84) [31]	−0.46 (−0.73 to −0.18)	0.002	—	—
Aerobic training group	7.00 (0.40) [32]	6.90 (0.78) [31]	6.90 (0.79) [28]	−0.10 (−0.38 to 0.19)	0.50	—	—
Resistance training group	6.95 (0.37) [28]	6.93 (0.78) [27]	6.87 (0.82) [26]	−0.08 (−0.38 to 0.22)	0.59	—	—
Control group	6.85 (0.33) [30]	6.88 (0.75) [29]	7.02 (0.81) [29]	0.17 (−0.11 to 0.46)	0.24	—	—
Combined exercise vs. aerobic training	—	—	—	—	—	−0.36 (−0.76 to 0.04)	0.074
Combined exercise vs. resistance training	—	—	—	—	—	−0.38 (−0.78 to 0.03)	0.070
Aerobic training vs. control	—	—	—	—	—	−0.27 (−0.67 to 0.14)	0.191
Resistance training vs. control	—	—	—	—	—	−0.25 (−0.66 to 0.16)	0.23
No change in oral hypoglycemic medication							
Combined exercise group	7.47 (1.32) [54]	6.95 (1.36) [51]	6.63 (1.39) [48]	−0.84 (−1.11 to −0.57)	<0.001	—	—
Aerobic training group	7.45 (1.34) [50]	6.99 (1.32) [48]	7.02 (1.31) [39]	−0.43 (−0.72 to −0.14)	0.004	—	—
Resistance training group	7.50 (1.30) [52]	7.32 (1.36) [51]	7.24 (1.36) [46]	−0.26 (−0.54 to 0.02)	0.064	—	—
Control group	7.38 (1.20) [50]	7.25 (1.19) [49]	7.56 (1.30) [47]	0.18 (−0.09 to 0.46)	0.19	—	—
Combined exercise vs. aerobic training	—	—	—	—	—	−0.41 (−0.81 to −0.01)	0.044
Combined exercise vs. resistance training	—	—	—	—	—	−0.58 (−0.97 to −0.19)	0.004
Aerobic training vs. control	—	—	—	—	—	−0.62 (−1.02 to −0.21)	0.003
Resistance training vs. control	—	—	—	—	—	−0.44 (−0.83 to −0.05)	0.026

* Results are estimated means from linear mixed-effects models, adjusted for age, sex, exercise training site, body mass index, and use or nonuse of oral hypoglycemic medication. Data are estimated means at each time point.

† Values in brackets are numbers of patients with complete data.

sition from the run-in phase to the intervention phase involved 4 changes in the exercise prescription: increasing frequency of resistance training from 2 to 3 days per week, increasing the number of sets from 2 to 3, increasing the amount of weight lifted, and decreasing the number of repetitions. During the intervention phase, weight or resistance for a given exercise was increased by 5 to 10 pounds when the participant could perform more than 8 repetitions of that exercise while maintaining proper form,

and it was decreased by 5 to 10 pounds if the participant could not perform at least 8 repetitions of that exercise while maintaining proper form.

Combined Aerobic and Resistance Training

This group performed the full aerobic and resistance training programs as described earlier. The aerobic and resistance components were performed on the same days, in varying orders.

Appendix Table 2. Changes to Medication Regimens*

Medication	Treatment Initiated or Dose Increased†	Treatment Discontinued or Dose Decreased‡	Both Increase and Decrease in Dose	No Change to Regimen
Oral hypoglycemic agents				
Combined exercise group	4 (6)	4 (6)	2 (3)	54 (84)
Aerobic training group	5 (8)	5 (8)	0 (0)	50 (83)
Resistance training group	5 (8)	6 (9)	1 (2)	52 (81)
Control group	9 (14)	3 (5)	1 (2)	50 (79)
Antihypertensive agents				
Combined exercise group	6 (9)	4 (6)	1 (2)	53 (83)
Aerobic training group	10 (17)	1 (2)	1 (2)	48 (80)
Resistance training group	5 (8)	0 (0)	0 (0)	59 (92)
Control group	4 (6)	2 (3)	3 (5)	54 (86)
Lipid-altering agents				
Combined exercise group	9 (14)	4 (6)	0 (0)	51 (83)
Aerobic training group	6 (10)	1 (2)	1 (2)	52 (93)
Resistance training group	4 (6)	0 (0)	1 (2)	59 (86)
Control group	7 (11)	2 (3)	0 (0)	54 (84)

* Data are the number (percentage) of participants and are based on 64 combined exercise training participants, 60 aerobic exercise participants, 64 resistance training participants, and 63 control participants. No intergroup difference was statistically significant by the Fisher exact test.

† Initiation of therapy with new medication or an increase in the dose of a medication taken at baseline, with no decrease in dose of or discontinuation of therapy with any other medication in the same class.

‡ Discontinuation of therapy with new medication or decrease in the dose of a medication taken at baseline, with no increase in dose of or initiation of therapy with any other medication in the same class.

Appendix Table 3. Changes in Nutritional Variables*

Variable	Mean Estimated Intake (SD)			Difference from Baseline to 6 Months (95% CI)	P Value
	Baseline	3 mo	6 mo		
Total caloric intake, kcal/d					
Combined exercise group	2073 (786)	1940 (748)	1904 (761)	–	–
Aerobic training group	2027 (785)	1979 (747)	1955 (774)	–	–
Resistance training group	2109 (773)	1950 (737)	1881 (751)	–	–
Control group	2067 (733)	1958 (700)	1896 (694)	–	–
Intergroup comparisons					
Aerobic training vs. control	–	–	–	100 (–99 to 300)	0.32
Resistance training vs. control	–	–	–	–57 (–250 to 137)	0.57
Combined exercise training vs. aerobic training	–	–	–	–98 (–302 to 106)	0.34
Combined exercise training vs. resistance training	–	–	–	58 (–140 to 257)	0.56
Carbohydrate intake, % of total calories					
Combined exercise group	49 (11)	48 (11)	49 (11)	–	–
Aerobic training group	46 (11)	46 (11)	47 (11)	–	–
Resistance training group	47 (11)	47 (11)	48 (11)	–	–
Control group	47 (10)	49 (10)	47 (10)	–	–
Intergroup comparisons					
Aerobic training vs. control	–	–	–	1.7 (–1.4 to 4.7)	0.28
Resistance training vs. control	–	–	–	1.2 (–1.7 to 4.2)	0.42
Combined exercise training vs. aerobic training	–	–	–	–2.2 (–5.3 to 1.0)	0.175
Combined exercise training vs. resistance training	–	–	–	–1.7 (–4.7 to 1.3)	0.27
Protein intake, % of total calories					
Combined exercise group	18 (8)	19 (6)	19 (6)	–	–
Aerobic training group	19 (8)	21 (6)	19 (6)	–	–
Resistance training group	19 (7)	20 (6)	20 (6)	–	–
Control group	20 (7)	18 (6)	19 (5)	–	–
Intergroup comparisons					
Aerobic training vs. control	–	–	–	0.6 (–1.9 to 3.1)	0.63
Resistance training vs. control	–	–	–	0.6 (–1.8 to 3.0)	0.62
Combined exercise training vs. aerobic training	–	–	–	1.1 (–1.4 to 3.6)	0.38
Combined exercise training vs. resistance training	–	–	–	1.1 (–1.3 to 3.6)	0.37
Total fat intake, % of total calories					
Combined exercise group	33 (11)	33 (10)	32 (11)	–	–
Aerobic training group	36 (11)	34 (10)	34 (11)	–	–
Resistance training group	34 (10)	33 (10)	32 (11)	–	–
Control group	34 (10)	33 (10)	33 (10)	–	–
Intergroup comparisons					
Aerobic training vs. control	–	–	–	–1.4 (–4.4 to 1.6)	0.37
Resistance training vs. control	–	–	–	–0.9 (–3.8 to 2.1)	0.56
Combined exercise training vs. aerobic training	–	–	–	1.2 (–1.9 to 4.3)	0.44
Combined exercise training vs. resistance training	–	–	–	0.7 (–2.3 to 3.7)	0.64
Saturated fats, % of total calories					
Combined exercise group	9.9 (5.8)	9.3 (5.2)	8.9 (5.2)	–	–
Aerobic training group	9.6 (5.8)	9.6 (5.2)	9.3 (5.3)	–	–
Resistance training group	9.8 (5.7)	9.8 (5.1)	9.6 (5.1)	–	–
Control group	10.6 (5.4)	8.6 (4.9)	9.2 (4.7)	–	–
Intergroup comparisons					
Aerobic training vs. control	–	–	–	1.1 (–0.8 to 3.1)	0.27
Resistance training vs. control	–	–	–	–0.9 (–3.8 to 2.1)	0.56
Combined exercise training vs. aerobic training	–	–	–	–0.7 (–2.7 to 1.3)	0.48
Combined exercise training vs. resistance training	–	–	–	–0.8 (–2.8 to 1.1)	0.39
Polyunsaturated fats, % of total calories					
Combined exercise group	2.8 (2.2)	2.3 (2.1)	2.8 (2.2)	–	–
Aerobic training group	3.1 (2.2)	2.9 (2.0)	2.7 (2.2)	–	–
Resistance training group	2.8 (2.1)	2.7 (2.0)	2.2 (2.1)	–	–
Control group	2.3 (2.0)	2.6 (1.9)	2.7 (2.0)	–	–
Intergroup comparisons					
Aerobic training vs. control	–	–	–	–0.7 (–1.5 to 0.0)	0.050
Resistance training vs. control	–	–	–	–0.4 (–1.1 to 0.3)	0.28
Combined exercise training vs. aerobic training	–	–	–	0.3 (–0.4 to 1.1)	0.38
Combined exercise training vs. resistance training	–	–	–	0.0 (–0.7 to 0.7)	0.97

Continued on following page

Appendix Table 3—Continued

Variable	Mean Estimated Intake (SD)			Difference from Baseline to 6 Months (95% CI)	P Value
	Baseline	3 mo	6 mo		
Monounsaturated fats, % of total calories					
Combined exercise group	5.7 (3.9)	5.4 (4.4)	5.5 (4.4)	–	–
Aerobic training group	5.5 (4.0)	6.2 (4.4)	6.0 (4.5)	–	–
Resistance training group	6.1 (3.9)	5.8 (4.3)	5.6 (4.3)	–	–
Control group	5.7 (3.7)	5.5 (4.2)	5.8 (4.0)	–	–
Intergroup comparisons					
Aerobic training vs. control	–	–	–	0.3 (–1.0 to 1.6)	0.64
Resistance training vs. control	–	–	–	–0.6 (–1.8 to 0.6)	0.33
Combined exercise training vs. aerobic training	–	–	–	–0.7 (–2.0 to 0.6)	0.30
Combined exercise training vs. resistance training	–	–	–	0.2 (–1.0 to 1.5)	0.73

* Results are estimated means from a linear mixed-effects model, adjusted for age, sex, exercise training site, body mass index, and use or nonuse of oral hypoglycemic medication. The sample for analysis consisted of 64 combined exercise training participants, 60 aerobic training participants, 64 resistance training participants, and 63 control participants at baseline for all variables.

Appendix Table 4. Exercise Program during the Run-in and Intervention Phases

Week	Aerobic Training			Resistance Training			
	Duration, min/d	Intensity, % of maximum heart rate*	Frequency, d/wk	Sets, n	Repetitions, n	Weight, maximum repetition†	Frequency, session/wk
Run-in phase							
1–2	15	60	3	1	15	15	2
2–4	20	60	3	2	15	15	2
Intervention phase							
5–6	25	70	3	3	12	12	3
7–8	30	70	3	3	12	12	3
9–10	35	70	3	3	12	12	3
11–12	40	70	3	3	10	10	3
13–16	45	70	3	3	8	8	3
17–19	40	75	3	3	8	8	3
20–26	45	75	3	3	8	8	3

* The maximum heart rate achieved during the maximal treadmill exercise test performed at baseline.

† The maximum weight that can be lifted the slated number of times while maintaining proper form. For example, 15 maximum repetitions is the maximum weight that can be lifted 15 times while maintaining proper form.

Appendix Table 5. Resistance Training Regimens

Regimen	Muscles Worked
Group A	
Abdominal crunches	Abdominal
Seated row	Back
Seated biceps curls	Biceps
Supine bench press	Chest
Leg press	Leg
Shoulder press	Shoulders and neck
Leg extension	Quadriceps
Group B	
Abdominal crunches	Abdominal
Lateral pulldown	Back
Triceps pushdown	Triceps
Sitting chest press	Chest
Leg press	Leg
Upright row	Shoulders and neck
Leg curls	Hamstrings