Effects of Exercise on Cardiovascular Risk Factors in Type 2 Diabetes

A meta-analysis

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OBJECTIVE—Exercise is a cornerstone of diabetes management and the prevention of incident diabetes. However, the impact of the mode of exercise on cardiovascular (CV) risk factors in type 2 diabetes is unclear.

RESEARCH DESIGN AND METHODS—We conducted a systematic review of the literature between 1970 and October 2009 in representative databases for the effect of aerobic or resistance exercise training on clinical markers of CV risk, including glycemic control, dyslipidemia, blood pressure, and body composition in patients with type 2 diabetes.

RESULTS—Of 645 articles retrieved, 34 met our inclusion criteria; most investigated aerobic exercise alone, and 10 reported combined exercise training. Aerobic alone or combined with resistance training (RT) significantly improved HbA_{1c} −0.6 and −0.67%, respectively (95% CI −0.98 to −0.27 and −0.93 to −0.40, respectively), systolic blood pressure (SBP) −6.08 and −3.59 mmHg, respectively (95% CI −10.79 to −1.36 and −6.93 to −0.24, respectively), and triglycerides −0.3 mmol/L (95% CI −0.48 to −0.11 and −0.57 to −0.02, respectively). Waist circumference was significantly improved −3.1 cm (95% CI −10.3 to −1.2) with combined aerobic and resistance exercise, although fewer studies and more heterogeneity of the responses were observed in the latter two markers. Resistance exercise alone or combined with any other form of exercise was not found to have any significant effect on CV markers.

CONCLUSIONS—Aerobic exercise alone or combined with RT improves glycemic control, SBP, triglycerides, and waist circumference. The impact of resistance exercise alone on CV risk markers in type 2 diabetes remains unclear.

Diabetes Care 34:1228–1237, 2011

Diabetes is a chronic condition brought about by the body's inability to produce enough insulin or to use the insulin that it produces. As a result of this insulin insufficiency, there is an increase in the concentration of glucose in the blood (known as hyperglycemia), as well as other metabolic abnormalities. According to the World Health Organization, the number of individuals with diabetes worldwide has increased from 30 million in 1985 to 171 million in 2000 (1); these rates are expected to further increase, with the World Health Organization predicting that the worldwide prevalence in adults will reach 6.4% by 2030, corresponding to a 39% increase from 2000 to 2030 (2). Of the diagnosed cases of diabetes, it is estimated that approximately 90–95% of individuals have type 2 diabetes (3).

Type 2 diabetes is an independent risk factor for both macrovascular disease (e.g., myocardial infarction and stroke) and microvascular disease (e.g., retinopathy and nephropathy), and is often associated with other cardiovascular (CV) disease (CVD) risk factors, including high blood pressure (BP), dyslipidemia, obesity, lack of physical activity, and smoking (4,5). Although glycemic control is a key therapeutic target for individuals with type 2 diabetes, the major cause of morbidity and mortality among this patient population is CVD, not metabolic dysregulation (6). CVD is the leading cause of mortality among individuals with diabetes (7,8), accounting for 65% of all deaths among this patient group (9). Furthermore, diabetes is twice as common among populations of patients with heart failure when compared with matched control subjects (10), and patients with diabetes are more likely to develop heart failure after a myocardial infarction than nondiabetic individuals (11).

Exercise has long been recognized as a cornerstone of diabetic management and the prevention of incident diabetes. For example, the American College of Sports Medicine currently recommends that individuals with type 2 diabetes expend a minimum cumulative total of 1,000 kcal per week of energy from physical activities (12). Meta-analyses have shown that aerobic or resistance training (RT) is related to statistically significant improvements in glycemic control (13–15). Support for the effect of exercise on other CV risk factors, however, is lacking. Therefore, we conducted this review to investigate the effects of aerobic exercise, RT, and combined aerobic and RT on CV risk factors in type 2 diabetes.

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Received 6 November 2010 and accepted 19 February 2011.
DOI: 10.2337/dc10-1881
This article contains Supplementary Data online at http://care.diabetesjournals.org/lookup/suppl/doi:10.2337/dc10-1881/-/DC1.

RESEARCH DESIGN AND METHODS

Search strategy

The databases SPORTDiscus, SCOPUS, PubMed, and CINAHL were searched using similar search strategies focusing on exercise interventions conducted with individuals who were diagnosed with type 2 diabetes. The searches were limited to studies taking place from 1970 to

October 2009 and studies published as full reports in the English language. References of relevant review articles and trials were screened to identify articles that were not found through the database searches.

Inclusion and exclusion criteria

The study populations consisted of individuals aged ≥18 years who have a diagnosis of type 2 diabetes and are engaging in a structured exercise program consisting of aerobic exercise, progressive RT, or combined aerobic and progressive RT. Because we were interested in exercise programs that had the potential to meet the American College of Sports Medicine's recommendation that individuals with type 2 diabetes expend a minimum cumulative total of 1,000 kcal per week of energy from physical activities, forms of exercise that did not meet this definition (i.e., tai-chi) were not included. To be included, the exercise intervention had to be quantifiable in terms of frequency, intensity, time, and duration. Only studies whose treatment was allocated using a randomized procedure and whose control group was not prescribed exercise as part of the study were eligible for inclusion. Because HbA_{1c} reflects the average blood glucose level during the preceding 8–12 weeks, and given that we were interested in the effects of sustained exercise as opposed to acute bouts, we only included trials in which the exercise intervention had a minimum duration of 8 weeks. Finally, we only included studies that measured at least one of the following outcome measures.

Outcome measures

The chronic hyperglycemia that characterizes type 2 diabetes is related to a significant long-term sequelae, including damage to and eventual failure of various organs (macrovascular), and directly related to the likelihood of developing microvascular complications (8). Therefore, our primary outcome measure was HbA_{1c}, which not only provides an estimate of overall control of blood glucose levels within the preceding 8–12 weeks but also is considered the gold standard for measuring long-term glycemic control (8,16).

Our secondary outcomes included dyslipidemia (HDL cholesterol [C] levels, LDL-C levels, triglyceride levels), systolic BP (SBP), BMI, waist circumference, and weight. Although there is strong evidence to support the notion that improved glycemic control reduces the risks of microvascular complications, a relationship between improved glycemic control and reduction in macrovascular complication has not been demonstrated through randomized controlled trials (8,16). Therefore, our secondary outcomes included dyslipidemia, a condition that is commonly characterized in patients with type 2 diabetes by the "atherogenic lipid triad" of hypertriglyceridemia, low levels of HDL-C, and a predominance of small, dense, LDL-C particles (17) and that has an established relationship with risk of macrovascular complications (8). SBP is a marker of hypertension that has a stronger association with risk of CVD and renal disease than diastolic BP (DBP) (18). Obesity is a prominent risk factor of type 2 diabetes, with an estimated 86% of individuals with type 2 diabetes being overweight or obese, of whom 52% are obese and 8.1% are morbidly obese (19). Moreover, obesity is an independent risk factor for CVD (20), and weight loss among patients with diabetes is often associated with reduced clinical symptoms and mortality risk (21). Therefore, our secondary outcomes included BMI and weight as measures of changes in body composition.

Statistical analysis

Statistical analysis was performed using Review Manager 5 software (RevMan 5.0.17, Cochrane Collaboration, Oxford, U.K.). For continuous outcomes presented on the same scale, we used a weighted mean difference (WMD) calculated using the final follow-up *P* values provided for the intervention and control groups to analyze the size of the intervention effects. When continuous outcomes were not presented on the same scale, standardized mean differences (SMDs) were used to analyze the size of the intervention effects for the intervention and control groups at the studies' last reported end points. In the event that study outcomes were presented as change scores, the first author of the study was contacted with a request for prepost data. Studies whose authors did not respond within 1 month's time or whose prepost data could not be obtained from the Cochrane Collaboration's Library of reviews (13) were excluded (22,23). All data were initially analyzed with a fixed effects model. A standard χ^2 test was used to assess the presence of heterogeneity between studies, with an α significance level of 0.05 used as an indicator of the presence of significant heterogeneity. The degree of inconsistency among study results was estimated using the I^2 parameter, where an I^2 parameter >50% was considered indicative of substantial heterogeneity. Where heterogeneity was found, the analysis was redone using a random effects model.

RESULTS—In the initial search of the databases, 645 articles were initially identified. The most common reasons for excluding articles were lack of a no-exercise or standard care control group; exercise intervention could not be quantified in terms of frequency, intensity, duration, and time; study investigating the effects of acute exercise; wrong study design; and irrelevant study population. A total of 34 articles were included in the review, with two studies (24,25) including three treatment arms (a combined aerobic and RT arm, an aerobic exercise arm, and an RT arm) and one study (26) including two treatment arms (a combined aerobic and RT arm and an aerobic exercise arm). Therefore, 21 studies (24–26, Supplementary Refs. S1–S18) reported outcomes on the effects of aerobic exercise, eight studies looked at the effects of RT (24,25, Supplementary Refs. S19–S24), and 10 studies reported on the effects of combined aerobic and RT in type 2 diabetes (24–26, Supplementary Refs. S25–S31). Four studies reported results through separate publications (Supplementary Refs. S1–S3, S12, and S13).

Characteristics of included studies

Aerobic exercise. The majority of studies (21 studies) included investigated the effects of aerobic exercise among patients with type 2 diabetes (Table 1). The frequency of prescribed exercise ranged from a minimum of one to a maximum of seven sessions per week, with 13 of the studies prescribing exercise 3 days per week. Exercise intensity was reported in terms of percentage of V_{O_2} max, V_{O_2} peak, or maximum heart rate (HR); one study reported exercise intensity in terms of kilocalories expended per week. The intensity of exercise ranged between 50 and 85% V_{O_2} max or V_{O_2} peak and 55 and 85% maximum HR. Length of exercise sessions ranged between 40 and 75 min, and duration of exercise intervention ranged between 2 months and 1 year.

RT. All eight studies looking at the effects of RT (Table 2) involved three supervised

Table 1—*Characteristics of aerobic exercise trials*

Study	Intervention	Frequency, intensity, time, duration	Adherence
Kaplan et al., 1985 (Supplementary Ref. S7)	Diet vs. exercise (walking) vs. diet + exercise vs. control	Exercise group: 8/10 sessions; 2 sessions unknown F: 1 day/week I: 60–70% Vo_2 max T: 40–60 min D: 10 weeks	Directly supervised; log book
Ronnemaa et al., 1986 and 1988 (lipid results for 1986 study) (Supplementary Refs. S12 and S13)	Exercise (walking, jogging, or skiing) vs. control (no instructions re: exercise)	F: 5–7 sessions/week I: 70% Vo_2 max T: 45 min D: 4 months	Exercise diaries
Wing et al., 1988 (Supplementary Ref. S15)	Diet + exercise (walking) vs. diet	F: 4 days/week I: ~1,561 kcal/week T: 3 miles/session D: 10 weeks	3/4 days supervised for first 10 weeks
Raz et al., 1994 (Supplementary Ref. S11)	Exercise (bicycle, treadmill, rowing machine) vs. control	F: 3 days/week I: 65% of Vo_2 max T: 60 min D: 12 weeks	2/3 directly supervised sessions/week
Ligtenberg et al., 1997 (Supplementary Ref. S8)	Aerobic exercise (e.g., bicycle ergometer, swimming, rowing) vs. no exercise control	F: 3 days/week I: 60–80% Vo_2 max T: 50 min D: 26 weeks	Supervised group exercise first 6 weeks, then training at home; log book
Mourier et al., 1997 (Supplementary Ref. S10)	Training + BCAA supplement vs. training + placebo vs. sedentary + BCAA supplement vs. sedentary + placebo	Pretraining period, then: F: 2 days/week I: 75% of Vo_2 peak supervised 45-min cycling class plus F: 1 day/week I: 5 exercises at 85% of Vo_2 peak (on an ergocycle) separated by 3 min of exercise at 50% Vo_2 peak. Both for: D: 2 months	Directly supervised
Boudou et al., 2001 (lipid results) and 2003 (Supplementary Refs. S1 and S2)	Continuous + intermittent exercise vs. control (exercised on ergometer at a constant rate of 60 r.p.m. for 20 min at low intensity [30 W])	F: 2 days/week I: 75% of Vo_2 peak supervised 45-min cycling class plus F: 1 day/week I: 5 exercises at 85% of Vo_2 peak separated by 3 min of exercise at 50% Vo_2 peak. Both for: D: 2 months	Directly supervised
Cuff et al., 2003 (22)	Aerobic (treadmill, bicycle, recumbent stepper, elliptical trainer, rowing machine) vs. combined aerobic + PRT vs. control (usual care)	F: 3 days/week I: 60–75% HRR T: 75 min D: 16 weeks	Directly supervised

Table 1—*Continued*

Study	Intervention	Frequency, intensity, time, duration	Adherence
Van Rooijen et al., 2004 (Supplementary Ref. S14)	Home exercise (walking) + hospital-based aerobics vs. control (relaxation exercises)	Home exercise: F: 2×/day I: moderate RPE of 12–14 ("somewhat hard" on Borg scale) T: start at 10 and work up to 45 min/session D: 12 weeks Hospital aerobics: F: 6 sessions I: 55–69% max HR (RPE 12–14) T: 45 min D: 6 sessions	Physical activity log; attendance log
Middlebrooke et al., 2006 (Supplementary Ref. S9)	Exercise vs. no exercise control	F: 3 days/week I: 70–80% max HR T: 30 min D: 6 months	2 days/week of supervised group exercise; fitted with HR monitors to ensure correct intensity and duration
Brassard et al., 2007 (subjects have LV diastolic dysfunction) (Supplementary Ref. S3)	Exercise (bicycle ergometer) vs. control (no aerobic exercise or RT)	F: 3 days/week I: 60–70% V_{O_2} max T: 30 min D: 12 months	Directly supervised
Kadoglou et al., 2007 (Supplementary Ref. S5)	Exercise (mainly cycling, treadmill walking/running, calisthenics) vs. control (maintain habitual activities)	F: 4 days/week I: 50–85% V_{O_2} max T: 45–60 min D: 16 weeks	Directly supervised
Kadoglou et al., 2007 (Supplementary Ref. S6)	Exercise (treadmill, cycling, calisthenics) vs. control (maintain habitual activities)	F: 4 days/week I: 50–75% V_{O_2} peak T: 45–60 min D: 6 months	Directly supervised
Sigal et al., 2007 (24)	Aerobic (treadmill, bicycle ergometer) vs. RT vs. combined vs. control	F: 3 days/week I: start at 60%, work up to 75% max HR T: start at 15 min, work up to 45 min D: 22 weeks	Supervised weekly for first 4 weeks, biweekly thereafter; logs; identification scanning at gym; HR monitors
Brun et al., 2008 (Supplementary Ref. S4)	Exercise (walking, jogging, or gymnastics) vs. control (routine care)	1-month educational period (8 2-h sessions over 4 weeks): 1 h of exercise education + 1 h of learning to cycle at ventilator threshold for 20–45 min. Then: F: 2 days/week I: at the level of the ventilatory threshold T: 45 min/session D: 11 months	Activity log; HR monitor to ensure correct training intensity

Table 1—*Continued*

Study	Intervention	Frequency, intensity, time, duration	Adherence
Lambers et al., 2008 (26)	Combined endurance + strength training (circuit) vs. endurance (similar to circuit—same intensity but no strength training exercises) vs. control	F: 3 days/week I: 60–85% max HR; RT: started at 60%, increased to 85% 1 RM, 3 sets of 10–15 reps T: 60 min/session D: 3 months	Directly supervised
Nojima et al., 2008 (Supplementary Ref. S17)	Aerobic training (suggested walking, jogging, cycling, swimming) vs. control (routine care)	F: at least 3 days/week I: not stated T: at least 30 min/session D: 12 months	Not assessed
Wycherley et al., 2008 (Supplementary Ref. S18)	Aerobic training (walking/jogging) + caloric restriction vs. caloric restriction	F: 4–5 days/week I: 60–65% HR max increased to 75–80% HR max by week 12 T: 25–30 min/session increased to 55–60 min/session by week 12 D: 12 weeks	HR monitors; at least 1 directly supervised session/week

BCAA, branched-chain amino acid; D, duration; F, frequency; HRR, heart rate reserve; I, intensity; LV, left ventricular; PRT, progressive resistance training; reps, repetitions; RM, repetition maximum; RPE, rating of perceived exertion; T, time.

exercise sessions per week, with the study by Sigal et al. (24) switching to biweekly supervised sessions after 1 month of supervised training sessions. Exercise duration varied between each intervention and ranged between 8 weeks and 6 months. Exercise intensity ranged between 50 and 80% one repetition maximum among the studies.

Combined aerobic and RT. Ten studies were selected for inclusion within this exercise category (Table 3). The majority of the studies directly monitored the compliance of the subjects with the exercise protocol for at least one session per week, with one study switching to biweekly supervised exercise sessions after 1 month of training and one study relying on activity logs to monitor patient adherence to the exercise protocol. Six of the studies involved an exercise program carried out three times per week, two studies involved two weekly sessions, one study involved four weekly sessions, and one study involved a goal of participants engaging in exercise 5 days per week. Intensity of the prescribed aerobic exercise varied between an initial exercise intensity of 35% HR maximum to an upward maximum of 85% HR max. The resistance component of the interventions varied in terms of prescribed load, repetition, and number of sets. Duration of the interventions ranged between 8 weeks and 24 months, with nine of the ten studies having a duration of at least 3 months.

Outcomes

HbA_{1c}. Aerobic exercise reduced HbA_{1c} by 0.6% (−0.62 HbA_{1c} WMD, 95% CI −0.98 to −0.27). RT alone was not found to have a statistically significant effect on HbA_{1c} (−0.33 HbA_{1c} WMD, 95% CI −0.72 to 0.05). Combined aerobic and RT reduced HbA_{1c} by 0.67% (−0.67 HbA_{1c} WMD, 95% CI −0.93 to −0.40), which is considered both statistically and clinically significant.

Dyslipidemia. Aerobic exercise was not found to have a significant effect on HDL-C (−0 HDL WMD, 95% CI −0.05 to 0.05) and LDL-C (−0.10 WMD, 95% CI −0.44 to 0.24). However, aerobic exercise was related to a 0.3 mmol/L decrease (−0.29 WMD, 95% CI −0.48 to −0.11) in triglycerides. Estimates of the effects of RT on HDL-C and LDL-C were not made because only two studies investigated these outcomes. Because only Sigal et al. (24) investigated the effects of RT on triglyceride levels, a summary of effect was not calculated for this outcome. Combined aerobic and RT was not found to have a significant effect on HDL-C (0.05 HDL-C WMD, 95% CI −0.05 to 0.15) and LDL-C (−0.07 LDL-C WMD, 95% CI −0.25 to 0.11), but lowered triglycerides by 0.3 mmol/L (−0.30 triglycerides WMD, 95% CI −0.57 to −0.02). The number of trials in this analysis was small.

Body composition. No statistically significant relationships were found between any of the exercise categories and changes in BMI or body mass; because only one RT study reported BMI as an outcome, estimates of effect were not calculated for BMI within this exercise category. Aerobic exercise was not related to changes in BMI (−0.33 BMI WMD, 95% CI −1.26 to 0.61) or body mass (0.16 body mass WMD, 95% CI −3.43 to 3.76). RT was not related to changes in body mass (−0.48 body mass WMD, 95% CI −4.98 to 4.02). Combined aerobic and RT was not related to changes in BMI (−0.78 BMI WMD, 95% CI −1.89 to 0.33) or body mass (−1.02 body mass WMD, 95% CI −2.85 to 0.82). However, waist circumference did show improvement (−3.1 cm) after combined aerobic and RT (−3.1 WMD, 95% CI −10.3 to −1.2). This difference was significant.

SBP. Aerobic exercise was related to a decrease in SBP of 6 mmHg (−6.08 WMD, 95% CI −10.79 to −1.36). This decrease was found to be statistically significant, but there was significant heterogeneity present. RT was not related to a statistically significant change in SBP among patients with type 2 diabetes (−4.36 WMD, 95% CI −12.14 to 3.42). Combined aerobic and RT is related to a decrease in SBP of 3.59 mmHg

Table 2—*Characteristics of RT trials*

Study	Intervention	Frequency, intensity, time, duration	Adherence
Dunstan et al., 1998 (Supplementary Ref. S22)	RT vs. no exercise control	F: 3 days/week I: 50–55% of 1 RM T: 3 sets of 10–15 reps (2 sets only for first 2 weeks) D: 8 weeks	Directly supervised
Castaneda et al., 2002 (Supplementary Ref. S21)	RT vs. nontraining control	F: 3 days/week I: 60–80% of 1 RM progressing to 70–80% of midstudy 1 RM T: 3 sets of 8–10 reps D: 16 weeks	Directly supervised
Dunstan et al., 2002 (Supplementary Ref. S23)	Moderate weight loss + supervised high-intensity RT vs. moderate weight loss + control	F: 3 days/week I: 50–60% of 1 RM progressing to 75–85% of 1 RM T: 3 sets of 8–10 reps D: 6 months	Directly supervised
Baldi et al., 2003 (Supplementary Ref. S19)	Moderate intensity RT vs. nontraining control	F: 3 days/week I: max weight at which subject could complete 10 upper and 15 lower body sets; increased by 5% when subject completed prescribed circuits and reps T: 2 sets of 12 reps (1 set only for first week) D: 10 weeks	Directly supervised
Brooks et al., 2007 (Supplementary Ref. S20)	RT vs. nontraining control	F: 3 days/week I: 60–80% of 1 RM for 8 weeks, then 70–80% of midstudy 1 RM T: 3 sets of 8 reps D: 16 weeks	Directly supervised
Sigal et al., 2007 (24)	RT vs. control	F: 3 days/week I: max weight at which "T" can be done T: 2–3 sets of 7–9 reps D: 22 weeks	Supervised weekly for first 4 weeks, biweekly thereafter; logs; identification scanning at gym; HR monitors
Cheung et al., 2009 (Supplementary Ref. S24)	RT vs. routine care	F: 5 days/week + 2 supervised sessions 1st month then 1 supervised session each month I: increased tension of band when 12 reps performed with good form T: 2 sets of 12 reps D: 16 weeks	Diary

D, duration; F, frequency; I, intensity; reps, repetitions; RM, repetition maximum; RPE, rating of perceived exertion; T, time.

(−3.59 WMD, 95% CI −6.93 to −0.24). This decrease was statistically significant.

CONCLUSIONS—Management of CV risk factors is a priority among individuals with type 2 diabetes, because CVD is the leading cause of death among individuals with diabetes (8). Furthermore, individuals with type 2 diabetes are at an increased risk of microvascular complications. According to the 2008 Canadian Diabetes Association guidelines, the main interventions for reducing risk of CVD include controlling blood glucose and blood lipid levels, as well as controlling BP (8). Therefore,

Table 3—*Characteristics of combined aerobic and RT trials*

Study	Intervention	Frequency, intensity, time, duration	Adherence
Tessier et al., 2000 (Supplementary Ref. S30)	Mixed aerobic (rapid walking) + RT (2 sets of 20 reps of major muscle groups)	F: 3×/week I: 35–59% HR max progressing to 60–79% HR max at week 4 until the end of the study; 2 sets of 20 reps T: 60 min (20 aerobic, 20 RT) D: 16 weeks	Directly supervised
Maiorana et al., 2002 (Supplementary Ref. S29)	Circuit training (7 RT + 8 aerobic exercises) vs. control	F: 3 days/week I: 55% pretraining MVC to 65% by week 4 (RT); 70% peak baseline HR – 85% by week 6 (aerobic) T: 60 min D: 8 weeks Work:rest 45:15 s	Directly supervised
Cuff et al., 2003 (22)	Combined aerobic (treadmill, bicycle, recumbent stepper, elliptical trainer, rowing machine) + PRT (5 exercises of major muscle groups) vs. control (usual care)	F: 3 days/week I: 60–75% HRR; 2 sets of 12 reps T: 75 min D: 16 weeks	Directly supervised
Loimaala et al., 2003 (Supplementary Ref. S27)	Circuit training (8 exercises for upper and lower extremities) vs. no exercise control	F: 2 days/week I: 70–80% max voluntary contraction for 10–12 reps; 65–75% Vo_2 max T: minimum 30 min at target HR D: 12 months	One supervised session/week
Balducci et al., 2004 (Supplementary Ref. S25)	Aerobic exercise (treadmill, bicycle, or elliptical) + RT (6 exercises for major muscle groups) vs. standard care control	F: 3 days/week I: 40–80% HR reserve (aerobic); 3 sets of 12 reps (RT) at 40–60% 1 RM (retested every 3 weeks) T: 30 min aerobic + 30 min RT D: 12 months	Directly supervised
Loimaala et al., 2007 (Supplementary Ref. S28)	Exercise (jogging or walking + RT) vs. control	F: 2 days/week I: 65–75% Vo_2 max T: minimum 30 min at target HR or intensity D: 12 months RT: F: 2 days/week I: 70–80% 1 RM T: Three sets of 10–12 reps D: 12 months	Two (of four) supervised sessions/week; exercise diary; exercise HR and intensity controlled
Sigal et al., 2007 (24)	Aerobic exercise (treadmill, bicycle ergometer) + RT vs. control	F: 3 days/week I: start at 60, work up to 75% max HR T: start at 15 min, work up to 45 min D: 22 weeks RT:	Supervised weekly for first 4 weeks, biweekly thereafter; logs; identification scanning at gym; HR monitors

Table 3—*Continued*

Study	Intervention	Frequency, intensity, time, duration	Adherence
		F: 3 days/week I: max weight at which "T" can be done T: 2–3 sets of 7–9 reps D: 22 weeks	
Krousel-Wood et al., 2008 (Supplementary Ref. S26)	Exercise tapes (combined aerobic + PRT) vs. no exercise control	F: goal of 5 days/week I: 3–6 METs while using tape T: 10-, 20-, and 30-min tapes D: 3 months	Activity logs
Lambers et al., 2008 (28)	Circuit training (combined endurance + RT) vs. control	F: 3 days/week I: 60–85% max HR; RT: started at 60%, increased to 85% 1 RM, 3 sets of 10–15 reps T: 60 min D: 3 months	Directly supervised

D, duration; F, frequency; HRR, heart rate reserve; I, intensity; max, maximum; METs, metabolic equivalents; MVC, maximum voluntary contraction; PRT, progressive resistance training; reps, repetitions; RM, repetition maximum; T, time.

we selected our outcome measures in this review on the basis of these modifiable risk factors for CVD.

For each 1% increase in the level of HbA_{1c}, the relative risk of CVD increases by 1.18% (27), whereas each 1% decrease in HbA_{1c} levels is associated with a 37% reduction in microvascular complications and a 14% reduction in myocardial infarctions (28). Further, lowering HbA_{1c} in patients with type 2 diabetes decreases the absolute risk of developing coronary heart disease by 5–17% and all cause mortality by 6–15% (29). Because the relationship between the risk of CVD and death from CV causes is linear (28), we can extend our findings of the effects of exercise on HbA_{1c} levels to the associated reductions in CVD risk. The 0.67% reduction in HbA_{1c} levels associated with combined aerobic and RT is related to a 26% decrease in risk of microvascular complications and a 10% decrease in rate of myocardial infarctions. Similarly, the 0.6% decrease in HbA_{1c} levels related to involvement in aerobic exercise is associated with a 22% decrease in microvascular complications risk and an 8% reduction in myocardial infarction rate. These effects are comparable to that of drug monotherapy, which is related to a 0.5–1.5% decrease in HbA_{1c}, depending on the pharmaceutical agent used and the baseline HbA_{1c} level of the individual (30). Because the extent of HbA_{1c} reduction is positively related to the baseline value of HbA_{1c}, combined aerobic and strength training, as well as aerobic training, may be the preferred first-line treatment option for individuals with lower baseline HbA_{1c} values who want to delay the onset of pharmaceutical treatment. Future studies should also consider the impact of concomitant use of nonpharmacologic and drug therapy on CV causes of type 2 diabetes.

According to the Canadian Diabetes Association, BP treatment targets for individuals with type 2 diabetes include maintenance of SBP <130 mmHg (8). Both aerobic and combined aerobic and RT exercise were related to statistically significant declines in SBP (6 mmHg and 3.59 mmHg, respectively). Moreover, the mean SBP of the aerobic exercise trials ranged between 126 and 133 mmHg at last follow-up (mean SBP = 130 mmHg), whereas the mean SBP of the combined aerobic and RT ranged between 129 and 138 mmHg (mean SBP = 134 mmHg) at last follow-up. Therefore, aerobic and combined aerobic and RT exercise have the potential to have a clinically significant impact on the presence of hypertension among individuals with type 2 diabetes. Both combined aerobic and RT, as well as aerobic exercise, were found to decrease triglyceride levels by 0.3 mmol/L. However, we did not find statistical support for the existence of a relationship between aerobic or RT and improved HDL-C and LDL-C among individuals with type 2 diabetes. In a randomized controlled trial of the effects of aerobic exercise on lipid levels in overweight individuals with mild-to-moderate dyslipidemia, it was found that improvements in lipid levels were more closely associated with exercise quantity than exercise intensity or improvements in fitness (31). Therefore, perhaps exercise interventions prescribing higher levels of exercise quantity need to be carried out to positively affect lipid levels in individuals with type 2 diabetes.

Our meta-analysis found little support for the benefits of RT on CV risk factors in type 2 diabetes. The energy expenditure of RT is affected by the number of sets and repetitions, rest interval, number of repetitions, velocity of movement, and load involved in the workout (32). Moreover, the energy expenditure of RT exercises also depends on the combinations of muscle groups worked (e.g., exercises involving greater muscle mass are associated with significantly larger energy expenditure) (33). Therefore, perhaps the RT interventions included in this analysis were not conducted at an intensity high enough to elicit meaningful increases in energy expenditure. Bloomer (34) carried out a randomized cross-over trial involving 10 healthy men to compare the energy expenditure and physiologic responses to moderate-duration resistance versus aerobic exercise. They found that despite being matched for total time and relative intensity, the energy cost of continuous aerobic

exercise was greater than that of intermittent resistance exercise (34). Therefore, future studies on the effect of RT in type 2 diabetes should investigate the effects of high-repetition, high-set weight lifting, which is carried out at higher aerobic levels than the more traditional power-lifting approach. When designing future aerobic exercise interventions, endurance exercises should be prescribed in terms of V_{O_2} reserve, not V_{O_2} max, because V_{O_2} reserve has been established as being directly related to other relative (HR reserve, HR max, the Borg rating of Perceived Exertion 6–20 scale) and absolute (metabolic equivalents) classifications of exercise intensity (35). Further, future studies could identify individual metabolic targets, such as the maximal level of lipid oxidation during exercise. This in turn would allow future meta-analysts to more accurately compare the effects of different intensity levels of exercise on outcomes of interest.

Combined aerobic exercise and RT, as well as aerobic exercise carried out on its own, taking place at least two times per week at an intensity of 60–85% of an individual's HR maximum, is related to statistically significant declines in HbA_{1c}, triglyceride levels, waist circumference, and SBP among individuals with type 2 diabetes; however, these exercise approaches are not related to significant changes in weight or BMI, or to statistically significant changes in HDL-C and LDL-C levels. When RT is not combined with other forms of exercise, it is not significantly related to changes in HbA_{1c} levels or to changes in SBP. More research needs to be conducted before the effects of RT on HDL-C, LDL-C, and triglyceride levels can be discerned.

Additional reference sources can be found in the Supplementary Data.

Acknowledgments—No potential conflicts of interest relevant to this article were reported.

A.C. was involved in the construction and search strategy and contributed to writing the manuscript. R.J.P. was involved in the conception and construction of the search strategy, adjudication of articles included in the analysis, and writing and editing the manuscript.

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