Preventive Medicine 48 (2009) 9–19

Contents lists available at ScienceDirect

Preventive Medicine

journal homepage: www.elsevier.com/locate/ypmed

Review

Impact of progressive resistance training on lipids and lipoproteins in adults: A meta-analysis of randomized controlled trials

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ARTICLE INFO

Available online 1 November 2008

Keywords:
Exercise
Lipids
Cholesterol
Meta-analysis
Systematic review
Adults

ABSTRACT

Objective. Given the discrepant findings of progressive resistance training (PRT) on lipids and lipoproteins in adults, we used the meta-analytic approach to examine this issue.

Methods. Randomized controlled trials ≥4 weeks dealing with the effects of PRT on lipids and lipoproteins in adult humans ≥18 years of age and published between January 1, 1955 and July 12, 2007 were included. Primary outcomes included total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), ratio of total cholesterol to high-density lipoprotein cholesterol (TC/HDL-C), non-high-density lipoprotein cholesterol (non-HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides (TG). A random-effects model was used for analysis with data reported as means and 95% confidence intervals.

Results. Twenty-nine studies representing 1329 men and women (676 exercise, 653 control) were included. Statistically significant improvements were found for TC (−5.5 mg/dl, −9.4 to −1.6), TC/HDL-C (−0.5, −0.9 to −0.2), non-HDL-C (−8.7 mg/dl, −14.1 to −3.3), LDL-C (−6.1 mg/dl, −11.2 to −1.0) and TG (−8.1 mg/dl, −14.5 to −1.8) but not HDL-C (0.7 mg/dl, −1.2 to 2.6). Changes were equivalent to −2.7%, 1.4%, −11.6%, −5.6%, −4.6%, and −6.4%, respectively, for TC, HDL-C, TC/HDL-C, non-HDL-C, LDL-C, and TG.

Conclusions. Progressive resistance training reduces TC, TC/HDL-C, non-HDL-C, LDL-C and TG in adults.

Contents

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doi:10.1016/j.ypmed.2008.10.010

Introduction

Cardiovascular disease (CVD), the number one cause of mortality in the United States (US), is responsible for more than 600,000 deaths per year (Minino et al., 2006). In addition, 80.7 million adults in the US have CVD (Rosamond et al., 2008). Furthermore, the costs associated with CVD are enormous, with annual total direct and indirect costs estimated to be $287.3 billion in 2008 (Rosamond et al., 2008). One of the major risk factors for CVD is less than optimal lipid and lipoprotein levels, a common problem in the US. For example, it is estimated that more than 80 million adults ages 20 years and older have low-density lipoprotein cholesterol (LDL-C) levels ≥130 mg/dl (Rosamond et al., 2008). Exercise, primarily aerobic exercise, is a low-cost therapeutic lifestyle change that has been recommended for improving lipid and lipoprotein levels in adults (Rosamond et al., 2008). While previous meta-analytic research has reported significant improvements in lipids and lipoproteins among both men (Kelley and Kelley, 2006) and women (Kelley et al., 2004) as a result of aerobic exercise, the effects of progressive resistance training (PRT), i.e., weight training, on lipids and lipoproteins in adults have been underwhelming. For example, previous randomized controlled trials addressing the effects of PRT on lipid and lipoprotein outcomes have reported conflicting findings with regards to total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), the ratio of TC to HDL-C (TC/HDL-C), LDL-C and triglycerides (TG) (Blessing et al., 1987; Boardley et al., 2007; Boyden et al., 1993; Bunout et al., 2001; Campbell, 1965; Castaneda et al., 2002; Crowder, 1989; Durak et al., 1990; Elliott et al., 2002; Ensign, 1993; Fahlman et al., 2002; Fenkci et al., 2006; Hagerman et al., 2000; Hersey et al., 1994; Hong, 2004; Johnson et al., 1983; Katznelson et al., 2006; LeMura et al., 2000; Maesta et al., 2007; Manning et al., 1991; Martin, 1994; Olson et al., 2006; Prabhakaran et al., 1999; Sallinen et al., 2007; Sigal et al., 2007; Stone et al., 1982; Thomas et al., 2005; Vincent et al., 2003; Wosornu et al., 1996). Given the conflicting findings regarding the effects of PRT on lipids and lipoproteins in adults, we used the meta-analytic approach (Sacks et al., 1987) to examine the effects of this intervention on lipids and lipoproteins in adults.

Methods

Data sources

Studies for potential inclusion in this meta-analysis were retrieved by searching six computerized databases (PubMed, Embase, SportDiscus, Cochrane Central Register of Controlled Clinical Trials, Current Contents, Dissertation Abstracts International), as well as cross-referencing from retrieved studies, including review articles. The search for relevant studies was conducted from January 1, 1955 forward. The last search was conducted on July 12, 2007. We chose 1955 as the starting date for our literature search since this appeared to be the first year in which an intervention study examined the effects of exercise on cholesterol levels in adults (Mann et al., 1955). While the keywords and terms used varied depending upon the database being queried, terms germane to all searches included "weight training," "lipids," "cholesterol," "resistance exercise," and "resistance training."

Study selection

The inclusion criteria for this study were: (1) randomized controlled trials, (2) PRT ≥4 weeks as the only intervention, (3) adult humans ≥18 years of age, (4) published and unpublished studies (master's theses and dissertations), (5) studies in any language, (6) studies published between January 1, 1955 and July 12, 2007, and (7) one or more of the following lipids and lipoproteins assessed in the fasting state (TC, HDL-C, ratio of TC/HDL-C, LDL-C, TG). In addition we also included non-HDL-C (TC minus HDL-C) as a primary outcome. Exclusion criteria for this meta-analysis were (1) non-randomized trials, (2) animal studies, (3) studies conducted in humans less than 18 years of age, and (4) studies in which additional interventions beyond PRT were implemented in the same group. From each study, we only included those groups that met our inclusion criteria.

Data extraction

Prior to the extraction of data, a codebook that could hold up to 421 items from each study was developed. The major categories of items that were coded included (1) study characteristics (for example, year of publication), (2) subject characteristics (for example, age), (3) lipid and lipoprotein assessment characteristics (for example, time of assessment), (4) PRT program characteristics (for example, length of training) and (5) our primary outcomes (TC, HDL-C, LDL-C, TC/HDL-C, TG, non-HDL-C). In cases where lipid and lipoprotein data were assessed but insufficient data were available for pooling, contact was made with the corresponding author of each study and a request was made for such. All studies were coded by both authors, independent of each other. The authors then reviewed every item for accuracy and precision. Disagreements were resolved by consensus. Using Cohen's kappa statistic (Cohen, 1968), the overall agreement rate prior to correcting discrepant items was 0.91.

Study quality was assessed using a quality index developed by others (Jadad et al., 1996). This assessment is a 3-item questionnaire designed to assess bias, specifically, randomization, blinding, and withdrawals/dropouts. The minimum number of points possible is 0 and the maximum 5, with the higher number representing greater study quality. All questions are designed to elicit a yes (1 point) or no (0 points) response. The questionnaire has been shown to be both valid (face validity) and reliable (researcher inter-rater agreement, $r=0.77$, 95% confidence interval 0.60 to 0.96). However, since no gold standard currently exists for determining study quality, especially for exercise training studies, we believe, as do others, that all scales should be interpreted with extreme caution and should not be used to weight outcomes (Herbison et al., 2006). Study quality was assessed by both authors. Using Cohen's kappa statistic (Cohen, 1968), the overall agreement rate prior to adjudication was 0.90.

Data synthesis

Calculation of study-level effect estimates for lipids and lipoproteins

For this study, the primary outcomes (treatment effects) were changes in lipids and lipoproteins (TC, HDL-C, LDL-C, ratio of TC/HDL-C, TG, non-HDL-C), analyzed separately. Treatment effects for our lipid and lipoprotein variables for each group from each study were

calculated by subtracting the change score in the exercise group from the change score in the control group. Variances were calculated from the pooled standard deviations of change scores in the exercise and control groups. If change score standard deviations were not available, these were calculated from 95% confidence intervals or pre and post standard deviation values according to procedures developed by others (Follmann et al., 1992). Since only one study reported data for non-HDL-C (Sigal et al., 2007), we calculated this as TC minus HDL-C and used previously developed procedures to estimate variances (Follmann et al., 1992). Each treatment effect was then weighted by the inverse of its variance. We used the original metric (milligrams per deciliter) versus some type of standardized metric because we believe it is more clinically meaningful (Mosteller and Colditz, 1996). Secondary outcomes (changes in body weight, body mass index (BMI) in kilogram meters squared, percent body fat, lean body mass) were calculated using the same approach as for our lipid and lipoprotein outcomes.

Pooled estimates for lipids and lipoproteins

After calculating treatment effects and variances for each outcome from each study, all results were pooled using random effects meta-regression (intercept-only model), an approach that accounts for between-study heterogeneity (Hunter and Schmidt, 2000). If the two-tailed, 95% confidence intervals did not cross zero (0) for the intercept, we considered our results to be statistically significant.

Heterogeneity based on a fixed effects model was also examined. This was accomplished using the Q statistic and an alpha value for statistical significance of 0.10 versus 0.05 because this test tends to suffer from low power (Hedges and Olkin, 1985). In addition, we examined the consistency of our between study findings for all outcomes using an extension of Q known as I^2 (Higgins et al., 2003). Generally, I^2 values of 25%, 50%, and 75% may be considered to represent small, medium, and large amounts of inconsistency (Higgins et al., 2003).

If a significant finding was identified for any of our outcomes, we then examined for potential publication bias using random effects meta-regression whereby the criterion variable was the outcome of interest, for example, changes in LDL-C, and the inverse of the sample size was the potential predictor variable (Peters et al., 2006). Ninety-five percent confidence intervals that did not cross zero (0) for the slope of the unstandardized regression coefficients (B) were considered to be suggestive of publication bias. In addition, cumulative meta-analysis, ranked by year, was performed in order to examine results over time (Lau et al., 1995).

Meta-regression

Simple, random-effects meta-regression was used to examine the potential relationship between changes in lipids and lipoproteins and potential predictors. Potential study characteristics that were examined included study quality, year the study was conducted, percent dropout, source of study (published journal article versus dissertation/master's thesis), country study was conducted (USA versus other) type of analysis (intention-to-treat versus per-protocol) and number of hours exercise was avoided prior to lipid assessment. Subject characteristics included age, gender, baseline lipid and lipoprotein levels, changes in body weight, BMI, percent fat, lean body mass, VO_{2max} in $ml \cdot kg^{-1}$ min^{-1} and upper and lower body strength, drugs that could affect lipid and lipoprotein metabolism, cigarette smoking, alcohol consumption, menopausal status of participants (pre versus post), whether the participants were defined by the authors as apparently healthy, changes in diet, whether the participants were physically active prior to taking part in the study and whether the participants were overweight/obese, had type 2 diabetes or cardiovascular disease. Because of a lack of data, we were unable to examine race/ethnicity. Training program characteristics that were examined included length, frequency and intensity of training, defined as a percentage of one-repetition maximum (1 RM), number of sets, number of repetitions, rest period between sets, number of exercises performed, compliance, defined as the percentage of exercise sessions attended, amount of resistance training per week (frequency × sets × repetitions × number of exercises), amount of resistance training per week, adjusted for intensity, and whether the exercise sessions were supervised or unsupervised. We were unable to conduct any type of multiple meta-regression analysis because of missing data. For all meta-regression analyses in which potential predictors were included, we report the slope of the unstandardized regression coefficients (B) along with their 95% confidence intervals. Confidence intervals that did not cross zero (0) were considered to be statistically significant.

Data reporting

With the exception of study quality, which was reported as the median, continuous descriptive statistics are reported as the mean ($\overline{X}$) ± standard deviation (SD) while changes in primary outcomes are reported as $\overline{X}$ and 95% confidence intervals. All meta-analytic analyses were conducted using Stata/SE for Windows (version 8.2).

Results

Study characteristics

Of the 612 studies reviewed, a total of 31 exercise groups from 29 studies met our inclusion criteria (Fig. 1) (Blessing et al., 1987; Boardley et al., 2007; Boyden et al., 1993; Bunout et al., 2001; Campbell, 1965; Castaneda et al., 2002; Crowder, 1989; Durak et al., 1990; Elliott et al., 2002; Ensign, 1993; Fahlman et al., 2002; Fenkci et al., 2006; Hagerman et al., 2000; Hersey et al., 1994; Hong, 2004;

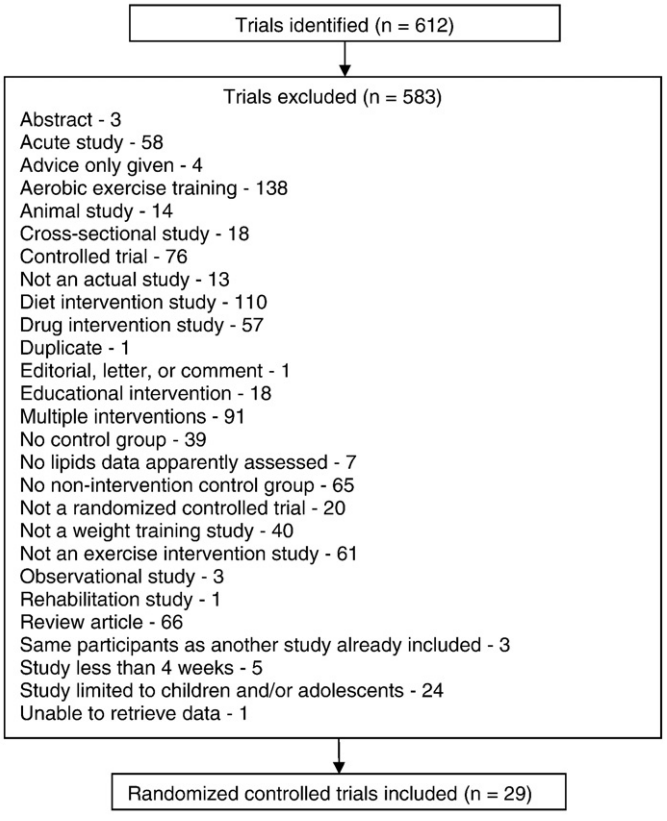

Fig. 1. Description of the number of studies excluded in our meta-analysis, with reasons. The number of reasons (937) exceeds the number of studies excluded because some studies were excluded for more than one reason. The date of the last search for potentially eligible studies was July 12, 2007.

Table 1
Baseline characteristics of participants from studies included in meta-analysis

Variable	Exercise			Control		
	N	$\overline{X}$ ± SD	Range	N	$\overline{X}$ ± SD	Range
Age (yrs)	30	53.0 ± 16.8	20 to 74	29	52 ± 16	20 to 75
Height (cm)	15	164.5 ± 7.4	151 to 178	14	165 ± 7.0	154 to 178
Weight (kg)	25	74.3 ± 9.8	57 to 99	24	74.9 ± 10.8	59 to 101
BMI (kg/m^2)	24	27.0 ± 3.4	21 to 34	23	26.8 ± 3.8	22 to 36
Body fat (%)	22	30.5 ± 6.9	19 to 45	21	30.5 ± 7.0	19 to 45
LBM (kg)	23	48.7 ± 10.4	18 to 65	22	48.6 ± 11.2	18 to 65
TC (mg/dl)	30	204.3 ± 26.8	165 to 268	29	200.6 ± 21.5	170 to 256
HDL-C (mg/dl)	28	50.2 ± 7.6	38 to 77	27	49.7 ± 7.6	37 to 72
TC/HDL-C	28	4.3 ± 0.8	3 to 6	27	4.1 ± 0.7	3 to 6
Non-HDL-C (mg/dl)	28	154.8 ± 26.1	103 to 209	27	150.6 ± 20.1	120 to 205
LDL-C (mg/dl)	23	133.1 ± 21.7	104 to 170	23	129.2 ± 19.6	104 to 172
TG (mg/dl)	26	126.9 ± 52.9	65 to 341	26	131.0 ± 51.4	68 to 341

N, total number of groups reporting data for that variable; $\overline{X}$ ± SD, mean ± standard deviation; Range represents the means for each group from each study; BMI, body mass index; LBM, lean body mass; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; TC/HDL-C, ratio of total cholesterol to high-density lipoprotein cholesterol; Non-HDL-C, non-high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglycerides; To convert TC, HDL-C, non-HDL-C and LDL-C to millimoles per liter (mmol/L) divide by 38.67; To convert TG to millimoles per liter (mmol/L) divide by 88.57.

Johnson et al., 1983; Katznelson et al., 2006; LeMura et al., 2000; Maesta et al., 2007; Manning et al., 1991; Martin, 1994; Olson et al., 2006; Prabhakaran et al., 1999; Sallinen et al., 2007; Sigal et al., 2007; Stone et al., 1982; Thomas et al., 2005; Vincent et al., 2003; Wosornu et al., 1996) while with multiple retrieval attempts the necessary data was not received for one (Baldi and Snowling, 2003). The total number of men and women included in the studies was 1329 (676 exercise, and 653 control). Eleven studies (38%) were limited to females (Boyden et al., 1993; Elliott et al., 2002; Ensign, 1993; Fahlman et al., 2002; Fenkci et al., 2006; LeMura et al., 2000; Maesta et al., 2007; Manning et al., 1991; Martin, 1994; Olson et al., 2006; Prabhakaran et al., 1999), 9 (31%) to males (Blessing et al., 1987; Campbell, 1965; Durak et al., 1990; Hagerman et al., 2000; Johnson et al., 1983; Katznelson et al., 2006; Sallinen et al., 2007; Stone et al., 1982; Wosornu et al., 1996), while 9 (31%) were mixed (Boardley et al., 2007; Bunout et al., 2001; Castaneda et al., 2002; Crowder, 1989; Hersey et al., 1994; Hong, 2004; Sigal et al., 2007; Thomas et al., 2005; Vincent et al., 2003). One mixed study reported data separately for males and females (Hong, 2004). We were unable to calculate the exact number of males and females because of missing data in some studies. Twenty-five studies were published in journals (Blessing et al., 1987; Boardley et al., 2007; Boyden et al., 1993; Bunout et al., 2001; Campbell, 1965; Castaneda et al., 2002; Durak et al., 1990; Elliott et al., 2002; Fahlman et al., 2002; Fenkci et al., 2006; Hagerman et al., 2000; Hersey et al., 1994; Johnson et al., 1983; Katznelson et al., 2006; LeMura et al., 2000; Maesta et al., 2007; Manning et al., 1991; Olson et al., 2006; Prabhakaran et al., 1999; Sallinen et al., 2007; Sigal et al., 2007; Stone et al., 1982; Thomas et al., 2005; Vincent et al., 2003; Wosornu et al., 1996), two as dissertations (Crowder, 1989; Ensign, 1993), and one as a master's thesis (Martin, 1994). Twenty studies (69%) were conducted in the United States (Blessing et al., 1987; Boardley et al., 2007; Boyden et al., 1993; Campbell, 1965; Castaneda et al., 2002; Crowder, 1989; Durak et al., 1990; Ensign, 1993; Fahlman et al., 2002; Hagerman et al., 2000; Hersey et al., 1994; Johnson et al., 1983; Katznelson et al., 2006; LeMura et al., 2000; Manning et al., 1991; Martin, 1994; Olson et al., 2006; Prabhakaran et al., 1999; Stone et al., 1982; Vincent et al., 2003), two each in China (Hong, 2004; Thomas et al., 2005) and the United Kingdom (Elliott et al., 2002; Wosornu et al., 1996), and one each in Brazil (Maesta et al., 2007), Canada (Sigal et al., 2007), Chile (Bunout et al., 2001), Finland (Sallinen et al., 2007), and Turkey (Fenkci et al., 2006). For those studies in which data were available, 21 (81%) used a per-protocol analysis when analyzing their data (Blessing et al., 1987; Boardley et al., 2007; Boyden et al., 1993; Bunout et al., 2001; Crowder, 1989; Durak et al., 1990; Elliott et al., 2002; Ensign, 1993; Fahlman et al., 2002; Fenkci et al., 2006; Hagerman et al., 2000; Hersey et al., 1994; Hong, 2004; Johnson et al., 1983; LeMura et al., 2000; Maesta et al., 2007; Manning et al., 1991; Martin, 1994; Prabhakaran et al., 1999; Sallinen et al., 2007; Vincent et al., 2003) while five (19%) used the intention-to-treat approach (Castaneda et al., 2002; Katznelson et al., 2006; Sigal et al., 2007; Thomas et al., 2005; Wosornu et al., 1996). Study quality ranged from 1 to 5 (median = 2).

Subject characteristics

Baseline characteristics of the participants are shown in Table 1. For race/ethnicity, four studies reported that more than one racial/ethnic group was included (Boardley et al., 2007; Katznelson et al., 2006; Martin, 1994; Sigal et al., 2007), three were limited to Hispanics (Bunout et al., 2001; Castaneda et al., 2002; Maesta et al., 2007), while two each were limited to either Asians (Hong, 2004; Thomas et al., 2005) or Whites (Boyden et al., 1993; Ensign, 1993). Five studies reported that some participants were taking drugs during the study that might affect lipid metabolism (Boardley et al., 2007; Castaneda et al., 2002; Fahlman et al., 2002; Sallinen et al., 2007; Sigal et al., 2007), while six reported that none were (Boyden et al., 1993; Crowder, 1989; Fenkci et al., 2006; LeMura et al., 2000; Manning et al., 1991; Olson et al., 2006). For cigarette smoking, eleven studies reported that none of the participants smoked cigarettes (Boardley et al., 2007; Castaneda et al., 2002; Crowder, 1989; Fahlman et al., 2002; Fenkci et al., 2006; Hong, 2004; LeMura et al., 2000; Maesta et al., 2007; Martin, 1994; Olson et al., 2006; Prabhakaran et al., 1999), while three reported that some participants smoked (Boyden et al., 1993; Hong, 2004; Wosornu et al., 1996). Three studies reported that some participants consumed alcohol during the study (Boyden et al., 1993; Crowder, 1989; Hong, 2004), while two others reported that none of the participants consumed alcohol (Fenkci et al., 2006; Martin, 1994). Only one study reported changes in diet that may have affected lipid and lipoprotein levels (Crowder, 1989). Twenty-three studies reported that none of the participants were physically active prior to taking part in the study (Blessing et al., 1987; Boardley et al., 2007; Boyden et al., 1993; Castaneda et al., 2002; Crowder, 1989; Elliott et al., 2002; Ensign, 1993; Fahlman et al., 2002; Fenkci et al., 2006; Hagerman et al., 2000; Hersey et al., 1994; Hong, 2004; Johnson et al., 1983; Katznelson et al., 2006; LeMura et al., 2000; Manning et al., 1991; Martin, 1994; Olson et al., 2006; Prabhakaran et al., 1999; Sigal et al., 2007; Stone et al., 1982; Thomas et al., 2005; Vincent et al., 2003), while one reported that participants were physically active (Sallinen et al., 2007). For menopausal status, ten studies included women who were postmenopausal (Boardley et al., 2007; Bunout et al., 2001; Castaneda et al., 2002; Durak et al., 1990; Fahlman et al., 2002; Hersey et al., 1994; Hong, 2004; Maesta et al., 2007; Thomas et al., 2005; Vincent et al., 2003), five included women who were premenopausal (Boyden et al., 1993; Ensign, 1993; LeMura et al., 2000;

Table 2
Training program characteristics of studies included in meta-analysis

Variable	*N*	$\overline{X}$ ± SD	Range
Length (weeks)	31	24.0 ± 19.0	8 to 78
Frequency (times/week)	30	2.9 to 0.4	2 to 3
Intensity (%1RM)	15	70.3 ± 10.4	50 to 87
Duration (minutes/session)	12	47.7 ± 11.5	24 to 60
Sets (#)	29	2.6 ± 1.1	1 to 5
Repetitions (#)	29	11.5 ± 6.6	7 to 30
Exercises (#)	30	9.2 ± 3.1	3 to 16
Rest between sets (seconds)	13	82.9 ± 37.6	22 to 150
Compliance (%)	20	85.5 ± 11.6	56 to 100

N, total number of groups reporting data for that variable; $\overline{X}$ ± SD, mean ± standard deviation; %1RM, percentage of 1-repetition maximum; #, number; Compliance, percentage of exercise sessions attended.

Table 3
Changes in primary and secondary outcomes for studies included in meta-analysis

Variable	*N*	$\overline{X}$(95% CI)	*Q* (*p*)	I^2
Primary outcomes (mg/dl)				
- TC	30	−5.5 (−9.4, −1.6)*	102.6 (<0.001)**	71.7
- HDL-C	28	0.7 (−1.2, 2.6)	211.5 (<0.001)**	87.2
- TC/HDL-C	14	−0.5 (−0.9, −0.2)*	96.7 (<0.001)**	86.6
- Non-HDL-C	26	−8.7 (−14.1, −3.3)*	234.2 (<0.001)**	89.3
- LDL-C	23	−6.1 (−11.2, −1.0)*	152.2 (<0.0001)**	85.5
- TG	26	−8.1 (−14.5, −1.8)*	89.4 (<0.001)**	72.0
Secondary outcomes				
- Body weight (kg)	21	0.003 (−0.4, 0.4)	8.2 (0.99)	<0.0001
- BMI (kg/m^2)	14	−0.2 (−0.2, 0.1)	14.5 (0.34)	10.6
- Body fat (%)	15	−1.8 (−2.5, −1.1)*	30.6 (0.006)**	54.2
- LBM (kg)	15	1.0 (0.4, 1.5)*	25.1 (0.03)**	44.1

N, total number of groups reporting data in which a treatment effect could be calculated; $\overline{X}$(95% CI), mean and 95% confidence interval; *Q*, heterogeneity value; *p*, significance value for Q; I^2, percentage (%) of inconsistency for study results, calculated from Q statistic; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; TC/HDL-C, ratio of total cholesterol to high-density lipoprotein cholesterol; Non-HDL-C, non-high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglycerides; BMI, body mass index; LBM, lean body mass.

* significantly different from zero (0).

** statistically significant at $p<0.10$; To convert TC, HDL-C, non-HDL-C and LDL-C to millimoles per liter (mmol/L) divide by 38.67; To convert TG to millimoles per liter (mmol/L) divide by 88.57.

Olson et al., 2006; Prabhakaran et al., 1999), and two included both (Manning et al., 1991; Sigal et al., 2007). Fourteen studies reported that participants were apparently healthy prior to participation (Boyden et al., 1993; Bunout et al., 2001; Elliott et al., 2002; Ensign, 1993; Fahlman et al., 2002; Hersey et al., 1994; Hong, 2004; LeMura et al., 2000; Manning et al., 1991; Olson et al., 2006; Prabhakaran et al., 1999; Sallinen et al., 2007; Thomas et al., 2005; Vincent et al., 2003). While none of the studies reported that all participants were hyperlipidemic, seven included some participants that were hyperlipidemic (Boardley et al., 2007; Castaneda et al., 2002; Hong, 2004; Maesta et al., 2007; Sallinen et al., 2007; Sigal et al., 2007; Thomas et al., 2005), while two apparently had no participants that were hyperlipidemic (Boyden et al., 1993; Olson et al., 2006). Three studies reported that all participants had diabetes (Castaneda et al., 2002; Durak et al., 1990; Sigal et al., 2007), another three reported that some participants had diabetes (Hong, 2004; Thomas et al., 2005; Wosornu et al., 1996), while six others reported that none of the participants had diabetes (Bunout et al., 2001; Ensign, 1993; Fenkci et al., 2006; Katznelson et al., 2006; Olson et al., 2006; Sallinen et al., 2007). For CVD, one study reported that participants had a history of CVD (Wosornu et al., 1996), two reported that some participants had a history (Castaneda et al., 2002; Hagerman et al., 2000), while 10 reported that none of the participants had such a history (Boardley et al., 2007; Elliott et al., 2002; Ensign, 1993; Fahlman et al., 2002; Fenkci et al., 2006; Hersey et al., 1994; Martin, 1994; Olson et al., 2006; Thomas et al., 2005; Vincent et al., 2003). Four studies reported that all participants were overweight or obese (Fenkci et al., 2006; Maesta et al., 2007; Manning et al., 1991; Olson et al., 2006), seven included some participants that were overweight or obese (Boardley et al., 2007; Castaneda et al., 2002; Hong, 2004; Katznelson et al., 2006; Sallinen et al., 2007; Sigal et al., 2007; Thomas et al., 2005), while none of the participants were overweight or obese in two studies (Boyden et al., 1993; Ensign, 1993).

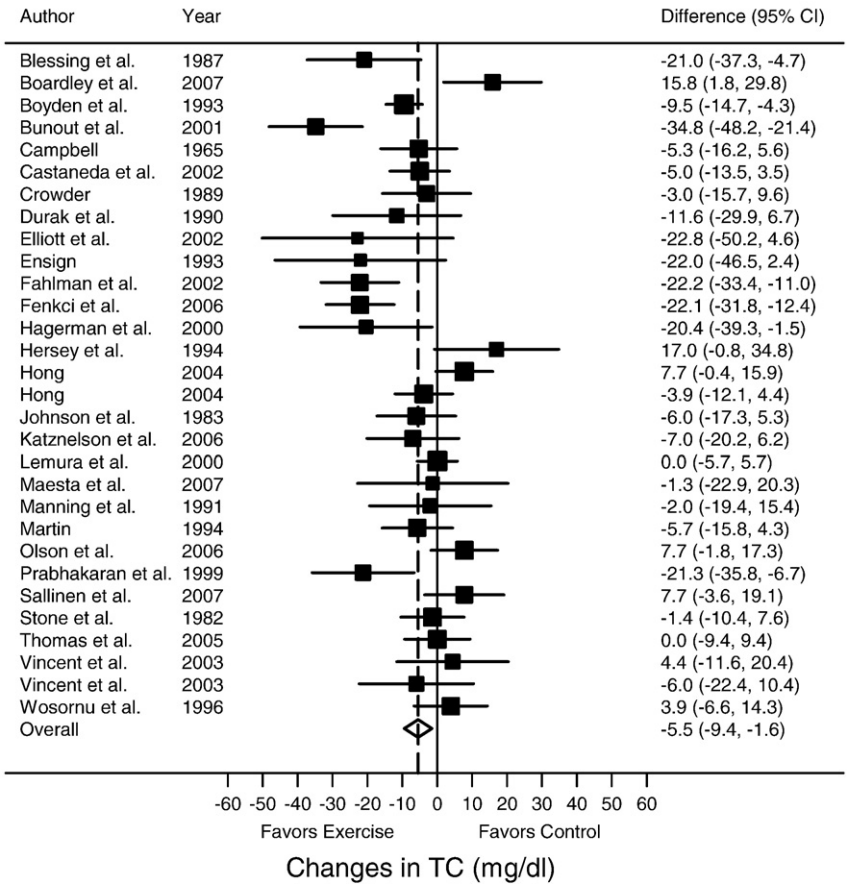

Fig. 2. Forest plot for changes in TC and 95% confidence intervals for each outcome as well as the overall weighted mean difference and 95% confidence interval for studies included in our meta-analysis. The size of the black boxes for each outcome represents the weight given to that outcome. The overall mean difference is shown by the middle of the diamond while the left and right extremes of the diamond represent the corresponding 95% confidence interval. The vertical dashed line represents the overall mean change. To convert to millimoles per liter (mmol/L) divide by 38.67.

Lipid assessment characteristics

Lipids and lipoproteins were typically assessed in the morning after an overnight fast of approximately 12 h. The number of hours that exercise was avoided prior to the assessment of lipids and lipoproteins ranged from 24 to 168 h ($\overline{X}$ ± SD, 55.9 ± 36.4 h) for those studies that provided this information (Blessing et al., 1987; Boyden et al., 1993; Elliott et al., 2002; Fahlman et al., 2002; Hersey et al., 1994; LeMura et al., 2000; Olson et al., 2006; Prabhakaran et al., 1999; Sallinen et al., 2007; Sigal et al., 2007). The Friedewald method was used almost exclusively to estimate LDL-C (Friedewald et al., 1972).

Training program characteristics

Training program characteristics are shown in Table 2. For those studies that reported data, 17 were supervised (Blessing et al., 1987; Boyden et al., 1993; Bunout et al., 2001; Campbell, 1965; Castaneda et al., 2002; Crowder, 1989; Ensign, 1993; Fenkci et al., 2006; Hagerman et al., 2000; Hersey et al., 1994; Hong, 2004; Maesta et al., 2007; Prabhakaran et al., 1999; Sallinen et al., 2007; Sigal et al., 2007; Thomas et al., 2005; Wosornu et al., 1996), two were unsupervised (Katznelson et al., 2006; Martin, 1994), and two included both (Boardley et al., 2007; Olson et al., 2006).

Outcomes analysis

Primary outcomes

Statistically significant reductions were found for TC, the ratio of TC/HDL-C, non-HDL-C, LDL-C, and TG. However, no statistically significant changes in HDL-C were observed (Table 3, Figs. 2–7). Based on a fixed-effects model, a large and statistically significant amount of heterogeneity was observed across all lipid and lipoprotein outcomes. Using the absolute changes in Table 3 and the baseline values for the exercise groups in Table 1, relative changes in lipids and lipoproteins were equivalent to −2.7% (95% CI, −4.6 to −0.8), 1.4% (−2.4 to 5.2), −11.6% (−20.9 to −4.7), −5.6% (−9.1 to −2.1), −4.6% (−8.4 to −0.8), and −6.4% (−11.4 to −1.4) respectively, for TC, HDL-C, TC/HDL-C, non-HDL-C, LDL-C, and TG. No statistically significant publication bias was observed for any of our lipid and lipoprotein outcomes. Cumulative meta-analysis, ranked by year, showed that statistically significant pooled decreases have consistently been present since 1993 for TC, 1999 for TC/HDL-C, 1993 for non-HDL-C, 2002 for LDL-C and 2005 for TG (results not shown). Within the time frame of included studies in this meta-analysis (January 1, 1955 and July 12, 2007) changes in HDL-C have been non-significant.

Secondary outcomes

Statistically significant decreases were found for percent body fat while a statistically significant increase in lean body mass was observed (Table 3). No statistically significant changes were found for body weight or BMI. Based on a fixed-effects model, a moderate and statistically significant amount of heterogeneity was observed for changes in both percent body fat and lean body mass. Using the same approach for calculating relative changes in lipids and lipoproteins, differences in our secondary outcomes were equivalent to 0.0003% (−0.06 to 0.6), −0.2% (−0.7 to 0.4), −5.6% (−8.2 to −3.1) and 2.0% (0.6 to 3.4), respectively, for body weight, BMI, percent body fat, and lean body mass.

Meta-regression for primary outcomes

Statistically significant associations were found between decreases in TC and decreases in BMI (B, 14.7, 3.7 to 25.7), increases in upper

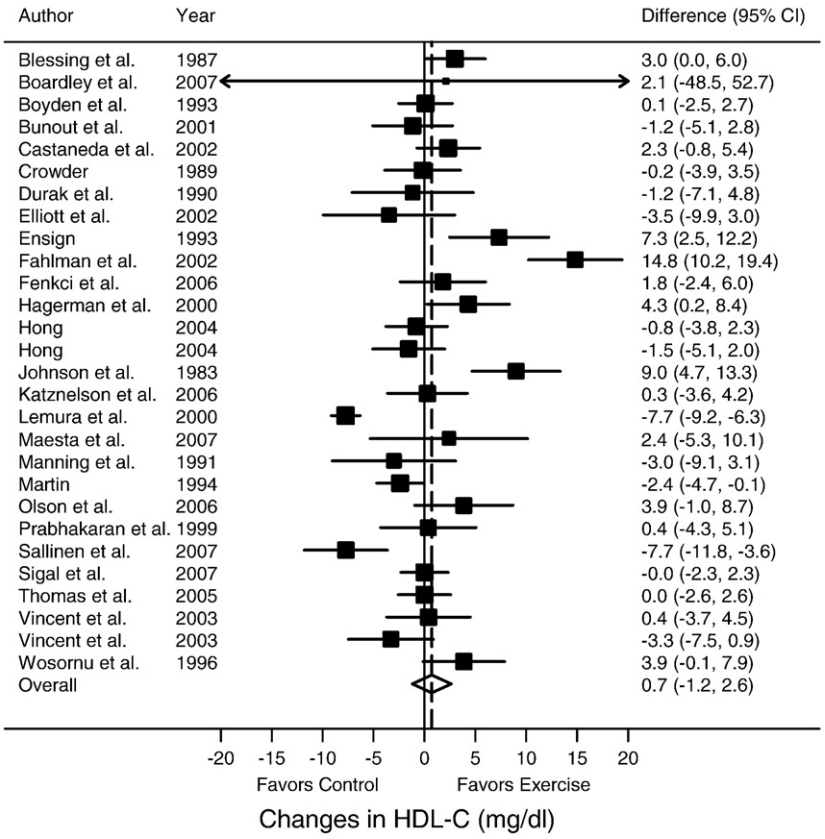

Fig. 3. Forest plot for changes in HDL-C and 95% confidence intervals for each outcome as well as the overall weighted mean difference and 95% confidence interval for studies included in our meta-analysis. The size of the black boxes for each outcome represents the weight given to that outcome. The overall mean difference is shown by the middle of the diamond while the left and right extremes of the diamond represent the corresponding 95% confidence interval. The vertical dashed line represents the overall mean change. To convert to millimoles per liter (mmol/L) divide by 38.67.

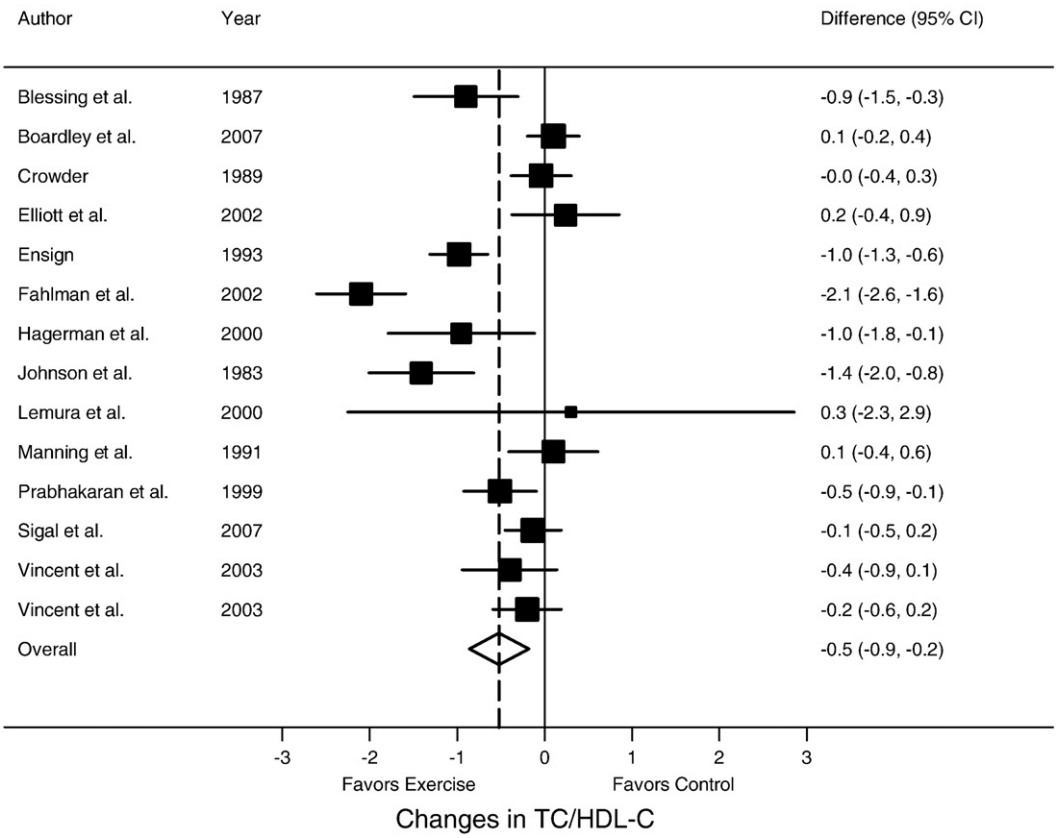

Fig. 4. Forest plot for changes in the ratio of TC/HDL-C and 95% confidence intervals for each outcome as well as the overall weighted mean difference and 95% confidence interval for studies included in our meta-analysis. The size of the black boxes for each outcome represents the weight given to that outcome. The overall mean difference is shown by the middle of the diamond while the left and right extremes of the diamond represent the corresponding 95% confidence interval. The vertical dashed line represents the overall mean change.

body strength (B, −0.5, −0.7 to −0.2), fewer exercises (B, 1.6, 0.1 to 3.1) and greater dropout rates (B, −0.5, −0.9 to −0.1). For HDL−C, increases were associated with lower initial levels of HDL−C (B, −0.3, −0.5 to −0.02) and decreases in BMI (B, −4.9, −9.5 to −0.3). Decreases in the ratio of TC/HDL−C were associated with decreases in BMI (B, 1.6, 0.4 to 2.7), increases in LBM (B, −0.4, −0.7 to −0.2), and greater dropout rates (B, −0.01, −0.02 to −0.005). For non-HDL-C, greater decreases were associated with greater decreases in body weight (B, 6.7, 0.7 to 12.8), BMI (B, 19.1, 7.2 to 31.0), greater dropout rates (B, −0.6, −1.0 to −0.3) and increases in upper body strength (B, −0.4, −0.7 to −0.04). For LDL-C, greater decreases were associated with studies conducted in the US versus other countries (B, −16.3, −26.0 to −6.6), higher intensity training (B, −1.1, −1.9 to −0.2), and greater compliance to the exercise protocol (B, −0.7, −1.3 to −0.02). No other statistically significant associations were found for any of our other potential predictors or for TG.

Discussion

Evaluation and interpretation of findings

The overall results of our study suggest that PRT reduces TC, the ratio of TC/HDL-C, non-HDL-C, LDL-C and TG in adults. This is in contrast to two recent narrative reviews that have suggested that PRT has little or no effect on lipids and lipoproteins in adults (Braith and Stewart, 2006; Williams et al., 2007). One possible reason for this discrepancy may be the fact that these previous reviews were based on the more subjective, narrative approach versus the more objective meta-analytic approach (Sacks et al., 1987). More specifically, these previous reviews based their conclusions on whether results were statistically significant or not (vote-counting approach), an approach that has been shown to be less valid and reliable than the statistical pooling of findings in meta-analysis (Hedges and Olkin, 1985). Based on previous research, our reported changes are equivalent to the following in relation to reducing the risk of coronary heart disease: (1) a reduction of an average of 5% (95% CI, 2% to 20%) as a result of decreases in TC (Consensus Development Panel, 1985) (2) a reduction of 21% in men (95% CI, 6% to 45%) as a result of reductions in TC/HDL-C (Kinosian et al., 1995), (3) a reduction of approximately 5% in men and women (95% CI, 2% to 8%) as a result of decreases in non-HDL-C (Bezafibrate Infarction Research Group, 2000), (4) a reduction of approximately 9% (95% CI, 2% to 24%) as a result of decreases in non-HDL-C (National Cholesterol Education Program et al., 2002), and (5) a reduction of 3% in men (95% CI, <1% to 6%) and 7% in women (95% CI, 1% to 14%) as a result of reductions in TG (Hokanson and Austin, 1996).

The reductions in non-HDL-C are noteworthy since recent research has suggested that non–HDL-C may be a better predictor of CVD morbidity (Pischon et al., 2005) and mortality (Cui et al., 2001) than LDL-C. This seems plausible given that non-HDL-C contains all known lipid particles considered to be atherogenic (low-density lipoprotein cholesterol, lipoprotein (a), intermediate-density lipoprotein, very-low-density lipoprotein) (Frost and Havel, 1998). In addition, patient burden is reduced because fasting isn't usually necessary prior to assessment (Frost and Havel, 1998). The improvements in LDL-C are also especially relevant given that LDL-C is currently the primary target of lipid lowering therapy in adults (National Cholesterol Education Program et al., 2002).

The lack of a statistically significant increase in HDL-C suggests that aerobic exercise may be the more appropriate type of exercise for increasing HDL-C in adults. For example, our previous meta-analytic work dealing with the effects of aerobic exercise on lipids

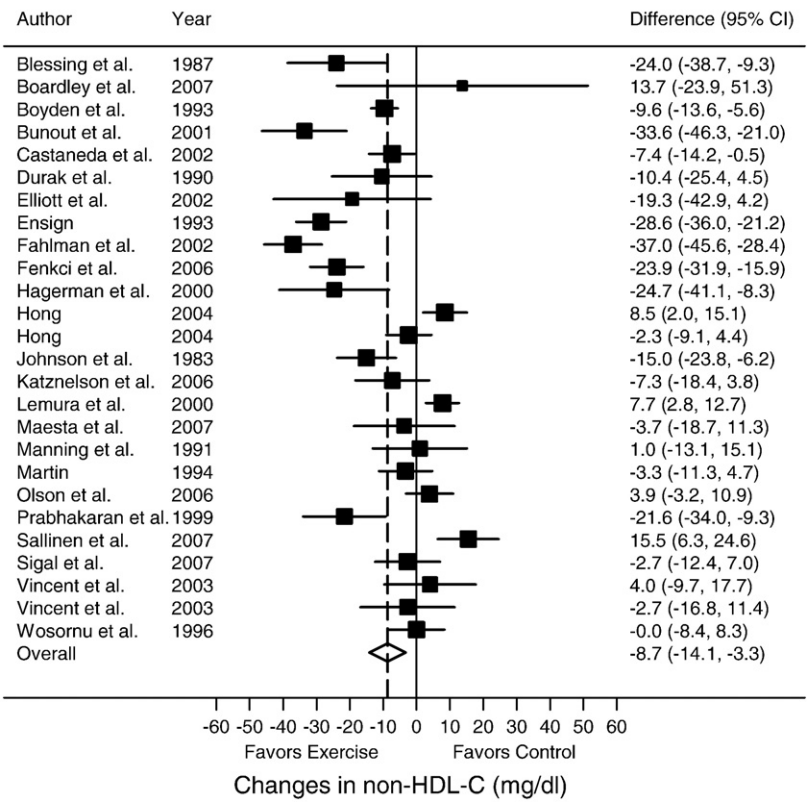

Fig. 5. Forest plot for changes in non-HDL-C and 95% confidence intervals for each outcome as well as the overall weighted mean difference and 95% confidence interval for studies included in our meta-analysis. The size of the black boxes for each outcome represents the weight given to that outcome. The overall mean difference is shown by the middle of the diamond while the left and right extremes of the diamond represent the corresponding 95% confidence interval. The vertical dashed line represents the overall mean change. To convert to millimoles per liter (mmol/L) divide by 38.67.

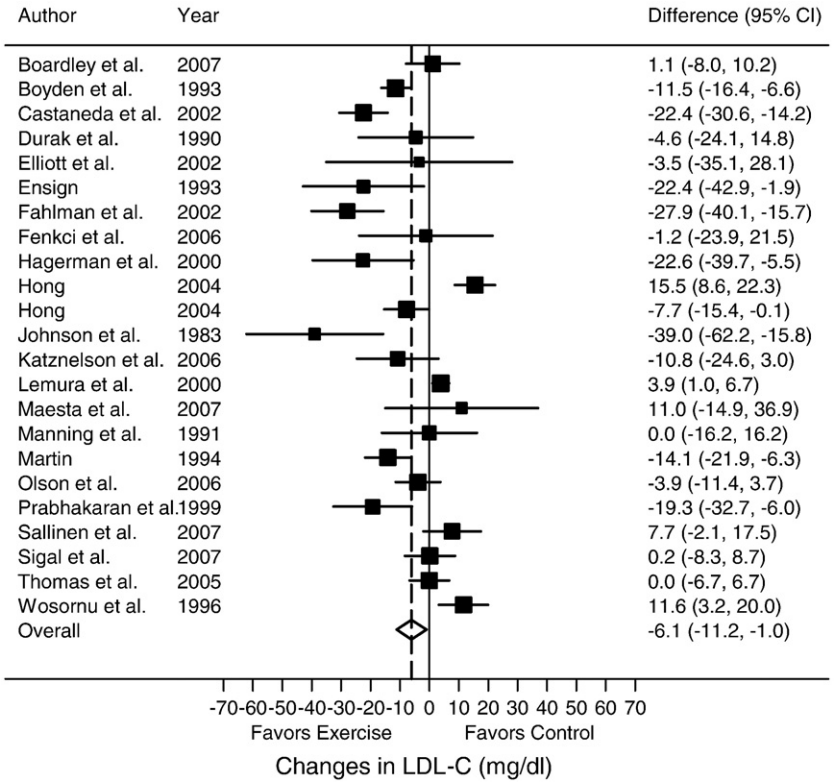

Fig. 6. Forest plot for changes in LDL-C and 95% confidence intervals for each outcome as well as the overall weighted mean difference and 95% confidence interval for studies included in our meta-analysis. The size of the black boxes for each outcome represents the weight given to that outcome. The overall mean difference is shown by the middle of the diamond while the left and right extremes of the diamond represent the corresponding 95% confidence interval. The vertical dashed line represents the overall mean change. To convert to millimoles per liter (mmol/L) divide by 38.67.

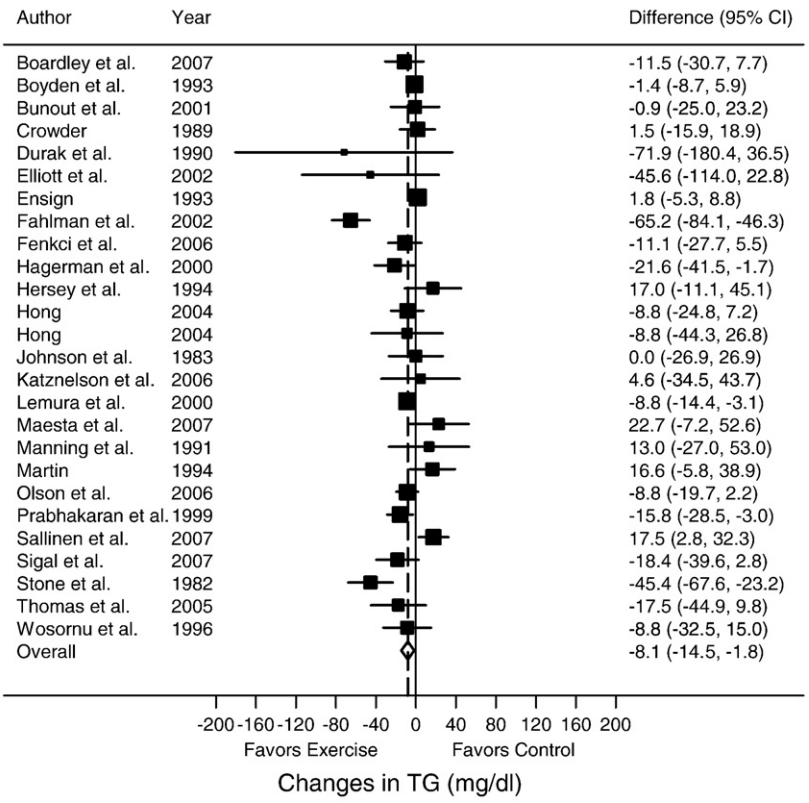

Fig. 7. Forest plot for changes in TG and 95% confidence intervals for each outcome as well as the overall weighted mean difference and 95% confidence interval for studies included in our meta-analysis. The size of the black boxes for each outcome represents the weight given to that outcome. The overall mean difference is shown by the middle of the diamond while the left and right extremes of the diamond represent the corresponding 95% confidence interval. The vertical dashed line represents the overall mean change. To convert to millimoles per liter (mmol/L) divide by 88.57.

and lipoproteins in men and women found statistically significant increases in HDL-C of 2% in men (Kelley and Kelley, 2006) and 3% in women (Kelley et al., 2004). However, we're not aware of any definitive reasons as to how HDL-C may be improved as a result of aerobic exercise but not PRT. Therefore, it is suggested that future research explore this issue.

Given our findings and current exercise guidelines recommending participation in both aerobic and PRT (Haskell et al., 2007; Nelson et al., 2007), the greatest overall benefits on lipids and lipoproteins may best be derived from participation in both. However, we are not aware of any consensus regarding such benefits. Regardless, participation in aerobic and PRT should almost always be recommended because of the numerous other benefits that can be derived from such (Pedersen and Saltin, 2006).

Despite the fact that we observed important improvements in lipids and lipoproteins as a result of PRT, changes in other lifestyle factors (for example, reduction in saturated fat intake) and possibly the prescription of lipid lowering agents such as hydroxymethyl glutaryl coenzyme A reductase inhibitors (statins) may be necessary to meet current lipid and lipoprotein goals (National Cholesterol Education Program et al., 2002).

We found several interesting associations between potential predictors and changes in lipids and lipoproteins. First, the inverse relationship between decreases in TC, TC/HDL-C and non-HDL-C with greater dropout rates may be reflective of more difficult exercise regimens in which greater benefits were derived but resulted in a greater loss of participants completing the exercise intervention. Second, the fact that decreases in BMI were associated with greater improvements in TC, HDL-C, TC/HDL-C, and non-HDL-C suggests that the changes observed for these primary outcomes may have been influenced by changes in BMI as a result of PRT versus PRT itself. However, it's important to note that the changes in BMI observed in our study were small (<1%) and non-significant. Third, the association between upper body strength and changes in TC and non-HDL-C suggests that greater decreases in TC and non-HDL-C are associated with greater increases in upper body strength. This was an interesting finding to us since one might have expected a greater association with changes in lower body strength given the larger amount of muscle mass that is generally involved in performing lower body exercises. Fourth, the fact that we found an association between changes in HDL-C and baseline levels of HDL-C suggests that greater increases in HDL-C may be achieved in those individuals with lower baselines values. Intuitively, this seems plausible. Fifth, the association between changes in HDL-C and LBM suggests that greater increases in HDL-C are associated with greater increases in LBM. Sixth, the association between changes in body weight and non-HDL-C suggests that greater decreases in bodyweight are associated with greater decreases in non-HDL-C. However, similar to changes in BMI, the changes in body-weight observed in this study were small and non-significant. Seventh, the fact that greater decreases in LDL-C were associated with studies published in the US versus other countries may be reflective of what is known as country bias (Vickers et al., 1998). Eighth, the association between changes in LDL-C and training intensity suggests that greater decreases in LDL-C may be achieved by training at a higher intensity of one's 1RM. However, this has to be considered with respect to the increased dropout rates associated with higher-intensity training (Haskell et al., 2007). Ninth, the association between greater decreases in LDL-C with higher compliance rates may reflect the greater benefits derived from a greater commitment to the PRT intervention. Lastly, we have no scientific explanation for the association between greater decreases in TC and fewer exercises performed.

Study strengths and limitations

The strengths of our study include the use of the meta-analytic approach for examining the effects of PRT on lipids and lipoproteins in adults. Such an approach allowed us to (1) improve power for our primary outcomes and selected subgroup analyses, (2) resolve uncertainty where studies disagreed, (3) improve estimates of treatment effectiveness, and (4) provide direction for future research based on a quantitative approach for reviewing the literature. However, while the results of our study provide important findings, they must be viewed with respect to the following potential limitations. First, despite the fact that a large amount of heterogeneity was observed for our primary outcomes we were unable to identify any significant sources of this heterogeneity based on the meta-regression tests we conducted. While we used a random-effects model that accounts for this heterogeneity and leads to more conservative (wider) confidence intervals when heterogeneity is present, some believe that heterogeneous results should not be combined, regardless of the model chosen (Higgins and Green, 2006).

Second, we conducted a large number of simple versus multiple meta-regression tests because of our desire to include as much data as possible for each potential predictor. However, by using this approach, some of our significant associations could be nothing more than the play of chance given the large number of tests we performed. However, we believe, as do others, that adjustments for these comparisons should not be made and that limiting the number of analyses is not in the best interest of science (Rothman, 1990; Sterne and Davey, 2001). Regardless, the associations we observed for our meta-regression tests and potential predictors should be viewed with caution and thus, need to be tested in large, well-designed randomized controlled trials before they can be confirmed. Third, the results of our study should not be generalized beyond the characteristics of our included studies. For example, we do not believe that it's appropriate to try and generalize our results to children and adolescents. Fourth, meta-analysis, like any review, is limited by the data that is available or can be obtained. For example, less than half of the data were available on the intensity of training and rest period between each set and exercise. Since these are important factors in determining the amount of work performed as well as the degree of pressure versus volume load on the cardiovascular system (Braith and Stewart, 2006; Williams et al., 2007), it is suggested that future studies collect and report this information. In addition, sufficient data on compliance to the PRT protocol were reported for only 65% of the exercise groups. Since compliance to the exercise protocol could have a significant impact on the results, future studies should collect and report this information. Furthermore, since less than half of the groups reported complete data on changes in percent body fat and lean body mass, future studies should also collect and report this information since changes in body composition may have an influence on changes in lipids and lipoproteins.

Conclusions

The results of our study suggest that PRT reduces TC, the ratio of TC/HDL-C, non-HDL-C, LDL-C and TG in adults.

Conflict of interest statement
The authors declare that there are no conflicts of interest.

Acknowledgments

The authors would like to thank Dr. William Haskell of Stanford University for reviewing our reference list and codebook.

This study was funded by Grant-in-Aid #0755207B from the American Heart Association (G.A. Kelley, Principal Investigator).

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.ypmed.2008.10.010.

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