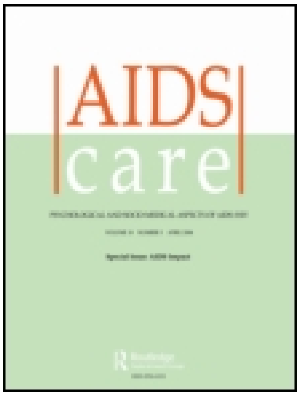

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Effects of progressive resistive exercise in adults living with HIV/AIDS: systematic review and meta-analysis of randomized trials

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Effects of progressive resistive exercise in adults living with HIV/AIDS: systematic review and meta-analysis of randomized trials

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This systematic review examined the effectiveness and safety of progressive resistive exercise (PRE) interventions on immunological/virological, cardiopulmonary, weight, and body composition, strength and psychological outcomes in adults living with HIV. Using Cochrane Collaboration protocol, we included randomized controlled trials from 1980–2006 comparing PRE interventions with no PRE or another intervention. Ten studies met inclusion criteria. Seventeen meta-analyses were performed. Results indicated that PRE or a combination of PRE and aerobic exercise may lead to statistically significant increases in weight (WMD: 2.68 kg; 95%CI: 0.40, 4.97) and arm and thigh girth (WMD: 7.91 cm; 95%CI: 2.18, 13.65) among exercisers versus non-exercisers. Trends toward improvement in submaximum heart rate and exercise time also were found. Individual studies suggested that PRE contributed to improved strength and psychological status. Findings are limited to participants who continued to exercise. Progressive resistive exercise appears to be safe and may be beneficial for medically-stable adults living with HIV.

Introduction

Due to medical advances, many people living with HIV who are able to access and tolerate highly active antiretroviral therapy (HAART) are living longer (Palella et al., 1998). This increased longevity has been mirrored by an increase in the prevalence and impact of disability experienced by this population (Rusch et al., 2004).

Exercise is one management strategy used by health professionals to address disablement. Progressive resistive exercise (PRE) could be used to address unwanted changes in body composition and fitness for people living with HIV. Progressive resistive exercise interventions have been associated with increases in lean body mass, muscle mass and strength in normal aging, frail and arthritic populations (Fiatarone et al., 1990, 1994; Rall, Meydani, Kehayias, Dawson-Hughes, & Roubenoff, 1996), however, the safety and effect of PRE among adults living with HIV is not well established. The purpose of this systematic review was to examine the safety and effectiveness of PRE interventions on immunological/virological, cardiopulmonary, strength, weight and body composition and psychological outcomes in adults living with HIV/AIDS.

Methods

Search strategy

We performed a systematic review and meta-analysis using the Cochrane Collaboration protocol (Cochrane Collaboration, 2006). We searched 14 electronic databases from 1980 to June 2006.

Selection criteria of studies and data abstraction

Titles and abstracts of all citations were reviewed independently by two reviewers to identify studies that met four inclusion criteria: (1) people who were HIV-positive; (2) 18 years of age or older; (3) a PRE intervention performed at least three times per week for at least four weeks; and (4) a randomized comparison group. All languages were included.

Two reviewers independently assessed entire papers if one or both reviewers believed a study met eligibility criteria; in the case of disagreements, a third reviewer read the paper and rendered a decision.

Progressive resistive exercise was defined as a regimen containing physical resistive activity performed at least three times per week for at least four weeks. Interventions could include, but were not limited to, weight training and isotonic and isometric strengthening exercises. Two reviewers independently

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abstracted data on: study design, participants, exercise interventions, outcomes and methodological quality from included studies.

Data analysis

Meta-analysis is defined as a statistical combination of results from two or more individual studies (Cochrane Collaboration, 2006). We used RevMan software (Cochrane Collaboration, 2002) for meta-analyses when sufficient data were available and when comparisons made sense in terms of participants, interventions and outcomes. Outcomes were analyzed as continuous using a random effects model to calculate a weighted mean difference (WMD) and 95% confidence interval (CI). A p-value less than 0.05 indicated statistical significance for an overall effect, and a p-value less than 0.1 indicated statistical significance for heterogeneity between studies (Lau, Ioannidis, & Schmid, 1997). In instances of lack of statistical significance for an overall effect, CIs were assessed for potential trends that may suggest movement towards an increase or decrease in overall effect. In instances of statistical significance for heterogeneity, sensitivity analyses were performed.

Results

Searches of all sources retrieved a total of 1658 citations, 106 of which were judged to merit scrutiny of the full article; 17 articles met inclusion criteria (Agin et al., 2001; Bhasin et al., 2000; Dolan et al., 2006; Driscoll, Meininger, Lareau et al., 2004; Driscoll, Meininger, Ljungquist et al., 2004; Fairfield et al., 2001; Grinspoon et al., 2000; Jaque et al., 2002; Lox, McAuley, & Tucker, 1995, 1996; Rigsby, Dishman, Jackson, Maclean, & Raven, 1992; Sattler et al., 1999, 2002; Schroeder et al., 2001; Schroeder, Terk, & Sattler, 2003; Shevitz et al., 2005; Spence, Galantino, Mossberg, & Zimmerman, 1990). Of these studies, four groups of citations were identified as replicate studies: (1) Lox, McAuley, & Tucker, 1995 & 1996; (2) Jaque et al., 2002; Sattler et al., 1999; Sattler et al., 2002; Schroeder et al., 2001; Schroeder, Terk, & Sattler, 2003; (3) Fairfield et al., 2001; Grinspoon et al., 2000; and (4) Driscoll, Meininger, Lareau et al., 2004; Driscoll, Meininger, Ljungquist et al., 2004, resulting in a total of 10 studies included in this review (Table 1 and Table 2).

All studies in this review were randomized trials that compared (1) PRE or PRE combined with another intervention with either (2) no PRE or (3) another exercise or treatment intervention. Types of PRE interventions included a combination of resistance training of major muscle groups in the upper and lower body for approximately 20–25 minutes ranging from 1–5 sets of 4–18 repetitions three times per week for 6–16 weeks. Exercise intensity ranged between 50–80% 1 repetition maximum (1-RM) or minimum-maximum setting of a hydraulic resistance training unit. Aerobic intensity ranged from 60–70% VO_{2max} or 60–75% submaximum heart rate.

Characteristics of participants

A total of 332 participants were included in the review, ranging from 18–66 years old. CD4 counts ranged from under 100 to greater than 1000 cells/mm^3. Women comprised less than 30% of the total number of participants (87/332 participants) in our review.

Three of the 10 studies included participants who were diagnosed with AIDS-wasting at baseline (either $>5\%$ or $>10\%$ involuntary weight loss or body weight $<90\%$ ideal body weight) (Agin et al., 2001; Bhasin et al., 2000; Grinspoon et al., 2000). One study included participants with elements of fat redistribution (truncal obesity defined as waist-to-hip ratio [WHR] >0.90 in men and >0.85 in women and a lipodystrophy score greater than two) (Driscoll, Meininger, Lareau et al., 2004). One study included participants with low testosterone levels (serum total testosterone levels less than 12.1 nmol/L) (Bhasin et al., 2000).

Four of the ten studies reported that greater than 70% of participants were on HAART (Dolan et al., 2006; Grinspoon et al., 2000; Sattler et al., 1999; Shevitz et al., 2005). Agin and colleagues (2001) reported that recruitment of participants occurred after the introduction of protease inhibitors but did not report the proportion of participants taking HAART. Three studies reported that most participants were taking some form of antiretroviral therapy (ART) (Bhasin et al., 2000; Driscoll, Meininger, Lareau et al., 2004; Lox, McAuley, & Tucker, 1995). Spence and colleagues (1990) included participants who were taking AZT monotherapy. Rigsby and colleagues (1992) did not report on whether participants were taking ART.

Methodological quality of included studies

We assessed study quality using the Jadad checklist (Jadad et al., 1996). All studies used randomization to allocate participants to a comparison group, however, only six described the randomization process (Agin et al., 2001; Bhasin et al., 2000; Dolan et al., 2006; Driscoll et al., 2004; Grinspoon et al., 2000; Sattler et al., 1999).

Table 1. Characteristics of studies included in the systematic review.

Study	Method	Sample size (at baseline)	% Male	Participants (at study completion)	Type of exercise	Time & intensity of exercise	Frequency & duration of exercise	Supervision (by whom)	Notes
Spence (1990)	Randomized exercise and control groups (2 groups)	$n=24$	100%	PRE group: $n=12$ (not confirmed) Non-exercising control group: $n=12$ (not confirmed)	Resistance training (bilateral and bi-directional concentric contractions throughout the range of motion)	*PRE*: resistance loading was uniformly increased throughout the training period from 1 set of 15 reps on the minimum setting of the Total Power hydraulic resistance training unit through 3 sets of 10 reps on the maximum setting. Maximum effort was encouraged.	3 times per week for 6 weeks	Yes (not specified)	Further clarification was sought from authors to confirm the number of participants at study completion (and potential withdrawal rate). For the purposes of this review, we assumed the number of participants at study completion were equal to those at baseline.
Rigsby (1992)	Randomized exercise and control (counselling) groups (2 groups)	$n=45$ (37 HIV+)	100%	PRE + Aerobic group: $n=16$ (13 HIV+) Non-exercising counselling control group: $n=15$ (11 HIV+)	Resistance training (chest press and leg extension) and stationary bike (aerobic)	Combined PRE and aerobic exercise for 60 minutes total. *PRE*: strengthening for a total of 20–25 minutes consisting of 3 sets of reps at maximal voluntary force with 1 minute rest period in between. Each set was performed for 30 seconds and the number of reps ranged from 15–18 for the first set to 6–8 for the third set. *Aerobic exercise*: 20 minutes at 60–80% HR reserve (2 min warm up and 3 min cool down at low intensity). Stretching times 10–15 min.	3 times per week for 12 weeks	Yes (not specified)	"Control" group received 90–120 minutes of counselling 1–2 times per week for 12 weeks.
Lox (1995)	Randomized 2 exercise groups and 1 control group (3 groups)	$n=34$	100%	PRE group: $n=12$ Aerobic group: $n=11$ Non-exercising control group: $n=10$	Isotonic resistance to major muscle groups in legs, arms and upper body	*PRE*: isotonic variable resistance to major muscle groups of legs, arms and upper body. Resistance was initiated at 60% of an individual's 1-RM and increased by either 5 or 10 pounds at a time after	3 times per week for 12 weeks	Yes (not specified)	For the purposes of this review, only the PRE group and the control group were included in meta-analyses.

Table 1 (*Continued*)

Study	Method	Sample size (at baseline)	% Male	Participants (at study completion)	Type of exercise	Time & intensity of exercise	Frequency & duration of exercise	Supervision (by whom)	Notes
						successfully performing 3 sets of 10 reps at constant weight.			The non-exercising control group engaged in stretching and flexibility exercise. Two articles that reported on the same study were incorporated as one study for this review.
Sattler (1999)	Randomized combined exercise plus testosterone and testosterone only groups (2 groups)	$n=33$	100%	PRE+ Testosterone group: $n=15$ Testosterone only group: $n=15$	Upper and lower body free weight training	*PRE*: warm-up of 5–8 reps at 50% 1-RM for each exercise, 3 sets of 8 reps at 80% 1-RM with the final set of reps performed to failure, with 2 minute rests in between all sets. Intensity of PRE began at 70% 1-RM at baseline and increased to 80% 1-RM by the end of week 2. 1-RM was assessed every 2 weeks to adjust training load to maintain intensity. *Testosterone*: weekly injections of nandrolone at a dose of 200mg in week 1, 400mg in week 2 and increased to 600mg for weeks 3–12.	3 times per week for 12 weeks	Yes (exercise physiologist)	Five articles that reported on the same study were incorporated as one study for this review.
Bhasin (2000)	Randomized combined exercise plus testosterone, testosterone only, exercise only and control groups (4 groups)	$n=61$	100%	PRE+ Testosterone group: $n=12$ Testosterone only group: $n=15$ PRE only group (exercise+ placebo):	Resistance training (Five upper and lower body exercises)	*PRE*: week 1–4: High volume (3 sets of 12–15 reps), low intensity (60% of initial 1-RM) resistance exercise. Week 5–10: Progressive periodic, high intensity (90% of 1-RM on heavy days, 80% on medium days, and 70% on light days), low volume	3 times per week for 16 weeks	Not recorded	

Table 1 (*Continued*)

Study	Method	Sample size (at baseline)	% Male	Participants (at study completion)	Type of exercise	Time & intensity of exercise	Frequency & duration of exercise	Supervision (by whom)	Notes
				$n=11$ Non-exercising control group: $n=11$		(4 sets of 4–6 reps each). Week 11–16: Resistance loads were increased by 7% for upper body and 12% for lower body exercises and the number of sets increased to 5. *Testosterone*: intramuscular injections of 100mg/wk of testosterone.			Further clarification was sought from authors to provide data for body weight and health-related quality of life.
Grinspoon (2000)	Randomized combined exercise plus testosterone, testosterone only, exercise only and control groups (4 groups)	$n=54$	100%	PRE+ Aerobic+ Testosterone group: $n=11$ Testosterone only group: $n=10$ PRE+ Aerobic only group (exercise+ placebo): $n=10$ Non-exercising control group: $n=12$	Isotonic resistance training to upper and lower body and stationary bike (aerobic)	*PRE*: resistance training using computerized equipment (Life Fitness) isotonically training the upper and lower body. Intensity of PRE: 2 sets of 8 reps each with increased intensity from Week 1–2: at 60% 1-RM. Week 3–6: at 70% 1-RM. Week 7–12: at 80% 1-RM. *Aerobic exercise*: 20 min aerobic exercise on stationary cycle at 60–70% HR_{max}, 15 min cool down. *Testosterone*: intramuscular injections of 200mg/wk of testosterone.	3 times per week for 12 weeks	Yes (not specified)	Two articles that reported on the same study were incorporated as one study for this review.
Agin (2001)	Randomized combined exercise plus whey protein, whey protein only and PRE only groups (3 groups)	$n=43$	0%	PRE group: $n=10$ Whey group: $n=10$ PRE+Whey group: $n=10$	Resistance training of seven major muscle groups	*PRE*: resistance training of 7 major muscle groups: 3 sets of 10 exercises at 8–10 reps/set as per ACSM guidelines. Week 1: loads were 50% of baseline 1-RM. Loads increased approximately 75% of 1-RM with adjustments based on number of reps and percentages of 1-RM. Loads were increased a minimum of 2.5 pounds when	3 times per week for 14 weeks.	Yes (exercise physiologist)	

Table 1 (*Continued*)

Study	Method	Sample size (at baseline)	% Male	Participants (at study completion)	Type of exercise	Time & intensity of exercise	Frequency & duration of exercise	Supervision (by whom)	Notes
						a participant completed 10 consecutive reps for a muscle group without fatigue. *Whey protein*: 1 g/kg of whey protein powder per day for 14 weeks.			
Driscoll (2004)	Randomized combined exercise plus metformin and metformin only groups (2 groups)	$n=37$	80%	PRE+ Aerobic+ Metformin group: $n=11$ Non-exercising metformin only group: $n=14$	Resistance training of six upper and lower body exercises and stationary bike (aerobic)	5 min warm-up on stationary bike, standard flexibility routine followed by aerobic and PRE exercise. *Aerobic exercise*: 20min (week 1–2) at 60% HR_{max} then progressed to 30 min (week 3–12) at 75% HR_{max} aerobic exercise according to ACSM guidelines. *PRE*: resistance training using external resistance Life Circuit equipment for six upper and lower body exercises: 3 sets of 10 reps each for every muscle group, resting 20 seconds between reps, 2 minutes between sets and 4 minutes between muscle groups. Week1: Initial intensity of PRE was 60% 1-RM. Week 2–4: Intensity increased to 70% of 1-RM. Week 4–12: Intensity increased to 80% of 1-RM. 1-RM was measured every other week and load adjusted to maintain relative intensity at 80% 1-RM.	3 times per week for 12 weeks	Yes (physical therapist)	Two articles that reported different outcomes on the same participants were incorporated as one study for this review.
Shevitz (2005)	Randomized combined nutrition plus exercise,	$n=50$	70%	Nutrition+ PRE group: $n=15$ Nutrition+	Resistance training of six major muscle groups	Warm-up period followed by PRE exercise. *PRE*: 6 resistance exercisers for upper and lower body (leg press,	3 times per week for 12 weeks	Yes (research technician)	Due to the involved nature of the nutrition intervention we

Table 1 (*Continued*)

Study	Method	Sample size (at baseline)	% Male	Participants (at study completion)	Type of exercise	Time & intensity of exercise	Frequency & duration of exercise	Supervision (by whom)	Notes
	nutrition plus oxandrolone, and nutrition only groups (3 groups)			Oxandrolone group: $n=16$ Nutrition only group: $n=16$		chest press, knee extension, seated row, leg press): 3 sets of 8 reps each with progressive increase in intensity to 80% 1-RM, on each and (modified abdominal curl-ups): 2 sets of 10 reps each with gradual increase with weight plate over chest. Strength was assessed at sessions 3 and 25 to adjust resistive intensity accordingly. *Oxandrolone*: 10 mg Oxandrolone tablets taken twice daily. *Nutrition*: weekly visits 30–60 minutes in length. Encouraged to meet dietary recommendations based on weight to promote weight gain; 40–50 kcal/kg/day calories and 1.6g/kg/day protein, oral liquid supplement 2 times daily that contained 240 kcal, 15 g of protein and 3 g of fat. Weekly visits counselled on good dietary intake.			classified this group as "another intervention" rather than a "non-exercising control." Hence, for the purposes of this review, the PRE plus nutrition group was classified as a "combined PRE intervention group" and the nutrition only group as "another intervention" group.
Dolan (2006)	Randomized exercise and control groups (2 groups)	$n=40$	0%	PRE+Aerobic group: $n=19$ Non-exercising control group: $n=19$	Resistance training of six upper and lower body exercises and stationary bike (aerobic)	Combined PRE and aerobic exercise for 2 hours total. 5 minute warm-up on stationary bike at 50% estimated HR_{max}, followed by standard flexibility routine and aerobic and PRE exercise according to ACSM guidelines followed by a cool down period. *PRE*: concentric and eccentric phases of 6 selective upper and lower	3 times per week for 16 weeks	Yes (study staff)	The intervention was a home-based exercise program. Participants completed 96% of the total exercise sessions.

Table 1 (*Continued*)

Study	Method	Sample size (at baseline)	% Male	Participants (at study completion)	Type of exercise	Time & intensity of exercise	Frequency & duration of exercise	Supervision (by whom)	Notes
						body muscle groups (knee hip extensors, bench press, knee flexors, shoulder abduction, ankle plantarflexors, and elbow flexors). Week 1: 3 sets of 10 reps for each muscle group at 60% 1-RM, 3–5 seconds between reps rest, 2 min rest between sets, 4 min rest between muscle groups. Week 3–16: 4 sets of 8 reps for each muscle groups at 70% 1-RM (Week 2–3) and 80% 1-RM (Week 4–16), 2–3 seconds between reps rest, 1 min rest between sets, 2 min rest between muscle groups. Each repetition lasted 6–10 seconds each. *Aerobic exercise*: stationary cycle for 20 minutes at 60% HR_{max} (Week 1–2), and 30 minutes at 75% HR_{max} (Week 3–16).			

+ = plus; PRE = progressive resistive exercise; HR_{max} = maximum heart rate; 1-RM = 1 repetition maximum; ACSM = American College of Sports Medicine; reps = repetitions.

Table 2. Outcomes and author's conclusions of individual studies included in the systematic review.

Study	Immunological/ virological	Cardiopulmonary	Strength	Weight & body composition	Psychological	Author's conclusions
Spence (1990)	NA	NA	*Upper and lower extremity strength*: significant increases in all lower extremity variables (12/12) and most upper extremity variables (10/12) in the exercise group. Significant decreases in upper extremity (6/12) and lower extremity (7/12) variables in the non-exercising control group.	*Weight and girth*: significant increases in weight and arm and thigh girth in the exercise group compared to significant decreases in the non-exercising control group.	NA	PRE improves muscles function and anthropometry in persons living with HIV in the PRE group compared to persons living with HIV in the control group.
Rigsby (1992)	*CD4 count*: no significant changes.	*Aerobic capacity*: significant increases in aerobic capacity in the exercise group and no change in the non-exercising control group. *Submaximum HR & total time to voluntary exhaustion*: significant decrease in HR and increase in total time exercise to voluntary exhaustion in the exercise group.	*Upper and lower extremity strength*: significant increases in chest press (50.3 Nm) and leg extension (47.5 Nm) in the exercise group compared with the non-exercising control group.	NA	NA	HIV positive men can experience increases in cardio-respiratory fitness. Increased fitness may occur without negative effects on immune status.
Lox (1995)	*CD4 count*: no significant changes.	*Submaximum HR*: non-significant decrease in HR in the PRE group compared to a non-significant increase in the non-exercising control group. *VO2max*: significant improvements among exercisers compared to non-exercisers. Significantly greater improvements in the aerobic group compared to the PRE and non-exercising control groups.	*Upper and lower extremity strength*: significant improvements in the PRE and aerobic exercise groups compared to the non-exercising control group. Significantly greater improvements as measured by 1-RM in the PRE group (U/E: $+31.5$ lbs, L/E: $+90.7$ lbs) compared to the aerobic and non-exercising control groups (U/E: -6.8 lbs, L/E: -14.7 lbs).	*Body mass index, fat mass & average body fat percentage*: no change among groups (PRE and aerobic and control) in average body mass index, fat mass and body fat percentage. *Weight, lean body mass & girth*: significant increases in weight, lean body mass and sum of chest, arm and thigh circumference among PRE and aerobic exercise groups	*Mood and life satisfaction*: significant improvements in mood and life satisfaction in both the PRE and aerobic exercise groups compared to the non-exercising control group. Significantly higher life satisfaction in the aerobic group compared to the PRE group.	Exercise results in improvements in body composition, strength, cardiopulmonary fitness, and mood and life satisfaction for people living with HIV

Table 2 (*Continued*)

Study	Immunological/ virological	Cardiopulmonary	Strength	Weight & body composition	Psychological	Author's conclusions
				compared to the non-exercising control group.		
Sattler (1999)	*CD4 count*: no significant changes.	NA	*Upper and lower extremity strength*: significant increases in upper and lower body strength in both groups with significantly greater increases in strength in the combined PRE and testosterone group (14–53%) compared with the testosterone only group (10–31%).	*Weight, body cell mass & muscle area*: significant increases in body weight, body cell mass and thigh muscle area within both groups. No significant difference between groups. *Fat mass*: significant decrease in fat mass in the combined PRE and testosterone group and no change in fat mass in the testosterone only group. *Lean body mass*: significantly greater increases in lean body mass in the combined PRE and testosterone group compared with the testosterone only group.	NA	Testosterone resulted in significant increases in total weight, lean body mass, body cell mass, muscle area and strength. Increases in lean body mass and muscular strength were significantly greater with PRE.
Bhasin (2000)	*CD4 count & viral load*: no significant changes.	NA	*Upper and lower extremity strength*: increases in the PRE only group by 29–36%, and in the testosterone only group by 17–28% for 5 variables of strength. Increases in the combined PRE and testosterone group by 10–32% (not significantly greater than either intervention alone). No	*Weight & fat free mass*: significant increase in the testosterone only and PRE only groups. No change in the non-exercising control group. Combined PRE and testosterone group did not show a greater increase in weight compared to one intervention alone.	*Health-related quality of life*: no association between the change in HRQL and testosterone administration or exercise in any group.	Testosterone and resistance exercise promotes gains in body weight, muscle mass, muscle strength and lean body mass in HIV-infected men with moderate weight loss and low testosterone levels. The effect of testosterone and exercise were not additive in this study.

Table 2 (*Continued*)

Study	Immunological/ virological	Cardiopulmonary	Strength	Weight & body composition	Psychological	Author's conclusions
			change in the non-exercising control group.	*Muscle volume*: greater increase in thigh muscle volume in testosterone only group, PRE only and combined PRE and testosterone group compared to the non-exercising control group. *Lean body mass*: increase in the testosterone only and combined testosterone and PRE group, and no change in the non-exercising control group.		
Grinspoon (2000)	*CD4 count & viral load*: No significant changes.		*Upper and lower extremity strength*: no significant change in strength for 7/7 variables (note strength was tested isometricly which may underestimate change in strength).	*Lean body mass & muscle area*: Significant increases in lean body mass, arm and leg muscle area in the exercise only group. *Weight & fat mass*: no significant changes in the exercise or non-exercising control groups.	NA	Exercise has a significant effect on lean body mass and muscle area independent of testosterone. Muscle mass and strength may increase in response to combined exercise and testosterone therapy. Exercise may be a strategy to reverse muscle loss in this population.
Agin (2001)	NA	NA	*Upper and lower extremity strength*: increase in muscle strength ranging from 40.6–95.3% for all 7 muscle groups assessed in the PRE only and combined PRE and whey protein groups.	*Weight*: significant increase in weight in the whey protein group. Body cell mass: significant increase in the PRE only and combined PRE and whey protein groups. Fat mass: significant increase in the whey only group and	*Health-related quality of life*: (measured by the MOS-HIV Scale) Significant increases in the physical activity scores for the PRE only group and significant decrease in the whey only and combined PRE and whey groups.	Resistance exercise significantly increased body cell mass, muscle mass, muscle strength and HRQL in HIV-infected women with reduced body cell mass. Whey protein had little effect on body cell mass gain and combined PRE and whey protein did not increase

Table 2 (*Continued*)

Study	Immunological/ virological	Cardiopulmonary	Strength	Weight & body composition	Psychological	Author's conclusions
				significant decrease in the PRE only group. No changes in the combined PRE and whey protein group. *Fat free mass*: significant increase in all three groups.	Significant improvements in the PRE group for general health perception and vitality scores.	body cell mass beyond gains achieved by PRE alone.
Driscoll (2004)	*CD4 count & viral load*: no significant changes.	*Exercise time*: significant improvements in endurance time on cycle ergometer during sub-maximal stress test in the exercise and metformin group compared with the metformin only group.	*Upper and lower extremity strength*: significant increases in 5 out of 6 strength indices in the exercise and metformin group compared with the metformin only group.	*Cross-sectional muscle area*: significant increases in the exercise and metformin group compared with the metformin only group. *Waist-to-hip ratio & abdominal fat area*: significant decreases in the exercise and metformin group compared with the metformin only group. *Weight, body mass index*: no significant change in either group.	NA	Exercise training and metformin significantly improves cardiovascular parameters more than metformin alone in persons living with HIV with fat redistribution and hyperinsulinemia. Exercise training (PRE and aerobic) is well tolerated and improves muscle strength and size as well as aerobic fitness in persons living with HIV.
Shevitz (2005)	*CD4 count & viral load*: no significant changes.	*Endurance tolerance*: significant improvements in all 3 groups but significantly greater improvements in 6MWT distance and chair stand time in the combined PRE and nutrition group versus the nutrition only group. *Self-reported physical function*: significant improvements in the combined PRE and nutrition group only.	*Upper and lower extremity strength*: significant improvements in all 7 upper and lower strength measures in the combined PRE and nutrition group, 1/7 strength measures for the nutrition only group, and 2/7 for the oxandrolone and nutrition group.	*Weight*: statistically significant increase within all three groups. *Body mass index*: no significant change within the three groups. *Fat free mass*: significant increase in within the combined oxandrolone and nutrition group and the nutrition only group. *Mid thigh cross sectional muscle area*: significant increases within the combined	*Quality of life adjusted years*: no significant change in QALYs within groups, however the increase was greatest in the PRE and nutrition group demonstrating most favourable cost-effectiveness (lowest cost/QALY).	Oxandrolone and PRE demonstrate similar improvements in body composition however PRE is superior over oxandrolone to improve strength, physical function, lean body mass and dietary intake with a lower cost and low risk of adverse effects. Results should encourage providers, patients and third party payers to use PRE as a medical intervention.

Table 2 (*Continued*)

Study	Immunological/ virological	Cardiopulmonary	Strength	Weight & body composition	Psychological	Author's conclusions
				PRE and nutrition group and the combined oxandrolone and nutrition group. There were no significant differences between groups for weight and body composition.		
Dolan (2006)	*CD4 count & viral load*: no significant changes.	*Exercise time*: significant improvements in submaximal exercise time and 6MWT distance among exercisers compared with non-exercisers. *VO2max*: significant improvements among exercisers compared with non-exercisers.	*Upper and lower extremity strength*: significant improvements in all 7 upper and lower strength measures among exercisers compared with non-exercisers.	*Weight*: no significant change in weight between groups. *Total cross sectional muscle area & muscle attenuation*: significantly increased among exercisers compared with non-exercisers. *Waist circumference*: significantly decreased among exercisers compared with non-exercisers. *Body mass index, abdominal visceral tissue area, subcutaneous adipose ttissue area, & total fat*: no significant difference between groups.	NA	A sixteen week supervised home-based PRE and aerobic exercise program improves measures of strength, cardio-respiratory fitness, and body composition among women living with HIV.

NA = not assessed; + = plus; VO2max = maximum oxygen consumption; HR = heart rate; BMI = body mass index; PRE = progressive resistive exercise; HRQL = health-related quality of life; 1-RM = 1 repetition maximum; MOS-HIV = Medical Outcomes Study HIV Health Survey; 6MWT = Six minute walk test; QALY; Quality of Life Adjusted Year; U/E = upper extremities; L/E = lower extremities.

No studies were double-blinded since the intervention was exercise. However, studies that included a co-intervention of testosterone and oxandrolone achieved participant blinding by using a placebo. Assessor blinding was described for two studies (Agin et al., 2001; Rigsby et al., 1992).

All but one study (Spence et al., 1990) reported on participants who withdrew from the study or were non-adherent with the exercise intervention. Withdrawal rates ranged from 3–35% and total outcome data were not available for 69 (17%) participants.

Seven studies reported that comparison groups were similar at baseline (Agin et al., 2001; Bhasin et al., 2000; Dolan et al., 2006; Driscoll et al., 2004; Rigsby et al., 1992; Sattler et al., 1999; Spence et al., 1990).

Results of meta-analyses

Seventeen meta-analyses were performed for outcomes of immunological and/or virological status (CD4 count, viral load), cardiopulmonary status (submaximum heart rate, maximum oxygen consumption, exercise time) and weight and body composition (weight, body mass index, lean body mass, fat mass, arm and thigh girth). Our results focus on four sub-group analyses: (1) PRE versus non-exercise, (2) combined PRE and aerobic exercise versus non-exercise, (3) PRE or combined PRE and aerobic exercise versus non-exercise and (4) PRE plus testosterone or combined PRE and aerobic exercise plus testosterone versus testosterone only.

Immunological and/or virological status

Eight of the 10 studies assessed changes in immunological and/or virological status in the form of CD4 count (Bhasin et al., 2000; Dolan et al., 2006; Driscoll, Meininger, Lareau et al., 2004; Grinspoon et al., 2000; Lox et al., 1995; Rigsby et al., 1992; Sattler et al., 1999; Shevitz et al., 2005) and/or viral load (Bhasin et al., 2000; Dolan et al., 2006; Driscoll, Meininger, Lareau et al., 2004; Grinspoon et al., 2000; Shevitz et al., 2005).

CD4 count. Three meta-analyses were performed (Table 3). Results demonstrated no difference in change in CD4 count for participants in the combined aerobic and PRE group compared to the non-exercising control group (WMD: 24.83 cells/mm^3; 95%CI: -23.70, 73.36; $p=0.32$; $n=84$) and for participants in the PRE or combined PRE and aerobic exercise group compared to the non-exercising control group (WMD: 38.51 cells/mm^3; 95%CI: -7.54, 84.56; $p=0.10$; $n=106$). A significant decrease in CD4 count was found in the combined PRE plus testosterone or combined PRE and aerobic exercise plus testosterone group compared with the testosterone only group (WMD: -32.13 cells/mm^3; 95%CI: -56.96, -7.30; $p=0.01$; $n=51$). These results did not reach our pre-specified threshold for clinical importance (50 cells/mm^3).

Viral load. One meta-analysis was performed for viral load. Results demonstrated no difference in change in viral load among participants in the combined PRE and aerobic exercise group compared with the non-exercising control group (WMD: 0.31 log^{10} copies; 95%CI: -0.13; 0.74; $p=0.17$; $n=60$). Individual studies also showed no differences in changes in viral load among exercisers compared with non-exercisers (Table 2).

Cardiopulmonary status

Five of the 10 studies assessed cardiopulmonary outcomes (Dolan et al., 2006; Driscoll, Meininger, Lareau et al., 2004; Lox et al., 1995; Rigsby et al., 1992; Shevitz et al., 2005) and three meta-analyses were performed for submaximum heart rate, maximum oxygen consumption and exercise time.

Submaximum heart rate. Two studies assessed submaximum heart rate (Lox et al., 1995; Rigsby et al., 1992). Meta-analysis showed a non-significant reduction in heart rate of -13.02 beats/minute (95%CI: -26.67, 0.64; $p=0.06$; $n=46$) for participants in the PRE or combined PRE and aerobic exercise group compared to the non-exercising control group. The confidence interval indicated a trend towards a clinically important improvement in submaximum heart rate among exercisers compared with non-exercisers (10 beats/min). This meta-analysis reported statistical significance for heterogeneity ($p=0.0005$; $I^2=91.8\%$) using a random effects model. Heterogeneity was likely attributed to the different exercise interventions between the studies.

Maximum oxygen consumption ($VO2_{max}$). Two studies measured $VO2_{max}$ (Dolan et al., 2006; Lox et al., 1995). Meta-analysis showed no difference in change in $VO2_{max}$ among participants in the PRE or combined PRE and aerobic exercise group compared to the non-exercising control group (WMD: 81.99 ml/kg/min; 95%CI: -155.34, 319.33; $p=0.50$; $n=60$).

Exercise time. Two studies assessed exercise time (Dolan et al., 2006; Rigsby et al., 1992). Meta-analysis showed a non-significant increase in exercise time of 3.92 minutes (95%CI: -0.63, 8.47; $p=0.09$; $n=62$) for participants in the combined PRE and

Table 3. Results of meta-analyses.

Outcomes	Sub-group comparisons of meta-analysis	Individual studies included in meta-analysis	Number of participants included in meta-analysis	Weighted mean difference	95% confidence interval	*P* value of overall effect	I^2 statistic and *P* value for heterogeneity	Interpretation
Immunological /virological status								
CD4 count (cells/mm^3)	Combined PRE and aerobic exercise compared with non-exercise	Rigsby (1992) Grinspoon (2000) Dolan (2006)	84	24.83 cells/mm^3	−23.70, 73.36	0.32	$I^2 = 0\%$ 0.46	No difference in change in CD4 count among exercisers compared with non-exercisers. Confidence interval indicates a positive trend towards an improvement in CD4 count among exercisers.
	PRE or combined PRE and aerobic exercise compared with non-exercise	Rigsby (1992) Lox (1995) Grinspoon (2000) Dolan (2006)	106	38.51 cells/mm^3	−7.54, 84.56	0.10	$I^2 = 8.1\%$ 0.35	No difference in change in CD4 count among exercisers compared with non-exercisers. Confidence interval indicates a positive trend towards an improvement in CD4 count among exercisers.
	PRE plus Testosterone or Combined PRE and aerobic exercise plus Testosterone compared with Testosterone only	Sattler (1999) Grinspoon (2000)	51	−32.13 cells/mm^3	−56.96, −7.30	0.01*	$I^2 = 0\%$ 0.96	Statistically significant decrease in CD4 count among exercisers taking testosterone compared with testosterone only. Note this does not indicate a clinically important difference in CD4 count.[a]
Viral load (log10copies)	Combined PRE and aerobic exercise compared with non-exercise	Grinspoon (2000) Dolan (2006)	60	0.31 log^{10}copies	−0.13, 0.74	0.17	$I^2 = 0\%$ 0.77	No difference in change in viral load among exercisers compared with non-exercisers.
Cardiopulmonary status								
Submaximum heart rate (HR) (beats/min)	PRE or combined PRE and aerobic exercise compared with non-exercise	Lox (1995) Rigsby (1992)	46	−13.02 beats/min	−26.67, 0.64	0.06	$I^2 = 91.8\%$ 0.0005**	Non-significant decrease in submaximum HR among aerobic exercisers compared with non-exercisers. Confidence interval indicates a trend towards a potential clinically important improvement in submaximum HR among exercisers.[b]

Table 3 (*Continued*)

Outcomes	Sub-group comparisons of meta-analysis	Individual studies included in meta-analysis	Number of participants included in meta-analysis	Weighted mean difference	95% confidence interval	*P* value of overall effect	I^2 statistic and *P* value for heterogeneity	Interpretation
Maximum oxygen consumption ($VO2_{max}$) (ml/kg/min)	PRE or combined PRE and aerobic exercise compared with non-exercise	Lox (1995) Dolan (2006)	60	81.99 ml/kg/min	−155.34, 319.33	0.50	$I^2 = 58.6\%$ 0.12	No difference in change in $VO2_{max}$ among exercisers compared with non-exercisers.
Exercise time (min)	Combined PRE and aerobic exercise compared with non-exercise	Rigsby (1992) Dolan (2006)	62	3.92 minutes	−0.63, 8.47	0.09	$I^2 = 98.4\%$ <0.00001**	Non-significant increase in exercise time among exercisers compared with non-exercisers. Confidence interval indicates a trend towards an improvement in exercise time among exercisers.[c]
Weight and body composition								
Body weight (kg)	PRE compared with non-exercise	Lox (1995) Spence (1990)	46	4.24 kg	1.82, 6.66	0.0006*	$I^2 = 39.2\%$ 0.20	Statistically significant and potential clinically important increase (improvement) in body weight among PRE exercisers compared with non-exercisers.[d]
	PRE or combined PRE and aerobic exercise compared with non-exercise	Spence (1990) Lox (1995) Grinspoon (2000) Dolan (2006)	106	2.68 kg	0.40, 4.97	0.02*	$I^2 = 81.4\%$ 0.001**	Statistically significant increase (improvement) in body weight among exercisers compared with non-exercisers.
	Combined PRE and aerobic exercise compared with non-exercise	Grinspoon (2000) Dolan (2006)	60	0.96 kg	−1.39, 3.30	0.42	$I^2 = 58.2\%$ 0.12	No difference in change in body weight among exercisers compared with non-exercisers.
	PRE plus testosterone or combined PRE and aerobic exercise plus testosterone compared with	Sattler (1999) Grinspoon (2000)	51	0.42 kg	−0.92, 1.77	0.54	$I^2 = 0\%$ 0.48	

Table 3 (*Continued*)

Outcomes	Sub-group comparisons of meta-analysis	Individual studies included in meta-analysis	Number of participants included in meta-analysis	Weighted mean difference	95% confidence interval	*P* value of overall effect	I^2 statistic and *P* value for heterogeneity	Interpretation
	testosterone only							No difference in change in body weight among exercisers taking testosterone compared with testosterone only.
Mean arm and thigh girth (cm)	PRE or combined PRE and aerobic exercise compared with non-exercise	Lox (1995) Spence (1990)	46	7.91 cm	2.18, 13.65	0.007*	$I^2=67.4\%$ 0.08**	Statistically significant and potential clinically important increase in mean arm and thigh girth among exercisers compared with non-exercisers.[e]
Mean body mass index (kg.m2)	PRE or combined PRE and aerobic exercise compared with non-exercise	Lox (1995) Dolan (2006)	60	1.06 kg.m2	−0.52, 2.64	0.19	$I^2=51.4\%$ 0.15	No difference in change in mean body mass index among exercisers compared with non-exercisers.
Mean lean body mass (kg)	PRE plus testosterone or combined PRE and aerobic exercise plus testosterone compared with testosterone only	Sattler (1999) Grinspoon (2000)	51	0.64 kg	−0.97, 2.26	0.44	$I^2=0\%$ 0.63	No difference in change in lean body mass among exercisers taking testosterone compared with testosterone only.
Mean fat mass (kg)	PRE or combined PRE and aerobic exercise compared with non-exercise	Lox (1995) Grinspoon (2000) Dolan (2006)	82	0.84 kg	−0.31, 1.98	0.15	$I^2=0\%$ 0.71	No difference in change in fat mass among exercisers compared with non-exercisers.
	Combined PRE and aerobic exercise compared with non-exercise	Grinspoon (2000) Dolan (2006)	60	0.07 kg	−1.22, 1.36	0.92	$I^2=0\%$ 0.35	

Table 3 (*Continued*)

Outcomes	Sub-group comparisons of meta-analysis	Individual studies included in meta-analysis	Number of participants included in meta-analysis	Weighted mean difference	95% confidence interval	*P* value of overall effect	I^2 statistic and *P* value for heterogeneity	Interpretation
	PRE plus testosterone or combined PRE and aerobic exercise plus testosterone compared with testosterone only	Sattler (1999) Grinspoon (2000)	51	−0.73 kg	−1.50, 0.04	0.06	$I^2 = 0\%$ 0.86	No difference in change in fat mass among exercisers taking testosterone compared with testosterone only.

*Indicates statistical significance $p < 0.05$; **Indicates statistical significance for heterogeneity $p < 0.10$

PRE = progressive resistive exercise; HR = heart rate; I^2 = I squared statistic (proportion of total variation in the study estimates due to heterogeneity rather than sampling error); $VO2_{max}$ = maximum oxygen consumption.

For the purposes of this review, the following values indicated clinically important changes: [a] CD4 count = 50 cells/mm^3; [b] submaximum heart rate = 10 beats/minute; [c] exercise time = 5 minutes; [d] body weight = 3 kilograms; [e] body composition (girth) = 5 centimetres (values based on consultation with clinical and research community and are consistent with values used in previous literature).

aerobic exercise group compared to the non-exercising control group. The confidence interval indicated a trend towards an improvement in exercise time among exercisers compared with non-exercisers. This meta-analysis reported statistical significance for heterogeneity ($p < 0.00001$; $I^2 = 98.4\%$) using a random effects model. Heterogeneity was likely attributed to differences in the outcomes measured (total time to voluntary exhaustion versus exercise time).

Individual study results – cardiopulmonary outcomes. Individual studies also suggested improvements in cardiopulmonary status among exercisers compared to non-exercisers. Greater improvements were seen with aerobic exercise interventions compared with PRE or no exercise (Table 2).

Strength

All studies reported on strength outcomes but meta-analyses could not be performed due to differences in outcomes and participants; however, nine of the 10 studies suggested improvements in strength among exercisers compared to non-exercisers (Table 2). Grinspoon and colleagues (2000) found no significant differences in strength for participants in the combined aerobic and PRE exercise group compared with participants in the non-exercising control group. The lack of statistical significance was attributed to the isometric method of strength testing versus isotonic methods of testing used in the other studies. Isometric testing is known to underestimate changes in strength (Hortobagyi, Lambert, & Hill, 1997).

Weight and body composition

Nine of the 10 studies assessed weight and/or body composition. Ten meta-analyses were performed: four for weight and six for body composition (Table 3).

Weight. Nine studies assessed body weight (Agin et al., 2001; Bhasin et al., 2000; Dolan et al., 2006; Driscoll, Meininger, Lareau et al., 2004; Grinspoon et al., 2000; Lox et al., 1995; Sattler et al., 1999; Shevitz et al., 2005; Spence et al., 1990). Meta-analyses showed a statistically significant and clinically important increase in body weight of 4.24 kg (95%CI: 1.82, 6.66; $p = 0.0006$; $n = 46$) for participants in the PRE group compared to non-exercising controls, and a statistically significant increase in body weight of 2.68 kg (95%CI: 0.40, 4.97; $p = 0.02$; $n = 106$) for participants in the PRE or combined PRE and aerobic exercise intervention compared to non-exercising controls (Table 3). The latter meta-analysis reported statistical significance for heterogeneity ($p = 0.001$; $I^2 = 81.4\%$) using a random effects model, which may be attributed to slight differences in the weight of participants at baseline. Two additional meta-analyses demonstrated no difference in change in body weight (Table 3).

Body composition. The same nine studies assessed body composition. Meta-analysis showed a statistically significant and clinically important increase in arm and thigh girth of 7.91cm (95%CI: 2.18, 13.65; $p = 0.007$; $n = 46$) for participants in the PRE or combined PRE and aerobic exercise intervention group compared to the non-exercising control group. Given that many participants in the individual studies were diagnosed with AIDS-related wasting syndrome, increases in weight and body composition may be interpreted as favourable outcomes. This meta-analysis was statistically significant for heterogeneity ($p = 0.08$; $I^2 = 67.4\%$) using a random effects model. Reasons for heterogeneity may be attributed to the different methods in which mean arm and thigh girth was measured between studies. The other five meta-analyses for body composition showed no difference among groups (Table 3).

Psychological status

Four of the 10 studies reported on psychological status (Agin et al., 2001; Bhasin et al., 2000; Lox et al., 1995; Shevitz et al., 2005). Meta-analysis was not possible due to differences in comparison groups and participants.

Individual study results – psychological outcomes. Individual study results showed significant improvements in health-related quality of life (HRQL) in the PRE intervention group compared to participants in the whey protein only and whey protein and PRE groups (Agin et al., 2001). Bhasin and colleagues (2000) reported no association between changes in HRQL measures between comparison groups. Lox and colleagues (1995) reported improvements in mood in the PRE group compared to the non-exercising control group. Shevitz and colleagues (2005) showed no significant change in quality of life adjusted years. The greatest increase was in the combined PRE and nutrition group (Table 2).

Discussion

The results of these meta-analyses indicate that PRE with or without aerobic exercise is associated with improvements in selected outcomes of weight and body composition (arm and thigh girth) and a trend toward improvements in selected outcomes of cardiopulmonary fitness (submaximum heart rate and exercise time) for adults living with HIV/AIDS. Individual studies that could not be included in meta-analysis supported these findings. The majority of individual studies also demonstrated improvements in strength and psychological outcomes. Neither CD4 count nor viral load appeared to be significantly affected by PRE or combined PRE and aerobic exercise.

Implications for practice

This systematic review suggests that performing PRE or a combination of PRE and aerobic exercise three times a week for at least six weeks appears to be safe and may lead to clinically important improvements in selected outcomes of weight and body composition for medically stable adults living with HIV/AIDS.

Results for other meta-analyses were not statistically significant and could not confirm an overall effect. However, meta-analysis for cardiopulmonary outcomes of submaximum heart rate suggested that exercise interventions may lead to clinically important improvements in cardiopulmonary fitness. Individual studies suggested that PRE interventions with or without aerobic exercise also contributed to improvements in strength and psychological status for adults living with HIV/AIDS. These findings coincide with results of a previous systematic review that found significant improvements in cardiopulmonary fitness and symptoms of depression among participants who engaged in aerobic or combined aerobic and PRE compared with non-exercise (O'Brien, Nixon, Tynan, & Glazier, 2006).

Individual studies also indicate that PRE or a combination of PRE and aerobic exercise appears to be safe for adults living with HIV/AIDS who are medically stable. This finding is based on the absence of reported adverse events attributed to exercise within the individual studies. The stability of CD4 count and viral load within individual studies and in three of four meta-analyses may also contribute to the evidence of the safety of PRE.

Limitations

Results of this review should be interpreted cautiously for a number of reasons. First, results are based on a small number of studies ($n = 10$). Meta-analyses were limited due to variation among individual studies in the types of interventions, participants and outcomes. Only 2–4 studies could be combined in each meta-analysis resulting in sample sizes ranging from 46 to 106 participants.

Second, individual studies included small sample sizes and high withdrawal or non-adherence rates. Half of the included studies had withdrawal rates greater than 15%. Participants who withdrew were often excluded from the final results by the authors, resulting in a per protocol analysis, limiting the ability to detect the effectiveness of exercise within some studies.

The inability to blind participants to the PRE intervention may have resulted in the Hawthorne effect. Individual studies could be susceptible to performance bias due to increased levels of interaction between the study investigators and participants in the exercise groups resulting in more favourable outcomes in exercisers compared to non-exercisers.

The maximum duration of intervention within the included studies was 16 weeks. Thus, the long-term effects of PRE remain unclear. Furthermore, the majority of study participants in the individual studies were men between 18 and 66. This limits the external validity and ability to generalize results to females, children, youth or older adults living with HIV. Finally, only four of the studies assessed HRQL, a clinically important outcome that acknowledges participants' perceptions of PRE on their own health.

Conclusion

In summary, results from this systematic review suggest that PRE or a combination of PRE and aerobic exercise is safe and may lead to clinically important improvements in selected outcomes of weight and body composition for medically stable adults living with HIV/AIDS. Individual study results suggest potential benefits to cardiopulmonary, strength and psychological outcomes. Further research is needed using an intention-to-treat analysis, to explore the effects of exercise in women, the long-term effects of exercise and clinically important outcomes of HRQL. Research is also required to develop recommendations pertaining to the parameters of frequency, intensity, time and type of PRE interventions that might be most beneficial to people living with HIV and to further investigate the effects of PRE in conjunction with interventions such as testosterone, whey protein, metformin and oxandrolone.

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References

Agin, D., Gallagher, D., Wang, J., Heymsfield, S.B., Pierson, R.N., Jr., & Kotler, D.P. (2001). Effects of whey protein and resistance exercise on body cell mass, muscle strength and quality of life in women with HIV. *Aids, 15*, 2431–2440.

Bhasin, S., Storer, T.W., Javanbakht, M., Berman, N., Yarasheski, K.E., Phillips, J., et al. (2000). Testosterone replacement and resistance exercise in HIV-infected men with weight loss and low testosterone levels. *Journal of the American Medical Association, 283*, 763–770.

Cochrane Collaboration (2002). *Review Manager (RevMan). Version 4.2 for Windows*. Oxford, England: The Cochrane Collaboration, 2002.

Cochrane Collaboration (2006). *The Cochrane Manual Issue 2, 2006 [updated 22 February 2006]*. Retrieved March 6, 2006 from http://www.cochrane.org/admin/manual.htm

Dolan, S.E., Frontera, W., Librizzi, J., Ljungquist, K., Juan, S., Dorman, R., et al. (2006). Effects of a supervised home-based aerobic and progressive resistance training regimen in women infected with human immunodeficiency virus: A randomized trial. *Archives of Internal Medicine, 166*, 1225–1231.

Driscoll, S.D., Meininger, G.E., Lareau, M.T., Dolan, S.E., Killilea, K.M., Hadigan, C.M., et al. (2004). Effects of exercise training and metformin on body composition and cardiovascular indices in HIV-infected patients. *Aids, 18*, 465–473.

Driscoll, S.D., Meininger, G.E., Ljungquist, K., Hadigan, C., Torriani, M., Klibanski, A., et al. (2004). Differential effects of metformin and exercise on muscle adiposity and metabolic indices in human immunodeficiency virus-infected patients. *Journal of Clinical Endocrinology & Metabolism, 89*, 2171–2178.

Fairfield, W.P., Treat, M., Rosenthal, D.I., Frontera, W., Stanley, T., Corcoran, C., et al. (2001). Effects of testosterone and exercise on muscle leanness in eugonadal men with AIDS wasting. *Journal of Applied Physiology, 90*, 2166–2171.

Fiatarone, M.A., Marks, E.C., Ryan, N.D., Meredith, C.N., Lipsitz, L.A., & Evans, W.J. (1990). High-intensity strength training in nonagenarians. Effects on skeletal muscle. *Journal of the American Medical Association, 263*, 3029–3034.

Fiatarone, M.A., O'Neill, E.F., Ryan, N.D., Clements, K.M., Solares, G.R., Nelson, M.E., et al. (1994). Exercise training and nutritional supplementation for physical frailty in very elderly people. *New England Journal of Medicine, 330*, 1769–1775.

Grinspoon, S., Corcoran, C., Parlman, K., Costello, M., Rosenthal, D., Anderson, E., et al. (2000). Effects of testosterone and progressive resistance training in eugonadal men with AIDS wasting. A randomized, controlled trial. *Annals of Internal Medicine, 133*, 348–355.

Hortobagyi, T., Lambert, N.J., & Hill, J.P. (1997). Greater cross education following training with muscle lengthening than shortening. *Medicine & Science in Sports & Exercise, 29*, 107–112.

Jadad, A.R., Moore, R.A., Carroll, D., Jenkinson, C., Reynolds, D.J., Gavaghan, D.J., et al. (1996). Assessing the quality of reports of randomized clinical trials: Is blinding necessary? *Controlled Clinical Trials, 17*, 1–12.

Jaque, S.V., Schroeder, E.T., Azen, S.P., Dube, M.P., Olson, C., Afghani, A., et al. (2002). Magnitude and timing of regional body composition changes during anabolic therapies in HIV positive males. *Clinical Exercise Physiology, 4*, 50–59.

Lau, J., Ioannidis, J.P., & Schmid, C.H. (1997). Quantitative synthesis in systematic reviews. *Annals of Internal Medicine, 127*, 820–826.

Lox, C.L., McAuley, E., & Tucker, R.S. (1995). Exercise as an intervention for enhancing subjective well-being in an HIV-1 population. *Journal of Sport & Exercise Psychology, 17*, 345–362.

Lox, C.L., McAuley, E., & Tucker, R.S. (1996). Aerobic and resistance exercise training effects on body composition, muscular strength and cardiovascular fitness in an HIV-1 population. *International Journal of Behavioural Medicine, 3*, 55–69.

O'Brien, K., Nixon, S., Tynan, A.M., & Glazier, R.H. (2006). Aerobic exercise interventions for people living with HIV/AIDS: Implications for practice, education, and research. *Physiotherapy Canada, 58*, 114–129.

Palella, F.J., Jr., Delaney, K.M., Moorman, A.C., Loveless, M.O., Fuhrer, J., Satten, G.A., et al. (1998). Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIV Outpatient Study Investigators. *New England Journal of Medicine, 338*, 853–860.

Rall, L.C., Meydani, S.N., Kehayias, J.J., Dawson-Hughes, B., & Roubenoff, R. (1996). The effect of progressive resistance training in rheumatoid arthritis. Increased strength without changes in energy balance or body composition. *Arthritis & Rheumatism, 39*, 415–426.

Rigsby, L.W., Dishman, R.K., Jackson, A.W., Maclean, G.S., & Raven, P.B. (1992). Effects of exercise training on men seropositive for the human immunodeficiency virus-1. *Medicine & Science in Sports & Exercise, 24*, 6–12.

Rusch, M., Nixon, S., Schilder, A., Braitstein, P., Chan, K., & Hogg, R.S. (2004). Impairments, activity limitations and participation restrictions: Prevalence and associations among persons living with HIV/AIDS in British Columbia. *Health and Quality of Life Outcomes, 2*, 46.

Sattler, F.R., Jaque, S.V., Schroeder, E.T., Olson, C., Dube, M.P., Martinez, C., et al. (1999). Effects of pharmacological doses of nandrolone decanoate and progressive resistance training in immunodeficient patients infected with human immunodeficiency virus. *Journal of Clinical Endocrinology & Metabolism, 84* 1268–1276.

Sattler, F.R., Schroeder, E.T., Dube, M.P., Jaque, S.V., Martinez, C., Blanche, P.J., et al. (2002). Metabolic effects of nandrolone decanoate and resistance training in men with HIV. *American Journal of Physiology – Endocrinology and Metabolism, 283*, E1214–E1222.

Schroeder, E.T., Jaque, S.V., Hawkins, S.A., Olsen, C., Wiswell, R.A., & Sattler, F.R. (2001). Regional DXA and MRI in assessment of muscle adaptation to anabolic stimuli. *Clinical Exercise Physiology, 3*, 199–206.

Schroeder, E.T., Terk, M., & Sattler, F.R. (2003). Androgen therapy improves muscle mass and strength but not muscle quality: Results from two studies. *American Journal of Physiology – Endocrinology and Metabolism, 285*, E16–E24.

Shevitz, A.H., Wilson, I.B., McDermott, A.Y., Spiegelman, D., Skinner, S.C., Antonsson, K., et al. (2005). A comparison of the clinical and cost-effectiveness of 3 intervention strategies for AIDS wasting. *Journal of Acquired Immune Deficiency Syndromes, 38*, 399–406.

Spence, D.W., Galantino, M.L., Mossberg, K.A., & Zimmerman, S.O. (1990). Progressive resistance exercise: Effect on muscle function and anthropometry of a select AIDS population. *Archives of Physical Medicine and Rehabilitation, 71*, 644–648.

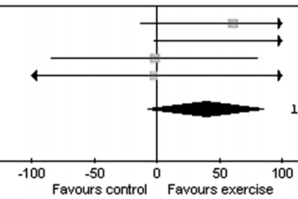
Appendix

Examples of forest plots of meta-analyses for sub-group comparison: PRE or combined PRE and aerobic exercise versus non-exercise.

CD4 count (cells/mm^3)

Study or sub-category	N	Treatment Mean (SD)	N	Control Mean (SD)	WMD (random) 95% CI	Weight %	WMD (random) 95% CI
Rigsby 1992	13	58.07(72.07)	11	-2.00(105.28)		34.70	60.07 [-13.45, 133.59]
Lox 1995	12	22.91(114.00)	10	-77.90(130.25)		18.63	100.81 [-2.52, 204.14]
Grinspoon 2000	10	31.00(125.00)	12	33.00(50.00)		28.25	-2.00 [-84.48, 80.48]
Dolan 2006	19	8.00(161.28)	19	11.00(165.64)		18.42	-3.00 [-106.95, 100.95]
Total (95% CI)	54		52			100.00	38.51 [-7.54, 84.56]

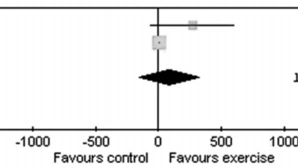
Test for heterogeneity: Chi² = 3.27, df = 3 (P = 0.35), I² = 8.1%
Test for overall effect: Z = 1.64 (P = 0.10)



VO$_2$max (ml/kg/min)

Study or sub-category	N	Treatment Mean (SD)	N	Control Mean (SD)	WMD (random) 95% CI	Weight %	WMD (random) 95% CI
Lox 1995	12	190.00(282.33)	10	-80.00(475.66)		29.32	270.00 [-65.31, 605.31]
Dolan 2006	19	1.50(3.49)	19	-2.50(6.97)		70.68	4.00 [0.50, 7.50]
Total (95% CI)	31		29			100.00	81.99 [-155.34, 319.33]

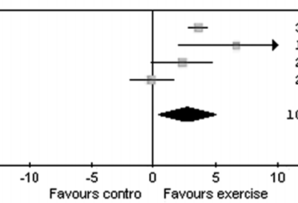
Test for heterogeneity: Chi² = 2.42, df = 1 (P = 0.12), I² = 58.6%
Test for overall effect: Z = 0.68 (P = 0.50)



Body weight (kg)

Study or sub-category	N	Treatment Mean (SD)	N	Control Mean (SD)	WMD (random) 95% CI	Weight %	WMD (random) 95% CI
Spence 1990	12	1.70(0.79)	12	-1.90(1.08)		32.93	3.60 [2.84, 4.36]
Lox 1995	12	2.12(2.85)	10	-4.50(6.87)		14.50	6.62 [2.07, 11.17]
Grinspoon 2000	10	1.70(3.20)	12	-0.60(2.50)		24.61	2.30 [-0.14, 4.74]
Dolan 2006	19	1.12(3.85)	19	1.23(1.38)		27.97	-0.11 [-1.95, 1.73]
Total (95% CI)	53		53			100.00	2.68 [0.40, 4.97]

Test for heterogeneity: Chi² = 16.09, df = 3 (P = 0.001), I² = 81.4%
Test for overall effect: Z = 2.30 (P = 0.02)



Arm and thigh girth (cm)

Study or sub-category	N	Treatment Mean (SD)	N	Control Mean (SD)	WMD (random) 95% CI	Weight %	WMD (random) 95% CI
Spence 1990	12	3.50(2.22)	12	-2.20(2.64)		63.59	5.70 [3.75, 7.65]
Lox 1995	12	5.19(4.32)	10	-6.59(9.74)		36.41	11.78 [5.27, 18.29]
Total (95% CI)	24		22			100.00	7.91 [2.18, 13.65]

Test for heterogeneity: Chi² = 3.07, df = 1 (P = 0.08), I² = 67.4%
Test for overall effect: Z = 2.71 (P = 0.007)