Progressive resistive exercise interventions for adults living with HIV/AIDS (Review)

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TABLE OF CONTENTS

[Intervention Review]

Progressive resistive exercise interventions for adults living with HIV/AIDS

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ABSTRACT

Background

Due to medical advancements, many people living with HIV infection in developed countries are living longer (Palella 1998). HIV infection can now present as a chronic illness with an uncertain natural disease history. The changing course of HIV infection has lead to a potential increase in the prevalence and impact of disability in people living with HIV infection. Exercise is one key management strategy used by health care professionals to address impairments (problems with body function or structure as a significant deviation or loss such as pain or weakness), activity limitations (difficulties an individual may have in executing activities such as inability to walk) and participation restrictions (problems an individual may experience in life situations such as inability to work) in this population (World Health Organization 2001). Exercise may also be used to address unwanted changes in weight and body composition in people living with HIV infection.

Aerobic exercise has been associated with improvements in strength, cardiovascular function, and psychological status in general populations (Bouchard 1993). Results of a systematic review suggested that aerobic exercise interventions appeared to be safe and may lead to improvements in cardiopulmonary fitness for adults living with HIV/AIDS (Nixon 2002). But what are the effects of progressive resistive exercise (PRE) for adults living with HIV infection?

A better understanding of the effectiveness and safety of progressive resistive exercise will enable people living with HIV and their health care workers to practice effective and appropriate exercise prescription, thus contributing to improved overall outcomes for adults living with HIV infection.

Objectives

To examine the safety and effectiveness of progressive resistive exercise interventions on weight, body composition, strength, immunological/virological, cardiopulmonary and psychological parameters in adults living with HIV infection.

Search methods

To identify studies to be included in this review, we searched the following databases: MEDLINE, EMBASE, CINAHL, COCHRANE, SCIENCE CITATION INDEX, PSYCHINFO, SOCIOLOGICAL ABSTRACTS, SSCI, ERIC, DAI and HEALTHSTAR. We also reviewed both published and unpublished abstracts and proceedings from major international and national HIV/AIDS conferences

such as the Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), the Conference on Retroviruses and Opportunistic Infections (CROI), the Infectious Diseases Society of America Conference (IDSA), and the International AIDS Conference (IAC). Reference lists from pertinent articles and books were reviewed, as well as Collaborative Review Group databases. Targeted journals were also hand searched for relevant articles. No language restriction was applied. The search strategy covered literature from 1980-August 2003.

Selection criteria

We included studies that were randomized controlled trials (RCTs) comparing progressive resistive exercise interventions with no progressive resistive exercise or another exercise or treatment modality, performed at least three times per week, and lasting at least four weeks among adults (18 years of age or older) living with HIV/AIDS.

Data collection and analysis

Data collection forms were used by reviewers to abstract data pertaining to study design, participants, interventions, outcomes and methodological quality from the studies that met inclusion criteria. Whenever possible, meta-analyses were conducted on outcomes using RevMan 4.2.2 computer software.

Main results

Seven studies met the inclusion criteria for this systematic review. Meta-analysis was limited due to the following differences among the studies: types of exercise interventions, inclusion of co-intervention groups, level of exercise supervision, baseline body composition and testosterone levels of participants, types of outcomes assessed, and methodological quality of the individual studies.

Main results indicated that performing progressive resistive exercise or a combination of progressive resistive exercise and aerobic exercise at least three times a week for at least four weeks appears to be safe and may lead to statistically and possibly clinically important increases in body weight and composition. Results also indicate exercise interventions may lead to clinically important improvements in cardiopulmonary fitness. Individual studies included in this review suggest that progressive resistive exercise interventions with or without aerobic exercise also contribute to improvements in strength and psychological status for adults living with HIV/AIDS. Individual studies indicate that progressive resistive exercise or a combination of progressive resistive and aerobic exercise appears to be safe for adults living with HIV/AIDS who are medically stable as a result of no change seen in immunological/virological status. These results are limited to those who continued to exercise and for whom there were adequate follow-up data.

Authors' conclusions

Progressive resistive exercise or a combination of progressive resistive exercise and aerobic exercise appear to be safe and may be beneficial for adults living with HIV/AIDS. These findings are limited by the small number of studies that could be included in meta-analyses, small sample sizes and variable participant withdrawal rates among included studies. Future research would benefit from including participants at various stages of HIV infection, a greater proportion of female participants, and participants in a variety of age groups to increase the generalizability of results. Furthermore, future research would benefit from studies with larger sample sizes that conduct an "intention-to-treat" analysis (analysis of participants based on the groups to which they were originally allocated) to better understand outcomes of participants that withdraw from exercise interventions.

PLAIN LANGUAGE SUMMARY

Progressive resistive exercise interventions for adults living with HIV/AIDS

Due to medical advancements, many people living with HIV infection in developed countries are living longer (Palella 1998). HIV infection can now present as a chronic illness with an uncertain natural disease history. The changing course of HIV infection has lead to a potential increase in the prevalence and impact of disability in people living with HIV infection. Exercise is one key management strategy used by health care professionals to address impairments (problems with body function or structure as a significant deviation or loss such as pain or weakness), activity limitations (difficulties an individual may have in executing activities such as inability to walk) and participation restrictions (problems an individual may experience in life situations such as inability to work) in this population (World Health Organization 2001). Exercise may also be used to address unwanted changes in weight and body composition in people living with HIV infection.

Aerobic exercise has been associated with improvements in strength, cardiovascular function, and psychological status in general populations (Bouchard 1993). Results of a systematic review suggested that aerobic exercise interventions appeared to be safe and may

lead to improvements in cardiopulmonary fitness for adults living with HIV/AIDS (Nixon 2002). But what are the effects of progressive resistive exercise (PRE) for adults living with HIV infection?

A better understanding of the effectiveness and safety of progressive resistive exercise will enable people living with HIV and their health care workers to practice effective and appropriate exercise prescription, thus contributing to improved overall outcomes for adults living with HIV infection.

In this review, we included studies that were randomized controlled trials (RCTs) comparing progressive resistive exercise interventions with no progressive resistive exercise or another exercise or treatment modality, performed at least three times per week, and lasting at least four weeks among adults (18 years of age or older) living with HIV/AIDS. Seven studies met the inclusion criteria for this systematic review. Progressive resistive exercise or a combination of progressive resistive exercise and aerobic exercise appear to be safe and may be beneficial for adults living with HIV/AIDS. These findings are limited by the small number of studies that could be included in meta-analyses, small sample sizes and variable participant withdrawal rates among included studies. Future research would benefit from including participants at various stages of HIV infection, a greater proportion of female participants, and participants in a variety of age groups to increase the generalizability of results. Furthermore, future research would benefit from studies with larger sample sizes that conduct an "intention-to-treat" analysis (analysis of participants based on the groups to which they were originally allocated) to better understand outcomes of participants that withdraw from exercise interventions.

BACKGROUND

Due to medical advancements, many people living with HIV infection in developed countries are living longer (Palella 1998). HIV infection can now present as a chronic illness with an uncertain natural disease history. The changing course of HIV infection has led to a potential increase in the prevalence and impact of disability in people living with HIV infection. Exercise is one key management strategy used by health care professionals to address impairments (problems with body function or structure as a significant deviation or loss such as pain or weakness), activity limitations (difficulties an individual may have in executing activities such as inability to walk) and participation restrictions (problems an individual may experience in life situations such as inability to work) in this population (WHO 2001).

Exercise may also be used to address unwanted changes in weight and body composition in people living with HIV infection. AIDS wasting is a condition associated with HIV infection and is defined as an "involuntary loss of more than 10% of baseline body weight in combination with diarrhea, weakness or fever." (CDC 1987). AIDS wasting may lead to increased energy expenditure (Grunfeld 1992), increased energy intake (Macallan 1995), decreased functional capacity (Grinspoon 1999), and even death (Palenicek 1995). Highly active antiretroviral therapy (HAART) has been associated with a reduction in the severity of weight loss and malnutrition and improvements in immune status for people living with HIV infection (Schwenk 1998). However, antiretroviral therapy may also be associated with unwanted changes in body composition known as lipodystrophy.

Lipodystrophy is a syndrome associated with physical and metabolic changes in the body (Boufassa 2001). Lipodystrophy is characterized by a reduction in subcutaneous fat (fat stores under the skin) in the face, arms, legs and buttocks, and an increase in visceral fat (fat stores that surround organs) in the abdomen, back of neck and breasts. Such changes in body composition can have an impact on body image for persons living with HIV/AIDS. Furthermore, the potential long term effects of the accumulation of visceral fat associated with lipodystrophy for people living with HIV infection are unknown. Certain pharmacological interventions, such as growth hormones, have been used among people living with HIV infection to increase lean body mass (parts of the body limited of stored fat such as: muscle, bone, connective tissue, organs and water). However, these medications are often expensive and may be fraught with unwanted adverse events (Roubenoff 1999).

In addition to other potential benefits, exercise is an alternative intervention for addressing changes in body composition. Aerobic exercise is associated with improvements in strength, cardiovascular function, and psychological status in general populations (Bouchard 1993). Results of a systematic review suggested that performing constant or interval aerobic exercise, or a combination of aerobic and progressive resistive exercise interventions at least 3 times per week for at least 4 weeks appeared to be safe and may lead to clinically important improvements in cardiopulmonary fitness for adults living with HIV/AIDS (Nixon 2002). But what are the effects of progressive resistive exercise (PRE) for adults living with HIV infection?

Progressive resistive exercise is a type of exercise that involves

strengthening of muscle tissue that may include, but is not limited to activities such as: isotonic strengthening exercises (muscular contraction with constant tension while length of muscle changes), and isometric strengthening exercises (muscular contraction where tension increases while length of muscle remains constant). Examples of weight training activities include: leg presses (extension), leg curls (flexion), biceps and triceps curls, and chest presses. 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 1990; Fiatarone 1994; Rall 1996). But how does progressive resistive exercise impact on outcomes such as the quality of life for adults living with HIV infection? What are the appropriate frequency, intensity, duration and types of exercise? At which stages of HIV infection may progressive resistive exercise be most beneficial, least beneficial or even harmful?

Progressive resistive exercise may be a strategy used to address unwanted changes in body composition, and may also be used as a general way to maintain health and fitness. However, the effectiveness and safety of progressive resistive exercise for people living with HIV infection are largely unknown.

A better understanding of the effectiveness and safety of progressive resistive exercise will enable people living with HIV and their health care workers to practice effective and appropriate exercise prescription, thus contributing to improved overall outcomes for adults living with HIV infection.

OBJECTIVES

To examine the safety and effectiveness of progressive resistive exercise interventions on weight, body composition, strength, immunological/virological, cardiopulmonary and psychological parameters in adults living with HIV infection.

METHODS

Criteria for considering studies for this review

Types of studies

Randomized controlled trials (RCTs) comparing progressive resistive exercise with no progressive resistive exercise or another exercise or treatment modality performed at least three times per week, and lasting at least four weeks were included.

Types of participants

Studies of adults (18 year and older) with HIV infection were included. Studies of men only, women only, or both at all stages of infection were included.

Types of interventions

Progressive resistive exercise was defined as a regimen containing resistive exercise interventions performed at least three times per week for at least four weeks. Progressive resistive exercise interventions may have included but were not limited to: weight training, isotonic and isometric strengthening exercises. Interventions may or may not have been supervised.

Types of outcome measures

Based on consultation with persons living with HIV infection, physiotherapists, physicians, and exercise researchers, we decided to include the following outcome measures in this review: weight, body composition, strength, immunological/virological indicators, cardiopulmonary measures, psychological measures and safety.

1) Weight measures that were considered for this review included but were not limited to: change in weight status (kg).

2) Body composition measures that were considered for this review included but were not limited to: body mass index (kg/m2), lean body mass (kg), girth, skinfolds (subcutaneous fat), and cross-sectional muscle area (mm2). Note, for the purposes of this review, we defined body composition broadly as any outcome that contributes to the direct or indirect measurement of muscle, fat, bone or other tissues of the body.

3) Strength measures that were considered for this review included but were not limited to: strength (amount of weight able to resist in kilograms).

4) Immunological and virological indicators that were considered for this review included but were not limited to: CD4 count (cells/mm3), and viral load (log10copies).

5) Cardiopulmonary measures that were considered for this review included but were not limited to: maximal oxygen consumption (VO2max) (ml/kg/min), maximum heart rate (beats/min), dyspnea (rate of perceived exertion and FEV1), fatigue (time on treadmill) and stamina.

6) Psychological measures that were considered for this review included but were not limited to measures of health related quality of life, and anxiety and depression. Measures included but were not be limited to: Medical Outcomes Study-HIV Health Survey (MOS-HIV), Short Form-20 Health Survey (SF-20), Short Form-36 Health Survey (SF-36), Quality of Well-Being Scale, Quality-adjusted Time Without Symptoms of disease or Toxicity of treatment (Q-TWIST), Quality of Life Index, EuroQoL, Sickness Impact Profile (SIP), Health Utility Assessment, and the Montgomery-Asberg Scale for Depression.

7) Safety measures that were considered for this review included but were not limited to the following adverse events: joint, muscle, tendon, ligament, nerve, vascular or bone injury, a deterioration in immune status (decrease in CD4 count), progression to AIDS, hospitalization and mortality.

Search methods for identification of studies

To identify studies to be included in this review, we searched the following databases: MEDLINE, EMBASE, CINAHL, COCHRANE, SCIENCE CITATION INDEX, PSYCHINFO, SOCIOLOGICAL ABSTRACTS, SSCI, ERIC, DAI and HEALTHSTAR. Two arms of the search strategy were developed and intersected using the Boolean term "AND":
i) Exercise subject headings (exploded): exertion, physical fitness, sports, physical education and training.
ii) HIV subject headings (exploded): HIV long term survivors, HIV, HIV infections.
We also reviewed both published and unpublished abstracts and proceedings from major international and national HIV/AIDS conferences such as the Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), the Conference on Retroviruses and Opportunistic Infections (CROI), the Infectious Diseases Society of America Conference (IDSA), and the International AIDS Conference (IAC). Reference lists from pertinent articles and books were reviewed, as well as Collaborative Review Group databases. Targeted journals were also hand searched for relevant articles.
No language restriction was applied. The search strategy covered literature from 1980-August 2003. Some databases required slight modifications to the search strategy.

Data collection and analysis

All abstracts retrieved from the search strategy were reviewed independently by two investigators who applied the following four inclusion criteria to determine if the abstract warranted further investigation:
a) Does the study include human participants who are HIV positive?
b) Does the study include adults 18 years of age and older?
c) Does the study include a progressive resistive exercise intervention performed at least three times per week for at least four weeks? and
d) Was there a randomized comparison group?
When the review based on the abstract alone (or title and keywords if no abstract was available from the search) indicated that one or both raters believed that the study may meet eligibility criteria (i.e. if the reviewers answered "yes" or "unsure" to the four questions), then hard copies of entire papers were independently reviewed by two reviewers. In instances where there was disagreement between the two reviewers, a third reviewer was asked to review the full paper and to make the final determination on whether the article met inclusion criteria. Full papers were not examined in instances where both raters agreed that the study did not meet the inclusion criteria.
From the group of studies retrieved that met the inclusion criteria, at least two reviewers reviewed each article independently to determine final inclusion. From the final group of included studies, data were abstracted onto standard data abstraction forms independently by at least two reviewers. Extracted data included the study citation, study design, length of study, times at which participants were assessed, inclusion and exclusion criteria for participants, characteristics of included participants (i.e. stage of disease, gender, age), objectives of the study, description of interventions (i.e. type, duration, intensity, frequency, level of supervision), types of outcome variables used and their values at baseline and study completion, and number of participants at baseline and study completion (including number of drop-outs). Methodological quality of the studies was also extracted using methodological criteria suggested by Jadad 1996. Instead of generating a formal methodological score, reviewers provided a description of the methodological quality of the studies using the Jadad criteria as follows:
a) Was the study described as randomized? If yes, describe the method of randomization.
b) Was the study described as blinded or double-blinded? If yes, describe how the double blinding was attained.
c) Was there a description of the withdrawals and drop-outs?
We also assessed whether groups were similar at baseline. Meetings took place to achieve consensus regarding any differences that arose between the reviewers in data interpretation or abstraction.
Outcomes were analyzed both as continuous and dichotomous/binary outcomes whenever possible. Where there was sufficient data available in the studies, when similar or comparable outcome measures were used, and analysis was performed using random effects models for outcomes. In the case of missing data, authors were contacted in an attempt to obtain further information where required.
Standard statistical analyses included:
1) For continuous outcomes: the weighted mean difference (WMD) and 95% confidence intervals for the means were calculated whenever possible.
2) For dichotomous/binary outcomes: the odds ratio, absolute difference in odds, relative risk (RR), risk difference (RD), and number needed to treat (NNT) including 95% confidence intervals were calculated whenever possible.
A p value of less than 0.05 was considered statistically significant for overall effect. A p value of less than 0.1 was considered statistically significant for testing heterogeneity (Lau 1997). In instances of statistically significant heterogeneity, we explained potential reasons for differences among the individual studies that might account for the heterogeneity between studies. Where meta-

analyses were not possible, we described results of the individual studies.

For the purposes of this review, we considered 3kg to indicate a clinically important change in body weight (which equals approximately 5% of the average baseline body weight of the participants), 5 cm to indicate a clinically important change in girth, 5kg to indicate a clinically important change in strength for lower extremities, 2kg to indicate a clinically significant change in strength for upper extremities, 50 cells/mm3 to indicate a clinically important change in CD4 count, 0.5 log10 copies to indicate a clinically important change in viral load, and 2ml/kg/min to indicate a clinically important change in VO2max.

SUBGROUP ANALYSES:

Subgroup analyses were performed whenever possible to estimate whether progressive resistive exercise interventions are associated with differences among groups using identified outcome measures. Possible subgroup analyses included: supervised vs. non-supervised exercise, symptomatic vs. asymptomatic HIV infection, males vs. females, older vs. younger participants, participants with HIV wasting vs. participants without HIV wasting and participants on antiretroviral therapy vs. participants not on antiretroviral therapy.

SENSITIVITY ANALYSES:

Sensitivity analyses were performed to determine whether particular studies may skew results. In situations where outliers were omitted or inclusion criteria for studies varied, sensitivity analyses were performed as needed to determine the robustness of findings. Exploratory analyses were performed based on the results of the review. Individual study design and procedures were taken into account to determine whether biases manifested. Potential biases in studies may have included: selection bias (systematic differences in the comparison groups), performance bias (systematic differences in the care provided apart from the intervention being evaluated), exclusion bias (systematic differences in withdrawals from the trial), and detection bias (systematic differences in outcome assessment). Reviewers also assessed whether or not an "intention-to-treat" analysis was performed for participants lost to follow-up.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies.

The search strategy resulted in 1414 citations. After abstract review, 58 full citations were reviewed to determine whether they met inclusion criteria. Of the 58 studies reviewed, 13 met the inclusion criteria (Lox 1995, Lox 1996, Agin 2001, Bhasin 2000, Sattler 1999, Schroeder 2001, Grinspoon 2000, Rigsby 1992 & Spence 1990, Fairfield 2001, Jaque 2002, Sattler 2002 and Schroeder 2003). Of the 13 included studies, there were three groups identified as duplicate studies (Grinspoon 2000 & Fairfield 2001, Sattler 1999, Schroeder 1999, Jaque 2002, Sattler 2002 & Schroeder 2003, and Lox 1995 & Lox 1996). In these instances, the earlier published study was included in the review, and any additional outcomes data reported in the later studies were also incorporated into the review. Thus there were a total of seven studies that met inclusion criteria (Spence 1990, Rigsby 1992, Lox 1995, Sattler 1999, Grinspoon 2000, Bhasin 2000 & Agin 2001 - see the table of characteristics of included studies). Studies that were excluded were either review articles, letters or editorials and therefore did not meet the inclusion criteria. Other studies were excluded because they did not include progressive resistive exercise interventions, did not include a comparison group, or were duplications of previously published studies (see table of excluded studies).

INCLUDED STUDIES:

Included studies were randomized trials that compared progressive resistive exercise with no progressive resistive exercise or another exercise or treatment modality performed at least three times per week, for at least four weeks among adults living with HIV/AIDS.

DESIGN OF INCLUDED STUDIES:

All seven included studies were randomized controlled trials (RCTs).

Five of the seven studies included a non-exercising control group (Spence 1990, Lox 1995, Grinspoon 2000, Bhasin 2000, Rigsby 1992) one of which included a counseling group (Rigsby 1992). Two of the seven studies included combined regimens of PRE and aerobic exercise (Grinspoon 2000 & Rigsby 1992). Exercise interventions in five studies included PRE interventions only (Agin 2001, Sattler 1999, Spence 1990, Lox 1995, & Bhasin 2000). One of the seven studies included an aerobic exercise only group along with a PRE only group (Lox 1995) of which the aerobic exercise group was not considered in this review. Four of the seven studies included comparison groups that assessed the effects of co-interventions of PRE with testosterone (Sattler 1999, Bhasin 2000 and Grinspoon 2000) and whey protein (Agin 2001). These studies also included comparison groups consisting of testosterone only and whey protein only, respectively. Three of the seven studies assess the effect of testosterone only (Sattler 1999, Grinspoon 2000, Bhasin 2000). In five studies (Agin 2001, Sattler 1999, Grinspoon 2000, Rigsby 1992 & Spence 1990), exercise was described as supervised and in the remaining two studies (Lox 1995 & Bhasin 2000) the level of supervision was not stated.

PARTICIPANTS OF INCLUDED STUDIES:

Participants included adults infected with HIV at various stages of the disease with CD4 counts ranging from <100 to >1000 cells/mm3. Six of the seven studies included all male participants (Grinspoon 2000, Spence 1990, Sattler 1999, Lox 1995, Bhasin 2000, Rigsby 1992) and the remaining study included all female participants (Agin 2001). Women comprised less than 15% of the to-

tal number of participants for this review. The age of participants ranged from 18-66 years. Three of the seven studies included participants with elements of wasting syndrome (either >5% or >10% involuntary weight loss or body weight <90% ideal body weight) (Grinspoon 2000, Agin 2001 & Bhasin 2000). One of the studies included participants with low testosterone levels (serum total testosterone levels less than 12.1nmol/L) (Bhasin 2000). Three of the seven studies included participants who were diagnosed with AIDS wasting at baseline (Bhasin 2000, Grinspoon 2000, & Agin 2001). Two of the seven studies reported that the majority of participants were on highly active antiretroviral activity (HAART) (Grinspoon 2000 & Sattler 1999). Agin (2001) reported that recruitment of participants occurred after the introduction of protease inhibitors but did not report on the proportion of participants who were taking HAART. Two studies reported that most if not all participants were taking some form of antiretroviral therapy (ART) (Lox 1995, Bhasin 2000). Spence (1990) included participants who were taking AZT monotherapy, and Rigsby (1992) did not report on whether participants were taking ART.

OUTCOMES OF INCLUDED STUDIES:

Five of the seven studies assessed immunological and/or virological outcomes (Lox 1995, Agin 2001, Sattler 1999, Rigsby 1992 & Grinspoon 2000). Six of the seven studies assessed body weight and composition outcomes (Spence 1990, Lox 1995, Agin 2001, Sattler 1999, Bhasin 2001 & Grinspoon 2000). All seven studies assessed strength outcomes. Two of the seven studies assessed cardiopulmonary outcomes (Lox 1995 & Rigsby 1992). Two of the seven studies assessed psychological outcomes in the form of health-related quality of life and well-being (Lox 1995 & Agin 2001). Adverse events to assess safety were reported in five of the seven studies (Agin 2001, Sattler 1999, Bhasin 2000, Rigsby & Grinspoon 2000).

Risk of bias in included studies

All studies that met the inclusion criteria were identified for full review by two reviewers. Each reviewer independently assessed the methodological quality of included studies based on the following criteria derived from the Jadad 1996 checklist (#1-3), and whether the groups were similar at baseline (#4). This methodological quality criteria is used by the Cochrane Collaborative Review Group on HIV Infection and AIDS. Instead of a formal score, a description of the methodological quality based on the four criteria is provided below.

1) Was the study randomized? If yes, was the randomization process described?

All seven studies reported using randomization to allocate participants to a comparison group. However, only four studies described the randomization process (Agin 2001, Grinspoon 2000 & Bhasin 2000 & Sattler 1999). Agin (2001) described the randomization process as sequential, generated by two research assistants using a random number table. Grinspoon (2000) described the randomization process as using a permuted-block algorithm with blocks of eight. Bhasin (2000) described the process of randomization as using schedules that generated random numbers from a uniform distribution on unit interval. Sattler (1999) described the randomization process as a list of random numbers, blocked in blocks of four.

2) Was the study double-blinded? If yes, how was the double-blinding attained?

None of the studies were double-blinded since the intervention of interest was exercise. However, the studies that included a co-intervention of testosterone (Sattler, 1999, Grinspoon 2000 & Bhasin 2000) achieved participant blinding to testosterone by using a placebo. Assessor blinding was specified for two of the seven studies (Rigsby 1992 & Agin 2001) whereby the study investigator was blinded to participant allocation to the comparison groups. For the other five studies, assessor blinding was not specified.

3) Was there a description of withdrawals and/or drop-outs?

Six of the seven studies reported on participants who withdrew from the study or were non-compliant with the exercise intervention (Rigsby 1992, Sattler, 1999, Lox 1995, Grinspoon 2000, Bhasin 2000 & Agin 2001). Spence (1990) did not report any withdrawals. Rates of withdrawal and a description of the reasons for withdrawal (when provided) are described below.

The withdrawal rate in Rigsby (1992) was 35% (13/37). Reasons for withdrawal included: "health reasons" among both exercise and counseling groups. Withdrawals reported from the exercise group were due to relocation of residence and withdrawals from the counseling group were due to lack of interest. There was one death reported during this study that was not attributed to exercise.

The withdrawal rate in Agin (2001) was 30% (13/43). Six participants withdrew at the point of randomization after an initial six week control period and seven withdrew during the intervention phase. Reasons for withdrawal included: dissatisfaction with group assignment, family constraints, non-compliance and death (n=1). The death reported in this study was a participant that was allocated to the co-intervention group of progressive resistive exercise and whey protein. Withdrawal rates were random in all three comparison groups.

The withdrawal rate in Spence (1990) was 0% (0/24). Clarification has been requested from the authors to confirm that there were no withdrawals from this study and that the number of participants at baseline was equal to the number of participants at study completion (n=24).

The withdrawal rate in Grinspoon (2000) was 20% (11/54). No participants withdrew from this study due to adverse events and the rates of withdrawal were similar among the comparison groups. Participants who did not receive the standard intervention were removed from the final analyses and were considered withdrawals.

The withdrawal rate in Bhasin (2000) was 20% (12/61). Characteristics of the participants that withdrew from this study were similar to those that completed the study except for age. Partici-

pants that withdrew from this study were older (41.4 years) compared to participants that completed the study (35.5 years) (p= 0.01).
The withdrawal rate in Lox (1995) was 3% (1/34). The one participant withdrew due to persistent infection.
The withdrawal rate in Sattler (1999) was 9% (3/33). Reasons for withdrawal included: an occupational hand injury (one participant in the testosterone only group), an abdominal injury (unrelated to exercise) and re-location of residence (two participants in the combined testosterone and progressive resistive exercise group).

4) Were the groups similar at baseline?
Five of the studies reported that the comparison groups were similar at baseline (Sattler 1999, Rigsby 1992, Agin 2001, Spence 1990 & Bhasin 2000). Grinspoon (2000) did not report on group similarity at baseline. Lox (1995) indicated significant differences between comparison groups for "most" participant characteristics, but variables that were different between the groups were not specified.

Effects of interventions

Six meta-analyses were completed in this review. The comparisons of the meta-analyses include: 1) PRE versus non-exercising control, 2) Combined PRE and aerobic exercise versus non-exercising control, and 3) PRE with or without aerobic exercise versus non-exercising control.
The number of meta-analyses were limited due to variability in: types of exercise interventions (PRE versus combined PRE and aerobic exercise), inclusion of co-intervention groups (whey protein and testosterone), level of exercise supervision, baseline body composition of participants (wasting versus non-wasting), baseline testosterone level of participants (low versus normal and/or not specified), types of outcomes reported, and methodological quality (see table of characteristics of included studies). Bhasin (2000) was not included in any of the meta-analyses because the participants in this study had low testosterone levels at baseline. As a result, we decided that these participants were not comparable to participants with other studies that had normal and/or testosterone levels not specified.
1) PROGRESSIVE RESISTIVE EXERCISE VERSUS NON-EXERCISING CONTROL
This section of the results presents the effect of progressive resistive exercise compared to non-exercising controls. When meta-analysis was not possible, results from individual studies are discussed. Three of the seven studies compared PRE with a non-exercising control group (Spence 1990, Lox 1995 & Bhasin 2000). Meta-analysis was only possible for body weight.
A) BODY WEIGHT STATUS
All three of the studies that compared PRE with a non-exercising control group assessed body weight (Spence 1990, Lox 1995, Bhasin 2000). Bhasin (2000) was not included in meta-analysis because the participants had low testosterone levels at baseline, unlike the other two studies in which participants had normal testosterone levels.
A-1) Body Weight:
Meta-analysis demonstrated a significant increase in body weight of 4.24kg (95% CI: 1.82, 6.66, p=0.0006, n=46) for participants in the PRE groups compared to the non-exercising control groups (Spence 1990 & Lox 1995) (see Figure 02.01). This increase in body weight of 4.24kg indicates a clinically important increase in body weight among exercisers compared to non-exercisers. See above discussion for individual study results for other body weight outcomes for all seven included studies.
Individual Study Results - Body Weight:
Spence (1990) found a significant increase in body weight of 1.7kg for participants in the PRE group compared to a significant decrease in body weight of 1.9kg for participants in the non-exercising control group. Grinspoon (2000) found an increase in body weight of 1.7kg for participants in the combined PRE and aerobic exercise group compared to a decrease in body weight of 0.6kg for participants in the non-exercising control group. These results were not statistically significant. Lox (1995) found a significant increase of 2.12kg in body weight for participants in the PRE group compared to a decrease of 4.5kg in the non-exercising control group. Bhasin (2000) found a significant increase in body weight of 2.2kg for participants in the PRE group compared to a decrease in body weight of 0.5kg in the non-exercising control group. Bhasin (2000) did not provide standard deviation data for body weight for participants in their study, and included participants with low testosterone levels, thus these results are not included in meta-analysis. Rigsby (1992) did not report body weight outcomes. Agin (2001) and Sattler (1999) did not include a non-exercising control group in their studies. Sattler (1999) found significant increases in body weight for both the combined testosterone and PRE group (4 kg), and the PRE only group (3.2kg), but there was no significant difference between the groups. Agin (2001) found a significant increase in body weight for the whey protein group (3.6kg) only.
B) BODY COMPOSITION STATUS:
Six of the seven included studies reported body composition outcomes (Lox 1995, Sattler 1999, Agin 2001, Spence 1990, Grinspoon 2000 & Bhasin 2000). Four of these studies included a non-exercising control group (Lox 1995, Spence 1990, Grinspoon 2000 & Bhasin 2000).
Individual Study Results - Body Composition:
Grinspoon (2000) found significant increases in lean body mass (2.3kg), arm muscle area (346mm2) and leg muscle area (797mm2) and a non-significant decrease in fat mass (-1.3kg) for participants in the combined PRE and aerobic exercise group compared to no changes in the non-exercising control group. Bhasin (2000) found significant increases in thigh muscle volume (62cm3) and fat free mass (2.0kg) for participants in the PRE group compared to no change in the non-exercising control group.

Bhasin (2000) found no significant changes in fat mass among the two comparison groups. Lastly, Bhasin (2000) found significant increases in lean body mass for the arms (0.5kg) and trunk (1.2kg) for participants in the PRE group compared to no change in lean body mass for participants in the non-exercising control group. Both Grinspoon (2000) and Bhasin (2000) included participants with wasting syndrome; thus results of increases in body weight, lean body mass, and fat free mass represent favourable results.

Spence (1990) found a significant increase in arm and thigh girth (3.5cm) and a non-significant increase in the sum of chest, abdomen and anterior thigh skinfold (5.1mm) for participants in the PRE group compared a significant decrease in arm and thigh girth (-2.2cm) and non-significant decrease in sum of chest, abdomen and anterior thigh skinfold (-4.9mm) for participants in the non-exercising control group. Lox (1995) found significant increases in girth (5.19cm) in the PRE group compared to the non-exercising control group, and no significant differences among PRE, aerobic or non-exercising control groups for average body fat, fat weight and mean body mass index, however, both exercise groups were significantly different than the non-exercising control group for measures of change in body weight and composition. Rigsby (1992) did not report body composition outcomes. Agin (2001) and Sattler (1999) did not include a non-exercising control group in their study. Agin (2001) found a significant increase in body cell mass for both the combined whey protein and PRE group (0.61kg) and PRE only group (0.74kg), significant increase in skeletal muscle for the PRE only group (1.2kg) with no change in the two whey protein groups, and a significant increase in fat mass for the whey protein only group (2.5kg) and decrease in fat mass for the PRE only group (-1.7kg). Sattler (1999) found a significant increase in lean body mass more in the combined PRE and testosterone group (5.2kg) versus the testosterone only group (3.9kg) and similar increases in body cell mass and cross-sectional muscle area for both groups.

C) STRENGTH STATUS:

All seven studies reported strength outcomes (Lox 1995, Sattler 1999, Rigsby 1992, Agin 2001, Spence 1990, Grinspoon 2000 & Bhasin 2000). Of these, five included a non-exercising control group (Lox 1995, Rigsby 1992, Spence 1990, Grinspoon 2000 & Bhasin 2000). Meta-analysis could not be performed for any strength outcomes due to differences in outcomes assessed and types of participants.

Individual Study Results - Strength:

Grinspoon (2000) found no significant differences in strength (7/7 variables) between the combined progressive resistive exercise (PRE) and aerobic exercise group and the non-exercising control group. The lack of statistical significance was attributed to the use of isometric methods of strength testing versus the alternative isotonic method of testing used in the other four studies. Isometric testing has been shown to underestimate changes in strength (Hortobagyi 1997). Bhasin (2000), which used one repetition isotonic methods to assess strength, found increases in strength by 29%-36% in the PRE intervention group compared to no change in strength in the non-exercising control group (-0.3%-4.0% increase) for five variables of strength. Rigsby (1992) found a significant increase in strength for chest press (50.27Nm) and leg press (47.54Nm) for the combined PRE and aerobic exercise intervention group compared to a non-significant increase in strength for chest press (19.22Nm) and leg press (6.92Nm) for the non-exercising control group. Lox (1995) found significant increases in strength in upper and lower extremities in the PRE group compared to the non-exercising control and aerobic exercise groups. Spence (1990) found significant increases in strength for all lower extremity variables (12/12) and for nearly all upper extremity variables (10/12) assessed in the PRE intervention group compared to significant decreases in strength seen in lower extremity variables (7/12) and upper extremity variables (6/12) assessed for the non-exercising control group. Agin (2001) and Sattler (1999) did not include a non-exercising control group in their study. Sattler (1999) found significantly greater increases in upper and lower extremity strength in the combined testosterone and PRE group (14-53% increase) compared to the testosterone only group (10-31%). Agin (2001) found significant increases in both the PRE only and combined PRE and whey protein groups for seven muscle groups with the increase ranging from 40.6-95.3%.

D) IMMUNOLOGICAL AND VIROLOGICAL STATUS:

Five of the seven studies reported immunological / virological outcomes. Three of the studies that included a non-exercising control group included combined PRE and aerobic exercise interventions (Rigsby 1992 & Grinspoon 2000), and one included PRE only (Lox 1995). Agin (2001) and Sattler (1999) also measured immunological / virological outcomes but did not include a non-exercising control group.

Individual Study Results

D-1) CD4 count:

Grinspoon (2000) found an increase of 31 cells/mm3 in the combined PRE and aerobic exercise intervention group compared to an increase of 33 cells/mm3 in the non-exercising control group. Rigsby (1992) found an increase of 58 cells/mm3 in the combined PRE and aerobic exercise intervention group as compared to a decrease of 2 cells/mm3 in the non-exercising control group. Lox (1995) found an increase of 23 cells/mm3 in the PRE group compared to a decrease of 78 cells/mm3 in the non-exercising control group. These results were statistically non-significant. In addition, Rigsby (1992) found non-significant differences in leukocytes, lymphocytes, CD4, CD8 and CD4:CD8 ratios. Agin (2001) and Sattler (1999) did not include a non-exercising control group. Sattler (1999) found a non-significant decrease of 10 cells/mm3 in the combined testosterone and PRE group and a non-significant increase of 22 cells/mm3 in the testosterone only group. No other studies reported pre and post exercise CD4 count outcomes.

D-2) Viral Load:

Grinspoon (2000) found an increase of 4.0 log10 copies in the

combined PRE and aerobic exercise intervention group and an increase of 3.1 log10 copies in the non-exercising control group. These results were not statistically significant. These results suggest a possible trend towards an increase in viral load for exercisers compared to non-exercisers. No other studies reported pre and post exercise viral load outcomes.

E) CARDIOPULMONARY STATUS:

Two studies reported cardiopulmonary outcomes (Rigsby 1992 & Lox 1995).

Individual Study Results -Cardiopulmonary Status:

Rigsby (1992) found significant increases in aerobic capacity, total time to voluntary exhaustion and decreases in heart rate in the combined PRE and aerobic exercise intervention group compared to the non-exercising control group. Lox (1995) found significantly lower VO2max changes in the PRE and non-exercising control groups compared to the aerobic exercise only group. No other studies reported cardiopulmonary outcomes.

F) PSYCHOLOGICAL STATUS:

Three studies reported health-related quality of life (HRQOL), mood and satisfaction outcomes in their studies (Agin 2001, Bhasin 2000 & Lox 1995). Bhasin (2000) included no actual presentation of HRQOL outcomes in the study. Meta-analysis was not possible because Agin (2001) did not include a non-exercising control group in their study, different outcome measures were used to assess psychological status, and Bhasin included participants that had low baseline testosterone levels which were different from the participants in the other studies.

Individual Study Results - Psychological Status:

Agin (2001) found significant improvements in the physical activity, general health perception and vitality scores for health-related quality of life for participants in the PRE intervention group compared to participants in the other two intervention groups (whey protein only & combination of whey protein and PRE). Significant decreases in physical activity scores were found for participants in the two groups that received whey protein. Bhasin (2000) reported no association between changes in health-related quality of life measures between comparison groups. No actual health-related quality of life data were provided by Bhasin (2000). Lox (1995) reported a higher positive mood and lower negative mood in the PRE group compared to the non-exercising control group. No other studies assessed psychological outcomes.

G) ADVERSE EVENTS (SAFETY):

Five of the seven studies reported on adverse events to assess safety (Sattler 1999, Rigsby 1992, Agin 2001, Grinspoon 2000 & Bhasin 2000). Meta-analysis was not possible due to the differences in reporting of adverse events.

Individual Study Results - Adverse Events:

Rigsby (1992) reported that participant withdrawal from the study was due to "health reasons" among the PRE intervention group (4 participants) and the non-exercising control group (5 participants). Three deaths were reported by Rigsby (1992): 2 deaths occurred after study completion (one participant in either comparison group) and 1 death occurred during the course of the study (non-exercising control group). Agin (2001) reported one death in their study of a participant who was allocated to the combined PRE and whey protein group. Grinspoon (2000) and Bhasin (2000) reported no deaths in their studies, no reductions in immunological status, and indicated that participant withdrawals were not attributed to adverse events or side effects from the exercise interventions. Bhasin (2000) reported adverse events such as breast enlargement for a participant receiving testosterone and acne for two participants, one who was receiving testosterone and the other, placebo. Hemoglobin levels also increased among participants in the testosterone groups. Sattler (1999) reported some minor adverse events such as acne and testicular shrinkage for participants in the testosterone groups. No participants developed urinary symptoms, breast enlargement, edema or changes in blood pressure. Spence (1990) and Lox (1995) did not report on any adverse events to assess safety.

2) COMBINED PROGRESSIVE RESISTIVE EXERCISE AND AEROBIC EXERCISE VERSUS NON-EXERCISING CONTROL

This section of the results presents the effect of combined progressive resistive exercise and aerobic exercise compared to non-exercising controls. Two of the seven studies compared combined PRE and aerobic exercise with a non-exercising control group (Rigsby 1992 & Grinspoon 2000). Meta-analysis was only possible for the immunological/virological outcome of CD4 count.

D) IMMUNOLOGICAL AND VIROLOGICAL STATUS:

D-1) CD4 Count:

Meta-analysis demonstrated a non-significant increase in CD4 count of 31.96 cells/mm3 (95% CI: -28.59, 92.52, n=46) for participants in the combined aerobic and progressive resistive exercise groups compared to non-exercising control groups (Rigsby 1992 & Grinspoon 2000) (see Figure 03.01). The confidence interval indicates a possible positive trend towards an increase in CD4 count for exercisers versus non-exercisers.

No other meta-analyses were possible to compare combined PRE and aerobic exercise versus non-exercising control groups for other outcomes. Please see above discussion for individual study results for outcomes of all seven included studies.

3) PROGRESSIVE RESISTIVE EXERCISE WITH OR WITHOUT AEROBIC EXERCISE VERSUS NON-EXERCISING CONTROL

This section presents the effects of progressive resistive exercise with or without combined aerobic exercise compared to non-exercising controls. Five of the seven studies compared PRE with a non-exercising control group (Spence 1990, Lox 1995 & Bhasin 2000), or compared combined PRE and aerobic exercise with a non-exercising control group (Rigsby 1992 & Grinspoon 2000). Four of the seven studies included a true non-exercising control group (Spence 1990, Lox 1995, Grinspoon 2000, Bhasin 2000). One study included a counseling group as a non-exercising control

group (Rigsby 1992). Two studies did not include a non-exercising control group (Agin 2001 & Sattler 1999). Four meta-analysis was possible for outcomes of body weight, body composition (mean arm and thigh girth), immunological outcomes (CD4 count), and cardiopulmonary measures (maximum heart rate).

A) BODY WEIGHT STATUS:

Six of the seven included studies reported body weight outcomes (Lox 1995, Sattler 1999, Agin 2001, Spence 1990, Grinspoon 2000 & Bhasin 2000). Four of these studies included a non-exercising control group (Lox 1995, Spence 1990, Grinspoon 2000 & Bhasin 2000).

A-1) Body Weight:

Meta-analysis demonstrated a statistically significant increase in body weight of 3.54kg (95% CI: 2.21, 4.87, p<0.00001, n=68) for participants in the PRE or combined PRE and aerobic exercise intervention groups compared to non-exercising control groups (Lox 1995, Grinspoon 2000 & Spence 1990) (see Figure 01.02). This increase in body weight of 3.54kg indicates a clinically important increase in body weight among exercisers compared to non-exercisers.

B) BODY COMPOSITION STATUS:

Six of the seven included studies reported body composition outcomes (Lox 1995, Sattler 1999, Agin 2001, Spence 1990, Grinspoon 2000 & Bhasin 2000). Four of these studies included a non-exercising control group (Lox 1995, Spence 1990, Grinspoon 2000 & Bhasin 2000).

B-1) Body Composition - Girth:

Meta-analysis demonstrated a significant 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 groups compared to non-exercising control groups. (Spence 1990 & Lox 1995) (see Figure 01.03). This increase in girth indicates a clinically important increase in arm and thigh girth among exercisers compared to non-exercisers. This meta-analysis was statistically significant for heterogeneity (p=0.08) using a random effects model. Reasons for heterogeneity may be attributed to the methods in which mean arm and thigh girth was measured between the studies.

C) STRENGTH STATUS:

All seven studies reported strength outcomes (Lox 1995, Sattler 1999, Rigsby 1992, Agin 2001, Spence 1990, Grinspoon 2000 & Bhasin 2000). Of these, five included a non-exercising control group (Lox 1995, Rigsby 1992, Spence 1990, Grinspoon 2000 & Bhasin 2000). Meta-analysis could not be performed for any strength outcomes due to differences in outcomes assessed and types of participants.

D) IMMUNOLOGICAL AND VIROLOGICAL STATUS:

Five of the seven studies reported immunological / virological outcomes. Three of the studies that included a non-exercising control group included combined PRE and aerobic exercise interventions (Rigsby 1992 & Grinspoon 2000), and one included PRE only (Lox 1995). Agin (2001) and Sattler (1999) also measured immunological / virological outcomes but did not include a non-exercising control group.

D-1) CD4 count:

Meta-analysis demonstrated a non-significant increase in CD4 count of 48.32 cells/mm3 (95% CI: -6.60, 103.23, n=68) for participants in the PRE or combined PRE and aerobic exercise intervention groups compared to non-exercising control groups. (Lox, 1995, Rigsby 1992 & Grinspoon 2000) (see Figure 01.01). The confidence interval demonstrates a positive trend towards improvement in CD4 count in the exercise groups. This improvement of 48.32 cells/mm3 represents a possible clinically important trend towards an improvement in CD4 count in the exercise groups compared to the non-exercising control groups.

E) CARDIOPULMONARY STATUS:

Two studies reported cardiopulmonary outcomes (Rigsby 1992 & Lox 1995).

E-1) Cardiopulmonary Status - Maximum Heart Rate

Meta-analysis demonstrated a non-significant reduction in maximum heart rate of 13.02 beats/minute (95% CI: -26.67, 0.64, n=56) for participants in the PRE or combined PRE and aerobic exercise intervention groups compared to the non-exercising control groups (Rigsby 1992 & Lox 1995) (see Figure 01.04). The confidence interval indicates a positive trend towards improvements in heart rate maximum in the exercise groups compared to non-exercising control groups. This improvement of 13.02 beats/minute represents a possible clinically important change in heart rate among exercisers compared to non-exercisers. This meta-analysis reported statistical significance for heterogeneity (p=0.0005) using a random effects model. Heterogeneity was likely attributed to the different exercise interventions between the two studies. Rigsby (1992), which consisted of, combined PRE and aerobic exercise demonstrated a larger improvement in maximum heart rate in the exercise group (reduction of 18.54 beats/min) compared to Lox (1995) which consisted of PRE only (reduction of 4.17 beats/min).

No other meta-analyses were possible to compare PRE with or without aerobic exercise versus non-exercising control groups for other outcomes. Please see above discussion for individual study results for outcomes of all seven included studies.

Subgroup Analyses:

We were unable to complete the subgroup analyses proposed in the protocol due to the small number of included studies, the variability of characteristics among studies, and/or because studies did not report results based on the variables of interest (gender, asymptomatic vs. symptomatic, supervised vs. non-supervised exercise, older vs. younger participants, wasting vs. non-wasting participants, participants on antiretroviral therapy vs. not on antiretroviral therapy).

Further Information Requested From Authors:

Further information or clarification was requested from the following authors regarding aspects of the studies. Data for strength was requested in units of kilograms from Rigsby (1992). Clarifi-

cation was requested with respect to whether there were any withdrawals in Spence (1990). Strength data was also requested in units of kilograms, as well as the raw data including standard deviations for health-related quality of life scores and body weight from Bhasin (2000). Body weight measures were requested from Jaque (2002). Body weight and composition measures were requested from Schroeder (2001). CD4 count and viral load, and body composition measures were requested from Agin (2001). Clarification was also requested from Grinspoon (2000) and Sattler (1999) to determine whether the participants in this study were similar to participants in Fairfield (2001), and Jaque (2002). To date we have received a response from one of the authors that we contacted. Grinspoon (2000) confirmed that participants in their study were the same participants in Fairfield (2001).

DISCUSSION

The results of this systematic review should be interpreted cautiously for a variety of reasons. First, this review is based on a small number of studies. Meta-analyses that were completed included a maximum of three studies and reported on less than 70 participants in each meta-analysis. The trials included in this review included relatively small number of participants and four of the seven studies were fraught with withdrawal rates greater than 15%. Thus, the generalizability of results is reduced because the overall findings among those who continued to exercise might not reflect the true experience of exercise among all adults living with HIV/AIDS. Additionally, publication bias may? have occurred if trials with negative results were suppressed in the published literature, leaving mostly small, but positive studies to include in the review.

Second, the ability to perform meta-analyses was limited due to the variability of characteristics of the studies pertaining to the exercise intervention, which included: type of exercise interventions, intensity of exercise, rate of progression of exercise intensity, length of follow-up to exercise, and participant compliance to exercise interventions. Meta-analysis was further limited by the breadth of outcomes used to assess the effects of exercise in the studies, and differences in baseline testosterone levels.

Third, the methodological quality of the included studies varied. Studies could not achieve participant blinding due to the nature of the intervention of interest, i.e. exercise. This may have led to bias in the results such as the Hawthorne effect whereby participants may perceive greater benefits associated with exercise based on the expectation that the intervention should be linked to positive outcomes. Authors were also vague in regard to describing the level of assessor blinding among the studies. If assessors were not blinded to the allocation of participants to groups, this may have resulted in detection bias whereby assessors that know group allocation may assess participants in the exercise intervention groups differently than participants in the non-exercising control group. This may lead to more positive outcomes in exercisers compared to non-exercisers based on the assessor's perception that exercise should be linked to positive outcomes. In addition, these studies are susceptible to performance bias due to the difference in the level of interaction between the study investigators among participants in the exercise groups and the non-exercising control groups. Participants in the exercise groups were followed three times per week resulting in much greater interaction with study investigators compared to the non-exercising control participants. Participants followed more closely by investigators may tend to report more positive subjective outcomes such as health-related quality of life compared to participants that had less extensive follow-up.

Fourth, although the majority of studies reported on strength, weight and body composition, only two of the studies assessed health-related quality of life, a clinically important outcome that acknowledges the participant's perception of progressive resistive exercise on his/her own health.

Lastly, the majority of study participants were male, thus results should be interpreted cautiously with respect to females.

Taking into account these limitations discussed above, we offer the following summary of our findings:

Results of meta-analysis of this systematic review indicated statistical and clinical important increases in mean body weight and arm and thigh girth among exercisers when compared to non-exercising controls. Despite statistical non-significance, results demonstrated possible clinically important improvements in cardiopulmonary fitness (HRmax) and a trend towards an increase in CD4 count among exercisers when compared to non-exercising controls.

Aside from the meta-analysis, individual studies reported significant results that demonstrated benefits of progressive resistive exercise interventions compared to non-exercise. All six studies that assessed weight and body composition found statistically significant improvements in weight and/or body composition among exercisers (Spence 1990, Grinspoon 2000, Lox 1995, Bhasin 2000, Agin 2001 & Sattler 1999). Six of the seven studies that assessed strength found statistically significant increases (improvements) in strength among exercisers (Bhasin 2000, Rigsby 1992, Lox 1995, Spence 1990, Agin 2001 & Sattler 1999). No significant changes were seen with respect to CD4 count or viral load for exercisers in the five studies that assessed these outcomes, although when combined, results of the meta-analysis indicated a non-significant trend towards an increase in CD4 count. The two studies that assessed cardiopulmonary measures found statistically significant improvements in cardiopulmonary status among exercisers with statistically greater improvements seen in interventions that included an aerobic exercise component compared to PRE. Two of the three studies that assessed psychological status found significant improvements in health-related quality of life among exercisers and reports of higher positive mood and lower negative

mood. Five of the seven studies that assessed safety by reporting adverse events attributed no adverse events to the exercise interventions. The study that reported adverse events found that withdrawals due to health reasons and deaths occurred in both exercisers and non-exercisers. Furthermore, this study was conducted in the early 1990s, prior to the emergence of highly active antiretroviral therapy, which has significantly altered the course of HIV infection. Thus adverse events associated with this study were likely attributed to the course of HIV infection rather than the exercise interventions. Lastly, results of meta-analysis that demonstrated no change in CD4 count suggest an element of safety with respect to immune status for adults living with HIV/AIDS.

AUTHORS' CONCLUSIONS

Implications for practice

This systematic review suggests that progressive resistive exercise interventions could play an important role in the care of adults living with HIV/AIDS. Meta-analysis suggests that performing progressive resistive exercise or a combination of progressive resistive and aerobic exercise three times a week for at least four weeks appears to be safe and may lead to statistically significant and possible clinically important improvements in body weight and composition for medically stable adults living with HIV/AIDS. Meta-analysis also suggests exercise interventions may lead to clinically important improvements in cardiopulmonary fitness. Individual studies included in this review suggest that progressive resistive exercise interventions with or without aerobic exercise also contribute to improvements in strength and psychological status for adults living with HIV/AIDS. Individual studies indicate that progressive resistive exercise or a combination of progressive resistive and aerobic exercise appears to be safe for adults living with HIV/AIDS who are medically stable as seen by no change in immunological / virological status. However, these results should be interpreted cautiously because the studies reviewed included outcome data only on those participants who continued to exercise and for whom there were adequate follow-up data.

Characteristics of participants included in this review varied pertaining to their stage of HIV infection, age, diagnosis of AIDS wasting syndrome, and whether they were taking HAART, thus heightening the external validity of this review. Results may be relevant to individuals who may or may not be taking HAART, and thus, may be applicable to persons living with HIV in developing countries who may not be on HAART. More broadly, the increasing advocacy for HIV care, treatment and support in the developing world, further supports the increasing relevance and importance of rehabilitation services for persons living with HIV in these countries.

Implications for research

The evidence pertaining to the effectiveness and safety of progressive resistive exercise for adults living with HIV/AIDS is limited by a small number of randomized controlled trials that include sample sizes and high withdrawal rates. In the majority of studies, participants who withdrew from exercise programs were not included in the final results of the study. This raises concerns about the safety of exercise among the participants that stopped exercising. This also limits the ability to determine the effectiveness of progressive resistive exercise versus the efficacy of progressive resistive exercise for adults living with HIV/AIDS. Future studies should make an effort to include all participants in an "intention-to-treat" analysis reporting results of participants who withdrawal from the exercise interventions.

Next, the results of this review include participants with widely ranging stages of HIV infection. An effect of exercise could not be distinguished according to stage of illness. Additional studies should further investigate the effects of progressive resistive exercise among adults at varying stages of HIV infection, particularly those that are severely immunocompromised.

Participants included in six of the seven studies were exclusively male adults, which limits the generalizability of results to females and people living with HIV/AIDS in other age groups. Additional studies should explore the effects of progressive resistive exercise among young adults and older adults living with HIV/AIDS. Studies should also attempt to recruit women to their studies to increase the external validity of results.

Lastly, a few of the included studies investigated the effects of progressive resistive exercise interventions in conjunction with alternative hormone or protein interventions. Future updates and inclusion of studies into this review will hopefully allow further exploration into the effects of progressive resistive exercise interventions compared to, and in conjunction with, alternative interventions such as testosterone and whey protein.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Agin 2001

Methods	Randomized trial.PRE vs. PRE + WHEY PROTEINvs. WHEY PROTEIN (3 groups) * note there is no non-exercising control group
Participants	43 HIV-infected women between 28-66 years with body cell mass (BCM) wasting.PRE EXERCISE GROUP: At study completion: n=10 WHEY GROUP: At study completion: n=10PRE+WHEY GROUP: At study completion: n=10
Interventions	PRE EXERCISE:(PRE of 7 major muscle groups). 3 sets of 10 ex's @ 8-10 reps/set as per ACSM guidelines.Week 1: loads were 50% of baseline 1-RM. Loads increased approx. 75% of 1-RM with adjustments based on # of reps and %ages of 1-RM. Loads were increased at least 2.5lbs when a participant completed 10 consective reps for a muscle group without fatigue. Frequency: 3 times per week for 14 weeks.Supervised by exercise physiologist.WHEY PROTEIN: 1 g/kg of whey protein powder for 14 weeks
Outcomes	WEIGHT AND BODY COMPOSITION: Significant increases in body weight (BW) were seen in the whey protein group. Body cell mass (BCM) significantly increased for both exercise groups (PRE and PRE + WHEY).Skeletal muscle significantly increased in the PRE group compared to no change in the other 2 groups. Fat mass (FM) significantly increased for the WHEY group and significantly decreased for the PRE group, and there was no change in the PRE + WHEY group. Fat free mass (FFM) increased in all 3 groups. STRENGTH:Muscle strength increased for all 7 groups assessed in the PRE and PRE + WHEY groups from 41-95%.HEALTH-RELATED QUALITY OF LIFE:Physical activity scores significantly increased for the PRE group but significantly declined for both WHEY groups. General health perception and vitality scores improved for the PRE group.ADVERSE EVENTS:1 death was reported in the PRE+WHEY group. No injuries were reported from resistance training or testing.AUTHOR'S CONCLUSIONS:Resistance exercise significantly increased BCM, muscle mass, muscle strength and HRQOL in HIV-infected women with reduced BCM. Whey protein had little effect on BCM gain and combined PRE + Whey protein did not increase BCM in excess of gains achieved by PRE alone
Notes	AUTHOR'S COMMENTS:No intention-to treat analysis was performed.A control period of 6 weeks prior to interventions showed no significant differences in outcomes.The PRE + WHEY group demonstrated a ceiling effect in the physical activity scale of the QOL assessment

Bhasin 2000

Methods	Double-blind, placebo- control, randomized trial.PRE vs. PRE+TEST vs. TEST vs. CONTROL(4 groups)
Participants	61 HIV-infected males between 18-50 years, with involuntary weight loss of at least 5% in the preceding 6 months, and low serum testosterone levels (less than 12.1nmol/L). Participants received stable ARV therapy for at least 12 weeks before enrollment.Participants were randomized to 4 groups: 1) CONTROL (placebo+no ex.) (n=14); 2) TEST. + no ex (n=17); 3) Placebo + EX (n=15); 4) TEST + EX (n=15)At study completion: n=49 1) n=12, 2) n=15, 3) n=11, 4) n=11) (# of withdrawls:12)
Interventions	PRE EXERCISE: (Groups #3&4) Weeks 1-4: High volume (3 sets of 12-15 reps), low intensity (60% of initial 1-RM) resistance ex. 3 times per week for 16 weeks. Week 5-10: Progressive, periodic, high intensity (90% of 1-RM on heavy days, 80% on medium days, and 70% on

Bhasin 2000 (*Continued*)

	light days), low volume (4 sets of 4-6 reps each) resistance exercise 3 times per week. Weeks 11-16: Loads were increased by 7% for upper body and 12% for lower body exercises and the number of sets was increased to 5. Frequency: 3X per week for 16 weeks. TESTOSTERONE INTERVENTION: (Groups #1&2) intramuscular injections of 100mg/wk of testosterone
Outcomes	WEIGHT AND BODY COMPOSITION:Body weight (BW) increased significantly by 2.6kg in men receiving testosterone alone, and 2.2kg in men who exercised alone, and did not change in the control group. Test + ex. group did not show a greater increase in BW compared to one intervention (either test or ex) alone.Fat free mass (FFM) increased significantly in the test alone and ex. alone groups and did not change in the non-exercising control group. The effect of test + ex together was not significantly different than either intervention alone.There was a greater increase of thigh muscle volume in men receiving testosterone alone (40cm3), exercise alone (62cm3), and test + ex (44cm3) than in men receiving placebo alone (5cm3). Average lean body mass (LBM) incresed by 2.3kg (testosterone alone) and 2.6kg (test.+ex.) and did not change in the non-exercising control group.STRENGTH:The ex. only group increased muscle strength by 29-36%, the testosterone only group increased strength by 17-28%. The testosterone + exercise group increased strength by 10-32% which was not significantly greater than either intervention alone.HRQOL: No association between the change in HRQL measures and testosterone administration or exercise were found in any group. ADVERSE EVENTS: No changes in immunological, physiological or virological measures. One participant that received test. and one participant that received placebo developed acne. One test. participant developed breast enlargement. No withdrawals were attributed to adverse events.AUTHOR'S CONCLUSIONS: Testosterone and resistance exercise promote 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 effects of testosterone and exercise were not additive in this study
Notes	AUTHOR'S COMMENTS:There were no withdrawals attributed to adverse events.Groups were similar at baseline.Participants that completed the study did not differ from those that withdrew from the study for many characteristics except that the withdrawals were older than those that completed the study.Exercise compliance: 7/11 participants in the ex alone group attended 90-100%, 5 attended 75-89% and 1 attended 70% of the scheduled sessions. 9/11 of the ex + test group attended more than 90% and 2 attended 75-89% of their scheduled sessions.Last available data for BW was carried forward for sensitivity analysis. **NOTE: Futher information has been requested from authors regarding 1) actual data for body weight (BW) with standard deviation for the groups & 2) actual data pertaining to HRQOL assessment.**NOTE: For the purposes of this review, we extracted results from the control gruop (no exercise + placebo) and exercise + placebo group to isolate the effects of exercise

Grinspoon 2000

Methods	Randomized control trialPRE+AEROBIC vs. PRE+AEROBIC+ TEST vs. TEST vs. CONTROL (4 groups)
Participants	54 HIV-infected males with AIDS-related wasting (weight<90% ideal body weight or self-reported weight loss>10%) and normal serum level of free testosterone. PRE+AEROBIC EXERCISE GROUP: 13 participants at baseline (10 participants analysed at week 12).NON-EXERCISING CONTROL GROUP:13 participants at baseline (12 participants analysed at week 12)
Interventions	PRE + AEROBIC EXERCISE: Supervised progressive strength training and constant aerobic conditioning consisting of 20 minutes aerobic exercise on stationary cycle at 60-70% HRmax, 15min cool-down followed by resistance training using computerized equipment (Life Fitness) training isotonically upper and lower body. Intensity of PRE: increased from Week 1-2: 2 sets of 8 reps each @ 60% 1-RM. Week 3-6: 2 sets of 8 reps each @ 70% 1-RM. Week 7-12: 3 sets of 8 reps each @ 80% 1-RM.

Grinspoon 2000 (*Continued*)

	Frequency: 3x per week for 12 weeks. TESTOSTERONE INTERVENTION: intramuscular injection of 200mg/wk of testosterone
Outcomes	WEIGHT AND BODY COMPOSITION: Participants in the exercise only group showed significant increases in lean body mass, arm muscle area, leg muscle area, HDL cholesterol and significant decreases in AST level compared to non-exercising control group. IMMUNE INDICES: No significant response in CD4 count or viral load to exercise or testosterone therapy either alone or together as a co-intervention. ADVERSE EVENTS: No deaths were reported and reasons for withdrawal were not due to adverse events or side effects. AUTHOR's CONCLUSIONS: Exercise has a significant effect on lean body mass and muscle area independent of testosterone. Muscle mass and strength may further increase in response to combined exercise and testosterone therapy. Exercise was associated with with an increase in HDL cholesterol whereas testosterone decreased HDL cholesterol. Exercise significantly increases muscle mass and offers cardio protective effects by increasing the HDL cholesterol in egonadal men with AIDS wasting. Exericse may be a strategy to reverse muscle loss in this population
Notes	AUTHOR'S COMMENTS:Participants in this study were men with AIDS-related wasting. The goal of exercise was to increase body composition.Withdrawal rates did not differ by group.No significant effects in strength may have been attributed to the fact that strength testing was done using isometric methods which has been known to underestimate change in strength compared to one repetition maximum (1-RM) of isotonic training which is used in the other four studies.NOTE:For the purposes of this systematic review, we extracted results from the control group (no exercise + placebo) and exercise + placebo group to isolate the effects of exercise

Lox 1995

Methods	Randomized control trial. AEROBIC vs. PRE vs. CONTROL (3 groups)
Participants	34 HIV-infected males. PRE GROUP: n=12 at baseline and study completion. AEROBIC GROUP: n=12 at baseline and n=11 at study completion NON-EXERCISING CONTROL GROUP: n=10 at baseline and study completion (1 withdrawal)
Interventions	PRE EXERCISE: Use of isotonic variable resistance to major muscle groups of legs, arms and upper body. Intensity: Resistance was increased by either 5 or 10 pounds at a time after successfully performing 3 sets of 10 repetitions at constant weight. Resistance was initially set at 60% of the indiviudual's 1-RM. AEROBIC EXERCISE: continuous 24 minutesof cycling exercise at constant pedal rate between 76-84rpm. Resistance was increased every 3-4 weeks as deemed appropriate by the physical therapist. Frequency: 3 times per week for 12 weeks. Each session included 5 min warm-up of flexibility and stretching, 24 minutes of AER or PRE and 15 minutes of cool down of stretching and flexibility exercises
Outcomes	WEIGHT AND BODY COMPOSITION: Significant increase in body weight and girth compared to the non-exercising control group. No significant differences in body fat, fat weight and mean body mass index between groups.

Lox 1995 (*Continued*)

	STRENGTH: Significant increases in upper and lower extremities in the PRE group compared to non-exercising control. IMMUNE INDICES: Non-significant increase in CD4 count in the PRE group and decrease in the non-exercising control group. CARDIOPULMONARY STATUS: Non-signficant decrease in HRmax in the PRE group compared to non-significant increase in HRmax in non-exercising control group. Significantly greater VO2max changes in the aerobic group compared to the PRE and non-exericising control group. HEALTH-RELATED QUALITY OF LIFE / MOOD / SATISFACTION: Higher positive mood and lower negative mood in the PRE group and aerobic group compared to non-exercising control group. Significant increases in positive mood an dlife satisfaction and negative mood decreased for the exercise groups. Positive mood decreased and negative mood increased and life satisfaction was unchanged in the non-exercising control group. AUTHOR'S CONCLUSIONS: Aerobic and weight training interventions enhanced self-efficacy, positive and negative modd and satisfaction with life, and improved lean muscle tissue, upper and lower body muscle strength, and predicted VO2max for exercise participants. Controls showed decrease in all physiological measures. Exercise may be a modality to combat the wasting process. Exercise may be capable of enhancing subjective well-being
Notes	AUTHOR'S COMMENTS:

Rigsby 1992

Methods	Randomized control trialPRE+AEROBIC vs. CONTROL/COUNSELING(2 groups)
Participants	45 male participants (37 HIV+, 8 HIV-), physically inactive for 6 months, median stage 3 disease (Walter Reed Scale) of CD4<200 to >400 cells/mm3.CD4 count range 8-804 cells/mm3.PRE EXERCISE GROUP: At baseline n=22: 19 HIV+, 3 HIV-At study completion n=16: 13 HIV+, 3 HIV-. COUNSELING GROUP: At baseline n= 23: 18 HIV+, 5 HIV- At study completion n=15: 11 HIV+, 4 HIV-
Interventions	PRE + AEROBIC EXERCISE: 60 min total: bike @ 60-80% HRreserve X 20min (2min warm-up & 3min cool down at low intensity), stretching X 10-15min, strengthening (PRE) X 20-25min. Frequency: 3 times / week for a total of 12 weeks.COUNSELING GROUP: 90-120min at 1-2 times / wk for a total of 12 weeks
Outcomes	STRENGTH: Significant increases in chest press and leg extension in th exercise group.IMMUNE INDICES:No significant change in CD4 count in either group.CARDIOPULMONARY MEASURES:Significant increases in aerobic capacity were shown in the exercise group with no change in the counseling group.Significant decreases in HR and increases in total time to voluntary exhaustion (TT) were seen in the exercise group.ADVERSE EVENTS: Withdrawals occurred from both groups due to "health reasons". Two deaths occurred during the course of the study (one from each group) and one death occurred after study completion (counseling group). AUTHOR'S CONCLUSIONS: HIV+ males including those symptomatic for AIDS-related complex can experience significant increases in strength and cardiopulmonary fitness. Increased fitness can occur without negative effects on immune status
Notes	AUTHOR'S COMMENTS:This study included participants along the entire range of disease severity.Only 1 participant with AIDS completed the exercise protocol and 2 completed the counseling sessions.The participant with AIDS that completed the exercise protocol demonstrated similar results to the others.The participants with AIDS in the counseling group (2) were similar to the exercising participants except for a decline in CD4 count.Exercise could have exerted an immune response that was not reflected in the clinical measures taken in this study.The medical

Rigsby 1992 (*Continued*)

	director was blinded to participant assignment to group. **NOTE** Further information has been requested from authors regarding strength data in units of kilograms.**

Sattler 1999

Methods	Randomized control trial PRE+TEST vs. TEST only (2 groups)
Participants	33 male participants. PRE+TEST GROUP: n=17 at baseline, n=15 at study completion; TEST ONLY GROUP: n=16 at baseline, n=15 at study completion.
Interventions	PRE EXERCISE: Supervised PRE included upper and lower body weight training using free weights. PRE included warm-up, 5-8 reps at 50% 1-RM for each exercise, 3 sets of 8 reps at 80% 1-RM with the final set performed to failure, with 2 min rest inbetween all sets. Intensity of PRE: participants started at 70% 1-RM at baseline and increased to 80% 1-RM by end of second week. 1-RM was assess every 2 weeks to adjust training load to maintain intensity at 80% 1-RM. Frequency: 3 times per week for 12 weeks. TESTOSTERONE INTERVENTION: Weekly injections of nandrolone - 200mg in week 1, 400mg in week 2. Dose increased to 600mg for weeks 3-12
Outcomes	WEIGHT AND BODY COMPOSITION: Participants in both the combined testosterone and PRE group and the PRE only group showed significant increases in body weight, thigh muscle area and body cell mass, but there was no significant difference between groups. There was no change in fat mass in the testosterone only group but a significant decrease in fat mass in the combined PRE and testosterone group. There were significantly greater increases in lean body mass in the combined PRE and testosterone group. STRENGTH: There were significant increases in upper and lower body strength in both groups with significantly greater gains in strength in the combined PRE and testosterone group. IMMUNE INDICES: Non-significant increases in CD4 count for both intervention groups. ADVERSE EVENTS: Acne and testicular shrinkage were found in testosterone groups. No participant developed urinary symptoms, breast enlargement, edema or changes in blood pressure. Other physiological measures resulted in no significant changes. AUTHOR'S CONCLUSIONS: Testosterone resulted in significant increases in total weight, lean body mass, body cell mass, muscle size and strength. Increases in lean body mass and muscular strength were significantly greater with PRE
Notes	AUTHOR'S COMMENTS:

Spence 1990

Methods	Randomized control trialPRE vs. CONTROL(2 groups)
Participants	24 HIV-infected male participantsPRE EXERCISE GROUP: n=12;NON-EXERCISING CONTROL GROUP: n=12

Spence 1990 (*Continued*)

Interventions	PRE EXERCISE: Resistance load 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 unit's maximum setting.All exercise was supervised and max effort by participants was encouraged.Frequency: 3 times per week for 6 weeks
Outcomes	WEIGHT AND BODY COMPOSITION:Exercise group showed significant in limb girth and body weight. The control group showed significant decreases in girth and body weight. There were no differences in the sum of skinfolds.STRENGTH:Significant declines in upper and lower extremity muscle function (6/12 variables, and 7/12 variables) for the non-ex. control group. Significant increases were seen for all (12/12) lower extremity variables for all variables in the upper extremity except for shoulder-arms extension and shoulder-arms flexion total work (10/12) in the exercise group.ADVERSE EVENTS:None specified.AUTHOR'S CONCLUSIONS:PRE improved muscle function and anthropometry in the PRE group compared to the non-exercising control group
Notes	AUTHOR'S COMMENTS:**NOTE** Further information has been requested from authors regarding: 1) strength data in units of kilograms for and 2) clarification of the number of participants at study completion: Were there no withdrawals?**

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Fairfield 2001	This study is a duplicate of the Grinspoon (2000) article. The participants are the same, but this study may report on different outcomes. Any new outcomes that were reported in this study were included in the review
Jaque 2002	This study is a duplicate of the Sattler (1999) article. The participants are the same, but this study may report on different outcomes. Any new outcomes that were reported in this study were included in the review
Lox 1996	This study is a duplicate of the Lox (1995) article. The participants are the same, but this study may report on different outcomes. Any new outcomes that were reported in this study were included in the review
Sattler 2002	This study is a duplicate of the Sattler (1999) article. The participants are the same, but this study may report on different outcomes. Any new outcomes that were reported in this study were included in the review
Schroeder 2001	This study is a duplicate of the Sattler (1999) article. The participants are the same, but this study may report on different outcomes. Any new outcomes that were reported in this study were included in the review
Schroeder 2003	This study is a duplicate of the Sattler (1999) article. The participants are the same, but this study may report on different outcomes. Any new outcomes that were reported in this study were included in the review

DATA AND ANALYSES

Comparison 1. Progressive Resistive Exercise OR Combined Prog. Resistive and Aerobic Exercise Vs Non-Exercising Control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 CD4 count (cells/mm3)	3	68	Mean Difference (IV, Random, 95% CI)	48.32 [-6.60, 103.23]
2 Weight Measures - Mean Body Weight (kg)	3	68	Mean Difference (IV, Random, 95% CI)	3.54 [2.21, 4.87]
3 Body Composition - Mean Girth (arm and thigh) (cm)	2	46	Mean Difference (IV, Random, 95% CI)	7.91 [2.18, 13.65]
4 Cardiopulmonary Measures - Maximum Heart Rate (beats/min)	2	46	Mean Difference (IV, Random, 95% CI)	-13.02 [-26.67, 0.64]

Comparison 2. Progressive Resistive Exercise Versus Non-Exercising Control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Weight Measures - Mean Body Weight (kg)	2	46	Mean Difference (IV, Random, 95% CI)	4.24 [1.82, 6.66]

Comparison 3. Combined Progressive Resistive Exercise and Aerobic Exercise Versus Non-Exercising Control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Immunological / Virological Indices - CD4 Count (cells/mm3)	2	46	Mean Difference (IV, Random, 95% CI)	31.96 [-28.59, 92.52]

Analysis 1.1. Comparison 1 Progressive Resistive Exercise OR Combined Prog. Resistive and Aerobic Exercise Vs Non-Exercising Control, Outcome 1 CD4 count (cells/mm3).

Review: Progressive resistive exercise interventions for adults living with HIV/AIDS

Comparison: 1 Progressive Resistive Exercise OR Combined Prog. Resistive and Aerobic Exercise Vs Non-Exercising Control

Outcome: 1 CD4 count (cells/mm3)

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Grinspoon 2000	10	31 (125)	12	33 (50)		34.7 %	-2.00 [-84.48, 80.48]
Lox 1995	12	22.91 (114)	10	-77.9 (130.25)		24.0 %	100.81 [-2.52, 204.14]
Rigsby 1992	13	58.07 (72.07)	11	-2 (105.28)		41.3 %	60.07 [-13.45, 133.59]
Total (95% CI)	**35**		**33**			**100.0 %**	**48.32 [-6.60, 103.23]**

Heterogeneity: $Tau^2 = 492.74$; $Chi^2 = 2.52$, df = 2 (P = 0.28); $I^2 = 21\%$

Test for overall effect: Z = 1.72 (P = 0.085)

Analysis 1.2. Comparison 1 Progressive Resistive Exercise OR Combined Prog. Resistive and Aerobic Exercise Vs Non-Exercising Control, Outcome 2 Weight Measures - Mean Body Weight (kg).

Review: Progressive resistive exercise interventions for adults living with HIV/AIDS

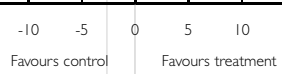
Comparison: 1 Progressive Resistive Exercise OR Combined Prog. Resistive and Aerobic Exercise Vs Non-Exercising Control

Outcome: 2 Weight Measures - Mean Body Weight (kg)

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Grinspoon 2000	10	1.7 (3.2)	12	-0.6 (2.5)		22.4 %	2.30 [-0.14, 4.74]
Lox 1995	12	2.12 (2.85)	10	-4.5 (6.87)		7.8 %	6.62 [2.07, 11.17]
Spence 1990	12	1.7 (0.79)	12	-1.9 (1.08)		69.8 %	3.60 [2.84, 4.36]
Total (95% CI)	**34**		**34**			**100.0 %**	**3.54 [2.21, 4.87]**

Heterogeneity: $Tau^2 = 0.51$; $Chi^2 = 2.77$, df = 2 (P = 0.25); $I^2 = 28\%$

Test for overall effect: Z = 5.22 (P < 0.00001)

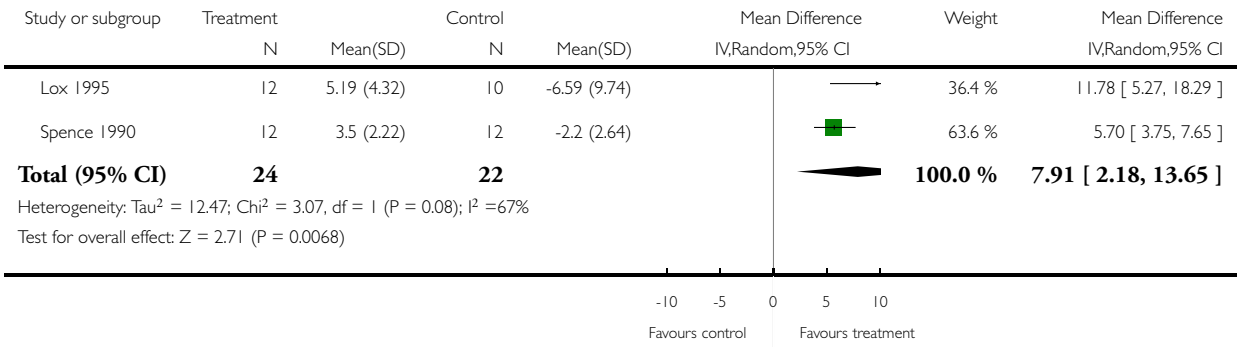


Analysis 1.3. Comparison 1 Progressive Resistive Exercise OR Combined Prog. Resistive and Aerobic Exercise Vs Non-Exercising Control, Outcome 3 Body Composition - Mean Girth (arm and thigh) (cm).

Review: Progressive resistive exercise interventions for adults living with HIV/AIDS

Comparison: 1 Progressive Resistive Exercise OR Combined Prog. Resistive and Aerobic Exercise Vs Non-Exercising Control

Outcome: 3 Body Composition - Mean Girth (arm and thigh) (cm)

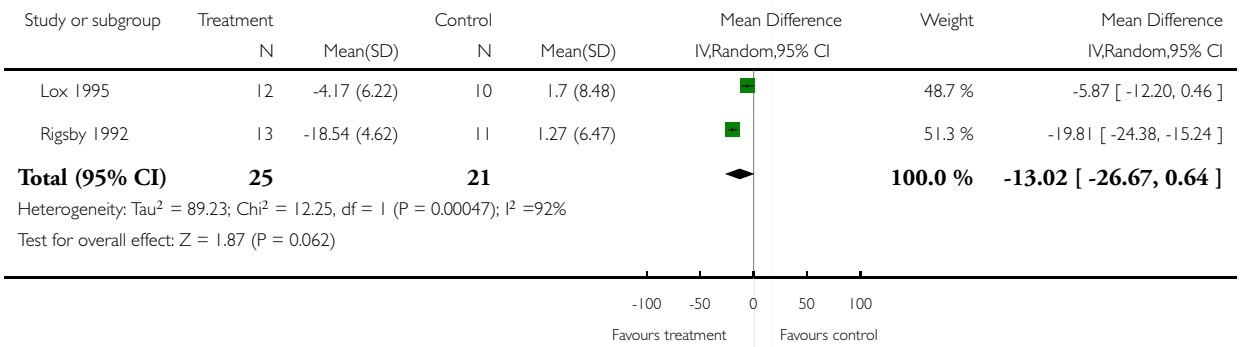


Analysis 1.4. Comparison 1 Progressive Resistive Exercise OR Combined Prog. Resistive and Aerobic Exercise Vs Non-Exercising Control, Outcome 4 Cardiopulmonary Measures - Maximum Heart Rate (beats/min).

Review: Progressive resistive exercise interventions for adults living with HIV/AIDS

Comparison: 1 Progressive Resistive Exercise OR Combined Prog. Resistive and Aerobic Exercise Vs Non-Exercising Control

Outcome: 4 Cardiopulmonary Measures - Maximum Heart Rate (beats/min)

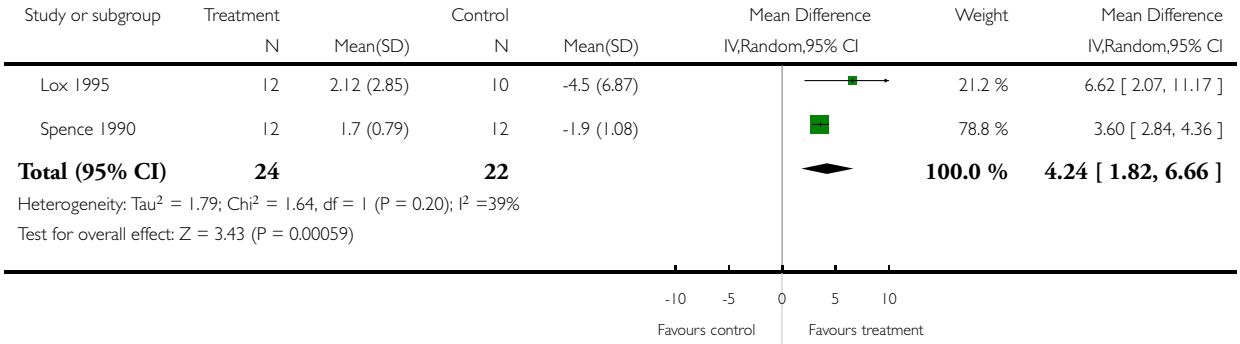


Analysis 2.1. Comparison 2 Progressive Resistive Exercise Versus Non-Exercising Control, Outcome 1 Weight Measures - Mean Body Weight (kg).

Review: Progressive resistive exercise interventions for adults living with HIV/AIDS

Comparison: 2 Progressive Resistive Exercise Versus Non-Exercising Control

Outcome: 1 Weight Measures - Mean Body Weight (kg)

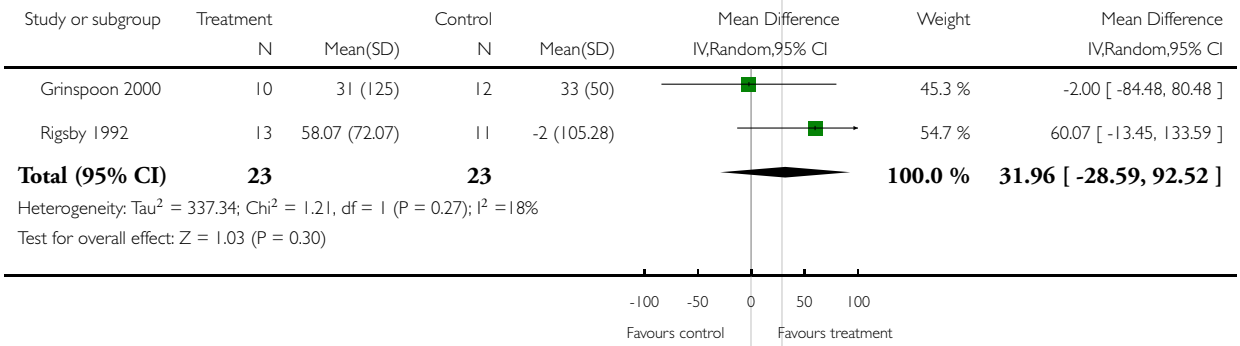


Analysis 3.1. Comparison 3 Combined Progressive Resistive Exercise and Aerobic Exercise Versus Non-Exercising Control, Outcome 1 Immunological / Virological Indices - CD4 Count (cells/mm3).

Review: Progressive resistive exercise interventions for adults living with HIV/AIDS

Comparison: 3 Combined Progressive Resistive Exercise and Aerobic Exercise Versus Non-Exercising Control

Outcome: 1 Immunological / Virological Indices - CD4 Count (cells/mm3)



WHAT'S NEW

Last assessed as up-to-date: 6 July 2004.

Date	Event	Description
10 November 2008	Amended	Converted to new review format.

HISTORY

Protocol first published: Issue 2, 2003

Review first published: Issue 4, 2004

Date	Event	Description
7 July 2004	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

Kelly O'Brien: contributions include: protocol development, abstract review, analysis of results and write-up of review

Stephanie Nixon: contributions include: protocol development, and write-up of review

Rick Glazier: contributions include: protocol development, write-up of review

Anne-Marie Tynan: contributions include: protocol development, abstract review, write-up of review

DECLARATIONS OF INTEREST

None

SOURCES OF SUPPORT

Internal sources

- Inner City Health Research Unit, St. Michael's Hospital, Toronto, Canada.

External sources

- The Ontario HIV Treatment Network, Canada.

INDEX TERMS

Medical Subject Headings (MeSH)

*Exercise; Acquired Immunodeficiency Syndrome [rehabilitation]; Exercise Therapy; HIV Infections [*rehabilitation]; Randomized Controlled Trials as Topic

MeSH check words

Female; Humans; Male