Effectiveness of Aerobic Exercise in Adults Living with HIV/AIDS: Systematic Review

KELLY O'BRIEN[1], STEPHANIE NIXON[1], ANNE-MARIE TYNAN[2], and RICHARD H. GLAZIER[3]

[1]Department of Physical Therapy, University of Toronto, Toronto, ON, CANADA; [2]St. Michael's Hospital, Inner City Health Research Unit, Toronto, ON, CANADA; [3]Department of Family and Community Medicine, University of Toronto, Toronto, ON, CANADA

ABSTRACT

O'BRIEN K., S. NIXON, A. M. TYNAN, and R. GLAZIER. Effectiveness of Aerobic Exercise in Adults Living with HIV/AIDS: Systematic Review. *Med. Sci. Sports Exerc.*, Vol. 36, No. 10, pp. 1659–1666, 2004. **Purpose:** The objective of this systematic review was to examine the effectiveness and safety of aerobic exercise interventions on immunological/virological, cardiopulmonary, and psychological outcomes in adults living with HIV/AIDS. **Methods:** Ten randomized trials of HIV-positive adults performing aerobic exercise three times per week for at least 4 wk were identified by searching 13 electronic databases, abstracts from conferences, reference lists, and personal contact with authors from 1980 to November 2002. At least two independent reviewers assessed articles for inclusion, extracted data, and assessed methodological quality. Random effects models were used for meta-analysis. **Results:** Main results indicated that aerobic exercise was associated with small nonsignificant changes in CD4 count (weighted mean difference: 14 cells·mm^{-3}, 95% CI: −26, 54), viral load (weighted mean difference: 0.40 log10 copies, 95% CI: −0.28, 1.07), and $\dot{V}O_{2max}$ (weighted mean difference: 1.84 mL·kg^{-1}·min^{-1}, 95% CI: −0.53, 4.20). Individual studies suggested that aerobic exercise may improve psychological well-being for adults living with HIV/AIDS. These findings are limited to those participants who continued to exercise and for whom there was adequate follow-up. **Conclusion:** In conclusion, performing constant or interval aerobic exercise, or a combination of constant aerobic exercise and progressive resistive exercise for at least 20 min, at least three times per week for 4 wk may be beneficial and appears to be safe for adults living with HIV/AIDS. However, these findings should be interpreted cautiously due to small sample sizes and large dropout rates within the included studies. Future research would benefit from increased attention to participant follow-up and intention-to-treat analysis. **Key Words:** COCHRANE COLLABORATION, META-ANALYSIS, SAFETY, HIV INFECTION, ACQUIRED IMMUNODEFICIENCY SYNDROME

The profile of HIV infection has changed dramatically since the advent of highly active antiretroviral therapy (HAART). Once viewed as an illness progressing steadily toward death, HIV infection can now present as a chronic and episodic disease for people who are able to access and tolerate HAART. These developments have been mirrored by a perceived increasing prevalence of impairments, activity limitations, and participation restrictions for many people living with HIV (19).

Exercise is one possible management strategy for addressing these issues. Exercise has potential prophylactic benefits associated with increased lean body mass and cardiovascular fitness. Exercise is also closely linked to body image, which has particular significance in certain HIV-affected communities (Shernoff, M. Pumped up: gay men and gym culture. *GayHealth*, December 18, 2000. Available at: www.gayhealth.com/iowa-robot/fitness/workout/?record = 340; accessed December 19, 2002). Exercise has been shown to improve strength, cardiovascular function, and psychological status in general populations (2), but the effectiveness and safety of aerobic exercise for adults living with HIV infection have not been established. If the risks and benefits of exercise for people living with HIV infection are better understood, appropriate exercise prescription may be practiced by health care providers and may enhance the effectiveness of HIV management, thus improving overall outcomes for adults living with HIV infection.

The purpose of this systematic review and meta-analysis was to examine the effectiveness and safety of aerobic exercise interventions on immunological/ virological, cardiopulmonary, and psychological outcomes in adults living with HIV.

Address for correspondence: Kelly O'Brien, Department of Physical Therapy, University of Toronto, 500 University Avenue, 8th Floor, Toronto, ON, M5G 1V7; E-mail: kelly.obrien@utoronto.ca.
Submitted for publication January 2004.
Accepted for publication June 2004.

0195-9131/04/3610-1659
MEDICINE & SCIENCE IN SPORTS & EXERCISE®

DOI: 10.1249/01.MSS.0000142404.28165.9B

METHODS

Search for primary studies. We performed a systematic review and meta-analysis using methods of the Cochrane Collaboration (3). We searched electronic databases for articles published between 1980 to November 2002 (MEDLINE, EMBASE, SCIENCE CITATION INDEX, AIDSLINE, CINAHL, HEALTHSTAR, PSYCHLIT, SOCIOFILE, SCI, SSCI, ERIC, DAI, and Cochrane Collaborative Review Group databases) using subject headings such as HIV, HIV infections, and exercise. We also reviewed abstracts from international and national AIDS conferences, searched reference lists from pertinent articles and books, made personal contact with authors, and hand searched targeted journals to identify potential studies for inclusion. All languages were included.

Selection of studies and abstraction of data. Titles and abstracts of all citations were reviewed independently by two reviewers to identify studies which met the following four inclusion criteria and included: 1) human participants who were HIV positive, 2) participants 18 yr of age or older, 3) an aerobic exercise intervention performed at least three times per week for at least 4 wk, and 4) a randomized comparison group. Two reviewers reviewed hard copies of an entire paper independently if one or both raters believed a study met eligibility criteria. Three of four possible reviewers examined full text to determine final inclusion. Disagreements were resolved through discussion and consensus.

Two reviewers (out of eight possible reviewers) abstracted relevant data from included studies onto standard data abstraction forms. Methodological quality of the studies was assessed using criteria developed by Jadad et al. (5). We also assessed whether the groups were similar at baseline. Our outcome measures included immunological/virological indicators (CD4 count, viral load), cardiopulmonary measures ($\dot{V}O_{2max}$), psychological measures, and adverse events including death.

Data analysis. We used RevMan (Version 4.1) software to perform statistical analyses. Where there were sufficient data available from the authors, and comparisons made practical sense, and in the absence of statistical heterogeneity ($P < 0.05$), meta-analyses were performed. For continuous variables, we used random effects models to calculate the weighted mean difference (WMD) and 95% confidence intervals. None of the outcomes were dichotomous variables.

Subgroups identified for separate analyses included: interval versus constant aerobic exercise and moderate versus heavy intensity aerobic exercise.

For the purposes of this review, we considered 50 cells·mm^{-3} to indicate a clinically important change in CD4 count, 0.5 log10 copies to indicate a clinically important change in viral load, and 2 mL·kg^{-1}·min^{-1} to indicate a clinically important change in $\dot{V}O_{2max}$. These values were based on extensive consultation with the clinical and research community, and are consistent with values used in previous literature (8,17,18). We considered a P value of less than 0.05 as statistically significant.

RESULTS

Trial characteristics. Searches of all sources retrieved a total of 1187 citations, 30 of which were judged to merit scrutiny of the full article and 12 of which met the inclusion criteria (1,4,6,7,9–16). Of the included studies, there were two groups of citations identified as being duplicate studies (LaPerriere et al. (6,7) and Lox et al. (9,10). In these instances, the earlier published study was included in the review, and any additional outcomes reported in the later studies were also incorporated into the review. Thus, there were a total of 10 studies that met inclusion criteria (1,4,6,9,11–16). Table 1 presents summary data from the 10 randomized trials eligible for this systematic review. Of the 10 studies, seven included a nonexercising control group (1,4,6,9,12,14,15). One of the studies included two additional study groups: exercise plus injection of 200 mg of testosterone enanthate per week, and a testosterone only group (4), which were not included in our analysis. One study included a nonexercising counseling group (exercise vs counseling group) (13), one study included a progressive resistive exercise (PRE) group (9), and two studies had comparison groups that compared heavy with moderate exercise (11,16). The studies included HIV-infected adults in various disease stages with CD4 counts ranging from less than 100 to greater than 1000 cells·mm^{-3}. Studies included both men and women, although women made up less than 15% of the total number of participants. The age of the participants ranged from 18 to 58 yr. Two studies included participants who were on HAART (72% of participants in Grinspoon et al. (4), and 23% of participants in Smith et al. (14)), five studies included participants who were not on HAART; however, most, if not all, participants were taking some form of antiretroviral therapy (ART) (1,9,11,12,15), and three studies did not report on whether participants were taking ART (6,13,16). Training intensities of participants in individual studies were reported in % HRmax (1,4,6,12,16), % heart rate reserve (9,13), % maximal oxygen uptake ($\dot{V}O_{2max}$) (11,14), % lactic acid threshold (LAT), and % difference between LAT and $\dot{V}O_{2max}$ (15). The way in which training intensities were established varied among individual studies and included submaximal testing (6,13,11), graded exercise testing (12,14), maximal exercise testing (1,15,16), and intensities prescribed based on the Karvonen formula and the American College of Sports Medicine guidelines (4,9). Other personal characteristics were reported inconsistently across studies.

Quality assessment of studies. Table 2 provides details of the assessment of quality. Only three studies described the randomization process and only two reported on blinding. Withdrawals and drop-outs were described in nine studies but drop-out rates were high, with six studies reporting drop-out rates greater than 20% and two studies greater than 50%.

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

Study	Method	Sample Size (at baseline)	% Male	Participants (at Study Completion)	Type of Exercise	Time and Intensity of Exercise	Frequency and Duration of Exercise	Supervision	Notes
LaPerriere et al. (6,7)	Randomized exercise and control groups	$N = 50$ (17 HIV+)	100%	Intervention group: $N = 30$ (10 HIV+) Non-exercising control group: $N = 20$ (7 HIV+)	Stationary bike	45 min total @ 80% HRmax × 3 min, then @ 69–79% HRmax × 2 min INTERVAL AEROBIC	3 × per week for 5 wk	NR	LaPerriere (1991) is a continuation of the study reported in 1990. Results were used from LaPerriere 1990 for this review to avoid skewed results
Rigsby et al. (13)	Randomized exercise and control groups	$N = 45$ (37 HIV+)	100%	Intervention group: $N = 16$ (13 HIV+) Nonexercising counseling control group: $N = 15$ (11 HIV+)	Stationary bike	60 min total @ 60–80% HR reserve × 20 min (2-min warm-up and 3-min cool-down at low intensity); stretching × 10–15 min CONSTANT AEROBIC + PRE	3 × per week for 12 wk	√ Yes	"Control" group received 90–120 min of counselling 1–2 × per week for 12 wk
MacArthur et al. (11)	Randomized—two exercise groups	$N = 25$	96%	(N = defined as "compliant with exercise program") High-intensity group: $N = 3$ Low-intensity group: $N = 3$	Walking, jogging, biking rowing, and stair-stepping	High-intensity exercise: 24 min total @ 75–85% $\dot{V}O_{2max}$ × 4 minute × 6 intervals Low-intensity exercise: 40 min total @ 50–60% $\dot{V}O_{2max}$ × 10 min × 4 intervals INTERVAL AEROBIC	3 × per week for 24 wk	NR	
Stringer et al. (15)	Randomized exercise and control groups	$N = 34$	NR	Moderate-intensity group: $N = 9$ Heavy-intensity group: $N = 9$ Nonexercising control group: $N = 8$	Stationary cycle ergometer	Moderate intensity exercise: 60 min @ 80% lactic acid threshold (LAT) Heavy-intensity exercise: 30–40 min @ 50% of difference between LAT and $\dot{V}O_{2max}$ CONSTANT AEROBIC	3 × per week for 6 wk	NR	For the meta-analysis of exercise versus nonexercising control; results of the moderate and heavy exercise groups were combined
Perna et al. (12)	Randomized exercise and control groups	$N = 43$	86%	Intervention group: $N = 18$ Nonexercising control group: $N = 10$	Stationary bike	45 min total @ 70–80% HRmax × 3 min then 2 min "off" (10-min stretch pre and post) INTERVAL AEROBIC	3× per week for 12 wk	√ Yes	For this review, a weighted average was calculated to combine data of complaint and noncompliant exercisers for analysis
Terry et al. (16)	Randomized—two exercise groups	$N = 31$	67%	Moderate-intensity group: $N = 10$ High-intensity group: $N = 11$	Walking, running, and stretching	Moderate-intensity exercise: 30 min walking @ 55–60% HRmax (15-min stretch pre and post) High-intensity exercise: 30 min running @ 75–85% HRmax (15-min stretch pre and post) CONSTANT AEROBIC	3× per week for 12 wk	NR	
Grinspoon et al. (4)	Randomized exercise and control groups	$N = 54$ (4 groups: ex+ testosterone; ex+ placebo; testosterone only; control	100%	Intervention group: ex. + placebo: $N = 10$ Nonexercising control group: $N = 12$	Stationary bike + progressive resistance exercise (PRE)	20-min aerobic ex. on stationary cycle at 60–70% HRmax, 15-min cool-down followed by resistance training CONSTANT AEROBIC + PRE	3× per week for 12 wk	√ Yes	For this review, results were extracted from the control group and exercise + placebo group to isolate the effects of exercise
Smith et al. (14)	Randomized exercise and control groups	$N = 60$	87%	Intervention group: $N = 19$ Nonexercising control group: $N = 30$	Walking/jogging, stationary bike, stair stepper, and cross-country machine.	Minimum of 30 min constant aerobic exercise at 60–80% $\dot{V}O_{2max}$ CONSTANT AEROBIC	3× per week for 12 wk	√ Yes	
Lox et al. (9,10)	Randomized—two exercise groups and one control group	$N = 34$	100%	Intervention groups: AER: $N = 11$, PRE: $N = 12$ Nonexercising control group: $N = 10$	Stationary bike	Approx. 45 min total: 5-min warm-up (stretching), 24-min cycle ergometer at 50–60% heart rate reserve (HRR), 15-min cool-down CONSTANT AEROBIC	3× per week for 12 wk	√ Yes	For the purposes of this review only the aerobic exercise group and the control group were included in meta-analyses; two articles that reported on the same study were incorporated as one study for this review
Baigis et al. (1)	Randomized exercise and control groups	$N = 123$	80%	Intervention group: $N = 35$ Nonexercising control group: $N = 34$	Ski machine	40 min total: 5-min stretching, 5-min warm-up on machine, 20 min constant aerobic exercise at 75–85% HRmax followed by 5-min cool-down and 5-min stretching CONSTANT AEROBIC	3× per week for 15 wk	√ Yes	

NR, not reported; PRE, progressive resistive exercise; AER, aerobic exercise.

TABLE 2. Methodological quality of studies included in the systematic review.

Quality Criteria	LaPerriere et al. (6,7)	Rigsby et al. (13)	MacArthur et al. (11)	Stringer et al. (15)	Perna et al. (12)	Terry et al. (16)	Grinspoon et al. (4)	Smith et al. (14)	Lox et al. (9,10)	Baigis et al. (1)
a) Study randomized? Randomization process described?	√ Yes	√ Yes	√ Yes	√ Yes √ Described randomization process	√ Yes	√ Yes	√ Yes √ Described randomization process	√ Yes	√ Yes	√ Yes √ Described randomization process
b) Study double-blind?	NR	NR	Single-blind (participants)	NR	NR	NR	NR	Single-blind (assessors)	NR	NR
c) Rate of withdrawal? Description of withdrawals/drop-outs provided?	NR No	35% √ Yes	76% √ Yes	24% √ Yes	51% √ Yes	32% √ Yes	15% √ Yes	18% √ Yes	4% √ Yes	44% √ Yes
d) Groups similar at baseline?	√ Yes	√ Yes	NR	√ Yes	√ Yes	√ Yes	NR	√ Yes	NR	√ Yes

NR, not reported.

Immunological/virological measures. All 10 studies used CD4 count as an outcome. Five meta-analyses were performed (Fig. 1), showing no difference in CD4 count for participants in any type of aerobic exercise intervention group compared with the nonexercising control group (weighted mean difference: 14 cells·mm^{-3}, 95% CI: −26, 54, $N = 209$), no difference in CD4 count of participants in the constant aerobic exercise group compared with nonexercising control group (weighted mean difference: −4 cells·mm^{-3}, 95% CI: −50, 42, $N = 164$) and nonsignificant improvement in CD4 count of 70 cells·mm^{-3} (95% CI: −11, 151, $N = 45$) for participants in the interval aerobic exercise group compared with the nonexercising control group. Although not statistically significant, the point estimate is above 50 cells·mm^{-3}, which represents a possible clinically important increase in CD4 count. There was no difference in CD4 count in the moderate intensity aerobic exercise group compared with the heavy-intensity exercise group (weighted mean difference: −34, 95% CI: −156, 89, $N = 39$) and no difference in CD4 count for participants in combined aerobic and progressive resistive exercise group compared with nonexercising control group (weighted mean difference: 6 cells·mm^{-3}, 95% CI: −71, 83, $N = 46$).

Meta-analysis of three studies demonstrated no difference in viral load for participants in the exercise intervention groups compared with the nonexercising control group (weighted mean difference: 0.40 log10 copies, 95% CI: −0.28, 1.07, $N = 63$) (Fig. 1).

Cardiopulmonary measures. Nine studies measured cardiopulmonary status (1,6,9,11–16). Significant improvements were found among individual trials of aerobic exercisers when compared with nonexercising controls, but meta-analysis could only be performed using $\dot{V}O_{2max}$ due to varying outcomes reported. Table 3 contains a description of cardiopulmonary status results for individual studies.

Seven studies assessed $\dot{V}O_{2max}$ as an outcome (1,6,9,11,12,14,15). Three meta-analyses were performed (Fig. 2), showing nonsignificant improvement in $\dot{V}O_{2max}$ of 1.84 mL·kg^{-1}·min^{-1} (95% CI: −0.53, 4.20, $N = 179$) for participants in the aerobic exercise intervention group compared with nonexercising control group, nonsignificant improvement in $\dot{V}O_{2max}$ of 1.56 mL·kg^{-1}·min^{-1} (95% CI: −0.94, 4.07, $N = 151$) for participants in the constant exercise group compared with the nonexercising control group, and statistically nonsignificant greater improvement in $\dot{V}O_{2max}$ of 4.29 mL·kg^{-1}·min^{-1} (95% CI: −1.23, 9.82, $N = 24$) for participants in the heavy-intensity aerobic exercise group compared with participants in the moderate-intensity exercise group. This finding reached clinical importance but not statistical significance.

Psychological measures. Meta-analysis was not possible for psychological status due to the breadth of outcomes used. Results of psychological measures of individual studies (Table 3) show improvement in anxiety and depression (6), general health (11), mood and life satisfaction (10), and quality of life (1,15) among those in the exercise intervention groups. In one study, exercise was not associated with change in depression (16).

Safety measures. The only death reported was in Rigsby et al. (13). This death was not attributed to aerobic exercise. No other adverse events such as sports injury, hospitalization or disease progression were reported.

DISCUSSION

We could not confirm an overall effect of aerobic exercise on CD4, viral load, or $\dot{V}O_{2max}$, either in individual studies or in meta-analysis. Despite statistical nonsignificance, results demonstrated the possibility of clinically important improvements in $\dot{V}O_{2max}$ among exercisers compared with nonexercising controls, and greater improvements in $\dot{V}O_{2max}$ among individuals exercising at heavy versus moderate intensity. Eight of the nine individual studies that measured cardiopulmonary status demonstrated statistically significant improvements in various cardiopulmonary parameters among exercisers. The fact that results did not reach statistical significance may have been due to a lack of statistical power to detect a difference secondary to small sample sizes, or inadequate intensity, duration, and mode of exercise prescribed within the individual studies. The five studies that measured psychological status among an exercise versus control group found statistically significant improvements in psychological parameters for the exercise intervention groups compared with the nonexercising control groups.

Results of this review indicate that aerobic exercise for adults living with HIV appears to be safe. This finding is based on the absence of reports of adverse events among

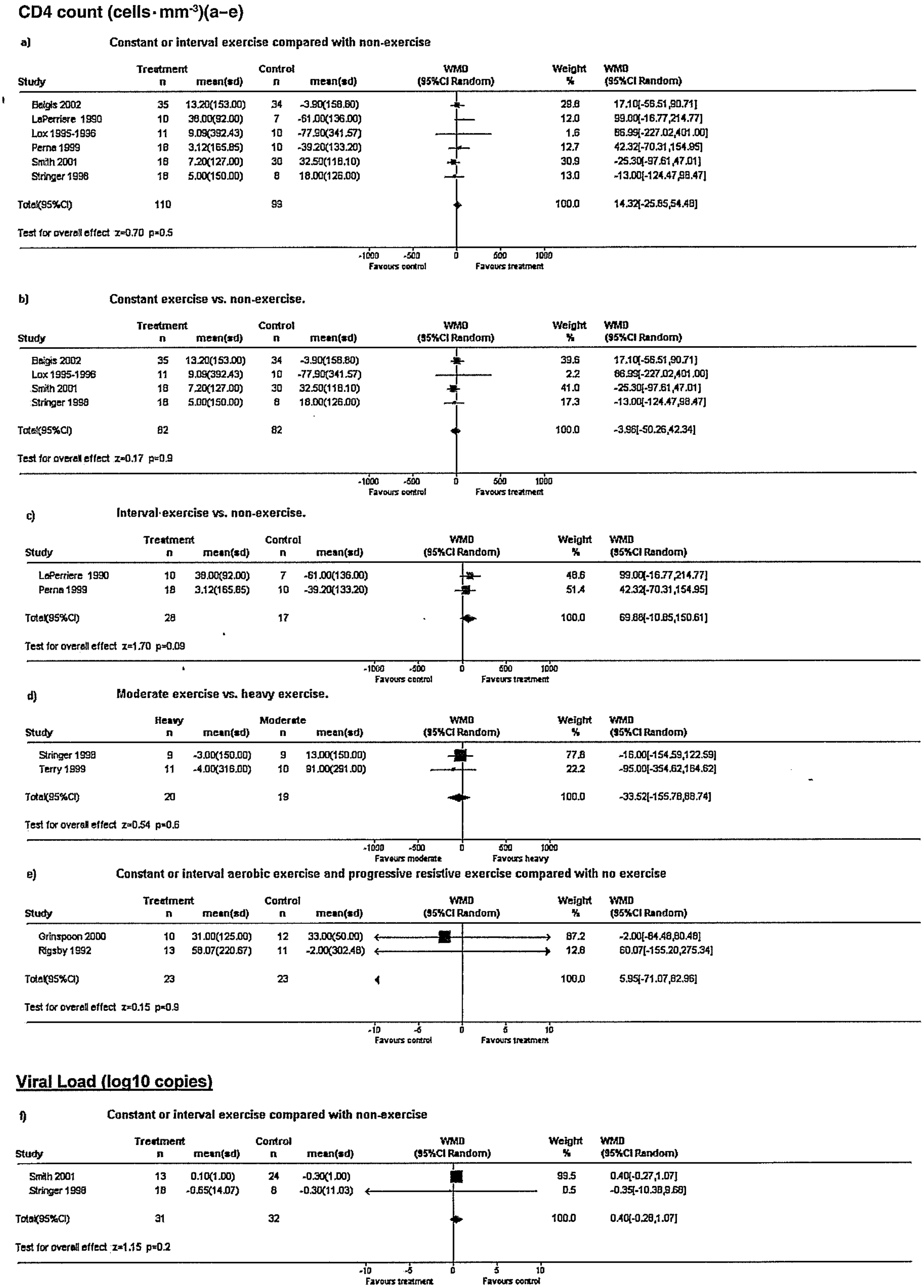

FIGURE 1—Immunological/virological measures: CD4 count (cells·mm^{-3}) (a–e) and viral load (log10 copies) (f) CD4 count (cells·mm^{-3}); WMD, weighted mean difference; CI, confidence interval; sd, standard deviation.

exercisers. The stability of immunological and virological measures during regular aerobic exercise can also be seen as evidence for the safety of this intervention. These results are based on those participants who completed the exercise programs and for those where there was adequate follow-up data.

TABLE 3. Outcomes and author's conclusions of individual studies included in the systematic review.

Study	Immunological/Virological	Cardiopulmonary	Psychological	Author's Conclusions
LaPerriere et al. (6)	CD4 count: HIV+ exercisers showed an increase in CD4 count by 38 cells/mm^3; HIV+ non-exercisers showed a decrease in CD4 count by 61 cells/mm^3	$\dot{V}O_{2max}$: 10% improvement in $\dot{V}O_{2max}$ in both HIV+ and HIV− exercisers No change in $\dot{V}O_{2max}$ in nonexercising controls	Anxiety and depression: HIV+ nonexercising controls showed significantly larger increases in anxiety and depression than the exercise groups	Aerobic exercise is a beneficial stress management intervention, which may be a useful strategy for attenuating an acute stressor such as postnotification of HIV status.
Rigsby et al. (13)	CD4 count: no significant changes	Significant increases in aerobic capacity were shown in the exercise group with no change in nonexercising control group Significant decreases in HR and increases in total time exercise to voluntary exhaustion	NA	HIV+ men can experience increases in cardiorespiratory fitness; increased fitness may occur without negative effects on immune status.
MacArthur et al. (11)	CD4 count: no significant changes	Significant increases in compliant exercisers (N = 6) for $\dot{V}O_{2max}$ (24%), minute ventilation (13%), oxygen pulse (24%)	General health questionnaire: scores improved for the six compliant participants	Exercise training is feasible and beneficial for moderately to severely immunocomprimised HIV+ individuals.
Stringer et al. (15)	CD4 count and viral load: no significant changes in all three groups	Intensity aerobic training effect seen (heavy > mod) relative to the nonexercising control group $\dot{V}O_{2max}$ and work rate max increased significantly in the heavy group LAT increased significantly in both intervention groups.	QOL questionnaire: significant improvements in both intervention groups compared with the nonexercising control group (no differences between the two intervention groups)	Exercise training resulted in a substantial improvement in aerobic function (heavy > mod) while immune indices were unchanged; QOL markers improved significantly with exercise; exercise training is safe and effective and should be promoted for HIV+ individuals.
Perna et al. (12)	CD4 count: compliant exercisers—increase in CD4 count by 13% and noncompliant exercisers—decreased by 18%. Controls—decrease in CD4 count of 10%	$\dot{V}O_{2max}$ (12%), O_2 pulse (13%), max TV (8%), $\dot{V}E$ (17%) significantly improved in compliant exercisers No significant differences were found in noncompliant exercisers and nonexercising control groups	Physician-rated health status: no significant differences	Aerobic exercise may significantly increase CD4 count amoung symptomatic HIV+ individuals; exercise noncompliance may be associated with faster CD4 decline.
Terry et al. (16)	CD4 count: no significant changes.	Peak HR unchanged for both groups Peak systolic BP increased significantly only in the high intensity group	Depression scale: no significant changes	Short-term aerobic exercise programs may be safely recommended to HIV+ individuals for improvement in functional capacity.
Grinspoon et al. (4)	CD4 count and viral load: no significant change in CD4 count or viral load	NA	NA	Exercise has a significant effect on lean body mass and muscle area independent of testosterone; muscle mass and strength may increase in response to combined exercise and testosterone therapy; exercise may be a strategy to reverse muscle loss in this population.
Smith et al. (14)	CD4 count and viral load: no significant changes.	$\dot{V}O_{2max}$: significant improvements in the experimental group (2.6 mL·kg^{-1}·min^{-1}) compared with control group (1 mL·kg^{-1}·min^{-1}) Significant decrease in fatigue in the exercisers compared to nonexercisers No significant effect on rate of perceived exertion (RPE) or dyspnea in either group	NA	Supervised aerobic exercise training safely decreases fatigue, in HIV-infected individuals.
Lox et al. (9,10)	CD4 count: no significant changes.	$\dot{V}O_{2max}$: significant improvements among exercisers compared to nonexercisers	Mood and life satisfaction: significant improvements in mood and life satisfaction in the aerobic exercise group compared with nonexercising controls	Exercise results in improvements in body composition, strength, cardiopulmonary fitness, and mood and life satisfaction for HIV-infected individuals.
Baigis et al. (1)	CD4 count: no significant changes.	$\dot{V}O_{2max}$: no significant differences between exercisers versus non-exercisers; results were attributed to the level of intensity and duration of exercise	HRQL: nonsignificant trend favouring exercisers compared with non-exercisers; significant improvement in overall health subscale of the MOS-HIV found among exercisers compared with nonexercisers	Exercise appears to be safe in HIV-infected individuals.

NA, not assessed.

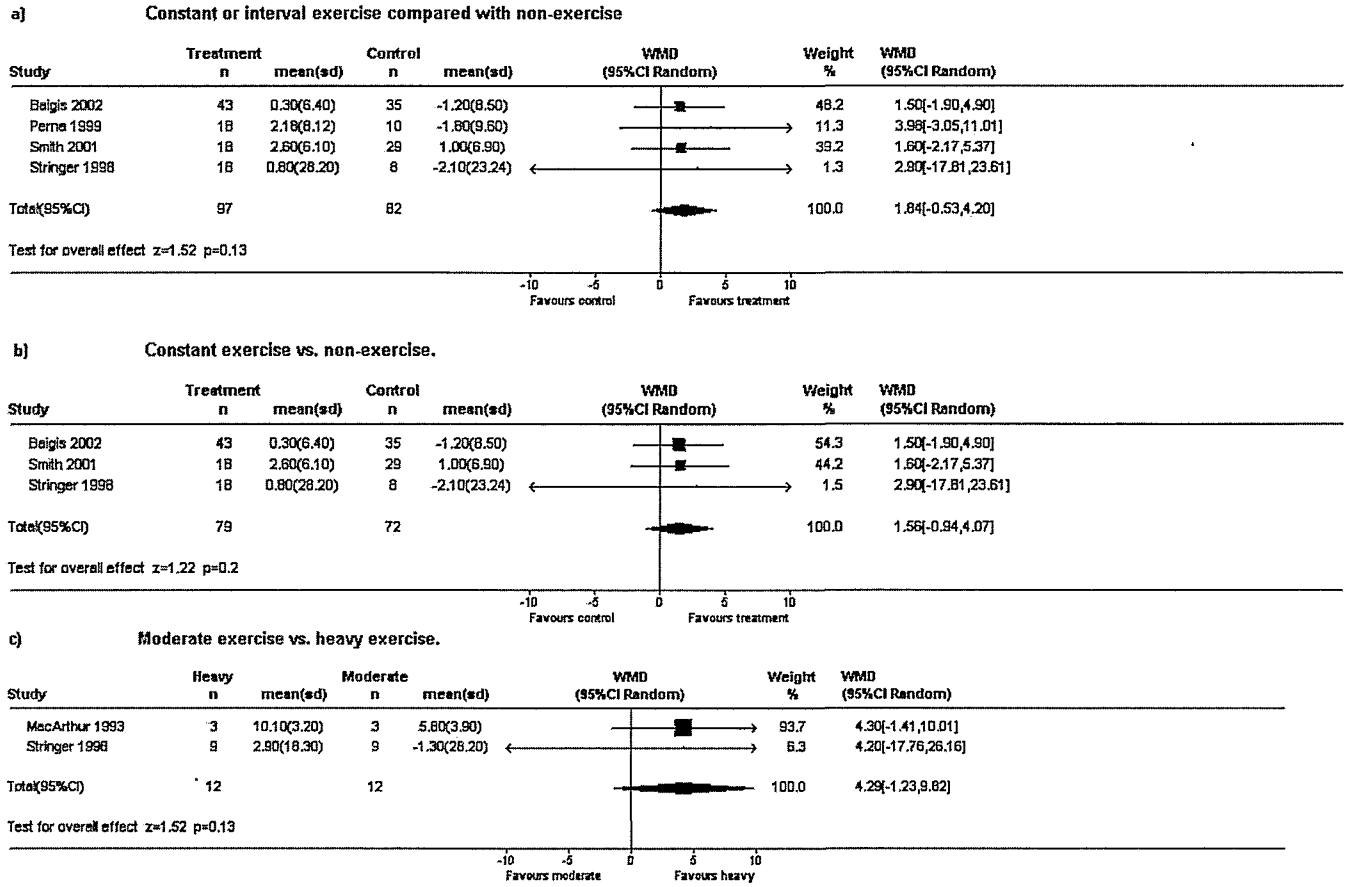

FIGURE 2—Cardiopulmonary measures: $\dot{V}O_{2max}$ ($mL \cdot kg^{-1} \cdot min^{-1}$); WMD, weighted mean difference; CI, confidence interval; sd, standard deviation.

Potential limitations and direction of future research. 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 trials. Furthermore, the trials included in this review involved relatively small numbers of participants, a variety of exercise interventions, and generally poor participant compliance with these interventions. The ability to perform meta-analyses was limited due to the breadth of outcome measures used in the trials. As a result, meta-analyses were underpowered to detect improvements in CD4 count and cardiopulmonary fitness that were of potential clinical importance. Additionally, publication bias may have occurred in this review if trials with negative results were suppressed in the published literature, leaving mostly small, but positive studies to include in the review.

It should also be emphasized that the exercise groups were fraught with high drop-out rates, and that for the most part, participants who dropped out of the exercise program were not included in the final results. This limited comparability of the remaining exercisers with nonexercising controls, which raises issues of effectiveness and safety of exercise among those who stop exercising. Future studies should make every effort to include all subjects in an intent-to-treat analysis with complete follow-up and reporting of results for those who drop out of exercise programs. Furthermore, training intensities were estimated using maximal testing in only three of the included studies. As a result, $\dot{V}O_{2max}$ might have been underestimated in other studies that used alternative methods (e.g. submaximal testing) to estimate their training intensities. This could have resulted in an overestimation of training intensities in these studies.

The vast majority of study participants were male and between the ages of 18 and 58. As such, findings should be interpreted cautiously with respect to females and/or people living with HIV/AIDS who are children, young adults, or older adults. Additional high-quality studies are required to further investigate the effects of aerobic exercise in adults at varying stages of HIV/AIDS, particularly those who are severely immunocompromised. The long-term effects of exercise also require attention. All studies were conducted for 12 wk or less, except for one 24-wk study. Further research should also explore the different effects of interval versus constant exercise, as well as aerobic exercise in conjunction with other exercise modalities. The purpose of this systematic review was to investigate the effects of aerobic exercise; however, future reviews should also explore the effects of progressive resistive exercise in this population.

CONCLUSION

Performing constant or interval aerobic exercise or a combination of constant aerobic exercise and progressive resistance exercise for at least 20 min three times per week for at least 4 wk may be beneficial and appears to be safe for adults living with HIV/AIDS. Results from the meta-analyses indicate that immunological and virological measures appear to be unaffected by aerobic exercise, a finding that should reassure those contemplating starting an exercise program. We found strong trends toward improved cardiopulmonary fitness and improved psychological health among those exercising, suggesting that adults living with HIV can expect to experience many of the well-established benefits of aerobic exercise. Given the lack of information on participants who dropped out of exercise, those exercising should be closely followed for changes in clinical status, especially in more advanced stages of immunosuppression. Furthermore, results should be interpreted cautiously due to the small sample sizes and large withdrawal rates within the individual studies.

Sources of support: The authors gratefully acknowledge the Ontario HIV Treatment Network, Ontario, Canada, and the Inner City Health Research Unit, St. Michael's Hospital, Toronto, Ontario, Canada, for their support.

The Inner City Health Research Unit is sponsored by the Ontario Ministry of Health and Long-Term Care. The opinions, results and conclusions are those of the authors and no endorsement by the Ministry is intended or should be inferred.

The authors would like to acknowledge the contributions of Jim Marianchuk, Sian Owen, Wayne Stump, and Tracy Xavier for their role in data abstraction in the original review; and Angela Eady, MLS, Health Information Research Unit, McMaster University, for her assistance in conducting the literature searches and refining the search strategy.

The following authors or coauthors were invaluable in providing additional data or information about their reviews that helped with this update: William Stringer, Sheldon Levine (for R. D. MacArthur), Allen Jackson (for L. W. Rigsby), Jorge Ribeiro (for L. Terry), and Frank Perna.

The results of the present study do not constitute endorsement of the product by the authors or ACSM.

REFERENCES

1. Baigis, J., D. M. Korniewicz, G. Chase, A. Butz, D. Jacobson, and A. Wu. Effectiveness of a home-based exercise intervention for HIV-infected adults: a randomised trial. *J. Assoc. Nurses AIDS Care* 13(2):33–45, 2002.
2. Bouchard, C., R. J. Shepherd, and T. Stephens. *Physical Activity, Fitness, and Health: International Proceedings and Consensus Statement.* Champaign, IL: Human Kinetics, 1994, pp. 9–76, 119–133.
3. Clarke, M., and A. D. Oxman (Eds.). *Cochrane Reviewers' Handbook 4.1.5* [updated April 2002]. In: *The Cochrane Library*, Issue 2, 2002. Oxford: Update Software, Updated quarterly.
4. Grinspoon, S., C. Corcoran, K. Parlman, et al. Effects of testosterone and progressive resistance training in eugonadal men with AIDS wasting. *Ann. Intern Med.* 133:348–355, 2000.
5. Jadad, A. R., A. Moore, D. Carroll, et al. Assessing the quality of reports or randomised clinical trials: is blinding necessary? *Controlled Clin. Trials* 17:1–12, 1996.
6. LaPerriere, A. R., H. Antoni, N. Schneiderman, et al. Exercise intervention attenuates emotional distress and natural killer cell decrements following notification of positive serologic status for HIV-1. *Biofeedback Self-Regul.* 15:229–242, 1990.
7. LaPerriere, A. R., M. A. Fletcher, M. H. Antoni, N. Klimas, and N. Schneiderman. Aerobic exercise training in an AIDS risk group. *Int. J. Sports Med.* 12:S53–S57, 1991.
8. Ledergerber, B., M. Egger, M. Opravil, et al. Clinical progression and virological failure on highly active antiretroviral therapy in HIV-1 patients: a prospective cohort study: Swiss HIV Cohort Study. *Lancet* 353:863–868, 1999.
9. Lox, C. L., E. McAuley, and R. S. Tucker. Aerobic and resistance exercise training effects on body composition, muscular strength, and cardiovascular fitness in an HIV-1 population. *Intern. J. Behav. Med.* 3:55–69, 1996.
10. Lox, C. L., E. McAuley, and R. S. Tucker. Exercise as an intervention for enhancing subjective well-being in an HIV-1 population. *J. Sport Exerc. Psychol.* 17:345–362, 1995.
11. MacArthur, R. D., S. D. Levine, and T. J. Birk. Supervised exercise training improves cardiopulmonary fitness in HIV-infected persons. *Med. Sci. Sports Exerc.* 25:684–688, 1993.
12. Perna, F. M., A. LaPerriere, N. Klimas, et al. Cardiopulmonary and CD4 changes in response to exercise training in early symptomatic HIV infection. *Med. Sci. Sports Exerc.* 31:973–979, 1999.
13. Rigsby, L. W., R. K. Dishman, A. W. Jackson, G. S. Maclean, and P. B. Raven. Effects of exercise training on men seropositive forthe human immunodeficiency virus-1. *Med. Sci. Sports Exerc.* 24:6–12, 1992.
14. Smith, B. A., J. L. Neidig, J. T. Nickel, G. L. Mitchell, M. F. Para, and R. J. Fass. Aerobic exercise: effects on parameters related to fatigue, dyspnea, weight and body composition in HIV-infected adults. *AIDS* 15:693–701, 2001.
15. Stringer, W. W., M. Bereszovskaya, W. A. O'Brien, C. K. Beck, and R. Casaburi. The effect of exercise training on aerobic fitness, immune indices, and quality of life in HIV+ patients. *Med. Sci. Sports Exerc.* 30:11–16, 1998.
16. Terry, L., E. Sprinz, and J. P. Ribeiro. Moderate and high intensity exercise training in HIV-1 seropositive individuals: a randomised trial. *Int. J. Sports Med.* 20:142–146, 1999.
17. Wood, E., R. S. Hogg, B. Yip, P. R. Harriigan, M. V. O'Shaughnessy, and J. S. Montaner. The impact of adherence on CD4 cell count responses among HIV-infected patients. *JAIDS* 35:261–268, 2004.
18. Wood, E., R. S. Hogg, B. Yip, et al. Discordant increases in CD4 cell count relative to plasma viral load in a closely followed cohort of patients initiating antiretroviral therapy. *JAIDS* 30:159–166, 2002.
19. World Health Organization. *International Classification of Functioning, Disability and Health: ICF Short Version.* Geneva: WHO, 2001, pp. 3–35.