SPECIAL SERIES

Aerobic Exercise Interventions for People Living with HIV/AIDS: Implications for Practice, Education, and Research

Kelly O'Brien, Stephanie Nixon, Anne-Marie Tynan, Richard H. Glazier

ABSTRACT

Purpose: The purpose of this article is to present the results of a systematic review that investigated the effects of aerobic exercise interventions in people living with HIV/AIDS and to discuss the implications for physical therapy practice, education, and research.

Summary of Key Points: A systematic review was conducted based on the Cochrane Collaboration protocol. Eleven randomized trials of HIV-positive adults who performed aerobic exercise three times per week for at least four weeks were identified. Thirteen meta-analyses were performed. The main results indicated that aerobic exercise was associated with significant improvements in some outcomes of cardiopulmonary status (maximum oxygen consumption) and psychological status (depression-dejection symptoms).

Conclusions: Performing continuous or interval aerobic exercise or a combination of continuous aerobic exercise and progressive resistive exercise for at least 24 minutes three times per week for at least five weeks appears to be safe and may be beneficial for adults living with HIV. These findings should be interpreted cautiously owing to small sample sizes and high withdrawal rates within individual studies. The results of this review support the role of exercise and, more broadly, the role of rehabilitation practice, education, and research in the care and treatment of persons living with HIV.

Key Words: aerobic, Cochrane Collaboration, effectiveness, exercise, HIV, AIDS, meta-analysis

RÉSUMÉ

Objectif: L'objectif de cet article est de présenter les résultats d'une revue systématique ayant évalué les effets des interventions par des exercices aérobiques chez des personnes vivant avec le VIH/SIDA et d'examiner les implications pour la pratique de la physiothérapie, l'éducation, et la recherche.

Résumé des points clés: Une revue systématique a été menée sur la base du protocole du Centre de collaboration Cochrane. Onze études randomisées menées auprès d'adultes VIH-positifs qui effectuaient des exercices aérobiques trois fois par semaine pendant au moins quatre semaines ont été identifiées. Treize méta-analyses ont été effectuées. Les principaux résultats ont indiqué que l'exercice aérobique était associé à une amélioration importante de certains paramètres de la fonction cardiopulmonaire (consommation maximale d'oxygène) et de l'état psychologique (symptômes de dépression-mélancolie).

Kelly O'Brien, B.Sc.PT, PhD(candidate): Department of Health Policy, Management and Evaluation, University of Toronto, and Lecturer, Department of Physical Therapy, University of Toronto, Toronto, Ontario.

Stephanie Nixon, B.HSc.PT, M.Sc., PhD: Lecturer, Department of Physical Therapy, University of Toronto, Toronto, Ontario.

Anne-Marie Tynan, BA: Research Co-ordinator, Centre for Research on Inner City Health, St. Michael's Hospital, Toronto, Ontario.

Richard H. Glazier, MD, MPH: Associate Professor, Department of Family and Community Medicine, University of Toronto and Centre for Research on Inner City Health, St. Michael's Hospital, Toronto, Ontario.

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Some results reported in this review were derived from a systematic review originally published and recently updated in *The Cochrane Library* (Nixon S, O'Brien K, Glazier RH, Tynan AM. Aerobic exercise interventions for adults living with HIV/AIDS. The Cochrane Database of Systematic Reviews 2005, Issue 2. Art. No.: CD001796. DOI: 10.1002/14651858.CD001796.pub2) and *Medicine & Science in Sports and Exercise* (O'Brien K, Nixon S, Tynan AM, Glazier RH. Effectiveness and safety of aerobic exercise in adults living with HIV/AIDS: systematic review and meta-analysis of randomized trials. Med Sci Sports Exerc 2004;36:1659-66).

Address for correspondence: *Kelly O'Brien*, Department of Physical Therapy, University of Toronto, 500 University Avenue, Room 160, Toronto, ON M5G 1V7; Tel: 416-978-0565; Fax: 416-946-8562; E-mail: kelly.obrien@utoronto.ca.

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Conclusions: La pratique d'exercices aérobiques continus ou par intervalle ou d'une association d'exercices aérobiques continus et d'exercices contre résistance progressifs pendant au moins 24 minutes trois fois par semaine pendant au moins cinq semaines est sûre et peut être bénéfique pour des adultes vivant avec le VIH. Ces constatations devraient être interprétées avec prudence en raison de la petite taille des échantillons et du taux élevé de retraits dans chaque étude. Les résultats de cette revue appuient le rôle bénéfique de l'exercice et, plus généralement, le rôle de la réadaptation, de l'éducation, et de la recherche dans les soins et le traitement des personnes vivant avec le VIH.

Mots clés: aérobie, Centre de collaboration Cochrane, efficacité, exercice, méta-analyse, SIDA, VIH

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At the end of 2003, an estimated 37.8 million people were living with human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) worldwide, with the majority living in sub-Saharan Africa, Asia, and the Pacific.[1] In the developed world, at the end of 2002, it was estimated that 56,000 individuals were living with HIV in Canada[2] and 385,000 were living with HIV in the United States.[3] Despite the stable incidence of new HIV infections in 1999 and 2002, the prevalence of HIV has increased 12% from an estimated 49,800 individuals living with HIV at the end of 1999 in Canada.

Effective treatments in the form of highly active antiretroviral therapy (HAART) have dramatically changed the experience of living with HIV.[4] Rather than an illness that traditionally resulted in a gradual progression to death, HIV can now present as a chronic illness characterized by fluctuating episodes of wellness and illness for people who can access and tolerate HAART.

Increased longevity associated with HAART means that a greater number of individuals are living longer with the day-to-day, health-related consequences and challenges associated with HIV. A range of health problems may arise from HIV disease itself, but individuals also commonly experience adverse events from the medications that may affect the physical, social, and/or psychological components of a person's health.

For example, lipodystrophy is a syndrome associated with physical and metabolic changes of the body that emerged after the introduction of HAART.[5] 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 the neck, and breasts. These changes in body composition may influence a person's self-esteem related to his/her body image. Lipodystrophy has also been associated with elevated triglycerides and low-density lipoproteins, placing individuals at risk of cardiovascular disease, potentially leading to myocardial infarction or stroke.[6]

Despite the medical benefits of HAART, the complex and demanding schedules for these medications may interfere with the performance of daily life tasks, including personal care and employment. This interruption of routine can lead to disclosure of HIV status, which may result in some form of stigmatization and discrimination. Thus, persons living with HIV may experience a range of physical, social, and psychological consequences associated with HIV and its associated conditions and treatments.

To illustrate the health-related challenges of HIV, a survey was conducted with persons living with HIV in British Columbia to assess the prevalence of impairments, activity limitations, and participation restrictions based on the International Classification of Functioning, Disability and Health.[7] Within this framework, an impairment is defined as any problem at the level of the body part, including its structure or function (such as pain or weakness). An activity limitation is defined as any difficulty an individual might have carrying out a task or action (such as walking or toileting). A participation restriction is defined as any problem an individual might have interacting within society in a life situation (such as maintaining employment).[7]

Results of this survey found a remarkably high prevalence of disablement, with at least 80% of respondents having experienced at least one impairment, activity limitation, or participation restriction within the previous month.[8] Examples of disablement included pain and generalized weakness (impairments), difficulty carrying out vigorous activities and household chores (activity limitations), and difficulty engaging in employment or leisure activities (participation restrictions).[8] Furthermore, mental health issues were found to be remarkably prevalent among persons living with HIV, with almost 60% of respondents having reported being diagnosed with depression by a physician.[8] Results of this study demonstrated an increased role for rehabilitation professionals to address the disability experienced by this population.

Exercise is one type of rehabilitation strategy that may be used to address disability, such as decreased strength and cardiovascular fitness, for persons living with HIV. Exercise is also important to people living with HIV because of links to disease prevention and health promotion, as seen in other populations. Furthermore, exercise is worthy of attention because of its connection to body image, which has been shown to be important in certain populations affected by HIV in Canada, such as gay men.[9-11]

Aerobic exercise has been shown to improve strength, cardiovascular function, and psychological status in general populations.[12] However, the safety and effects of aerobic exercise among adults living with HIV are not well-established. Knowing the effects of aerobic exercise for people living with HIV may facilitate the appropriate use of aerobic exercise interventions to enhance HIV care and treatment, with the overall goal of improving the health and quality of life of adults living with HIV. Therefore, the purpose of this article is to present the results of a systematic review[13,14] that investigated the effects of aerobic exercise interventions in people living with HIV/AIDS and to discuss the implications for physical therapy practice, education, and research. Earlier versions of this systematic review were originally published and recently updated in *The Cochrane Library*[13] and *Medicine & Science in Sports and Exercise*.[14]

METHODS

A systematic review was conducted following guidelines established by the Cochrane Collaboration.[15] Databases, abstracts from major HIV/AIDS conferences, and reference lists from pertinent articles and books were searched from 1980 to March 2005 to identify randomized controlled trials that compared aerobic exercise interventions with no exercise intervention or other treatment among adults (18 years of age or older) living with HIV/AIDS. For the purpose of this systematic review, aerobic exercise was defined as a regimen containing sustained physical activity performed at least three times per week for at least four weeks. Aerobic interventions may have included but were not limited to walking, jogging, cycling, or rowing. Data on study design, participants, exercise interventions, outcomes, and methodological quality were abstracted from studies that met the inclusion criteria. Outcomes of interest included immunological/virological outcomes, cardiopulmonary outcomes, strength, weight, body composition, and psychological outcomes. Meta-analyses were performed using *RevMan 4.2* computer software (The Nordic Cochrane Centre, Rigshospitalet, Copenhagen, Denmark) when sufficient data were available in the studies and when similar or comparable outcomes were used. Further details of these methods are published elsewhere.[13]

RESULTS

Evidence of the Effect of Aerobic Exercise in HIV/AIDS

Searches of all sources retrieved 1,572 articles, of which 16 studies met the inclusion criteria: LaPerriere and colleagues,[16,17] Rigsby and colleagues,[18] MacArthur and colleagues,[19] Lox and colleagues,[20,21] Stringer and colleagues,[22] Perna and colleagues,[23] Terry and colleagues,[24] Grinspoon and colleagues,[25] Smith and colleagues,[26] Fairfield and colleagues,[27] Baigis and colleagues,[28] Neidig and colleagues,[29] and Driscoll and colleagues.[30,31] Of these studies, five reported duplicate results: LaPerriere and colleagues[17] reported long-term data for the same study participants as LaPerriere and colleagues[16]; Fairfield and colleagues[27] used the same participants as Grinspoon and colleagues[25]; Lox and colleagues[21] used the same participants as Lox and colleagues[20]; Neidig and colleagues[29] used the same participants as Smith and colleagues[26]; and Driscoll and colleagues[30] used the same participants as Driscoll and colleagues.[31] In these instances, earlier published studies were included in the review. Any additional outcomes reported in later published studies were also incorporated. Thus, 11 studies were included in the overall systematic review. See Table 1 for the characteristics of included studies and Table 2 for the outcomes of individual studies.

Characteristics of Studies Included in the Review

Of the 11 studies, eight included a non-exercising control group,[16,18,20,22,23,25,26,28] one of which included a non-exercising counseling group.[18] Aerobic exercise was administered in the form of either continuous or interval training. Four of the 11 studies compared continuous aerobic exercise with non-exercising controls,[20,22,26,28] whereas two studies compared interval aerobic exercise with non-exercising controls.[16,23] Three of the 11 studies included combined regimens of continuous aerobic and progressive resistive exercise (PRE) compared with non-exercising controls.[18,25,30] One study included two additional comparison groups: an exercise plus injection of testosterone enanthate group and a testosterone-only group.[25] One study included a combined metformin and exercise group compared with a metformin-only group.[30] One study included a PRE-only group, compared with an aerobic group, compared with a non-exercising control group.[20] Three studies included comparison groups that compared heavy with moderate continuous aerobic exercise.[19,22,24] Seven of the 11 studies reported that the exercise interventions were supervised,[18,20,23,25,26,28,30] four of which specified that the supervision was conducted by laboratory assistants,[23] personal trainers,[26] nurses trained by exercise physiologists,[28] and physical therapists.[30] The level of supervision was not stated in the remaining four studies.[16,19,22,24]

Three hundred and eight participants were included in the review. Participants were living at various stages of HIV infection, with CD4 counts (measure of immune status) ranging from ≤ 100 to $\geq 1{,}000$ cells/mm^3. Studies included both men and women ranging from 18 to 58 years of age. However, women comprised less than 15% of the total number of participants. Two studies included participants who were on HAART, defined as a combination of three or more different types of HIV medications.[25,26] Six studies included participants who were not specified as being on HAART. However, most, if not all, participants were taking some form of antiretroviral therapy (ART).[19,20,22,23,28,30] Three studies did not report on whether participants were taking ART.[16,18,24]

The training intensity of participants was reported in per cent HR_{max},[16,23-25,28,30] per cent heart rate reserve,[18,20] per cent maximal oxygen uptake (VO_{2max}),[19,26] per cent lactic acid threshold (LAT), and the difference between LAT and VO_{2max}.[22] Training intensities were established based on varied methods, such as submaximal testing,[16,18,19] graded exercise testing,[23,26] maximal exercise testing,[22,24,28] and intensities prescribed based on the Karvonen formula[32] and the American College of Sports Medicine[33] guidelines.[20,25,30]

Methodological Quality of Included Studies

Methodological quality of included studies was assessed based on criteria derived from the Jadad checklist[34] and whether groups were similar at baseline. All 11 studies reported randomization to allocate participants to a comparison group, but only four studies described the randomization process.[22,25,28,30] Two studies reported on single blinding: participants in MacArthur and colleagues were not told to which exercise intensity they had been assigned (low or high),[19] and assessors of outcomes were blinded in Smith and colleagues.[26]

Ten of the 11 studies made reference to participants who withdrew from or were non-adherent with the exercise intervention.[18-20,22-26,28,30] Withdrawal rates ranged from 4 to 76%, and total outcome data were not available for 159 (34%) participants. The reasons for withdrawal or non-adherence included lack of interest, time required for participation, economic and family issues, transportation difficulties, employment or school, geographical relocation of residence, conflicting work schedules, lack of motivation to exercise, parole violation, geographical distance from the exercise intervention, health reasons, including hospitalizations and persistent infection, lack of interest, dissatisfaction being in the non-exercising group, and reports that the exercise interventions were too difficult. Withdrawal rates were similar across comparison groups for Stringer and colleagues,[22] Rigsby and colleagues,[18] and Perna and colleagues.[23] Eight of the 11 studies reported that comparison groups were similar at baseline.[16,18,22-24,26,28,30]

Results of Meta-Analyses

Thirteen meta-analyses were performed for outcomes of immunological and/or virological status, cardiopulmonary status, strength, weight and body composition, and/or psychological status.

Immunological and/or Virological Status

All 11 of the included studies assessed immunological and/or virological status in the form of CD4 count[16,18,19,20,22-26,28,30] or viral load.[22,25,26,30] CD4 count is a measure of immunological status and is measured in cells/mm^3. A rise in CD4 count represents an improvement in immune status. Viral load is a measure of virological status that reflects the amount of virus in the circulating blood and is measured in log^{10} copies. A decline in viral load represents an improvement in virological status.

CD4 Count. Five meta-analyses were performed (Table 3). Overall, no significant changes in CD4 count were found among comparison groups. The results showed no difference in change in CD4 count for participants in the continuous or interval aerobic exercise group, compared with the non-exercising control group (weighted mean difference: 24.27 cells/mm^3; 95% confidence interval [CI]: −9.52, 58.06; $p = .16$; $n = 209$); no difference in change in CD4 count for participants in the continuous aerobic exercise group, compared with the non-exercising control group (weighted mean difference: 0.04 cells/mm^3; 95% CI: −33.33, 33.41; $p = 1.00$; $n = 164$), and a significant trend towards an improvement in CD4 count for participants of 69.58 cells/mm^3 in the interval aerobic exercise group compared with the non-exercising control group (95% CI: 14.08, 125.09; $p = .01$; $n = 45$). Although not statistically significant, the point estimate is above 50 cells/mm^3, which suggests a potential clinically important increase in CD4 count for exercisers compared with non-exercisers.[13] The results showed no difference in change in CD4 count for participants exercising at moderate intensity compared with participants exercising at heavy intensity (weighted mean difference: −42.90 cells/mm^3; 95% CI: −116.28, 30.07; $p = .25$; $n = 39$) and no difference in change in CD4 count for participants in a combined aerobic exercise and PRE group compared with the non-exercising control group (weighted mean difference: 29.18 cells/mm^3; 95% CI: −31.65, 90.01; $p = .35$; $n = 46$). The majority of non-significant findings are consistent with individual study results.

Viral Load. One meta-analysis was performed for viral load (see Table 3) and resulted in no difference in change in viral load for participants in the aerobic exercise group compared with the non-exercising control group (weighted mean difference: 0.40 log^{10} copies; 95% CI: −0.28, 1.07; $p = .25$; $n = 63$). These non-significant findings are consistent with individual study results.

Cardiopulmonary Status

Ten of the 11 studies assessed cardiopulmonary outcomes[16,18-20,22-24,26,28,30] but used a variety of measures, so it was not always possible to combine results in meta-analysis. Eight of the 10 individual studies reported significant improvements in cardiopulmonary outcomes, such as VO_{2max}, work rate maximum, LAT, oxygen pulse, maximum tidal volume, minute ventilation, fatigue, maximum heart rate, time to voluntary exhaustion, and exercise time.[16,18-20,22,23,26,30]

VO_{2max}. Seven studies assessed VO_{2max},[16,19,20,22,23,26,28] and three meta-analyses were performed (see Table 3). The results showed a significant improvement in VO_{2max}

Table 1 Characteristics of Studies Included in the Systematic Review

Study (Year)	*Method*	*Sample Size (at Baseline)*	*% Male*	*Participants (at Study Completion)*	*Type of Exercise*
LaPerriere et al (1990 and 1991)[16,17]	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
Rigsby et al (1992)[18]	Randomized exercise and control groups	*N* = 45 (37 HIV+)	100	Intervention group: *n* = 16 (13 HIV+) Non-exercising counselling control group: *n* = 15 (11 HIV+)	Stationary bike
MacArthur et al (1993)[19]	Randomized, 2 exercise groups	*N* = 25	96	High-intensity group: *n* = 3 Low-intensity group: *n* = 3 (*n* = defined as ''compliant with exercise program'')	Walking, jogging, biking, rowing and stair-stepping
Stringer et al (1998)[22]	Randomized 2 exercise groups and 1 control group	*N* = 34	NR	Moderate-intensity group: *n* = 9 Heavy-intensity group: *n* = 9 Non-exercising control group: *n* = 8	Stationary cycle ergometer
Perna et al (1999)[23]	Randomized exercise and control groups	*N* = 43	86	Intervention group: *n* = 18 Non-exercising control group: *n* = 10	Stationary bike
Terry et al (1999)[24]	Randomized, 2 exercise groups	*N* = 31	67	Moderate-intensity group: *n* = 10 High-intensity group: *n* = 11	Walking, running, and stretching
Grinspoon et al (2000)[25] and Fairfield et al (2001)[27]	Randomized exercise and control groups	*N* = 54 (4 groups: exercise + testosterone; exercise + placebo; testosterone only; control)	100	Intervention group: (exercise + placebo): *n* = 10 Non-exercising control group: *n* = 12	Stationary bike + PRE
Smith et al (2001)[26] and Neidig et al (2003)[29]	Randomized exercise and control groups	*N* = 60	87	Intervention group: *n* = 19 Non-exercising control group: *n* = 30	Walking/jogging, stationary bike, stair-stepper, and cross-country machine
Lox et al (1995 and 1996)[20,21]	Randomized, 2 exercise groups and 1 control group	*N* = 34	100	Intervention groups: AER, *n* = 11; PRE, *n* = 12; Non-exercising control group: *n* = 10	Stationary bike
Baigis et al (2002)[28]	Randomized exercise and control groups	*N* = 123	80	Intervention group: *n* = 35 Non-exercising control group: *n* = 34	Ski machine
Driscoll et al (2004)[30,31]	Randomized combined exercise and metformin and metformin-only group	*N* = 37	80	Intervention group: *n* = 11 Non-exercising metformin-only group: *n* = 14	Stationary bike

AER = aerobic exercise; HIV = human immunodeficiency virus; HR_{max} = heart rate maximum; LAT = lactic acid threshold; NR = not reported; PRE = progressive resistive exercise; VO_{2max} = maximum oxygen consumption.

Time and Intensity of Exercise	*Frequency and Duration of Exercise*	*Supervision (by Whom)*	*Notes*
45 min total @ 80% HR_{max} × 3 min and then @ 69–79% HR_{max} × 2 min *Interval aerobic*	3 times per week for 5 wk	NR	LaPerriere et al (1991) is a continuation of the study reported in 1990; thus, results were used from LaPerriere et al (1990) for this review to avoid skewed results.
60 min total @ 60–80% heart rate reserve × 20 min (2 min warm-up and 3 min cool-down at low intensity); stretching × 10–15 min *Continuous aerobic + PRE*	3 times per week for 12 wk	√ Yes (not specified)	''Control'' group received 90–120 min of counseling 1–2 times per week for 12 wk.
High-intensity exercise: 24 min total @ 75–85% VO_{2max} × 4 min × 6 intervals Low-intensity exercise: 40 min total @ 50–60% VO_{2max} × 10 min × 4 intervals *Interval aerobic*	3 times per week for 24 wk	NR	
Moderate-intensity exercise: 60 min @ 80% LAT Heavy-intensity exercise: 30–40 min @ 50% of difference between LAT and VO_{2max} *Continuous aerobic*	3 times per week for 6 wk	NR	For the meta-analysis of exercise vs. non-exercising control, the results of the moderate- and heavy-intensity exercise groups were combined.
45 min total @ 70–80% HR_{max} × 3 min and then 2 min ''off'' (10 min stretch pre and post) *Interval aerobic*	3 times per week for 12 wk	√ Yes (laboratory assistants)	For this review, a weighted average was calculated to combine data of adherent and non-adherent exercisers for analysis.
Moderate-intensity exercise: 30 min walking @ 55–60% HR_{max} (15 min stretch pre and post) High-intensity exercise: 30 min running @ 75–85% HR_{max} (15 min stretch pre and post) *Continuous aerobic*	3 times per week for 12 wk	NR	
20 min aerobic exercise on stationary cycle at 60–70% HR_{max}; 15 min cool-down followed by resistance training. *Continuous aerobic + PRE*	3 times per week for 12 wk	√ Yes (not specified)	For the purposes of this review, we extracted results from the control group and exercise + placebo group to isolate the effects of exercise.
Minimum of 30 min continuous aerobic exercise at 60–80% VO_{2max} *Continuous aerobic*	3 times per week for 12 wk	√ Yes (personal trainers)	
Aerobic exercise: approx. 45 min total: 5 min warm-up (stretching), 24 min cycle ergometer at 50–60% heart rate reserve, 15 min cool-down *Continuous aerobic*	3 times per week for 12 wk	√ Yes (not specified)	For the purposes of this review, only the aerobic exercise group and the control group were included in meta-analyses. Also, two articles that reported on the same study[20,21] were incorporated as one study for this review.
40 min total: 5 min stretching, 5 min warm-up on machine, 20 min continuous aerobic exercise at 75–85% HR_{max} followed by 5 min cool-down and 5 min stretching. *Continuous aerobic*	3 times per week for 15 wk	√ Yes (nurses trained by exercise physiologists)	
20 min (weeks 1–2) at 60% HR_{max} and then progressed to 30 min (weeks 3–12) at 75% HR_{max} aerobic exercise; 5 min warm-up on stationary bike, standard flexibility routine followed by resistance training *Continuous aerobic + PRE*	3 times per week for 12 wk	√ Yes (physical therapists)	Two articles[30,31] that reported different outcomes on the same participants were incorporated as one study for this review.

Table 2 Outcomes and Authors' Conclusions of Individual Studies Included in the Systematic Review

Study (Year)	*Immunological/Virological*	*Cardiopulmonary*	*Strength*
LaPerriere et al (1990)[16]	*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.	*VO_{2max}*: 10% showed improvement in VO_{2max} in both HIV+ and HIV− exercisers. No change shown in VO_{2max} in non-exercising controls.	NA
Rigsby et al (1992)[18]	*CD4 count*: no significant changes	*Aerobic capacity*: significant increases in aerobic capacity were shown in the exercise group, with no change in the non-exercising control group. *HR and total time to voluntary exhaustion:* significant decreases in HR and increases in total time exercise to voluntary exhaustion	*Upper and lower extremity strength*: significant increases in chest press and leg extension in the exercise group
MacArthur et al (1993)[19]	*CD4 count*: no significant changes	Significant increases in adherent exercisers (n = 6) for *VO_{2max}* (24%), *VE* (13%), *oxygen pulse* (24%).	NA
Stringer et al (1998)[22]	*CD4 count and viral load*: no significant changes in all three groups	Intensity aerobic training effect seen (heavy > moderate) relative to the non-exercising control group *VO_{2max} and work rate maximum*: increased significantly in the heavy group. *LAT*: increased significantly in both intervention groups.	NA
Perna et al (1999)[23]	*CD4 count*: adherent exercisers: increase in CD4 count by 13%; non-adherent exercisers: decrease in CD4 count 18% Controls: decrease in CD4 count by 10%	*VO_{2max}* (12%), *O_2 pulse* (13%), *maximum TV* (8%), *VE* (17%) significantly improved in adherent exercisers No significant differences were found in non-adherent exercisers and non-exercising control groups.	*Lower extremity strength*: significant increase in leg power by 25% in adherent exercisers and no change in non-adherent exercisers or non-exercising controls
Terry et al (1999)[24]	*CD4 count*: no significant changes	*HR_{max}*: unchanged for both groups *Peak systolic BP*: increased significantly only in the high-intensity group	NA
Grinspoon et al (2000)[25]	*CD4 count and viral load*: no significant changes	NA	*Upper and lower extremity strength*: no significant change in strength (Note that strength was tested isometrically, which may underestimate change in strength.)
Smith et al (2001)[26]	*CD4 count and viral load*: no significant changes	*VO_{2max}*: significant improvements in the experimental group (2.6 mL/kg/min) compared with the control group (1 mL/kg/min). *Fatigue*: significant decrease in fatigue in exercisers compared with non-exercisers *RPE and dyspnea*: no significant effect on RPE or dyspnea in either group	NA

Weight and Body Composition	*Psychological*	*Authors' Conclusions*
NA	*Anxiety and depression:* HIV+ non-exercising controls showed significantly larger increases in anxiety and depression than the exercise groups.	Aerobic exercise is a beneficial stress management intervention that may be a useful strategy for attenuating an acute stressor such as post-notification of HIV status.
NA	NA	Men who are HIV+ can experience increases in cardiorespiratory fitness. Increased fitness may occur without negative effects on immune status.
NA	*General health questionnaire*: scores improved for the 6 adherent exercisers.	Exercise training is feasible and beneficial for moderately to severely immunocompromised individuals living with HIV.
NA	*QOL questionnaire*: significant improvements in both intervention groups compared with the non-exercising control group (no differences between the 2 intervention groups)	Exercise training resulted in a substantial improvement in aerobic function (heavy > moderate), whereas immune indices were unchanged. QOL markers improved significantly with exercise. Exercise training is safe and effective and should be promoted for individuals with HIV.
Body mass index: significant increase in adherent exercisers	*Physician-rated health status*: no significant differences (Note that this outcome was not considered a true measure of psychological status because it was not completed by participants.)	Aerobic exercise may significantly increase CD4 count among symptomatic individuals with HIV. Exercise non-adherence may be associated with faster CD4 decline.
Body mass, body fat percentage, and body density: no significant change in either intensity group	*Depression*: no significant changes on scores of the Montgomery-Asberg Depression Score.	Short-term aerobic exercise programs may be safely recommended to individuals with HIV for improvement in functional capacity.
Lean body mass and muscle area: significant increases in lean body mass, arm and leg muscle area *Weight and fat mass*: no significant changes in either the exercisers or non-exercising control group	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.
Weight, body mass index, skinfold thickness, and abdominal girth: significant decrease in waist-to-hip ratio among exercisers (Note that many participants were above ideal body weight prior to exercise; thus, decreases in both weight and body composition were considered favourable outcomes.)	*Anxiety and depression*: significant improvement in overall scores and depression-dejection subscale scores of the POMS and CES-D among exercisers; non-significant trend towards improvement in BDI scores among exercisers.	Supervised aerobic exercise training safely decreases fatigue in individuals affected with HIV.

(*continued on next page*)

Table 2 Continued

Study (Year)	*Immunological/Virological*	*Cardiopulmonary*	*Strength*
Lox et al (1995)[20]	*CD4 count*: no significant changes	*VO_{2max}*: significant improvements among exercisers compared with non-exercisers	*Upper and lower extremity strength*: significant improvements in the resistance and aerobic exercise groups compared with non-exercising controls (greater improvements in resistive group compared with aerobic and non-exercising control)
Baigis et al (2002)[28]	*CD4 count*: no significant changes	*VO_{2max}*: no significant differences between exercisers versus non-exercisers Results were attributed to the level of intensity and duration of exercise.	NA
Driscoll et al (2004)[30]	*CD4 count and viral load*: no significant changes	*Exercise time:* significant improvements in endurance time on cycle ergometer during submaximal stress test in the exercise and metformin group compared with the metformin-only group	*Upper and lower extremity strength*: significant increases in five of six strength indices in the exercise and metformin group compared with the metformin-only group

BDI = Beck Depression Inventory; BP = blood pressure; CES-D = Center for Epidemiological Studies-Depression Scale; HIV = human immunodeficiency virus; HR = heart rate; HRQOL = health-related quality of life; LAT = lactic acid threshold; MOS-HIV = Medical Outcomes Study HIV Health Survey; NA = not assessed; POMS = Profile of Mood States; PRE = progressive resistive exercise; QOL = quality of life; RPE = rate of perceived exertion; TV = tidal volume; VE = minute ventilation; VO_{2max} = maximum oxygen consumption.

of 1.64 mL/kg/min for participants in the continuous or interval aerobic exercise group, compared with the non-exercising control group (95% CI: 1.06, 2.22; $p < .00001$; $n = 179$), significant improvement in VO_{2max} of 1.53 mL/kg/min for participants in the continuous aerobic exercise group, compared with the non-exercising control group (95% CI: 0.94, 2.12; $p < .00001$; $n = 151$), and a significant trend towards a greater improvement in VO_{2max} of 4.30 mL/kg/min for participants in the heavy-intensity exercise group, compared with participants in the moderate-intensity exercise group (95% CI: 0.61, 7.98; $p = .02$; $n = 24$). The point estimate is above 2 mL/kg/min, which suggests a potential clinically important improvement in VO_{2max} among heavy-intensity exercisers compared with moderate-intensity exercisers.[13]

Maximum Heart Rate. Four studies assessed heart rate maximum (HR_{max}).[18,20,23,24] Meta-analysis showed a non-significant decrease in HR_{max}, with a reduction of −9.81 beats/min (95% CI: −26.28, 6.67; $p = .24$; $n = 49$) for participants in the aerobic exercise group, compared with participants in the non-exercising control group (see Table 3).

Strength

Five of the 11 studies assessed muscle strength.[18,20,23,25,30] Two of these studies compared the combined aerobic exercise and PRE intervention with the non-exercising control,[18,25] two studies compared aerobic exercise only with the non-exercising control,[20,23] and one study compared combined aerobic exercise and PRE with metformin, compared with metformin alone.[30] Meta-analysis could not be performed for strength owing to differences in the types of strength outcomes assessed, types of interventions, and types of participants. However, individual studies suggested improvements in strength among exercisers compared with non-exercisers. Rigsby and colleagues found a

Weight and Body Composition	*Psychological*	*Authors' Conclusions*
Body mass index, fat mass, and average body fat percentage: no change among groups (PRE and aerobic and control) in average body fat percentage, fat weight, and body mass index *Weight, lean body mass, and girth*: significant increases in weight, lean body mass, and sum of circumference among aerobic and resistive exercise groups compared with the non-exercising control group	*Mood and life satisfaction*: significant improvements in mood and life satisfaction in the aerobic exercise group compared with non-exercising controls.	Exercise results in improvements in body composition, strength, cardiopulmonary fitness, and mood and life satisfaction for individuals infected with HIV.
NA	*HRQOL*: non-significant trend favouring exercisers compared with non-exercisers. Significant improvement in overall health subscale of the MOS-HIV found among exercisers compared with non-exercisers.	Exercise appears to be safe in individuals infected with HIV.
Cross-sectional muscle area: significant increases in the exercise and metformin group compared with the metformin-only group *Waist-to-hip ratio and abdominal fat area*: significant decreases in the exercise and metformin group compared with the metformin-only group *Weight, body mass index*: no significant change in either group	NA	Exercise training and metformin significantly improve cardiovascular parameters more than metformin alone in persons living with HIV with fat redistribution and hyperinsulinemia. Exercise training (aerobic and PRE) is well-tolerated and improves muscle strength and size as well as aerobic fitness in persons living with HIV.

significant increase in strength as measured by chest press (50.3 nm) and leg press (47.5 nm) for participants in the combined aerobic exercise and PRE group compared with participants in the non-exercising control group.[18] Lox and colleagues showed significantly greater improvements in upper and lower extremity strength as measured by one repetition maximum for participants in the aerobic exercise group (upper extremity: +28.3 lb; lower extremity: +2.0 lb) compared with participants in the non-exercising control group (upper extremity: −14.7 lb; lower extremity: −6.8 lb).[20] Perna and colleagues found that leg power significantly improved by 25% in exercisers who were adherent with the program.[23] Driscoll and colleagues found significant improvements in five of six strength indices in the combined metformin and aerobic exercise and PRE group compared with metformin alone,[30] whereas Grinspoon and colleagues found no significant differences in strength (7/7 variables) for participants in the combined aerobic exercise and PRE group compared with participants in the non-exercising control group.[25] The lack of statistical significance in the latter study was attributed to the use of isometric methods of strength testing versus the alternative isotonic method of testing used in the other studies. Isometric testing is known to underestimate changes in strength.[35]

Weight and Body Composition

Six of the 11 studies assessed weight and/or body composition.[20,23-26,30] Two meta-analyses were performed, one for weight and one for body composition (see Table 3).

Weight. Five studies assessed body weight.[20,24-26,30] Meta-analysis showed no difference in change in body weight for participants in the aerobic exercise group compared with participants in the non-exercising control group (weighted mean difference: 0.37 kg; 95% CI: −5.32, 6.05; p = .90; n = 68) (see Table 3).

Table 3 Results of Meta-Analyses

Outcomes	*Comparisons of Meta-Analysis*	*Individual Studies Included in Meta-Analysis (Study and Year)*	*Number of Participants Included in Meta-Analysis*	*Weighted Mean Difference*	*95% Confidence Interval*	p *Value of Overall Effect*	*Interpretation*
Immunological/virological status							
CD4 count (cells/mm^3)	Continuous or interval aerobic exercise compared with non-exercise	Baigis et al (2002),[28] LaPerriere et al (1990),[16] Lox et al (1995),[20] Perna et al (1999),[23] Smith et al (2001),[26] Stringer et al (1998)[22]	209	24.27 cells/mm^3	−9.52, 58.06	.16	No difference in change in CD4 count among exercisers compared with non-exercisers
	Continuous aerobic exercise compared with non-exercise	Baigis et al (2002),[28] Lox et al (1995),[20] Smith et al (2001),[26] Stringer et al (1998)[22]	164	0.04 cells/mm^3	−33.33, 33.41	1.00	No difference in change in CD4 count among continuous aerobic exercisers compared with non-exercisers
	Interval aerobic exercise compared with non-exercise	LaPerriere et al (1990),[16] Perna et al (1999)[23]	45	69.58 cells/mm^3	14.08, 125.09	.01*	Significant trend demonstrating a potential increase in CD4 count among interval aerobic exercisers compared with non-exercisers
	Moderate-intensity aerobic exercise compared with heavy-intensity exercise	Stringer et al (1998),[22] Terry et al (1999)[24]	39	−42.90 cells/mm^3	−116.28, 30.47	.25	No difference in change in CD4 count among moderate-intensity exercisers compared with heavy-intensity exercisers
	Combined continuous or interval aerobic exercise compared with non-exercise	Grinspoon et al (2000),[25] Rigsby et al (1992)[18]	46	29.18 cells/mm^3	−31.65, 90.01	.35	No difference in change in CD4 count among combined aerobic and PRE compared with non-exercisers
Viral load (log^{10} copies)	Continuous or interval aerobic exercise compared with non-exercise	Smith et al (2001),[26] Stringer et al (1998)[22]	63	0.40 log^{10} copies	−0.28, 1.07	.25	No difference in change in viral load among exercisers compared with non-exercisers
Cardiopulmonary status							
VO_{2max} (mL/kg/min)	Continuous or interval aerobic exercise compared with non-exercise	Baigis et al (2002),[28] Perna et al (1999),[23] Smith et al (2001),[26] Stringer et al (1998)[22]	179	1.64 mL/kg/min	1.06, 2.22	< .00001*	Significant improvement in VO_{2max} among exercisers compared with non-exercisers

	Continuous aerobic exercise compared with non-exercise	Baigis et al (2002),[28] Smith et al (2001),[26] Stringer et al (1998)[22]	151	1.53 mL/kg/min	0.94, 2.12	< .00001*	Significant improvement in VO_{2max} among continuous aerobic exercisers compared with non-exercisers
	Moderate-intensity aerobic exercise compared with heavy-intensity exercise	MacArthur et al (1993),[19] Stringer et al (1998)[22]	24	4.30 mL/kg/min	0.61, 7.98	.02*	Significant trend towards a greater improvement in VO_{2max} among heavy-intensity exercisers compared with moderate-intensity exercisers (trend potentially clinically important)
HR_{max} (beats/min)	Continuous or interval aerobic exercise compared with non-exercise	Lox et al (1995),[20] Perna et al (1999)[23]	49	−9.81 beats/min	−26.28, 6.67	.24	Non-significant improvement in HR_{max} among aerobic exercisers compared with non-exercisers
Weight and body composition							
Weight (kg)	Continuous or interval aerobic exercise compared with non-exercise	Lox et al (1995),[20] Smith et al (2001)[26]	68	0.37 kg	−5.32, 6.05	.90	No difference in change in body weight among aerobic exercisers compared with non-exercisers
Mean body mass index (kg/cm^2)	Continuous or interval aerobic exercise compared with non-exercise	Lox et al (1995),[20] Perna et al (1999)[23]	49	0.85 kg	−0.62, 2.31	.26	Non-significant increase in lean body mass among aerobic exercisers compared with non-exercisers
Psychological status							
Depression-dejection subscale of the POMS	Continuous or interval aerobic exercise compared with non-exercise	LaPerriere et al (1990),[16] Smith et al (2001)[26]	65	−7.68 points	−13.47, −1.90	.009*	Significant improvement in the depressive symptoms as measured by a reduction in the depression-dejection subscale of the POMS among exercisers compared with non-exercisers (potentially clinically important)

HR_{max} = heart rate maximum; POMS = Profile of Mood States; PRE = progressive resistive exercise; VO_{2max} = maximum oxygen consumption.

*Indicates clinical significance, $p < .05$.

Body Composition. Six studies assessed body composition.[20,23-26,30] Meta-analysis showed a non-significant increase in the mean body mass index of 0.85 kg/cm^2 for participants in the aerobic exercise group compared with participants in the non-exercising control group (95% CI: −0.62, 2.31; p = .26; n = 49) (see Table 3). Given that many participants in the individual studies were diagnosed with AIDS-related wasting syndrome, increases in weight and body composition may be interpreted as favourable outcomes.

Psychological Status

Seven of the 11 studies assessed psychological status in the form of anxiety and depression, depression, general health status, mood and life satisfaction, and health-related quality of life.[16,19,20,22,24,26,28] Individual study results showed improvements in anxiety and depression,[16] general health,[19] mood and life satisfaction,[20] and quality of life[22,26] among participants in the aerobic exercise groups. A recent comprehensive narrative review also concluded that exercise might be useful to treat psychological conditions such as depression and anxiety in persons living with HIV.[36]

Profile of Mood States Scale. Meta-analysis was possible for the depression-dejection subscale of the Profile of Mood States (POMS). The results demonstrated a significant improvement in the depression-dejection subscale of the POMS by a reduction of 7.68 points (95% CI: −13.47, −1.90; p = .009; n = 65) for participants in the aerobic exercise intervention group, compared with the non-exercising control group (see Table 3). This represents a potential clinically important improvement in depression-dejection among exercisers compared with non-exercisers.[13]

Adverse Events

Five of the 11 studies reported on adverse outcomes. Meta-analysis was not possible owing to the scarcity and variability of the adverse events reported. Rigsby and colleagues reported one death during the study in the counseling group.[18] Perna and colleagues reported one hospitalization during the course of the study.[23] The three other studies reported no adverse events among participants.[22,25,26]

DISCUSSION

The results of this systematic review should be interpreted cautiously for a number of reasons. With this in mind, we offer the following summary:

Results of meta-analyses showed statistically significant improvements for some outcomes of cardiopulmonary status (maximum oxygen consumption) and psychological status (depression-dejection symptoms) among participants who were exercising compared with non-exercising controls. Cardiopulmonary status results demonstrated significant improvements in VO_{2max} among exercisers compared with non-exercising controls and greater improvements in VO_{2max} among individuals exercising at heavy compared with moderate intensity, which may be clinically important. Psychological status results demonstrated significant improvements in depression-dejection symptoms among exercisers compared with non-exercisers, which also may be clinically important. Weight and body composition results demonstrated non-significant increases in body weight and body mass index among exercisers compared with non-exercisers. No significant differences were found in all but one meta-analysis for outcomes of CD4 count or viral load, suggesting that aerobic exercise has little impact on immunological and/or virological status.

Aside from the meta-analyses, individual studies reported significant results that demonstrated the benefits of aerobic exercise interventions compared with non-exercise. Nine of 10 individual studies that measured cardiopulmonary status demonstrated statistically significant improvements in outcomes among exercisers. Four of the five individual studies that measured strength found significant increases in strength among exercisers. Five of the six studies that measured weight and/or body composition found significant changes among exercisers compared with non-exercisers. Furthermore, the seven individual studies that measured psychological status found significant improvements in outcomes measured for exercisers compared with non-exercisers.

Implications for Practice

This systematic review suggests that aerobic exercise may be an important intervention in the care and treatment of adults living with HIV. Performing continuous or interval aerobic exercise or a combination of continuous aerobic exercise and PRE for at least 24 minutes, three times per week for at least five weeks, may contribute to improvements in selected outcomes of cardiopulmonary and psychological status. The results for other meta-analyses were not significant. Thus, we could not confirm an overall effect. However, these results are based only on participants who completed the exercise interventions and for whom there were adequate follow-up data.

Results of this review also suggest that aerobic exercise appears to be safe among adults living with HIV who are medically stable. This finding is based on the absence of reports of adverse events among exercisers within the individual studies, yet it should be interpreted cautiously because six of the 11 studies did not report on adverse events, leaving the possibility that adverse events occurred but were not documented. Even so, the stability of CD4 count and viral load demonstrated may also contribute to the evidence of the safety of aerobic exercise.

Aerobic exercise interventions may be continuous (exercise at a continuous intensity for a duration of time) or interval (exercise at a varied high and low intensity for a duration of time) in nature. Types of aerobic interventions for persons living with HIV may include (as described in the included studies) a stationary bike, walking, jogging, running, rowing and stair-stepping, a stationary cycle ergometer, or a cross-country and ski machine. Exercise intensity in the included studies ranged between 50 and 85% VO_{2max} or 55 to 85% maximum heart rate, three times per week, for five to 24 weeks. Ultimately, the type of exercise intervention, frequency, duration, intensity, and progression of intensity will depend on the availability of equipment, the ability of the client, and his or her goals. Furthermore, any exercise program should be comprehensive and consist of aerobic exercise and PRE and stretching and/or flexibility components, complete with an adequate warm-up and cool-down. Finally, given the sometimes unpredictable and episodic nature of HIV infection, clients participating in an exercise intervention should be monitored by a physical therapist or other qualified health-care provider for potential changes in their health status, especially those in more advanced stages of immunosuppression, to prevent any potential adverse events of exercise. This may include recommending that persons living with HIV notify their health-care provider if they note a change in their health status, so that any exercise interventions may be modified accordingly.

Participants in this review varied in stage of HIV infection, age, diagnosis of AIDS wasting syndrome, and whether they were taking HAART, thus heightening the external validity of the results. For instance, the results of this review may be relevant to individuals who may or may not be taking HAART, including persons living with HIV in developing countries who might not have access to antiretroviral medications.

Results of this review illustrate the role of aerobic exercise and, more broadly, the role of rehabilitation for persons living with HIV. Persons living with HIV may simultaneously experience a range of impairments, activity limitations, and participation restrictions affecting multiple systems, including the musculoskeletal, neurological, and cardiorespiratory systems, requiring rehabilitation intervention. Thus, rehabilitation professionals working in outpatient, inpatient, rehabilitative, or community care settings have a role to play in working with this population, specifically related to aerobic exercise. Similar to all clients living with lifelong illnesses, aerobic exercise interventions may be designed to prevent the decline of functional ability.[37] Health promotion activities such as exercise and achieving optimal nutrition are two strategies that may be implemented via community programs to prevent a decline in health status while optimizing participation.[38] As a result, aerobic exercise may be applicable to persons living with HIV at any stage of the continuum and may be beneficial to all clients, whether in asymptomatic stages of infection or in palliative stages of care.

Contrary to some misperceptions, rehabilitation professionals require no special training in the field of HIV to work with this population. Assessment and treatment strategies used with this population are no different from those used with other populations. Physical therapists draw on the same tools but apply them in a different context, keeping in mind the multi-systemic, episodic, and unpredictable nature of the infection.[39]

Implications for Education

Despite the increasing role of rehabilitation for persons living with HIV, few physical therapists work with this population. The results of a national survey of physical therapists found that 59% reported that they had never knowingly served persons living with HIV.[40] Furthermore, half of physical therapist survey respondents believed that rehabilitation professionals are uncomfortable with the idea of working with persons living with HIV.[40] This gap clearly demonstrates the need for further education of current and future physical therapists on the role of rehabilitation in the context of HIV.

Despite the fact that education on HIV/AIDS has been gradually increasing in rehabilitation science curricula across Canada, two-thirds of physical therapists reported not receiving HIV training in their rehabilitation degree programs.[40] Thus, there is a need for greater education to increase the knowledge, awareness, and role of physical therapists in the care and treatment of persons living with HIV.

The International Classification of Functioning, Disability and Health[7] is a useful framework for conceptualizing disability and the role of rehabilitation for people living with HIV.[39,41] This framework has been used to guide a range of educational strategies implemented through leadership by the Canadian Working Group on HIV and Rehabilitation, a national, multi-sector working group that promotes innovation and excellence in the area of HIV rehabilitation.[42]

Implications for Research

The literature on aerobic exercise and HIV is gradually increasing, including recent narrative reviews that support the use of aerobic exercise interventions for people living with HIV.[6,36,43] However, the results of this review and, more broadly, the body of evidence pertaining to the safety and effectiveness of aerobic exercise interventions for adults living with HIV should be interpreted cautiously for a number of reasons.

The results of this systematic review are based on a small number of studies ($N = 11$). Meta-analyses were limited owing to variation among individual studies pertaining to the types of interventions and types of outcomes assessed, enabling only two to six studies to be combined in meta-analyses.

Individual studies in this review included small sample sizes and high withdrawal or non-adherence rates, thus reducing the internal validity of the results. Participants who withdrew from the exercise program were often excluded from the final results by the authors, resulting in a per protocol approach to the analysis. This limits the ability for a study to detect the effectiveness of exercise, because the overall findings among those who continued to exercise might not reflect the true experience of exercise among all adults living with HIV. Additionally, publication bias may result in fewer studies with negative results being published. The methodological quality of the studies also varied. Furthermore, the inability to blind participants to the aerobic exercise intervention may have resulted in the Hawthorne effect, whereby participants might perceive greater benefits associated with exercise based on the expectation that the intervention should be linked to positive outcomes. Moreover, the majority of study participants in the individual studies were males between the ages of 18 and 58 years. This limits the external validity and ability to generalize the results to females and other persons living with HIV, such as children, youth, or older adults. Finally, the maximum duration of aerobic exercise intervention within the included studies was 24 weeks. Thus, the long-term sustainable effects of aerobic exercise remain unclear.

As such, further research is needed that uses an intention-to-treat analysis to investigate the effect of aerobic exercise interventions for persons at varying stages of HIV disease, particularly those who are severely immunocompromised. Future research should make attempts to include women, to investigate the long-term effects of exercise, and to develop recommendations pertaining to optimal parameters of frequency, intensity, time, and type of exercise interventions that might be most beneficial to persons living with HIV.

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