Long-term effects of physical exercise on cardiorespiratory fitness among adults living with human immunodeficiency virus: a systematic review and meta-analysis

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ABSTRACT

BACKGROUND: People living with human immunodeficiency virus (HIV) (PLWH) may have lower cardiorespiratory fitness than HIV-negative individuals due to factors such as aging, chronic infection, antiretroviral therapy, and physical inactivity. Exercise can increase maximal oxygen consumption (VO_{2max}). However, the evidence comes from small, heterogeneous studies, making it difficult to determine optimal training parameters.

OBJECTIVES: To evaluate the chronic effects of different structured exercise interventions on VO_{2max} in PLWH.

DESIGN AND SETTING: Systematic review and meta-analysis.

METHODS: Four databases, PubMed, Web of Science, Embase, and LILACS, were searched through May 2025 for randomized controlled trials (RCTs) in PLWH reporting $VO_{2max.}$ We assessed risk of bias using RoB 2 and the certainty of evidence using Grading of Recommendations Assessment, Development and Evaluation. Random-effects meta-analyses with predefined subgroup comparisons were performed.

RESULTS: Nineteen trials (n = 1054) met inclusion criteria; nine RCTs (n = 333) were pooled. Aerobic training increased VO_{2max} by +1.94 $mL \cdot kg^{-1} \cdot min^{-1}$ (95% CI −1.17 to 5.06; I^2 = 0%). Concurrent training improved VO_{2max} by +3.93 $mL \cdot kg^{-1} \cdot min^{-1}$ (95% CI 3.19 to 4.68; I^2 = 0%), with a subgroup difference compared with aerobic training (p = 0.0499). Exercise duration was not associated with changes in VO_{2max} ($\beta = -0.08$; p = 0.76). Mean dropout was 15.2%. Funnel plots, Begg, Egger, and trim-and-fill showed no evidence of publication bias. The certainty of the evidence for VO_{2max} was very low.

CONCLUSION: Exercise interventions lasting ≥ 10 weeks may improve cardiorespiratory fitness in PLWH. Concurrent training may produce greater improvements in VO_{2max} than aerobic training, although the certainty of the evidence is very low due to the small number of studies and methodological limitations.

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INTRODUCTION

The human immunodeficiency virus (HIV), first identified in the 1980s,[1,2] compromises the immune system and increases susceptibility to chronic diseases, including cardiovascular,[3,4] metabolic,[5,6] and musculoskeletal disorders.[7,8] Despite the effectiveness of highly active antiretroviral therapy (HAART) in extending life expectancy, people living with HIV (PLWH) remain at heightened risk of comorbidities due to persistent systemic inflammation and treatment-related adverse drug effects.[6,9,10]

Cardiorespiratory fitness (CRF) is a key health marker that reflects the body's ability to use oxygen efficiently during exercise.[11,12] In PLWH, CRF is frequently impaired regardless of HAART use, contributing to reduced quality of life and increased morbidity.[9,13,14] Maximal oxygen consumption (VO_{2max}), a widely accepted measure of CRF, provides an objective measure of physiological adaptations to exercise.[15,16] While exercise is a promising non-pharmacological strategy to mitigate the adverse effects of HIV and its treatment, optimal training protocols remain undefined.

Current evidence suggests that both aerobic (AT) and resistance (RT), as well as concurrent training (CT), improve CRF. Yet there is no consensus on the most effective modality, intensity, or duration.[17–19] Additionally, high-intensity training (>70% of VO_{2max}) appears to enhance VO_{2max}

gains but may reduce adherence.[20–22] Methodological inconsistencies across studies, such as heterogeneous training protocols, small sample sizes, and high dropout rates, further limit the strength of existing conclusions.[23] Moreover, social stigma and treatment side effects negatively impact adherence to exercise programs, posing additional barriers to implementation.[17,24]

Previous reviews of exercise in PLWH frequently combined short interventions with non-randomized designs.[19,22,25] This heterogeneity limits conclusions on chronic cardiorespiratory responses. Consequently, the evidence on structured exercise and fitness outcomes in this population remains limited.

The distinction between acute and chronic exercise effects is crucial for understanding improvements in CRF.[15,26,27] Acute responses are temporary, involving increased heart rate and oxygen transport, while chronic adaptations, driven by sustained training, lead to structural changes such as increased mitochondrial density and capillary perfusion.[27] These adaptations are particularly relevant for PLWH, as systemic inflammation and the adverse effects of antiretroviral therapy may impair CRF.[9,13,16]

OBJECTIVE

This systematic review and meta-analysis evaluates the chronic effects of different exercise interventions on $VO_{2_{max}}$ in PLWH. By synthesizing the evidence and identifying key moderating factors, this review aims to inform evidence-based recommendations to optimize exercise prescription and improve CRF outcomes in this population.

METHODS

To ensure transparency and rigor, the review was registered in PROSPERO (CRD42022382419). This systematic review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement,[28] and the PERSiST guidelines.[29]

Literature search strategy

The search strategy was developed in collaboration with a librarian specializing in systematic reviews to ensure comprehensiveness and accuracy. Searches were conducted in PubMed, Web of Science, Embase, and LILACS. Medical Subject Headings terms and relevant keywords, including "HIV," "exercise," and "CRF," were combined using Boolean operators. The full search strategy for each database is detailed in **Supplementary Table S1** to ensure transparency and reproducibility.

The search strategy comprised two levels: a primary bibliographic search across the specified databases and a secondary search of the reference lists of shortlisted studies. Structured search terms and filters were applied across four domains: HIV infection, exercise, CRF, and randomized controlled trials (RCTs). After standardizing the search strategy for PubMed, adaptations were made for the other databases. The search was completed in June 2024 and updated in May 2025.

Selection of papers

Title, abstract, and full-text screening were conducted using Covidence®. Studies not meeting the PICO criteria were excluded. The following were deemed ineligible: studies unrelated to HIV and exercise, non-randomized studies, and studies that did not evaluate CRF parameters using VO_{2max} or did not describe the exercise intervention protocol. The number of studies excluded at each stage was documented in a PRISMA flowchart.

Subsequently, we retrieved and assessed the full texts of potentially relevant studies for eligibility. In sum, our inclusion and exclusion criteria were:

1. Population: PLWH or individuals with acquired immunodeficiency syndrome, aged 18 to 59 years, at any stage of infection, with or without antiretroviral therapy, and with or without clinical manifestations of the disease. Studies from all geographic regions were included to ensure global applicability.

2. Intervention: Any form of physical exercise, including AT, resistance or RT, CT, balance exercise, flexibility exercise, and stretching. All exercise modalities were considered eligible regardless of type.

3. Intervention Structure: Structured exercise programs with a minimum frequency of 3 weekly sessions for at least 10 weeks were included to ensure chronic adaptations in CRF, as recommended by international guidelines on physical training in PLWH.[15,27] Studies were excluded if they did not describe essential exercise parameters, including modality, session duration, frequency, intensity, and progression.

4. Comparator: Studies comparing exercise interventions with placebo (sham, no training), different training modalities (e.g., AT vs. CT), or non-exercise interventions (e.g., nutritional or psychological counseling) were eligible.

5. Outcomes: The primary outcome was CRF, measured by VO_{2max} or peak oxygen uptake (VO_{2peak}) pre- and post-training, using direct gas exchange analysis or validated predictive formulas for clinical populations. Secondary outcomes included blood biomarkers (e.g., CD4+ and CD8+ counts, viral load, lipid profile), mental health outcomes, and quality-of-life metrics.

6. Study Design: Only RCTs were included. Observational studies, case reports, case series, and reviews were excluded.

Two independent researchers conducted the selection process. In cases of disagreement, a third independent party resolved the conflict. Studies were excluded from the meta-analysis if VO_{2max} was not reported in a format that permitted direct comparison

across interventions, such as inconsistent units, missing baseline or post-training values, or missing standard deviations. These studies were retained in the systematic review.

Data extraction

Data were extracted using a standardized, pre-validated extraction form that systematically captured baseline characteristics, including study author(s), year of publication, country, study design, and demographic features (e.g., age, sex distribution, HAART treatment, and comorbidities). Dropout and adherence rates were also recorded. If adherence was not directly reported, it was inferred as the proportion of participants who completed the intervention relative to the initial sample.

Additionally, intervention-related data included the type of exercise, training components, intensity, duration, progression, monitoring, supervision, and equipment used. The intensity was classified based on $VO_{2max,}$ VO_{2peak}, maximum heart rate (HR_{max}), heart rate reserve (HR_{res}), resting heart rate (HR_{rest}), or one-repetition maximum (1 RM) and was categorized accordingly. Lastly, data related to the prespecified outcomes were abstracted, including VO_{2max} pre- and post-intervention, assessment protocols, and exploratory outcomes (e.g., changes in body composition, muscular strength, and cardiometabolic parameters). Whenever possible, missing or unclear data were clarified by contacting the corresponding authors.

Risk of bias assessment

The risk of bias in the included RCTs was assessed using Cochrane Collaboration's RoB 2 tool. This assessment covered five key domains: randomization process; deviations from intended interventions; missing outcome data; measurement of the outcome; and selection of the reported result.

Each study was categorized as "low risk of bias," "some concerns," or "high risk of bias." Two independent researchers conducted these assessments, with conflicts resolved by a senior researcher. The impact of identified biases on the overall findings is further discussed in the manuscript.[30,31]

Statistical analysis and certainty of evidence

All meta-analyses were performed using random-effects models with the Restricted Maximum Likelihood estimator and Hartung–Knapp adjustment to derive more accurate confidence intervals, particularly given the small number of studies included. Between-study heterogeneity was quantified using Cochran's Q test, tau², and the I^2 statistic. Subgroup analyses were conducted a priori to explore potential sources of heterogeneity, comparing pooled effects by exercise intervention type (aerobic vs. concurrent) and by the protocol used to assess VO_{2max} (direct vs. submaximal). Statistical differences between subgroups were evaluated using Q-tests for between-group heterogeneity.

Sensitivity analyses were conducted using a leave-one-out approach, in which each study was sequentially removed, and the pooled effect and heterogeneity were recalculated to assess the influence of each study on the overall results. Additionally, two meta-regression models were performed to explore the potential influence of continuous or categorical moderators: one using intervention duration (in weeks) as a continuous predictor, and another using risk of bias classification (categorized as "some concerns" or "high risk") as a moderator.

The certainty of evidence was rated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system, which evaluates methodological robustness across five domains: risk of bias, inconsistency, imprecision, indirectness, and potential publication bias. Publication bias was assessed through visual inspection of funnel plots and formal statistical testing using Begg's rank correlation test. For meta-analyses with at least four studies, the trim-and-fill method was applied to estimate the potential impact of small-study effects and to adjust the pooled estimates accordingly. All statistical analyses were conducted using the "meta" and "metafor" packages in RStudio (version 4.4.1).

RESULTS

Overall findings

Nineteen studies met the inclusion criteria and were included to assess the chronic effects of exercise on CRF in PLWH. **Figure 1** illustrates the PRISMA-based study selection process.[32–50] From 15,222 initial records, 5,888 duplicates were removed. After screening 9,334 studies, 9,302 were excluded based on eligibility criteria. Thirty-three studies were selected for full-text review, and 13 were excluded due to the wrong population ($n = 6$), inappropriate study design ($n = 6$), or insufficient intervention duration ($n = 1$).

Table 1 summarizes the characteristics of the included studies. Most studies were conducted in the United States ($n = 9$)[31–34,37,38,42,44,50] and Brazil ($n = 7$),[36,41,43,45,46,48,49] while Rwanda,[47] Mozambique,[39] Ireland,[40] and Italy[35] each had one study. The sample included 1054 participants, with a mean age ranging from 32 to 52 years. Twelve studies[32,36–39,42–44,46–48,50] reported sex distribution at baseline ($n = 546$), with 53.3% male. Seven studies[33–35,40,41,45,49] reported sex after the intervention ($n = 293$), with 54.9% male. One trial[33] included only men as participants, and two included only women.[38,39]

Adherence reporting was heterogeneous. Some trials quantified adherence as the percentage of exercise sessions completed, whereas others defined it based on the number of participants who

completed the study. The mean dropout rate was 15.2% (range 0–76%). Reported reasons for discontinuation included HIV-related complications, logistical barriers, socio-economic factors, and motivational challenges, which were the most frequently cited obstacles to sustained participation.

Seven studies[33,34,39,41,44,46,49] did not specify antiretroviral medication use. Among those who did, nucleoside reverse transcriptase inhibitors and protease inhibitors were the most frequently reported, and one study[40] did not report whether antivirals were used. Nine studies[32,33,37,41,45,48,49] documented HIV-associated comorbidities, including lipodystrophy,[42,44,49,50] hypertension,[47,48,49] metabolic syndrome,[37,47,50] dyslipidemia,[43,45,48] and diabetes,[45,48,49] while others did not report comorbidities.[34–36,38–40,46]

Intervention characteristics are summarized in **Table 2**. AT was implemented in eight studies (n = 126)[32–35,39,40,42,43] and CT in ten RCTs (n = 284).[36–39,41,44–50] One trial[33] evaluated the isolated effect of RT (n = 12), and another evaluated stretching[43] (n = 15). The mean intervention duration was 16 weeks (range

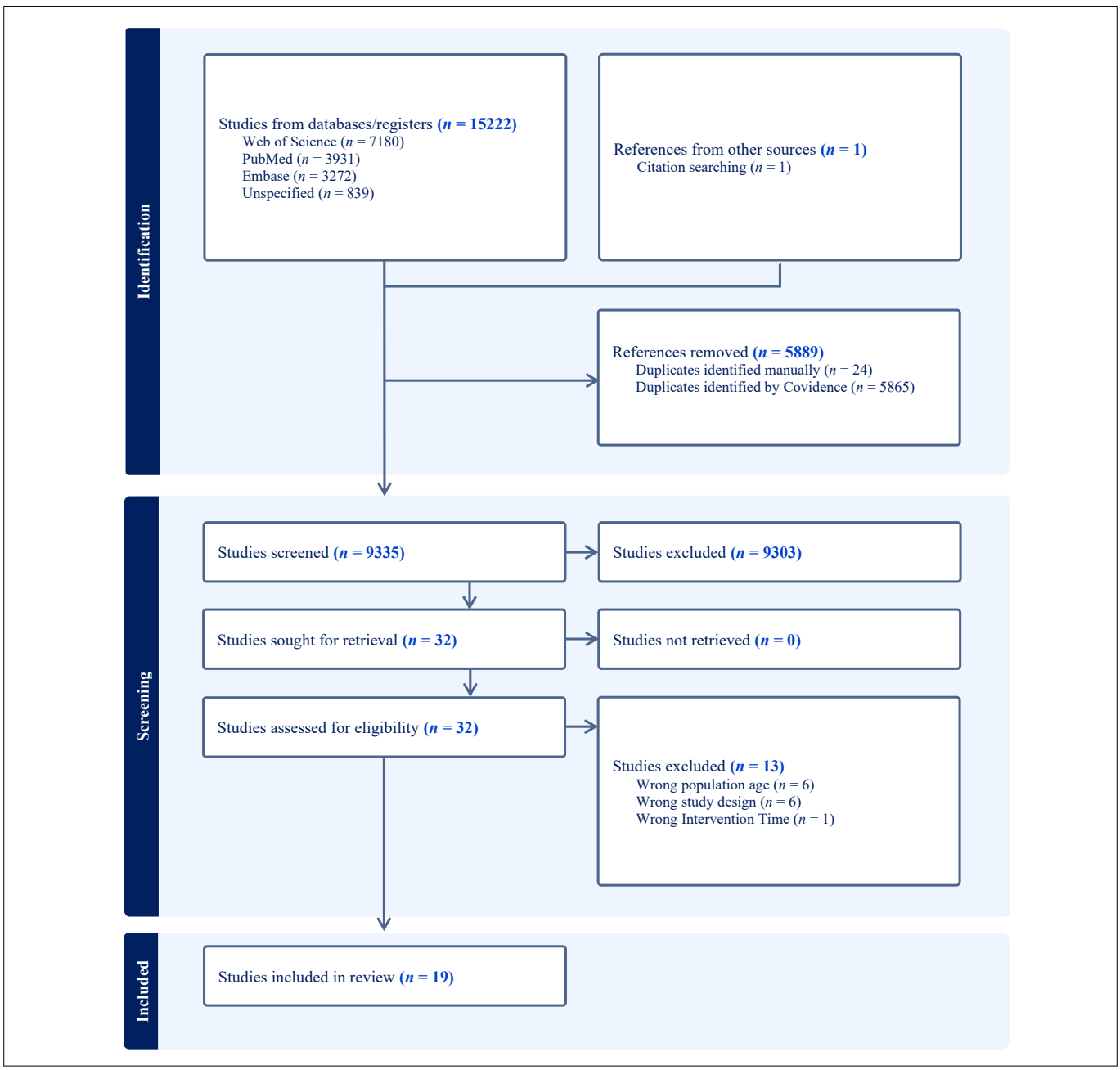


Figure 1. PRISMA 2020 flow diagram illustrating the identification, screening, and inclusion of randomized controlled trials on the effects of physical exercise on cardiorespiratory capacity in adults living with HIV.

Table 1. Characterization of studies that evaluated the chronic effects of physical exercise on CRF in adults living with HIV. Information on country, study design, mean age, HAART used, adverse effects, and age

Author (year)	Country	Groups	Mean age (years ± SD)	Initial sample size (male | female)	Final sample size (male | female)	Drop-out rate (%)	Adherence reported (%)	HAART (% of participants)	HIV-associated comorbidities (% of participants)
Aerobic training (AT); Resistance training (RT); Stretching training (ST)									
MacArthur et al., 1993a	USA	AT high intensity	38.8 ± 4.8	25 (24 | 1)	3	19	12% of participants completed at least 80% of the training sessions	Zidovudine (NR)	AIDS, ARC (36%)
		AT low intensity	38.8 ± 4.8	25 (24 | 1)	3	19			
		Partial adherence	32 ± 11.1		7				
		Low adherence	35.5 ± 11.9		12				
Lox et al., 1996 b	USA	AT	36.45 (Range: 25–58)	12	11 (33 | 0)	1/11 (8%)	2.62 sessions per week in all sessions	Unspecified (100%)	AIDS (58%)
		RT		12	12 (33 | 0)	12/12 (0%)			
		NE		10	10 (33 | 0)	10/10 (0%)			
Perna et al., 1999	USA	AT	36.75 ± 6.27	23	18 (18 | 10)	6/23 (26%)	61% of participants completed at least 50% of the training sessions	Unspecified (100%)	NR
		NE		20	10 (18 | 10)	9/20 (47.4%)			
Smith et al., 2001	USA	AT	36.6 ± 6.2	30 (52 | 8)	19	11/30 (37%)	27/36 sessions were completed	PI (23%)	NR
		NE	35.4 ± 7	30 (52 | 8)	30	30/30 (0%)			
Terry et al., 2006	Brazil	AT	36 ± 5	22 (26 | 16)	15	7/22 (32%)	36/36 sessions were completed (100%)	PI (93%); NNRTI (7%)	Dyslipidemia, Lipodystrophy (100%)
		ST	39 ± 7	20 (26 | 16)	15	5/20 (25%)			
McDermott et al., 2017	Ireland	AT	43 ± 4	6	5 (8 | 3)	1/6 (14%)	Supervised sessions (56%); Unsupervised sessions (68%)	Not Reported	NR
		NE	44 ± 11	7	6 (8 | 3)	1/7 (13%)			
Bonato et al., 2020 c	Italy	AT mobile application	52 (Range: 43–56)	20	18 (28 | 6)	2/20 (10%)	Supervised session (100%); Unsupervised session (60%)	2NRTI + PI (39%); 2NRTI + NNRTI (33%); Other (27%)	NR
		AT No. mobile application	50 (Range: 45–52)	18	16 (28 | 6)	2/18 (11%)	Supervised session (100%); Unsupervised session (54%)	2NRTI + PI (44%); 2NRTI + NNRTI (31%); Other (25%)	

It continues...

Table 1. Continuation.

Author (year)	Country	Groups	Mean age (years ± SD)	Initial sample size (male | female)	Final sample size (male | female)	Drop-out rate (%)	Adherence reported (%)	HAART (% of participants)	HIV-associated comorbidities (% of participants)
Concurrent training (CT)									
Cade et al., 2003	USA	CT	41 ± 6	12 (21 | 3)	8	4/12 (25%)	43/52 sessions	NRTI; PI; NNRTI	Metabolic complications (100%)
		NE	42 ± 7	12 (21 | 3)	12	0/12			
Dolan et al., 2006	USA	CT	43 ± 2	40 (0 | 40)	19	1/20 (5%)	45/48 sessions were completed	NRTI (25%); PI (55%); NNRTI (30%)	NR
		NE	40 ± 2	40 (0 | 40)	19	1/20 (5%)		NRTI (60%); PI (50%); NNRTI (40%)	
Mutimura et al., 2008	Rwanda	CT lipodystrophy	37.8 ± 5.5	50 (20 | 30)	48	2/50 (4%)	82% of participants completed at least 50% of the training sessions	NRTI; NNRTI (100%)	Redistribution of body fat (100%)
		NE lipodystrophy	37.5 ± 6.9	50 (20 | 30)	49	1/50 (2%)			
		NE non-lipodystrophy	NR	50	47	3/50 (6%)			
		NE non-HIV	NR	50	43	7/50 (14%)			
Ogalha et al., 2011	Brazil	CT	42.06 ± 7.45	35	35 (34 | 29)	0/35 (0%)	60% of participants completed at least one of the training sessions	Unspecified (100%)	Lipodystrophy (54%); Diabetes (14%); Hypertension (13%)
		NE	44.25 ± 11.45	35	28 (34 | 29)	7/35 (20%)			
Fitch et al., 2012	USA	CT placebo	49 ± 2	11 (8 | 3)	8	3/11 (27%)	121/144 sessions were completed	PI (56%); NRTI (86%); NNRTI (22%)	Metabolic Syndrome (100%); Coronary artery calcification (51%)
		CT metformin	47 ± 2	15 (13 | 2)	9	6/15 (40%)			
		NE placebo	47 ± 2	11 (7 | 4)	9	2/11 (18%)			
		NE metformin	45 ± 2	13 (10 | 3)	10	3/10 (23%)			
Mendes et al., 2013	Brazil	CT lipodystrophy	39.7 ± 9.3 (Male); 38.8 ± 11.6 (Female)	24	NR (29 | 51)	13/45 (29%)	Participants completed at least 70% of the training sessions	Unspecified (100%)	Lipodystrophy (45%)
		CT no lipodystrophy		21	NR (29 | 51)				
		NE lipodystrophy		27	NR (29 | 51)	6/54 (11%)			
		NE		27	NR (29 | 51)				

It continues...

Table 1. Continuation.

Author (year)	Country	Groups	Mean age (years ± SD)	Initial sample size (male | female)	Final sample size (male | female)	Drop-out rate (%)	Adherence reported (%)	HAART (% of participants)	HIV-associated comorbidities (% of participants)
Tiozzo et al., 2013	USA	CT	43.2 ± 9.5	18 (7 | 5)	12	6/18 (33%)	29/36 sessions were completed	Unspecified (100%)	NR
		NE	47.8 ± 4.5	19 (7 | 4)	11	8/19 (42%)			
Mangona et al., 2015	Mozambique	CT	39.5 ± 8.4 for all groups	20 (0 | 55)	19	1/20 (5%)	33/36 sessions were completed	Unspecified (100%)	NR
		AT		19 (0 | 55)	18	1/19 (5%)	31/36 sessions were completed		
		NE		16 (0 | 55)	16	0/16 (0%)			
Pedro et al., 2016 d	Brazil	CT	43.1 ± 7.2	25 (22 | 21)	20	5/25 (20%)	66% of participants in the exercise group and 72% in the control group completed the intervention (adherence not directly reported)	NRTI (100%); NNRTI (53%); PI (59%); INT (9%)	Dyslipidemia (CT, 32% | NE, 22%); Diabetes type-2 (8% | 6%); Hypertension (8% | 6%); Hepatitis C (24% | 11%); Hepatitis A (4% | 11%); Hepatitis B: (8 | 17%); Lupus: (4% | 6%)
		Physical Activity	45.8 ± 7.9	18 (22 | 21)	12	6/18 (33%)		NRTI (94%); NNRTI (47%); PI (58%); INT (0%)	
Zanetti et al., 2020	Brazil	CT Placebo	44.8 ± 10.7	20	18 (10 | 8)	2/20 (10%)	33/36 sessions were completed for exercise groups	NRTI (87%); NNRTI (87%); INT (80%); PI (7%)	Dyslipidemia (100%); Hypertension (22%); Diabetes (24%)
		CT Statin	43 ± 9.8	20	18 (10 | 8)	2/20 (10%)			
		NE Placebo	39.9 ± 10.1	21	18 (9 | 9)	3/21 (14%)			
		NE Statin	40 ± 10.8	21	18 (10 | 8)	3/21 (14%)			
Oliveira et al., 2020	Brazil	CT	45.5 ± 7.2 for all groups	25 (11 | 14)	14	11/25 (44%)	40/48 sessions were completed	NRTI + PI (28%); NRTI + NNRTI (26%)	NR
		NE		21 (10 | 11)	9	12/21 (57%)			
Santos et al., 2021e	Brazil	CT	32.6 ± 9.08	38 (33 | 5)	19	NR	Not Reported	Unspecified (100%)	NR
		NE			19	NR			

HAART, Highly Active Antiretroviral Therapy; HIV, Human Immunodeficiency Virus; AT, Aerobic Training; AIDS, Acquired Immunodeficiency Syndrome; ARC, AIDS-Related Complex; RT, Resistance Training; NE, Non-Exercise; NR, Not Reported; PI, Protease Inhibitor; ST, Stretching Training; NNRTI, Non-Nucleoside Reverse Transcriptase Inhibitor; NRTIs, Nucleoside Reverse Transcriptase Inhibitors; CT, Concurrent Training; INT, Integrase Inhibitor. [a] The author did not specify the initial number of participants in each subgroup (high- and low-intensity). The control group was not initially randomized but was formed by participants who discontinued the intervention (*n* = 19), with 12 classified as "low adherence" (drop-out before 12 weeks) and 7 as "partial adherence" (drop-out after 12 weeks). The weighted mean age was calculated across the high- and low-adherence groups and the two intervention groups that completed the study. The combined standard deviation was adjusted according to the total degrees of freedom. [b] This study compares aerobic training with resistance training and stretching training (group exercise used for a control group). [c] The values are expressed either as the number of participants (%) or as the median (Q1-Q3). [d] This study reported gender at an intermediate stage, after 15 participants dropped out, leaving 43 individuals (22 men and 21 women). At the end, 33 participants remained, and the gender was not reported. [e] For studies that did not report adherence directly, adherence was inferred as the proportion of participants who completed the intervention relative to the initial group size. This approach was used to standardize the data and ensure comparability.

Table 2. Characteristics of training and components of interventions performed by adults living with HIV

Author (Year)	Group | Type exercise | Equipment	Duration (Description of sessions in min)	Intensity	Progression and monitoring	Intervention time (Weeks) | Supervision (%)
Aerobic Training and Resistance Training					
McArthur et al., 1993	AT: Walking or jogging | Stationary bicycling (Schwinn air-dyne); Rowing (Concept II); Stair-stepping (Stairmaster 4000 PT)	60 min	High-Intensity Group: 6 sets with 4 min intervals at 75–85% VO_{2max} Low-Intensity Group: 4 sets with 10 min intervals at 50–60% VO_{2max}	Progressive increase in caloric expenditure (250 kcal/session in the first 8 weeks, 350 kcal/session in the next 8 weeks, 450–500 kcal/session in the final 8 weeks)	24 | 100%
Lox et al., 1996	AT: Cycling; Stretching; Flexibility | Ergometric bicycle lifecycle 9500	45 min (5 min of stretching + 24 min of AT + 15 min of stretching)	50–80% HRrest	Monitored with a favor HR monitor, Polar CIC, and using the Karvonen Formula for progression	12 | 100%
	RT: Hamstring curls; Extension of lower limbs; Leg press; Bench press; Lateral pull; Lateral bench press; Barbell curl; Triceps extension; Stretching; Flexibility | Weight isotonic equipment	45 min (5 min of stretching + 24 min of RT + 15 min of stretching)	Three sets of 10 repetitions at 60% of 1 RM	Progressive increments to RT of 5–10 pounds after successful completion of three sets of 10 reps	
Perna et al., 1999	AT: Interval cycling | Ergoline 800 electronically braked cycle ergometer	65 min (10 min of stretching + 45 min of AT + 10 min of stretching)	9 cycles alternating 3 min at 70–80% HR_{max}, 2 min recovery	HR monitoring with Polar Vantage XL	12 | 100%
Smith et al., 2001	AT: Walking; Jogging; running | Ran stationary cycle; Stair stepper; Cross-country machine	50 min (20 min of WP + 30 min of AT)	60–80% VO_{2max} based on graded exercise test	Progression based on HR monitoring with Polar Vantage XL, increasing every 3–4 weeks	12 | 100%
Terry et al., 2006	AT: Continuous running | Treadmill Imbramed KT 4000	60 min (15 min of stretching + 30 min of AT + 15 min of stretching)	70–85% HR_{max}, increased every 3–4 weeks	Progression based on HR_{max} from baseline maximal exercise test with HR watch, Cardiosport Heartsafe-T	12 | 100%
	ST: Soft stretching and relaxation	45 min			
McDermott et al., 2016	AT Supervised: Aerobic circuit; | Ergometric bicycle; Cross trainer; Treadmill; Polar T31; Polar electro oy	31–52 min (5 min of WP + 21–42 min of AT + 5 min of CD)	40–60% HRres, 21–24 min (weeks 1–4); 45–65% HRres, 26–30 min (weeks 3–4); 50–70% HRres; 30–42 min (weeks 5–8); 55–75% HRres; 42 min (weeks 9–16)	HR monitored with one Polar T31, and Borg scale used to monitor intensity and progression of training during unsupervised sessions	18 | 63% supervised
	AT Unsupervised: Running; Brisk walking; Cycling | Exercises diary				
Bonato et al., 2020	AT: Light running; Brisk walking using a smartphone app or printed program | Outdoor sessions with Polar Electro 2011	49–58 min (5 min of WP, 50 min of AT, + 5 min of CD)	Supervised: 60–70% HR_{max} (weeks 1–4), 70–80% HR_{max} (weeks 5–16). Unsupervised: 70–80% HR_{max} (weeks 5–16)	HR monitored with Polar FT4 in the first 4 weeks. Borg CR-10 scale used for perceived exertion (especially for participants on beta-blockers) in all programs	16 | Supervised (weeks 1–4); Unsupervised (weeks 5–16)

It continues...

Table 2. Continuation.

Author (Year)	Group | Type exercise | Equipment	Duration (Description of sessions in min)	Intensity	Progression and monitoring	Intervention time (Weeks) | Supervision (%)
Concurrent Training (Aerobic + Resistance)					
Cade et al., 2003	AT: Walking/jogging; | Stationary cycling; Treadmill; Stair-stepper climbing; Elliptical	90–120 min (AT + RT)	50–85% HRres (moderate to high intensity), based on percentage of predicted HR_{max}	HR was monitored continuously with a Polar monitor (Polar, Lake Success, NY). The audible alarm is outside the target zone; data were stored and reviewed daily. Trainers increased aerobic intensity progressively	16 | 100%
	RT: Four upper and three lower body exercises (not described) | Gym machines		Load inducing failure at ~8 reps (progressed when 12 reps completed)	1 RM measured in first 3–4 sessions; weight increased 10% whenever participant reached 12 reps with ease. Progressive 8–12 reps cycle maintained. Training was individualized based on initial fitness level	
Dolan et al., 2006	AT: Cycling | Stationary bicycle; Polar A1 heart monitor	120 min (5 min of WP + 20–30 min of AT + 60–95 min of RT + 5 min of stretching)	20 min at 60% HR_{max} (weeks 1–2); 30 min at 75% HR_{max} (weeks 3–16)	HR was monitored via Polar A1, and perceived exertion via the Borg scale was assessed by a study staff member at baseline, 10, 20, and 30 min, and after 5 min of recovery	16 | 100%
	RT: Knee extension; Bench press; Knee flexion; Shoulder abduction; Standing calf raises; Arm curls | Flexion-extension bench; Free-standing Squat stand; Weight sets; Resistance bands		Three sets of 10 repetitions of 60% of 1 RM (weeks 1–2); 3 sets of 10 repetitions of 70% of 1 RM (weeks 3–4); Four sets of 8 repetitions of 80% of 1 RM (weeks 5–16)	1 RM test every 2 weeks for progressive resistance	
Mutimura et al., 2008	AT: Jogging; Running; Stair climbing	90 min (15 min of stretching + 45–60 min of AT + 15 min of stretching)	45% of HR_{max} (weeks 1–3); 60% of HR_{max} (weeks 3–6); 75% of HR_{max} (weeks 6–24)	HR monitored weekly for all participants; Borg Rating of Perceived Exertion Scale was used for perceived effort (moderate-to-high intensity)	24 | 100%
	RT: Low back Abdominal stabilization; Strengthening exercises (calisthenics), stretching; Brisk walking		Not Specified	Not Specified	
Ogalha et al., 2011	AT: Brisk walking; Jogging; Running; Stair climbing	60 min	60–65% of HR_{max} (weeks 1–4), to 75% of HR_{max} (weeks 4–24)	HR monitored via physiological indicators such as oxygen consumption, ventilatory, lactate thresholds, and Borg scale	24 | 100%
	RT: Low back; abdominal stabilization; Strengthening exercises (Calisthenics); Stretching	Not Specified	Not Specified	Not Specified	

It continues...

Table 2. Continuation.

Author (Year)	Group | Type exercise | Equipment	Duration (Description of sessions in min)	Intensity	Progression and monitoring	Intervention time (Weeks) | Supervision (%)
Fitch et al., 2012	AT: Cycling | Cycle ergometer; Stationary Bicycle	50–60 min (10 min of WP + 20–30 min of AT + 20 min of RT)	60% of HR_{max} (weeks 0–2); 65% of HR_{max} (weeks 3–36)	Borg rate of perceived exertion scale, HR monitors	36 | 100%
	RT: Leg press; Chest press; Knee extension; Lateral pull-down; Knee flexion; Triceps dip | Free weight		Three sets of 10 reps at 60% of 1 RM (weeks 1–2); 80% of 1 RM (weeks 3–36)	1 RM measurements for baseline, 9, and 12 months	
Mendes et al., 2013	AT: Stationary treadmill; Cycle ergometer	75–80 min (10 min WP + 15–20 min of AT + 40 min of RT + 10 min CD)	50–80% of HRres	HRres calculated by the Karvonen formula and monitored continuously during exercise	24 | 100%
	RT: Squat; bench press; Hamstring extension; Back pulley; Knee flexion; calf press | Free weights and gym machines		Three sets of 8–10 reps at 80% of 1 RM	Resistance loads adjusted based on a 12-week strength test for recalibration of loads	
Tiozzo et al., 2013	AT: Running; Cycling | Stationary treadmill; Cycle ergometer	45–60 min. 0–2 weeks (5–45 min of AT + 5–10 min of core training + 20–45 min of RT); 3–6 weeks (5–50 min of AT + 5–10 min of core training + 25–50 min of RT); 7–12 weeks (5–50 min of AT + 5–10 min of core training + 25–50 min of RT)	60% of HR_{max} (weeks 0–2); 65% of HR_{max} (weeks 3–6); 70% of HR_{max} (weeks 7–9); 75% of HR_{max} (weeks 10–12)	HR was monitored during sessions with Polar FT2 devices	12 | 100%
	RT: Leg press; Leg extension; Leg curl; Chest press; Lat pull; Shoulder press; Seated row; Triceps press; Biceps curl; Chest fly. Core training; Back extension; Abdominal crunches | Lifestyle fitness 95T		60% of 1 RM (weeks 0–2); 65% of 1 RM (weeks 3–6); 70% of 1 RM (weeks 7–9); 75% of 1 RM (weeks 10–12)	1 RM tests performed at baseline with load progression supervised by researchers	
Mangona et al., 2015†	CT: Cycling; Horizontal bench press; horizontal row; Arm flexion; Arm extension; Squat; Curl-up | Monark stationary bike	60 min (15 min of WP + 40 min of CT + 5 min of CD)	60% of VO_{2peak} (weeks 1–4); 75% of VO_{2peak} (weeks 5–8); 80–85% of VO_{2peak} (weeks 8–12)	HR monitored with Polar FS1 Model; Borg scale used to adjust intensity. Repetition and weights adjusted for weight training every 4 weeks	13 | 100%
	AT: Dancing; Skipping and Pre-sports Games | Balls; Baskets; Flags; Cans; Bottles with Sand; Buckets; Ribbons	60 min (15 min of WP + 40 min of AT + 5 min of CD)	Not Specified	Intensity progression monitored through Borg scale	
Pedro et al., 2016	AT: Running | Stationary treadmill	60 min (15–20 min of AT + 20–40 min of RT)	50-60% HRrest (weeks 1–4); 60-65% HRrest (weeks 5–12); 65-70% HRrest (weeks 13–16)	Intensity adjustments, these, were made in the 8th week to ensure that the load remained progressive and adequate	16 | 100%
	RT: Bench Press; Leg press; Lat pulldown; Leg curl; Biceps curl; Sit-up; Low row; Squat hack | Free and machines weights		Two sets of 10–12 RM (weeks 1–4); three sets of 10–12 RM (weeks 5–12); three sets of 8–10 RM (weeks 13–16)	If the participant managed to exceed the prescribed number of repetitions in the last set, the load was increased.	
	Physical activity: Walking; Dancing; Stretching	60 min (once or twice a week optionally)			

It continues...

Table 2. Continuation.

Author (Year)	Group | Type exercise | Equipment	Duration (Description of sessions in min)	Intensity	Progression and monitoring	Intervention time (Weeks) | Supervision (%)
Zanetti et al., 2020	AT: Running | Stationary treadmill	40–65 min (10–25 min of AT + 30–40 min of RT)	One session per week (7 sets of 30 s at 85–90% of training heart rate, and 1 min of passive recovery); 2nd session (6 sets of 2 min at 70% of training HR, and 1 min of recovery at 50% of training heart rate); 3° session (25 min at 60% of training HR)	Adjusted based on the initial Bruce protocol. Use of HR monitors during sessions to ensure participants remain in target training zone	12 | 100%
	RT: Squats, Bench press; Hamstring curls; Frontal pull; Seated calf raises; Shoulder press | free weights and machines		One session per week (3 sets of 4–6 RM with a 180 s rest interval); 2nd session (3 sets of 15–20 RM with a 45 s rest interval); 3° session (3 sets of 8–12 RM with a 90 s rest interval)	Progression is based on RM tests, with load adjustments according to the participant's performance. Load increase of 1 kg for lower limbs and 0.5 kg for upper limbs for each extra repetition performed	
Oliveira et al., 2020	AT: Running | Stationary treadmill	50–70 min	50–60% HR_{max} (weeks 1–4) 50–60% HR_{max} (weeks 1–4) 20 min at 50–60% (weeks 5–8) 20 min at 60–65% HR_{max} (weeks 9–16)	Controlled using HRres, starting with continuous walking and progressing to jogging to maintain cardiovascular intensity	16 | 100%
	RT: Bench press; Leg press; Pulldown; leg curl; Arm curl; Sit-up | Free and Machines weights		Two sets at 12–15 RM (weeks 1–4) Three sets at 8–12 RM (weeks 5–12) Three sets at 10 RM (weeks 13–16)	Progressive training with exercises targeting major muscle groups. Load adjusted weekly using RM tests for strength.	
Santos et al., 2021	AT: Indoor or Outdoor running exercises; Bleachers; Stairs	60 min (30 min of AT + 25–30 min of RT)	70%–85% HR_{max}	Perceived effort was monitored using the OMNI Subjective Effort Scale. HR monitors were used for self-reported exertion and HR tracking	24 | When carried out in the clinic, training sessions were supervised; For training sessions in public places or at home, supervision was done remotely, via SMS
	RT: Knee extension/flexion; Ankle dorsiflexion; Shoulder flexion; Horizontal flexion shoulder; Scapular adduction/abduction; Inferior scapular rotation; Ulnar extension/flexion; Forward flexion of the trunk | Open-air gym equipment; bleachers; stairs; elastic bands		Training subjects, three sets of 10 reps at 70%–80% of 1 RM; Beginner Subjects, one set of 10 reps at 60%–70% of 1 RM		

VO_{2max}, Maximum oxygen consumption; AT, Aerobic training; RT, Resistance training; HR, heart rate; HRrest, Resting heart rate; RM, Maximum repetition; HR_{max}, Maximum heart rate; WP, Warm-up; ST, Stretching training; CD, Cool-down; HRres, Heart rate reserve; VO_{2peak}, Highest achieved oxygen consumption.

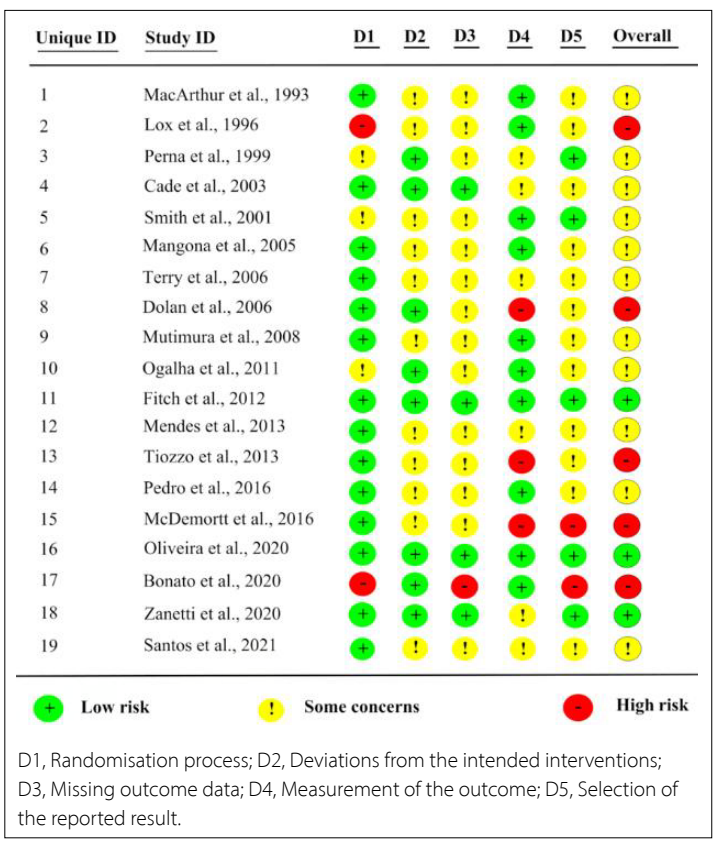
12–52), with three sessions per week and an average session duration of 55 min (range 40–120). Exercise intensity was described using VO_{2max} (50–85%), HR_{max} (70–85%), HR_{res} (40–75%), HR_{rest} (50–80%), and 1 RM (60%). Equipment included stationary ergometers, free weights, and gym machines, with some interventions incorporating outdoor activities.

Bias analysis

Figure 2 presents the RoB-2 assessment. Overall, 57.9% of trials were rated as "some concerns," 26.3% as "high risk," and 15.8% as "low risk." The most frequent concerns were deviations from intended interventions and selective reporting (68.4%). Randomization was adequate in most studies (63.2% low risk). Outcome measurement was the weakest domain, with 15.8% rated high risk.

Primary outcome: VO_{2max}

Table 3 summarizes the main findings related to pre- and post-intervention VO_{2max}. **Figure 3** presents the meta-analyses comparing AT vs. Control[34,39,40,42] and CT vs. Control[34,38–40,42,44,48,49] interventions for improving VO_{2max} in PLWH. Nine RCTs[34,38–40,42,44,45,48,49] were included, totaling 333 participants in the quantitative synthesis. Nine studies[32,34,35–37,41,43,46,47] were excluded from the meta-analysis due to inconsistent data, including incomplete control-group data,[32] incomplete VO_{2max} data,[33,35,45] comparisons only with other exercise groups,[43] reporting only changes in VO_{2max},[37,45,47] and absence of pre- and post-intervention data for the control group.[36,41,46]



D1, Randomisation process; D2, Deviations from the intended interventions; D3, Missing outcome data; D4, Measurement of the outcome; D5, Selection of the reported result.

Figure 2. Risk of bias assessment with the Cochrane RoB-2 tool.

AT × Control

Four studies (n = 117) were included,[34,39,40,42] with 54 participants in the AT group. Using a random-effects model, the meta-analysis showed that AT improved VO_{2max} by +1.94 $mL \cdot kg^{-1} \cdot min^{-1}$ (95% CI: −1.17 to 5.06; Qp = 0.14). Heterogeneity was low (I^2 = 0%; p = 0.83), indicating no evidence of between-study heterogeneity. The confidence interval crossing zero suggests that the effect did not reach statistical significance.

CT × Control

Five studies (n = 216)[38,39,48,49] were included, with 109 participants in the CT group. CT increased VO_{2max} by +3.93 $mL \cdot kg^{-1} \cdot min^{-1}$ (95% CI: 3.19 to 4.68; p = 0.0001). Heterogeneity was low (I^2 = 0%; Qp = 0.85), indicating no evidence of between-study heterogeneity. We applied a random-effects model (with Hartung–Knapp adjustment) to account for between-study variation. The absence of observed heterogeneity suggests that the effect estimates were similar across the included studies.

Subgroup analysis

Subgroup analysis revealed differences in training response by intervention type. AT was associated with a mean difference of +1.94 $mL \cdot kg^{-1} \cdot min^{-1}$ (95% CI: −1.17 to 5.06; I^2 = 0%). CT increased VO_{2max} by +3.93 $mL \cdot kg^{-1} \cdot min^{-1}$ (95% CI: 3.19 to 4.68; I^2 = 0%; p < 0.001). A test for subgroup differences (random-effects model) indicated that CT was associated with greater improvements than AT (p = 0.0499). The meta-regression analysis using intervention duration (in weeks) as a moderator showed no association with changes in $VO_{2max.}$ The regression coefficient was β = −0.0787 (95% CI: −0.59 to 0.43; p = 0.7617; I^2 = 0%).

Sensitivity analysis

A leave-one-out sensitivity analysis was performed to ensure the robustness of the meta-analysis findings. Excluding individual trials did not alter the direction or magnitude of effects. For instance, removing the largest CT study[38] reduced the pooled effect from +3.93 to +3.42 $mL \cdot kg^{-1} \cdot min^{-1}$, with heterogeneity unchanged.

Publication bias assessment

Funnel plots showed no evidence of asymmetry. Begg's test (AT: Kendall's τ = 0.333, p = 0.75; CT: τ = −0.400, p = 0.48). Egger's regression tests (p = 0.34 for AT; p = 0.42 for CT) and

Table 3. Maximal oxygen consumption values at baseline and post-intervention

Author (year)	Groups	VO_{2max} – baseline	VO_{2max} post-intervention	Outcome unit	Mean differences	Mean differences %	p value	Protocol used for measuring VO_{2max}	Description of protocol
Aerobic Training (AT); Resistance Training (RT)									
MacArthur et al., 1993	AT High intensity	35 ± 1.8	45.1 ± 3.2	VO_{2max} – mL·kg−1·min−1	b10.1 ± 1.9	b28.86	p < 0.05	Treadmill incremental protocol with direct gas exchange	Conducted on a Quinton Q-55 treadmill, with a 2-MET increment per stage until exhaustion. Gas collection was performed for ventilation analysis. Ventilation and gas exchange were measured directly. The Borg Scale was used to assess perceived exertion
	AT Low intensity	31.4 ± 3.9	37.2 ± 2		b5.8 ± 4	b18.47	p < 0.05		
	Partial adherence	29.8 ± 10	NR		NR	NR	NR		
	Low adherence	29.7 ± 8.3	NR		NR	NR	NR		
Lox et al., 1996	AT	2.31 ± 0.98	3.47 ± 1.23	Predicted VO_{2max} – l/min	1.16 ± b1.2	b49.35	NR	Astrand-Ryhming submaximal test on a cycle ergometer	HR monitoring during the test and perceived exertion were assessed using the Borg Scale. VO_{2max} was estimated indirectly based on the relationship between submaximal heart rate and applied workload
	RT	1.7 ± 0.59	1.89 ± 0.78		0.19 ± b0.9	b11.18	NR		
	NE	1.73 ± 0.92	1.65 ± 1.19		−0.08 ± b1.1	b−4.62	NR		
Perna et al., 1999	AT	28.7 ± 7.5	32.2 ± 7.3	VO_{2max} – mL·kg−1·min−1	b3.5 ± 7.5	b12.2	NR	Incremental test on SensorMedics 800 cycle ergometer	The test was performed using a SensorMedics (Yorba Linda, CA) Ergoline 800 electronically braked cycle ergometer, a SensorMedics 2900c metabolic cart, and a SensorMedics Marquette MAX-1 Stress ECG
	Non-compliant exercise	25.4 ± 9.1	25.5 ± 8.8		b0.1 ± 9.1	b0.39	NR		
	NE	28.3 ± 9.6	26.5 ± 8.4		b−1.8 ± 9.6	b−6.38	NR		
Smith et al., 2001	AT	34.9 ± 5.7	37.5 ± 6.1	VO_{2max} – mL·kg−1·min−1	b2.6 ± 5.7	b7.5	0.09	OSU Hi-Fit treadmill protocol with 2-min stages	Oxygen consumption, carbon dioxide production, and RER were continuously monitored. HR, blood pressure, and 12-lead ECG were recorded at each workload
	NE	31.2 ± 5.3	33.2 ± 5.9		b2 ± 5.3	b6.41	NR		
Terry et al., 2006	AT	32 ± 5	40 ± 8	VO_{2peak} – mL·kg−1·min−1	b8 ± 5	b25	NR	Maximal treadmill test with ramp protocol	Treadmill ramp protocol starting at 3 km/h and 2% incline, incremental increases until volitional fatigue for 10 min. Supervised by a cardiologist, and blood pressure monitored every 3 min. ECG and respiratory gases continuously monitored
	Stretching training	34 ± 7	35 ± 8		b1 ± 7	b2.94	NR		
Concurrent Training (CT)									
McDermott et al., 2016	AT	33.2 ± 9.6	37.4 ± 8.9	Predicted VO_{2max} – mL·kg−1·min−1	b4.2 ± 9.6	b12.65	NR	Modified Bruce treadmill protocol	Terminated at 85% predicted HR_{max}, measured with Polar T31. Gas analysis via Cosmed K4b2 system
	NE	36.7 ± 8.6	39 ± 9.6		b1 ± 7	b2.94	NR		
cBonato et al., 2020	AT app	1.8 IQR: 1.4–2.3	2.1 IQR: 1.6–2.6	VO_{2peak} – l/min	b0.3	b16.67	0.001	Cycle ergometer (E50, Cosmed, Italy)	The participants were connected to a 12-lead ECG for monitoring. After a 3-min rest, the participants started pedaling on the cycle ergometer at a rate of 60 revolutions per min, with 20-W increments every 2 min until exhaustion.
	AT no app	2.1 IQR: 1.2–2.3	2 IQR: 1.3–2.3		b−0.1	b−4.76	NR		
Cade et al., 2003	CT	23.3 ± 5.6	26 ± 7.9	VO_{2max} – mL·kg−1·min−1	b2.7 ± 5.6	b11.59	0.91	Not describable	Not describable
	Pioglitazone	24.30 ± 5.2	25.3 ± 6		b1 ± 5.2	b4.12	NR		

It continues...

Table 3. Continuation.

Author (year)	Groups	VO_{2max} – baseline	VO_{2max} post-intervention	Outcome unit	Mean differences	Mean differences %	p value	Protocol used for measuring VO_{2max}	Description of protocol
Dolan et al., 2006	CT	16.9 ± 1	18.4 ± 0.9	VO_{2max} – mL·kg−1·min−1	b1.5 ± 1.3	b8.88	NR	Submax cycle ergometer test	Participants cycled at 50 rpm with workload increments of 50 watts every 3 min. The test was stopped when participants reached 85% of their predicted HR_{max}. Separate readings of heart rate and blood pressure were taken at the end of each stage and at 1, 3, and 5 min of recovery.
	NE	15.3 ± 1.1	12.8 ± 1.3		b−2.5 ± 1.3	b−16.34	NR		
Mutimura et al., 2008	CT – lipodystrophy	NR	NR	VO_{2peak} – mL·kg−1·min−1	4.7 ± 0.6	NR	p < 0.0001	20 m multistage shuttle run test	Participants ran between two points 20 m apart. The pace increased incrementally by 0.14 m/s every min until exhaustion. The test was conducted on a synthetic surface in an indoor stadium. HR and blood pressure were measured before and after the test, and perceived exertion was recorded using the Borg Scale.
	NE – lipodystrophy	NR	NR		2 ± 1.2	NR	NR		
	NE – no lipodystrophy	NR	NR		2 ± 1.2	NR	NR		
	NE – no HIV	NR	NR		2 ± 1.2	NR	NR		
Ogalha et al., 2011	CT	31.55 ± 7.58	31.41 ± 6.1	VO_{2max} – mL·kg−1·min−1	b−0.14 ± 7.6	b−0.44	NR	Treadmill ergometer, ramp protocol	Continuous increments in speed and incline to reach volitional fatigue in 8–12 min. HR monitored every 3 min during the exercise test; twelve-lead electrocardiography continuously monitored
	NE	31.98 ± 7.62	30.36 ± 7.55		b−1.62 ± 7.7	b−5.07	NR		
Fitch et al., 2012	CT – placebo	22.1 ± 1.7	NR	VO_{2max} – mL·kg−1·min−1	2 ± 1.2	NR	0.05	Submaximal exercise stress test using a cycle ergometer	VO_{2max} was measured indirectly through endurance testing. Electrocardiograms were used during exercise testing to monitor any abnormal heart rhythms or other cardiovascular issues
	CT – metformin	22.1 ± 1.2	NR		3.7 ± 1.8	NR	NR		
	NE –Placebo	23.4 ± 1	NR		−0.7 ± 1.6	NR	NR		
	NE – metformin	23.7 ± 0.9	NR		−1.3 ± 0.9	NR	NR		
Mendes et al., 2013	CT – lipodystrophy	28.6 ± 7.1	34 ± 6.7	VO_{2max} – (mL×kg×m/n)−1	b5.4 ± 7.1	b18.88	0.0001	Modified multi-stage fitness test	Participants ran between two points 20 m apart. The pace increased incrementally by 0.14 m/s every min until exhaustion. The total number of completed stages was used to calculate peak velocity, which was then used to estimate VO_{2max}
	CT – no lipodystrophy	32 ± 7.6	36.3 ± 7.91		b4.3 ± 7.6	b13.44	0.0001		
	NE – lipodystrophy	NR	NR		NR	NR	NR		
	NE – no lipodystrophy	NR	NR		NR	NR	NR		
Tiozzo et al., 2013	Concurrent training	NR	NR	Estimated VO_{2max} – mL·kg−1·min−1	4.7	NR	0.01	Submax treadmill	Treadmill-based submaximal testing, increasing speed or incline until reaching 85% of age-predicted HR_{max}. HR was continuously monitored using a Polar FT2 chest band and wristwatch display to ensure the participants reached 85% of their HR_{max}
	NE	NR			0.4	NR			

It continues...

Table 3. Continuation.

Author (year)	Groups	VO_{2max} – baseline	VO_{2max} post-intervention	Outcome unit	Mean differences	Mean differences %	p value	Protocol used for measuring VO_{2max}	Description of protocol
Mangona et al., 2015	CT	31.3 ± 9.1	34.8 ± 9.9	VO_{2peak} – mL·kg−1·min−1	b3.5 ± 9.1	b11.18	0.008	Adapted Balke treadmill protocol	Speed constant at 5.3 km/h. Incline increased by 2% per min. Oxygen uptake measured with K4-Cosmed device
	AT	33.2 ± 5.5	38.1 ± 7.1		b4.9 ± 5.5	b14.76	0.01		
	NE	33 ± 5.5	33.2 ± 3.9		b0.2 ± 5.6	b0.61	0.85		
Pedro et al., 2016	CT	26.3 ± 4.7	31.6 ± 5.6	VO_{2peak} – mL·kg−1·min−1	b5.3 ± 4.7	b20.2	0.5	Incremental treadmill test (Cosmed TM, t170)	The test began at 5 km/h for 5 min, with the speed increased by 1 km/h every 3 min until exhaustion. Treadmill inclination was set to 1%. VO_{2peak} was measured using a gas analyzer (Metalyzer 3B, CPX System) and was calculated as the highest recorded value over 10 s
	Physical activity	26.3 ± 4.7	27.2 ± 7.6		b0.9 ± 4.7	b3.42			
Zanetti et al., 2020	CT – placebo	32.4 ± 3.9	NR	VO_{2peak} – mL·kg−1·min−1	11.1 ± 4.3	NR	0.5	Modified bruce protocol on treadmill	This protocol was performed on a treadmill and consists of six stages. Each stage lasted 3 min. The treadmill speed increased progressively (from 2.7 km/h in stage 1 to 6.8 km/h in stage 5), and the treadmill incline started at 0% and increased progressively (from 5% in stage 2 to 10% by stage 3, with 2% increments in subsequent stages)
	CT – statin	33.5 ± 2.7	NR		10.4 ± 3.2	NR	0.5		
	NE – placebo	30.9 ± 8.6	NR		0.3 ± 1.7	NR	NR		
	NE – statin	33.3 ± 3.6	NR		−0.2 ± 2	NR	NR		
Oliveira et al., 2020	CT	12.8 ± NR	15.6 ± NR	VO_{2max} – mL·kg−1·min−1	b2.8	NR	0.05	American College of Sports Medicine equations	Heart rate reserve and predicted HR_{max} (HR_{max} = 220 –age) were used to calculate Heart Rate Reserve, which was used to prescribe exercise intensity during training. The predicted VO_{2max} was calculated using the American College of Sports Medicine formula that incorporates both horizontal and vertical components of treadmill exercise
	NE	NR							
Santos et al., 2021	CT	Median 45.75	NR	VO_{2max} – mL·kg−1·min−1	NR	NR	NR	Ergospirometry test on a treadmill, using American College of Sports Medicine guidelines	Was measured using HR monitoring and gas exchange analysis to capture VO_{2max} at peak exercise intensity

VO_{2max}, Maximal oxygen consumption; NE, no exercise; NR, not reported; MET, Metabolic equivalent task; HR, Heart rate; ECG, Electrocardiogram; RER, Respiratory exchange ratio; VO_{2peak}, Maximal oxygen uptake; HR_{max}, Heart rate maximum; IQR, Interquartile range; HR_{max}; VO_{2max}. [a] In addition to reporting the adherence and dropout rates, the authors conducted an additional analysis to compare the non-compliant group (those with less than 50% attendance in exercise sessions) with the compliant group. [b] Calculated by the reviewer using reported baseline and post-intervention means and SDs. Correlation assumed to be r = 0.5 for SD_diff. [c] The values are expressed either as the number of participants (%) or as median (Q1-Q3).

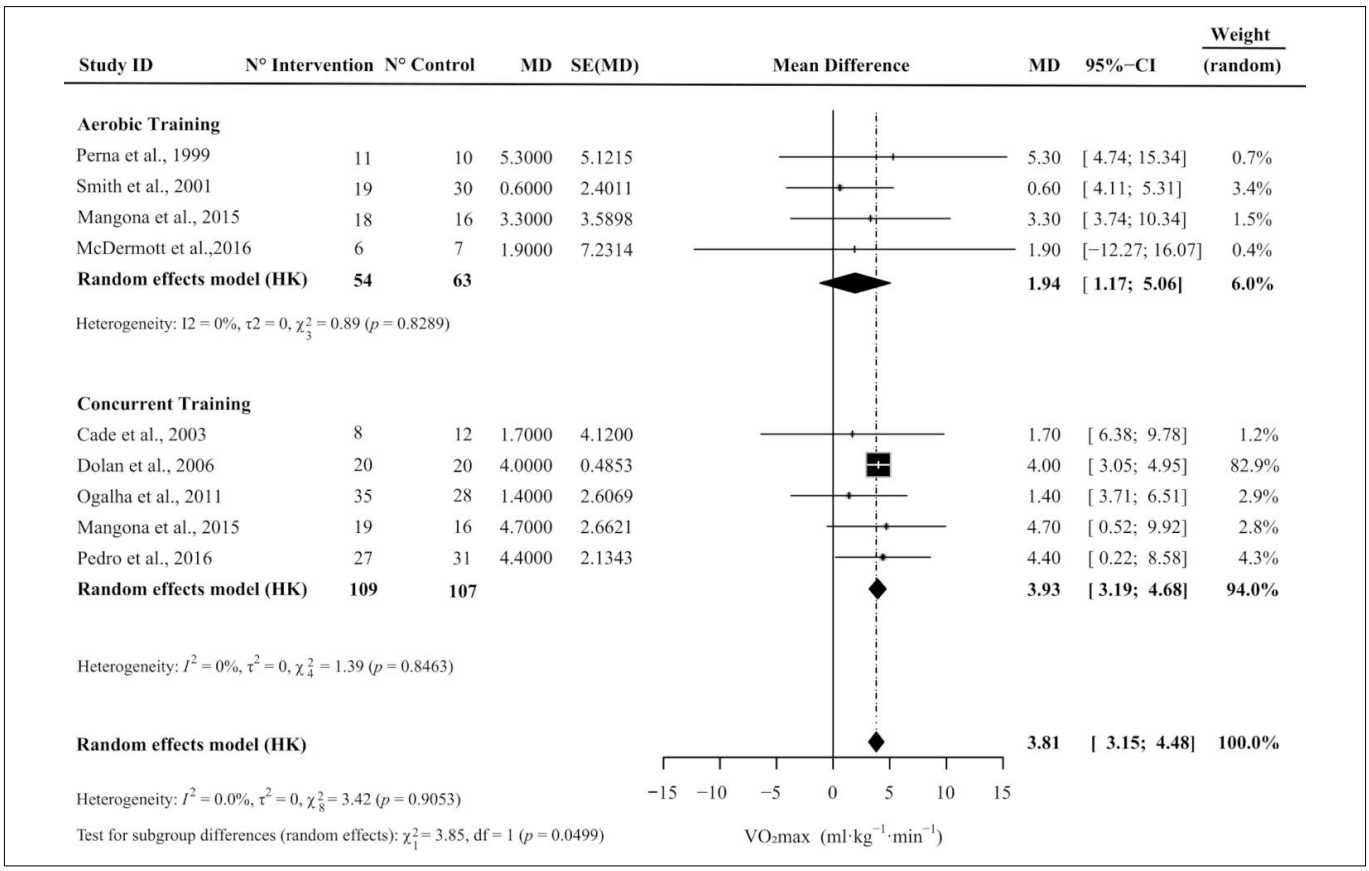


Figure 3. Forest plot of the effects of aerobic and concurrent training on Maximal oxygen consumption in people living with HIV.

trim-and-fill analyses did not indicate publication bias. The trim-and-fill method was further used to assess the potential impact of small-study effects. For AT, imputation of two hypothetical studies yielded an adjusted effect of +0.73 mL·kg^{-1}·min^{-1} (95% CI: −2.14 to 3.6). For CT, imputation of a single study yielded an adjusted effect of +4.01 mL·kg^{-1}·min^{-1} (95% CI: 3.21 to 4.81), consistent with the original result.

Subgroup analysis by study quality showed similar results. RCTs rated as "some concerns" (*n* = 7) reported a pooled effect of +2.92 mL·kg^{-1}·min^{-1} (95% CI: 0.8 to 5.04), while those rated as "High Risk" (*n* = 2) showed +3.99 mL·kg^{-1}·min^{-1} (95% CI: 3.04 to 4.94). The test for subgroup differences was not statistically significant (Q = 0.82; p = 0.3652).

Certainty of evidence (GRADE) – VO_{2max}

Supplementary Table S2 presents the evidence profile, where both AT and CT were rated as very low. Downgrading was applied due to methodological limitations across the included trials and imprecision associated with small sample sizes and wide confidence intervals. Heterogeneity was not considered a limiting factor, as I^2 was 0% in both subgroups. No evidence of publication bias was detected by funnel plot inspection, Egger's or Begg's tests, or trim-and-fill analyses. Although pooled estimates suggest improvements in VO_{2max}, the overall certainty of the evidence remains very low and warrants cautious interpretation.

Secondary results

In addition to VO_{2max}, the included studies evaluated secondary outcomes. These outcomes were grouped into physiological and functional domains to facilitate synthesis. The most assessed categories included:

1. Body composition: Most studies reported reductions in body mass index, body weight, fat mass, or waist circumference, though heterogeneity precluded pooling.

2. Immune function: CD4+ counts were assessed in 14 studies, with inconsistent results and no clear pooled effect.

3. Metabolic markers: Glucose, total cholesterol, triglycerides, low-density lipoprotein, and high-density lipoprotein were reported, with many trials indicating improvements but insufficient consistency for meta-analysis.

4. Muscle strength: Trials using 1 RM and isometric tests consistently reported gains in upper and lower limb strength.

Pooling of secondary outcomes was not feasible due to heterogeneous reporting and outcome measures.

DISCUSSION

This systematic review and meta-analysis examined the chronic effects of exercise on CRF in PLWH. The results demonstrated that AT led to a non-significant improvement (+1.9 $mL \cdot kg^{-1} \cdot min^{-1}$) in VO_{2max}, whereas CT led to a greater improvement (+3.93 $mL \cdot kg^{-1} \cdot min^{-1}$), consistent with previous reviews[18,19,25] that also suggested a greater effect for CT compared with other modalities.

The observed improvements are potentially clinically significant for PLWH, as chronic inflammation and mitochondrial toxicity associated with certain antiretroviral therapies can result in myopathy and muscle atrophy.[5–7,9] These pathological changes may impair oxygen extraction by the musculoskeletal system.[51–53] In response, RT increases motor unit recruitment and muscle cross-sectional area, thereby facilitating strength gains, preserving lean mass, reducing adiposity, and enhancing overall body composition.[19,25,52,53] These adaptations may enhance oxidative metabolism and peripheral oxygen extraction, thereby increasing the effectiveness of the aerobic component of CT during interventions and potentially contributing to improvements in VO_{2max} levels. However, these mechanisms derive from studies in healthy populations, leaving a gap in the direct evidence regarding whether they manifest similarly in PLWH.[18,19] The magnitude of this effect may depend on the aerobic modality, training volume, intensity, session order, sex, training status, and load progression.[11,12,25,51,52] While existing literature indicates that AT alone can improve CRF,[18,21] the absence of significant findings in this review warrants cautious interpretation.

Although the subgroup difference test indicated a potential advantage of CT over AT, the limited number of trials per group reduces the statistical power to consider this difference definitive. This limitation is evident in the GRADE analysis, which assigned very low certainty to the evidence due to imprecision related to the small total number of participants. In terms of assessment methods, the subgroup analysis did not identify a significant difference between the direct and submaximal protocols, suggesting insufficient statistical evidence to confirm a divergence between these measures. Similarly, the meta-regression found that intervention duration was not a significant predictor of VO_{2max} changes, suggesting that intervention duration was not significantly associated with variation in effect sizes in the available data.

This variation in effect sizes across studies may be explained by differences in training intensity and duration, as well as participant heterogeneity regarding HIV-related comorbidities and the use of different classes of antiretrovirals. These improvements may be clinically relevant for PLWH, as chronic inflammation associated with HIV persists even with HAART and may impair cardiorespiratory function and oxygen extraction and utilisation, potentially contributing to lower VO_{2max} compared with healthy individuals of the same age and level of physical activity.[11,12,25,51]

Dropout rates varied between groups, as reported in other studies,[18,23,24,51] suggesting that the choice between AT and CT should be individualized, considering not only the potential for VO_{2max} gain and other physiological variables, but also the clinical condition, personal preferences, and availability of resources.[24] Supervised community programs, remote follow-up, and low-cost interventions can facilitate exercise continuity, reinforcing the clinical feasibility of both approaches and the importance of integrating physical exercise as a complementary strategy in HIV treatment.

This review has limitations in the interpretation of the results. Despite low statistical heterogeneity ($I^2 = 0\%$) in the main comparisons, clinical and methodological heterogeneity were identified across the trials, including variations in training density, the duration of the aerobic component between CT and AT, sample characteristics, and outcome measures. Although no significant publication bias was detected by funnel plot inspection or the Begg test, the trim-and-fill analysis suggested that the pooled effect estimate for CT may be underestimated. However, these estimates remain unstable due to the small number of studies included in the meta-analysis. In addition, the absence of a systematic search for unpublished studies may have increased the risk of publication bias. External validity is limited by the geographic concentration of studies in Brazil and the United States, suggesting caution when generalizing the results to populations with different clinical profiles and varying access to antiretroviral therapy.

Future studies should prioritize standardizing training protocols, adopting validated tools for VO_{2max} measurement, and stratifying outcomes by sex, age, and immune status. Exploring the effects of exercise on immune modulation, systemic inflammation, and HIV disease progression should also be incorporated into research agendas. Moreover, feasible, low-cost interventions have the potential to promote sustained engagement in physical activity.

CONCLUSION

In summary, structured exercise interventions may improve CRF in adults living with HIV. In some trials, CT appears to yield greater gains than AT alone; however, the available evidence is limited and does not support definitive conclusions on the superiority of one modality over the other. In practice, the choice should be guided by clinical profile, preferences, resources, and adherence feasibility, which likely influences the magnitude of the observed benefit. Proposed physiological mechanisms provide plausibility to the findings but lack specific confirmation in this population. Overall certainty remains very low, given the combination of small samples, heterogeneous protocols, and inconsistent reporting of adherence and outcomes. Research priorities include larger randomized trials with comparable protocols and extended follow-up, evaluating clinically relevant outcomes (quality of life, cardiovascular events) and

moderators (sex, age, antiretroviral regimen, comorbidities). Standardized reporting of intensity, volume, and adherence, along with preregistration and data/code sharing, may strengthen inferences and accelerate translation into clinical practice.

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