Evidence profile: Benefits of physical activity for people living with HIV and AIDS for selected health outcomes

Prepared for the Guideline Development Group for the
WHO Guidelines on physical activity and sedentary behaviour for children and adolescents, adults and older adults

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Scoping question:

For people living with HIV and AIDS (PLWHA), what is the association between physical activity (PA) and health-related outcomes?

- *Is there a dose response association (volume, duration, frequency, intensity)?*
- *Does the association vary by type of physical activity?*

Part 1: Background

The human immunodeficiency virus (HIV), the virus that causes AIDS, continues to be a serious public health problem, with approximately 37.9 million people globally living with HIV at the end of 2018 *(1)*. HIV continues to be a global problem with approximately 770 000 deaths having been recorded in 2018 *(1)*. Regionally, Eastern and Southern Africa continue to be the most affected with approximately 20.6 million people living with HIV in these regions in 2018 *(1)*. Additionally, the Southern African region is the hardest hit by the epidemic, thus confirming that HIV/AIDS is a disease of inequality, since most of the countries in this region have high GINI coefficient indexes *(2)*. However, the number of people who die from AIDS-related illnesses continues to fall, from an approximated 32 million people, since the start of the epidemic, to approximately 770 000 in 2018 *(1)*, and this could be due to the advent of highly active anti-retroviral therapy (HAART).

Impairments caused by HIV can be managed pharmacologically *(3)* and non-pharmacologically or by self-care strategies *(4)*. Recently, there has been many advances in HIV therapy, with two generic fixed dose combinations of tenofovir disoproxil fumarate (TDF), lamivudine (3TC) and dolutegravir (DTG) (TLD) being tentatively approved by the US Food and Drug Administration (FDA) in August 2017 *(5)*. Pharmacological therapy can dramatically bring AIDS patients back from near death to almost normal health through inhibition of HIV replication *(6)* - a biblical analogy referred to as "the Lazarus effect" (7). This situation is especially exacerbated by the improved access to antiretroviral therapy, with an approximated 24.5 million people living with HIV and AIDS (PLWHA) accessing antiretroviral therapy (ART) by the end of June 2019 *(1)*. Thus, the use of HAART has been associated with significant improvements in the prognosis of the disease *(8)*. Medical developments have made it possible for people living with HIV and AIDS (PLWHA) to live longer *(9)*.

Unfortunately, the use of ART may be fraught with adverse effects *(10)*. This was especially the case in the earlier period of combination ART, where adverse effects were associated with switching or discontinuing therapy and medication non-adherence *(11)*. Some of the common and/or severe adverse effects associated with ART include bone density effects, bone marrow suppression, cardiac conduction effects, cardiovascular disease, cholethiasis, diabetes mellitus and insulin resistance, dyslipidemia, gastrointestinal effects, hepatic effects, hypersensitivity reaction, lactic acidosis, lipodystrophy, myopathy/elevated creatine phosphokinase, nervous system/psychiatric effects, rash and renal effects/urolithiasis *(12)*. Additionally, ART has been associated with teratogenicity risk in pregnant women *(13)*, an increase in both body fat mass and body mass index (BMI) *(14)*, increased blood pressure *(15)* and cardiovascular risk *(16)*. Thus, as HIV/AIDS has shifted to a chronic, largely manageable condition due to the advent of HAART, the long-term effects of living with HIV/AIDS and HAART treatment are now emerging *(17)*, and PLWHA are mostly succumbing to

non-AIDS related illnesses. Indeed, it has been shown that since the advent of ART, the primary cause of death among PLWHA are chronic diseases generally associated with aging such as cardiovascular disease (CVD) and kidney failure, among others *(18)*.

Physical activity (PA) is one cost-effective, non-pharmacological approach that has been shown to effectively address the impairments caused by HAART *(19)*. PA is important for maintaining good health and quality of life among PLWHA *(20)*. The benefits of PA for PLWHA also include improved metabolic profile and cardiorespiratory fitness *(21)*. A suitably graded exercise prescription may help with preserving lean tissue, improve cardiopulmonary function and immune status, and enhance quality of life in PLWHA *(22)*. Furthermore, an improvement in inflammation and cardio-metabolic health has been reported with increasing PA in PLWHA *(23; 24)*. Thus, regular PA can be a crucial aspect of lifestyle optimization in PLWHA, especially given the associations of physical inactivity with poor health and inconsistent adherence to medication in PLWHA. Given the foregoing, the aim of this umbrella review of systematic reviews is to search, identify, and synthesise the evidence currently available on the benefits of PA interventions (aerobic, resistance training or multicomponent physical activity) for PLWHA. Specifically, the following outcomes were targeted, health related quality of life (HRQOL), body composition, anxiety/depression, fitness and functional capacity, cardio metabolic markers, viral load and cognition.

Part 2: Establishing the PI/ECO

Scoping questions in PI/ECO format (population intervention/exposure, comparisons, outcomes)

For people living with HIV and AIDS (PLWHA), what is the association between physical activity (PA) and health-related outcomes?

- ***Is there a dose response association (volume, duration, frequency, intensity)?***
- ***Does the association vary by type of PA (aerobic, resistance, multimodal)?***

✓ P: People living with HIV/AIDS (PLWHA)
✓ I: Physical activity interventions (aerobic, resistance training or multicomponent physical activity)
✓ E: Greater volume, duration, frequency, or intensity of physical activity.
✓ C: No physical activity or lesser volume, duration, frequency, or intensity of physical activity.
✓ O: Outcomes (Critical)

- Health-related quality of life (HRQOL)
- Body composition
- Anxiety/Depression
- Fitness/Functional Capacity
- Cardiometabolic disease markers
- Viral Load
- Cognition

Part 3. Search Strategies

For the purposes of this umbrella review, we conducted searches in three reference databases, Pubmed, CINAHL and Web of Science. Where available, search strings were based on those used in the Physical Activity Guidelines for Americans 2018, with the following distinctions: no limits in terms of language, publications were limited to systematic reviews, meta-analyses, pooled analyses; and no restrictions on publication year or language. The searches were completed between the 12-16 October, 2019. We have provided the full set of search terms for each database below.

PubMed

Physical Activity Search Terms

((“Activity bouts”[tiab] OR “Daily steps”[tiab] OR “High intensity activity”[tiab] OR “Pedometer”[tiab] OR “Step count”[tiab] OR “Steps/day”[tiab] OR “Interval training”[tiab] OR “Walk”[tiab] OR “Walking”[tiab] OR (“High intensity”[tiab] AND “training”[tiab]) OR “Active living”[tiab] OR “Active travel”[tiab] OR “Exercise”[mh] OR “High intensity activities”[tiab] OR “Light intensity activity”[tiab] OR “Low intensity activity” [tiab] OR “Moderate to Vigorous Activities”[tiab] OR “Moderate to Vigorous Activity”[tiab] OR “Physical endurance”[mh] OR “Physical fitness”[mh] OR “Physical inactivity”[tiab] OR “Sedentary lifestyle”[mh] OR “Weight lifting”[mh] OR “Active commute”[tiab] OR “Active commuting”[tiab] OR “Moderate Activities” [tiab] OR “Moderate Activity” [tiab] OR “Vigorous Activities”[tiab] OR “Vigorous Activity”[tiab] OR “Aerobic activities”[tiab] OR “Aerobic activity”[tiab] OR “Anaerobic training”[tiab] OR “Cardiorespiratory activity”[tiab] OR “Cardiorespiratory fitness”[tiab] OR “Cardiovascular activities”[tiab] OR “Cardiovascular activity”[tiab] OR “Cardiovascular fitness” [tiab] OR “Endurance activities”[tiab] OR “Endurance activity”[tiab] OR “Energy expenditure”[tiab] OR “Exercise”[tiab] OR “Physical activity”[tiab] OR “Physical conditioning”[tiab] OR “Physical fitness”[tiab] OR “Resistance training”[tiab] OR “Sedentary lifestyle”[tiab] OR “Strength training”[tiab] OR “Weight training”[tiab]) OR “physical exercises”[tiab] OR “exercise intervention”[tiab]))

HIV Search Terms

((HIV Infections[MeSH] OR HIV[MeSH] OR hiv[tiab] OR hiv-1[tiab] OR hiv-2*[tiab] OR hiv1[tiab] OR hiv2[tiab] OR hiv infect*[tiab] OR "human immunodeficiency virus"[tiab] OR "human immune deficiency virus"[tiab] OR "human immuno-deficiency virus"[tiab] OR "human immune-deficiency virus"[tiab] OR ((human immun*) AND (deficiency virus[tiab])) OR "acquired immunodeficiency syndrome"[tiab] OR "acquired immune deficiency syndrome"[title/abstract] OR "acquired immuno-deficiency syndrome"[tiab] OR "acquired immune-deficiency syndrome"[tiab] OR "AIDS virus"[tiab] OR HIV[tiab] OR HIV/AIDS[tiab] OR HIV-positive[tiab] OR HIV[title] OR HIV/AIDS[title] OR HIV-positive[title]) OR AIDS[tiab]))

Systematic Review Search Terms

((HIV Infections[MeSH] OR HIV[MeSH] OR hiv[tiab] OR hiv-1[tiab] OR hiv-2*[tiab] OR hiv1[tiab] OR hiv2[tiab] OR hiv infect*[tiab] OR "human immunodeficiency virus"[tiab] OR "human immune deficiency virus"[tiab] OR "human immuno-deficiency virus"[tiab] OR "human immune-deficiency virus"[tiab] OR ((human immun*) AND (deficiency virus[tiab])) OR "acquired immunodeficiency syndrome"[tiab] OR "acquired immune deficiency syndrome"[title/abstract] OR "acquired immuno-deficiency syndrome"[tiab] OR "acquired immune-deficiency syndrome"[tiab] OR "AIDS virus"[tiab] OR HIV[tiab] OR HIV/AIDS[tiab] OR HIV-positive[tiab] OR HIV[title] OR HIV/AIDS[title] OR HIV-positive[title]) OR AIDS[tiab]))

Outcomes Search Terms

Health Related Quality of Life	(("HRQOL"[tiab] OR "Quality of life"[tiab] OR "Quality of life"[mh] OR "Life quality"[tiab] OR "life satisfaction"[tiab] OR "Satisfaction with life"[tiab]))
Anxiety/Depression	AND (("Affect"[mh] OR "Affect"[tiab] OR "Anxiety"[mh] OR "Anxiety"[tiab] OR "Mood"[tiab] OR "Mood disorders"[mh] OR "Bipolar disorder"[mh] OR "Trauma and Stressor Related Disorders"[mh] OR "Anxiety disorders"[mh] OR "Panic"[tiab] OR "Affect disorder"[tiab] OR "Affect disorders"[tiab] OR "Depression"[mh] OR "Antidepressant"[tiab] OR "Hypervigilance"[tiab] OR "Nervousness"[tiab] OR "Nervous"[tiab] OR "Worry"[tiab] OR "Worries"[tiab] OR "Worried"[tiab] OR "Arousal"[mh] OR "Pleasant"[tiab] OR "Pleasureable"[tiab] OR "Pleasure"[tiab] OR "Valence"[tiab] OR "Activate"[tiab] OR "Activated"[tiab] OR "Activation"[tiab] OR "Activates"[tiab] OR "Feelings"[tiab] OR "Emotion"[tiab] OR "Emotions"[tiab] OR "Emotional"[tiab] OR "Emotions"[mh] OR "Tension"[tiab] OR "Anger"[tiab] OR "Hostility"[tiab] OR "Dejection"[tiab] OR "Vigor"[tiab]) OR (("Affective"[tiab] OR "Mood disorder"[tiab] OR "Mood disorders"[tiab] OR "Bipolar disorders"[tiab] OR "Bipolar disorder"[tiab] OR "Adjustment disorder"[tiab] OR "Adjustment disorders"[tiab] OR "Traumatic stress disorder"[tiab] OR

	"Traumatic stress disorders"[tiab] OR "PTSD"[tiab] OR "Anxiety disorder"[tiab] OR "Anxiety disorders"[tiab] OR "Depression"[tiab] OR "Depressive"[tiab] OR "Depressed"[tiab] OR "Anxiolytic"[tiab] OR "Phobia"[tiab] OR "Phobic"[tiab] OR "Arousal"[tiab] OR "Aroused"[tiab] OR "Dysthymic Disorder"[tiab] OR "Dysthymia"[tiab]) NOT medline[sb]))
Body composition	("Body weight"[mh] OR "Body weight change"[tiab] OR "Weight gain"[tiab] OR "Weight status"[tiab] OR "Obesity"[tiab] OR "Overweight"[tiab] OR "Weight Control"[tiab] OR "Weight maintenance"[tiab] OR "Weight regulation"[tiab] OR "Weight stability"[tiab]) OR "body fat redistribution"[tiab] OR "central obesity"[tiab] OR "waist circumference"[tiab] OR "waist-to-hip ratio"[tiab] OR "waist to hip ratio"[tiab] OR "lipodystrophy"[tiab] OR "muscle wasting"[tiab] OR "wasting"[tiab])
Viral Load	("Viral load"[tiab] OR "CD4 count"[tiab] OR "CD4"[tiab] OR "Immunosuppression"[tiab])
Cardiometabolic Disease Markers	(("Arteriosclerosis"[mh] OR "Heart failure"[mh] OR "Myocardial ischemia"[mh] OR "myocardial infarction"[mh] OR "Stroke"[mh] OR "Subarachnoid hemorrhage"[mh] OR "Intracranial hemorrhages"[mh] OR "insulin resistance"[mh] OR "Blood glucose"[mh] OR "insulin resistance"[tiab] OR Hyperglycemia[mh] OR "Diabetes Mellitus, Type 2"[mh]) OR ((Arteriosclero*[tiab] OR Atherosclero*[tiab] OR "Cerebral infarction"[tiab] OR "Cerebrovascular diseases"[tiab] OR "Cerebrovascular disease"[tiab] OR "Coronary heart disease"[tiab] OR "Heart failure"[tiab] OR "Intracerebral Hemorrhage"[tiab] OR "Intracerebral Hemorrhages"[tiab] OR "Intracranial hemorrhage"[tiab] OR "Intracranial hemorrhages"[tiab] OR "myocardial infarction"[tiab] OR "Stroke"[tiab] OR "Subarachnoid hemorrhages"[tiab] OR "Subarachnoid hemorrhage"[tiab] OR "Ischemic heart diseases"[tiab] OR "Ischemic heart disease"[tiab] OR "metabolic syndrome"[tiab] OR "syndrome of insulin resistance"[tiab] OR "cardiometabolic disease"[tiab] OR "cardio-metabolic disease"[tiab] OR "hypertension" [tiab] OR "high blood pressure"[tiab]))
Physical fitness and functional capacity	("cardiorespiratory fitness"[All Fields] OR "fitness"[All Fields] OR "functional capacity"{ALL Fields])
Cognition	(("Academic achievement"[tiab] OR "Academic performance"[tiab] OR "Attentional control"[tiab] OR "Brain health"[tiab] OR "Brain function"[tiab] OR "Cognitive ability"[tiab] OR "Cognitive control"[tiab] OR "Cognitive function"[tiab] OR "Cognitive functioning"[tiab] OR "Cognitive health"[tiab] OR "Cognitive performance"[tiab] OR "Cognitive processing"[tiab] OR "Executive control"[tiab] OR "Executive function"[mh] OR "Information processing"[tiab] OR "Inhibitory control"[tiab] OR "Memory"[mh] OR "Mental flexibility"[tiab] OR "Mental recall"[tiab] OR "Neuro cognitive"[tiab] OR "Neurocognitive"[tiab] OR "Perceptual

	processing"[tiab] OR "Problem solving"[mh] OR "Problem solving"[tiab] OR "Scholastic achievement"[tiab] OR "Scholastic performance"[tiab]) OR (("Executive function"[tiab] OR "Executive functioning"[tiab] OR "Executive functions"[tiab] OR "Memory"[tiab]) NOT medline[sb]))

CINAHL

Physical Activity Search Terms

(“Activity bouts” OR “Daily steps” OR “High intensity activity” OR “Pedometer” OR “Step count” OR “Steps/day” OR “Interval training” OR “Walk” OR “Walking” OR (“High intensity” AND “training”) OR “Active living” OR “Active travel” OR “Exercise” OR “High intensity activities” OR “Light intensity activity” OR “Low intensity activity” OR “Moderate to Vigorous Activities” OR “Moderate to Vigorous Activity” OR “Physical endurance” OR “Physical fitness” OR “Physical inactivity” OR “Sedentary lifestyle” OR “Weight lifting” OR “Active commute” OR “Active commuting” OR “Moderate Activities” OR “Moderate Activity” OR “Vigorous Activities” OR “Vigorous Activity” OR “Aerobic activities” OR “Aerobic activity” OR “Anaerobic training” OR “Cardiorespiratory activity” OR “Cardiorespiratory fitness” OR “Cardiovascular activities” OR “Cardiovascular activity” OR “Cardiovascular fitness” OR “Endurance activities” OR “Endurance activity” OR “Energy expenditure” OR “Exercise” OR “Physical activity” OR “Physical conditioning” OR “Physical fitness” OR “Resistance training” OR “Sedentary lifestyle” OR “Strength training” OR “Weight training”) OR “physical exercises” OR “exercise intervention”)

HIV Search Terms

(“HIV Infections” OR “HIV” OR “human immunodeficiency virus” OR “human immune deficiency virus” OR “human immuno-deficiency virus” OR “human immune-deficiency virus” OR “acquired immunodeficiency syndrome” OR “acquired immune deficiency syndrome” OR “acquired immuno-deficiency syndrome” OR “acquired immune-deficiency syndrome” OR “AIDS virus” OR “HIV/AIDS” OR “HIV-positive” OR “AIDS”)

Systematic Review Search Terms

"PT (“systematic review” OR “systematic literature review” OR "metaanalysis" OR "metaanalysis" OR metanalyses OR "meta analyses" OR “meta-analyses” OR “meta-analysis”

Outcomes Search Terms

Health Related Quality of Life	("HRQOL" OR "Quality of life" OR "Life quality" OR "life satisfaction" OR "Satisfaction with life")
Anxiety/Depression	(("Affect" OR "Affect" OR "Anxiety" OR "Anxiety" OR "Mood" OR "Mood disorders" OR "Bipolar disorder" OR "Trauma and Stressor Related Disorders" OR "Anxiety disorders" OR "Panic" OR "Affect disorder" OR "Affect disorders" OR "Depression" OR "Antidepressant" OR "Hypervigilance" OR "Nervousness" OR "Nervous" OR "Worry" OR "Worries" OR "Worried" OR "Arousal" OR "Pleasant" OR "Pleasureable" OR "Pleasure" OR "Valence" OR "Activate" OR "Activated" OR "Activation" OR "Activates" OR "Feelings" OR "Emotion" OR "Emotions" OR "Emotional" OR "Emotions" OR "Tension" OR "Anger" OR "Hostility" OR "Dejection" OR "Vigor") OR (("Affective" OR "Mood disorder" OR "Mood disorders" OR "Bipolar disorders" OR "Bipolar disorder" OR "Adjustment disorder" OR "Adjustment disorders" OR "Traumatic stress disorder" OR "Traumatic stress disorders" OR "PTSD" OR "Anxiety disorder" OR "Anxiety disorders" OR "Depression" OR "Depressive" OR "Depressed" OR "Anxiolytic" OR "Phobia" OR "Phobic" OR "Arousal" OR "Aroused" OR "Dysthymic Disorder" OR "Dysthymia")
Body composition	("Body weight" OR "Body weight change" OR "Weight gain" OR "Weight status" OR “Obesity” OR "Overweight" OR "Weight Control" OR "Weight maintenance" OR "Weight regulation" OR "Weight stability") OR “body fat redistribution” OR “central obesity” OR “waist circumference” OR “waist-to-hip ratio” OR “waist to hip ratio” OR “lipodystrophy” OR “muscle wasting” OR “wasting”)
Viral Load	("Viral load" OR "CD4 count" OR "CD4" OR "Immunosuppression")
Cardiometabolic Disease Markers	Not done
Physical fitness and functional capacity	(“fatigue” OR "functional capacity" OR “cardiorespiratory fitness” or “fitness”)
Cognition	Not done

Web of Science

Physical Activity Search Terms

(("Activity bouts"OR "Daily steps"OR "High intensity activity" OR "Pedometer"OR "Step count"OR "Steps/day"OR "Interval training"OR "Walk" OR "Walking" OR "High intensity" AND "training"OR "Active living"OR "Active travel" OR "Exercise"OR "High intensity activities"OR "Light intensity activity"OR "Low intensity activity" OR "Moderate to Vigorous Activities"OR "Moderate to Vigorous Activity"OR "Physical endurance"OR "Physical fitness" OR "Physical inactivity" OR "Sedentary lifestyle" OR "Weight lifting" OR "Active commute"OR "Active commuting" OR "Moderate Activities" OR "Moderate Activity"OR "Vigorous Activities" OR "Vigorous Activity" OR "Aerobic activities" OR "Aerobic activity" OR "Anaerobic training" OR "Cardiorespiratory activity" OR "Cardiorespiratory fitness" OR "Cardiovascular activities"[tiab] OR "Cardiovascular activity" OR "Cardiovascular fitness" OR "Endurance activities"OR "Endurance activity" OR "Energy expenditure" OR "Exercise" OR "Physical activity" OR "Physical conditioning" OR "Physical fitness"OR "Resistance training" OR "Sedentary lifestyle"[tiab] OR "Strength training" OR "Weight training" OR "physical exercises" OR "exercise intervention"))

HIV Search Terms

(("HIV Infections" OR "HIV" OR "hiv" OR "hiv-1" OR "hiv-2" OR "hiv1" OR "hiv2" OR "hiv infect" OR “human immunodeficiency virus” OR “human immune deficiency virus” OR “human immuno-deficiency virus” OR “human immune-deficiency virus” OR "human immun" AND "deficiency virus" OR “acquired immunodeficiency syndrome” OR “acquired immune deficiency syndrome” OR “acquired immuno-deficiency syndrome” OR “acquired immune-deficiency syndrome” OR “AIDS virus” OR "HIV" OR "HIV/AIDS" OR "HIV-positive" OR "HIV" OR "HIV/AIDS" OR "HIV-positive"OR "AIDS"))

Systematic Review Search Terms

((systematic OR meta-analysis OR “systematic review” OR “systematic literature review” OR metaanalysis OR "meta analysis" OR metanalyses OR "meta analyses" OR “meta-analyses” OR "pooled analysis" OR “pooled analyses” OR "pooled data"))

Outcomes Search Terms

HRQOL	("HRQOL" OR "Quality of life" OR "Quality of life" OR "Life quality" OR "life satisfaction" OR "Satisfaction with life")
Anxiety/Depression	(("Affect" OR "Affect" OR "Anxiety" OR "Anxiety"OR "Mood" OR "Mood disorders"OR "Bipolar disorder" OR "Trauma and Stressor Related Disorders"OR "Anxiety disorders" OR "Panic" OR "Affect disorder"OR "Affect disorders" OR "Depression" OR "Antidepressant" OR "Hypervigilance" OR "Nervousness"OR "Nervous" OR "Worry" OR "Worries" OR "Worried" OR "Arousal" OR "Pleasant" OR "Pleasureable" OR "Pleasure" OR "Valence" OR "Activate" OR "Activated"OR "Activation" OR "Activates" OR "Feelings" OR "Emotion" OR "Emotions" OR "Emotional" OR "Emotions" OR "Tension" OR "Anger" OR "Hostility" OR

	"Dejection" OR "Vigor" OR "Affective" OR "Mood disorder" OR "Mood disorders" OR "Bipolar disorders" OR "Bipolar disorder" OR "Adjustment disorder" OR "Adjustment disorders" OR "Traumatic stress disorder" OR "Traumatic stress disorders" OR "PTSD" OR "Anxiety disorder" OR "Anxiety disorders" OR "Depression" OR "Depressive" OR "Depressed" OR "Anxiolytic" OR "Phobia" OR "Phobic" OR "Arousal" OR "Aroused" OR "Dysthymic Disorder" OR "Dysthymia" NOT "medline"))
Body Composition	(("Body weight" OR "Body weight change" OR "Weight gain"OR "Weight status" OR "Obesity" OR "Overweight" OR "Weight Control" OR "Weight maintenance" OR "Weight regulation" OR "Weight stability" OR "body fat redistribution" OR "central obesity" OR "waist circumference" OR "waist-to-hip ratio" OR "waist to hip ratio" OR "lipodystrophy" OR "muscle wasting" OR "wasting"))
Viral Load	(("Viral load" OR "CD4 count"OR "CD4" OR "Immunosuppression"))
Cardio-metabolic markers	("Arteriosclerosis" OR "Heart failure" OR "Myocardial ischemia" OR "myocardial infarction" OR "Stroke" OR "Subarachnoid hemorrhage"] OR "Intracranial hemorrhages" OR "insulin resistance" OR "Blood glucose" OR "insulin resistance" OR Hyperglycemia OR "Diabetes Mellitus, Type 2" OR "Arteriosclero" OR "Atherosclero" OR "Cerebral infarction" OR "Cerebrovascular diseases" OR "Cerebrovascular disease" OR "Coronary heart disease" OR "Heart failure" OR "Intracerebral Hemorrhage" OR "Intracerebral Hemorrhages" OR "Intracranial hemorrhage" OR "Intracranial hemorrhages" OR "myocardial infarction" OR "Stroke" OR "Subarachnoid hemorrhages" OR "Subarachnoid hemorrhage" OR "Ischemic heart diseases" OR "Ischemic heart disease" OR "metabolic syndrome" OR "syndrome of insulin resistance" OR "cardiometabolic disease" OR "cardio-metabolic disease" OR "hypertension" OR "high blood pressure")
Fitness & Functional Capacity	(("cardiorespiratory fitness" OR "fitness" OR "functional capacity"))
Cognition	(("Academic achievement" OR "Academic performance" OR "Attentional control" OR "Brain health" OR "Brain function" OR "Cognitive ability" OR "Cognitive control" OR "Cognitive function" OR "Cognitive functioning" OR "Cognitive health" OR "Cognitive performance" OR "Cognitive processing" OR "Executive control" OR "Executive function" OR "Information processing" OR "Inhibitory control" OR "Memory" OR "Mental flexibility" OR "Mental recall" OR "Neuro cognitive" OR "Neurocognitive" OR "Perceptual processing" OR "Problem solving" OR "Problem solving" OR "Scholastic achievement" OR "Scholastic performance" OR "Executive function" OR "Executive functioning" OR "Executive functions" OR "Memory" NOT "medline"))

Part 4. Study selection and reasons for inclusion and exclusion

We used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) for documenting the flow of information through the different phases of our review. We have mapped the total number of records identified, and those excluded at each stage, with reasons given for exclusion and inclusion (See the PRISMA diagram to the right, Figure 1).

Initial screening of titles and abstracts was done by two independent reviewers, and where consensus was not reached, a third reviewer was consulted.

Records were subsequently excluded where duplicates were found, and also if the articles did not specifically address the PICOS.

Finally, full-text articles were also excluded, for example, if they did not include PLWHA, or there was no comparator, or the study was not a systematic review. There were 24 studies that were found to be eligible for inclusion in the qualitative synthesis and underwent quality scoring.

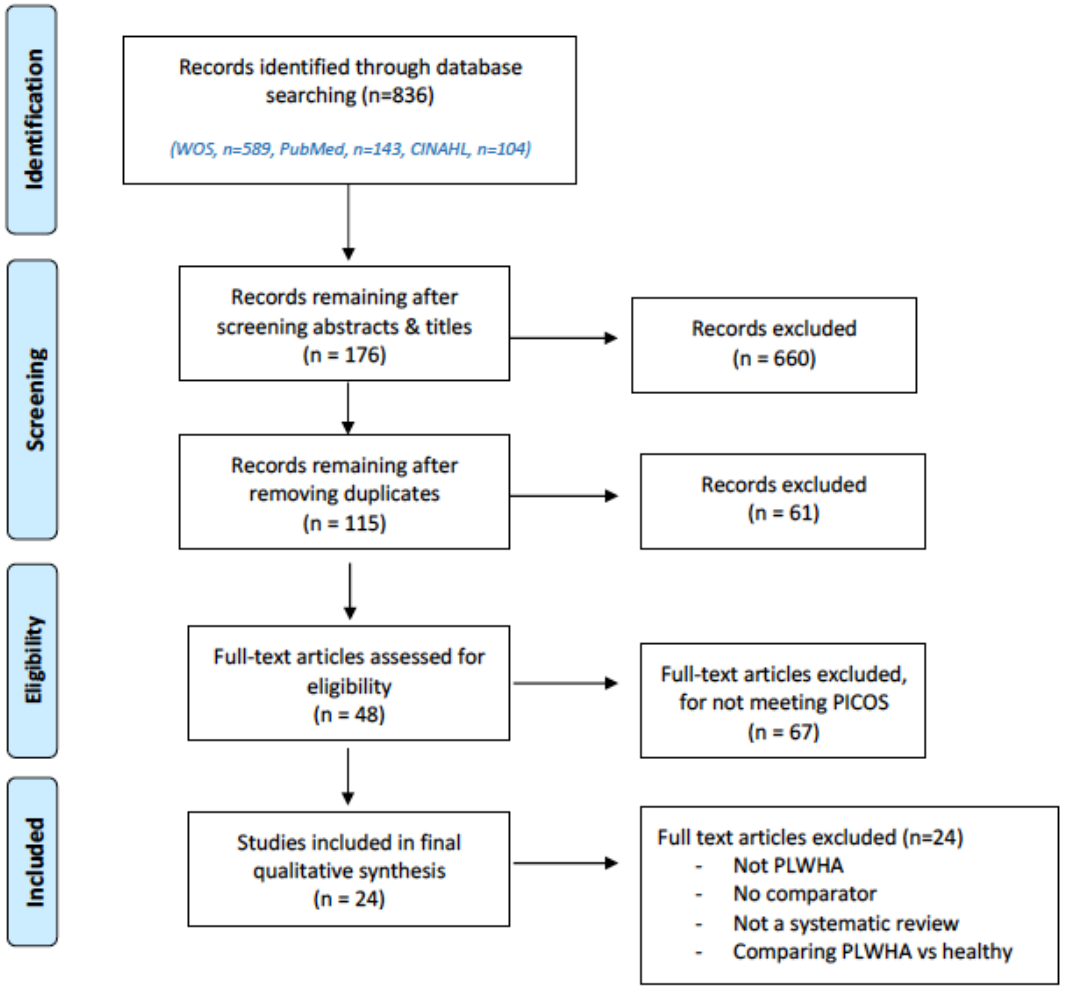

Figure 1. PRISMA flow diagram for the umbrella review on the association between physical activity (PA) and health-related outcomes for people living

with HIV and AIDS (PLWHA)

Part 5. Rating the quality of the included systematic reviews

An independent team of nine reviewers used the AMSTAR 2 (Assessment of Multiple Systematic Reviews) *(25)* tool to rate the quality of the final included systematic reviews. The AMSTAR 2 is a 16-item instrument designed for evaluating different aspects of systematic reviews of randomized trials. Of the 16 items, the following items are regarded as "critical" flaws which affect the quality of the review and therefore, the rating and subsequent interpretation. These included:

	AMSTAR 2 Questions
Apriori methods	Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?
Literature search strategy	Did the review authors use a comprehensive literature search strategy?
Excluded studies	Did the review authors provide a list of excluded studies and justify the exclusions?
Risk of Bias Assessment	Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?
Statistical methods	If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?
Risk of Bias Results	Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?
Publication Bias	If a quantitative synthesis was performed, did the review authors carry out adequate investigation of publication bias (small study bias) and discuss the likely impact on the results of the review?

According to the AMSTAR 2 guidance document (https://amstar.ca/Amstar-2.php), a systematic review rated "high" in quality has none or only one non-critical weakness, meaning that the systematic review "provides an accurate (unbiased) and comprehensive summary of the results of the available studies that address the question of interest". A systematic review rated "moderate" in quality "has more than one non-critical weakness, meaning that despite these weaknesses, the systematic the review has no critical flaws which would make interpretation of and confidence in the results open to question. As such, "it may provide an accurate summary of the results of the available studies that were included in the review". A systematic review rated "low" in quality has one critical flaw with or without non-critical weaknesses. As such, the review "may not provide an

accurate and comprehensive summary of the available studies that address the question of interest". A systematic review rated "critically low" in quality has more than one critical flaw with or without non-critical weaknesses. As such, the review "should not be relied on to provide an accurate and comprehensive summary of the available studies".

Two reviewers were assigned to review the quality of the systematic reviews included for each specific outcome. The two reviewers then completed the AMSTAR 2 tool independently for all included reviews. After reviewing, the reviewers then met to discuss the outcome of their AMSTAR 2 rating. Consensus was then met about the final rating of each systematic review. Where the reviewers did not agree, a third reviewer was consulted and the final decision regarding the rating of the systematic review was resolved by joint discussion and consensus among the reviewers collectively. Final results of AMSTAR 2 ratings are presented in Table 1 below, for the included systematic reviews for specific outcomes.

Table 1. Included Systematic Reviews

Author, Year	Outcomes							Last search date	# of included studies	AMSTAR 2
	HRQOL	BODY COMPOSITION	ANXIETY/ DEPRESSION	FITNESS AND FUNCTIONAL CAPACITY	CARDIO-METABOLIC MARKERS	VIRAL LOAD/ CD4 count	COGNITION*			
Ibemene, 2019a *(28)*				X				Jan 2018	23	high
Ibemene, 2019b *(29)*	X					X		June 2017	19	high
O'Brien, 2017 *(30)*	X	X		X		X		April 2013	20	high
O'Brien, 2016 *(31)*	X	X	X	X		X		April 2013	24	high
Gomes Neto, 2015 *(32)*	X			X				Aug 2014	7	High
O'Brien, 2010 *(33)*	X	X	X	X		X		June 2009	14	high
Nixon, 2005 *(34)*	X		X	X		X		Aug 2003	10	high
Bhatta, 2017 *(35)*	X							Dec 2015	28	high
Pedro, 2017 *(36)*	X	X		X	X	X		July 2016	5	High
O'Brien, 2004 *(37)*	X		X	X		X		NMR2002	10	high
O'Brien, 2008 *(38)*	X	X		X		X		Nov 2008	10	high
Zech, 2019 *(39)*				X				Aug 2017	27	high
Voigt, 2018 *(40)*				X				NR	15	moderate
Poton, 2017 *(41)*		X		X		X		June 2016	13	moderate
Gomes Neto, 2013b *(42)*	X			X				Aug 2012	8	low
Fillipas, 2010 *(43)*		X			X			Nov 2009	9	low
Heissel, 2019 *(44)*			X					Feb 2019	10	low
Quiles, 2019 *(45)*					X			Nov 2017	9	low
Chaparro, 2018 *(46)*				X				Dec 2017	13	low
Nosrat, 2017 *(47)*	X		X					Nov 2016	24	critically low
Gomes Neto, 2013a	X	X		X				Aug 2012	29	critically low

(48)										
Lopez, 2015 *(49)*	X		X	X		X		NMR 2015	18	critically low
Lofgren, 2018 *(50)*			X					Feb2017	18	critically low
Leyes, 2008 *(51)*	X	X		X		X		1996-2008	25	critically low

*No systematic review identified for cognition. ABBREVIATIONS: HRQOL = Health-related quality of life; NR= month and/or year not reported; NMR=No month reported

Twenty four reviews were identified (published from 2005 to 2019). The reviews examined the relationship between PA and health-related outcomes among PLWHA (Table 1) (28-51). All the reviews focused on PLWHA, and on a variety of outcomes, with most of the reviews addressing more than one outcome, including 15 reviews addressing HRQOL, 9 reviews addressing body composition, 8 reviews addressing anxiety/depression, 19 reviews addressing fitness and functional capacity, 4 reviews addressing cardiometabolic markers, and 11 reviews addressed viral load and /or CD4+ count. No reviews identified addressed cognition among PLWHA.

The included body of evidence for the reviews was relatively small ranging from 5 to 29 included studies. Initially, some studies *(28-30;33-35;37,38)* had scored either critically low or low on AMSTAR 2. We reviewed the scoring, with a specific focus on items 4 (literature search strategy) and 15 (Publication bias) or both. As reporting styles differ in journals, publication bias and the literature search strategy may be reported differently, but may not impact on the quality of the review. As such, for item number 4, we scored "YES", if the authors adhered to the following:

(a) Searched at least 2 databases.
(b) Provided key words
(c) Justified publication restrictions (e.g., language).

For critical item number 15, we concluded that if the authors did not explicitly state that they assessed publication bias, but did state that risk of bias in general was assessed, the assumption was that publication bias was also assessed. After applying this criteria throughout all the included reviews, studies *28-30*, *33-35*,*37* and *38* were revised to high quality status on AMSTAR 2 rating. However, some reviews remained critically low or low on AMSTAR 2 rating *(42-51)*. Consequently, the reviews that scored critically low and low for AMSTAR 2 were excluded from the GRADE rating, because they were considered by the panel to constitute poor evidence. In this review, we also decided to include the evidence from all the reviews, since

this is a virtually new area of research, with a few high quality studies. We also included all studies in order to cover all the outcomes of interest. Tables 2 (a) to(g) shows the AMSTAR 2 rating based on exercise modality for each outcome, and Tables 3 (a) to (g), the GRADE tables for each outcome.

In the next series of tables (Table 2a-2h), we present information regarding the critical items for the AMSTAR 2 scoring, for each health outcome and comparisons for different exercise modalities (aerobic exercise, resistance training, or multi-modal training).

Table 2a. AMSTAR 2 rating based on exercise modality, PICO: Effects of PA on HRQOL among PLWHA

Exercise modality	Study	No. of Studies No. of participants	QUALITY ASSESSMENT/AMSTAR 2 CRITICAL ITEMS							AMSTAR 2 Score
			Apriori Methods[2]	Literature Search Strategy[4]	Excluded Studies[7]	RoB Assessment[9]	Statistical Methods[11]	RoB Results[13]	Publication Bias[15]	
Aerobic Exercise	O'Brien, 2016	24 RCTs, N=1242	Y	Y	y	Y	Y	Y	Y	high
	O'Brien, 2010	14 RCTs, N=454	Y	Y	Y	Y	Y	Y	Y	high
	Nixon, 2005	10 RCTs, N=276	Y	Y	Y	Y	Y	Y	Y	high
	O'Brien, 2004	10 RCTs, N=458 HIV+ only participants	Y	Y	Y	PY	Y	Y	Y	high
Resistance Exercise	O'Brien, 2017	20 RCTS, N=764	Y	Y	Y	Y	N/A	Y	N/A	high
	O'Brien, 2008	10 RCTs, N=332	Y	Y	Y	Y	Y	Y		high
Multimodal Exercise	Ibemene, 2019b	19 RCTs, N=661 for participants	Y	Y	Y	Y	Y	Y	Y	high
	Nosrat, 2017	24 RCTs, N=1278	PY	Y	N	N	N/A	N	N/A	critically low
	Gomes Neto, 2015	7 RCTs, N=386	Y	Y	PY	Y	Y	Y	Y	high
	Gomes Neto,	29 RCTs + Clinical trials +	PY	Y	N	N	N/A	N	N/A	critically low

	2013a	Controlled trials, N=NR								
	Gomes Neto, 2013b	8 RCTs, N=NR	Y	Y	N	Y	N/A	Y	N/A	low
	Bhatta, 2017	28 RCTs, N=4136	Y	PY	PY	Y	Y	Y	Y	high
	Lopez, 2015	28 RCTs + Quasi experimental studies, N=493	Y	PY	PY	N	N/A	N	N/A	critically low
	Pedro, 2017	5 RCTs, N=253	Y	PY	Y	Y	N/A	Y	N/A	high
	Leyes, 2008	15 RCTs + 10 Open-label, N=1189	N	N	Y	N	N/A	N	N/A	critically low

Abbreviations: N = no; N/A = not applicable; PICO = population, intervention, comparator, outcome; PY = partial yes; RoB = risk of bias; RCTs = randomised controlled trials; Y = yes

[2] Did the report of the review contain an explicit statement that the review methods were established prior to conduct of the review and did report justify any significant deviations from protocol?
[4] Did the review authors use a comprehensive literature search strategy?
[7] Did the review authors provide a list of excluded studies and justify the exclusions?
[9] Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?
[11] If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?
[13] Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?
[15] If a quantitative synthesis was performed, did the review authors carry out adequate investigation of publication bias (small study bias) and discuss the likely impact on the results of the review?

Table 2b. AMSTAR 2 rating based on exercise modality, PICO: Effects of PA on body composition among PLWHA

Exercise modality	Study	No. of Studies No. of participants	QUALITY ASSESSMENT/AMSTAR 2 CRITICAL ITEMS							AMSTAR 2 Score
			Apriori Methods[2]	Literature Search Strategy[4]	Excluded Studies[7]	RoB Assessment[9]	Statistical Methods[11]	RoB Results[13]	Publication Bias[15]	
Aerobic Exercise	O'Brien, 2016	24 RCTs, N=1242	Y	Y	Y	Y	Y	Y	Y	high
	O'Brien, 2010	14 RCTs, N=454	Y	Y	Y	Y	Y	Y	Y	high
Resistance Exercise	O'Brien, 2017	20 RCTs, N=764	Y	Y	Y	Y	N/A	Y	N/A	high
	O'Brien, 2008	10 RCTs, N=332	Y	Y	Y	Y	Y	Y	Y	high
	Poton, 2017	13 RCTs, N=291	PY	Y	PY	Y	Y	Y	Y	moderate
Multimodal Exercise	Pedro, 2017	5 RCTs, N=253	Y	PY	Y	Y	N/A	Y	N/A	high
	Fillipas, 2010	9 RCTs, N=469	Y	PY	PY	Y	Y	Y	N	low
	Leyes, 2008	15 RCTs + 10 Open-label, N=1189	N	N	Y	N	N/A	N	N/A	critically low

	Gomes Neto, 2013	29 RCTs, N=1216	PY	Y	N	N	N/A	N	N/A	critically low

Abbreviations: N = no; N/A = not applicable; PICO = population, intervention, comparator, outcome; PY = partial yes; RoB = risk of bias; RCTs = randomised controlled trials; Y = yes

[2] Did the report of the review contain an explicit statement that the review methods were established prior to conduct of the review and did report justify any significant deviations from protocol?
[4] Did the review authors use a comprehensive literature search strategy?
[7] Did the review authors provide a list of excluded studies and justify the exclusions?
[9] Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?
[11] If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?
[13] Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?
[15] If a quantitative synthesis was performed, did the review authors carry out adequate investigation of publication bias (small study bias) and discuss the likely impact on the results of the review?

Table 2c. AMSTAR 2 rating based on exercise modality, PICO: Effects of PA on anxiety/depression among PLWHA

Exercise modality	Study	No. of Studies No. of participants	QUALITY ASSESSMENT/AMSTAR 2 CRITICAL ITEMS							AMSTAR 2 Score
			Apriori Methods[2]	Literature Search Strategy[4]	Excluded Studies[7]	RoB Assessment[9]	Statistical Methods[11]	RoB Results[13]	Publication Bias[15]	
Aerobic Exercise	O'Brien, 2016	24 RCTs, N=1242	Y	Y	Y	Y	Y	Y	Y	high
	O'Brien, 2010	14 RCTs, N=454	Y	Y	Y	Y	Y	Y	Y	high
	Nixon, 2005	10 RCTs, N=276	Y	Y	Y	Y	Y	Y	Y	high
	O'Brien, 2004	10 RCTs, N=458 HIV+ only participants	Y	Y	Y	PY	Y	Y	Y	high

	Lofgren, 2018	7 RCTs + 2 Comparison trials + 6 Intervention trials + 3 Cohort studies (1 study had 2 Cohorts) + 1 Intervention, N=1966	N	N	PY	N	N/A	N	N/A	critically low
Resistance Exercise	No systematic reviews identified									
Multimodal Exercise	Nosrat, 2017	24 RCTs, N=1278	PY	Y	N	N	N/A	N	N/A	critically low
	Lopez, 2015	28 RCTs + Quasi experimental studies, N= 493	Y	PY	PY	N	N/A	N	N/A	critically low
	Heissel, 2019	10 RCTs, N=479	Y	Y	N	Y	Y	Y	Y	low

Abbreviations: N = no; N/A = not applicable; PICO = population, intervention, comparator, outcome; PY = partial yes; RoB = risk of bias; RCTs = randomised controlled trials; Y = yes

[2] Did the report of the review contain an explicit statement that the review methods were established prior to conduct of the review and did report justify any significant deviations from protocol?
[4] Did the review authors use a comprehensive literature search strategy?
[7] Did the review authors provide a list of excluded studies and justify the exclusions?
[9] Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?
[11] If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?
[13] Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?
[15] If a quantitative synthesis was performed, did the review authors carry out adequate investigation of publication bias (small study bias) and discuss the likely impact on the results of the review?

Table 2d. AMSTAR 2 rating based on exercise modality, PICO: Effects of PA on fitness and functional capacity among PLWHA

Exercise modality	Study	No. of Studies No. of participants	QUALITY ASSESSMENT/AMSTAR 2 CRITICAL ITEMS							AMSTAR 2 Score
			Apriori Methods[2]	Literature Search Strategy[4]	Excluded Studies[7]	RoB Assessment[9]	Statistical Methods[11]	RoB Results[13]	Publication Bias[15]	
Aerobic	O'Brien, 2016	24 RCTs, N=1242	Y	Y	Y	Y	Y	Y	Y	High

Exercise	O'Brien, 2010	14 RCTs, N=454	Y	Y	Y	Y	Y	Y	Y	High
	Nixon, 2005	10 RCTs, N=276	Y	Y	Y	Y	Y	Y	Y	high
	O'Brien, 2004	10 RCTs, N=458 HIV+ only participants	Y	Y	Y	Y	Y	Y	Y	high
Resistance Exercise	Poton,2017	13 RCTs, N=291	PY	Y	PY	Y	Y	Y	Y	moderate
	O'Brien, 2008	10 RCTs, N=332	Y	PY	Y	Y	Y	Y	N	low
	O'Brien, 2017	20 RCTs, N=764	Y	Y	Y	Y	N/A	Y	N/A	high
	O'Brien, 2008	10 RCTs, N=332	Y	Y	Y	Y	Y	Y	Y	high
Multimodal Exercise	Chaparro, 2018	13 RCTs, N=NR	Y	Y	Y	Y	Y	Y	Y	high
	Zech, 2019	27 RCTs, N= 1294	Y	Y	PY	Y	Y	Y	Y	high
	Gomes Neto, 2015	7 RCTs, N=386	Y	Y	PY	Y	Y	Y	Y	high
	Voight, 2018	15 RCTs, N=537	PY	PY	PY	Y	N/A	Y	N/A	moderate
	Gomes Neto, 2013a	29 RCTs, N=1216	PY	Y	N	N	N/A	N	N/A	critically low
	Gomes Neto, 2013b	8 RCTs, N=NR	Y	Y	N	Y	N/A	Y	N/A	low
	Leyes, 2008	15 RCTs+ 10 Open-label, N=1189	N	N	Y	N	N/A	N	N/A	critically low
	Lopez, 2015	28 RCTs + Quasi experimental studies, N=493	Y	PY	PY	N	N/A	N	N/A	critically low
	Pedro, 2017	5 RCTs, N=253	Y	PY	Y	Y	N/A	Y	N/A	high
	Chaparro, 2018	13 RCTs, IG baseline = 249, IG post-intervention = 246; CG baseline = 1216, CG post-intervention = 246	Y	Y	Y	Y	Y	Y	Y	high
	Ibeneme, 2019a	23RCTs, N=1073	Y	Y	Y	Y	Y	Y	Y	high

Abbreviations: N = no; N/A = not applicable; PICO = population, intervention, comparator, outcome; PY = partial yes; RoB = risk of bias; RCTs = randomised controlled trials; Y = yes; IG=intervention group; CG=control group

[2] Did the report of the review contain an explicit statement that the review methods were established prior to conduct of review and did the report justify any significant deviations from protocol?
[4] Did the review authors use a comprehensive literature search strategy?
[7] Did the review authors provide a list of excluded studies and justify the exclusions?
[9] Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?
[11] If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?
[13] Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?
[15] If a quantitative synthesis was performed, did the review authors carry out adequate investigation of publication bias (small study bias) and discuss the likely impact on the results of the review?

Table 2f. AMSTAR 2 rating based on exercise modality, PICO: Effects of PA on cardio metabolic markers among PLWHA

Exercise modality	**Study**	**No. of Studies** **No. of participants**	**QUALITY ASSESSMENT/AMSTAR 2 CRITICAL ITEMS**	**AMSTAR 2 Score**

			Apriori Methods[2]	Lit Search Strategy[4]	Excluded Studies[7]	RoB Assessment[9]	Statistical Methods[11]	RoB Results[13]	Publication Bias[15]	
Aerobic Exercise	No systematic reviews identified									
Resistance Exercise	No systematic reviews identified									
Multimodal Exercise	Pedro, 2017	5 RCTs, N=253	Y	PY	Y	Y	N/A	Y	N/A	high
	Fillipas, 2010	9 RCTs, N=469	Y	PY	PY	Y	Y	Y	N	low
	Quiles, 2019	9 RCTs, N=638	N	PY	Y	Y	N/A	Y	N/A	low
	Leyes, 2008	15 RCTs+ 10 Open-label, N=1189	N	N	Y	N	N/A	N	N/A	critically low

Abbreviations: N = no; N/A = not applicable; PICO = population, intervention, comparator, outcome; PY = partial yes; RoB = risk of bias; RCTs = randomised controlled trials; Y = yes

[2] Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?
[4] Did the review authors use a comprehensive literature search strategy?
[7] Did the review authors provide a list of excluded studies and justify the exclusions?
[9] Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?
[11] If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?
[13] Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?
[15] If a quantitative synthesis was performed, did the review authors carry out adequate investigation of publication bias (small study bias) and discuss the likely impact on the results of the review?

Table 2g. AMSTAR 2 rating based on exercise modality, PICO: Effects of PA on viral load and CD4+ cell count among PLWHA

Exercise modality	Study	No. of Studies No. of participants	QUALITY ASSESSMENT/AMSTAR 2 CRITICAL ITEMS							AMSTAR 2 Score
			Apriori Methods[2]	Lit Search Strategy[4]	Excluded Studies[7]	RoB Assessment[9]	Statistical Methods[11]	RoB Results[13]	Publication Bias[15]	
Aerobic Exercise	Nixon, 2005	10 RCTs, N=276	Y	Y	Y	Y	Y	Y	Y	high
	O'Brien, 2004	10 RCTs, N=458 HIV+ only participants	Y	Y	Y	Y	Y	Y	Y	high
	O'Brien, 2016	24 RCTs, N=1242	Y	Y	y	Y	Y	Y	Y	high
	O'Brien, 2010	14 RCTs, N=454	Y	Y	Y	Y	Y	Y	Y	high
Resistance Exercise	Poton,2017	13 RCTs, N=291	PY	Y	PY	Y	Y	Y	Y	moderate
	O'Brien, 2017	20 RCTs, N=764	Y	Y	Y	Y	N/A	Y	N/A	high
	O'Brien, 2008	10 RCTs, N=332	Y	Y	Y	Y	Y	Y	Y	high
Multimodal Exercise	Ibemene, 2019b	19 RCTs, N=661 for participants	Y	Y	Y	Y	Y	Y	Y	high
	Pedro, 2017	5 RCTs, N=253	Y	PY	Y	Y	N/A	Y	N/A	high
	Lopez, 2015	28 RCTs + Quasi experimental studies, N=493	Y	PY	PY	N	N/A	N	N/A	critically low
	Leyes, 2008	15 RCTs+ 10 Open-label, N=1189	N	N	Y	N	N/A	N	N/A	critically low

Abbreviations: N = no; N/A = not applicable; PICO = population, intervention, comparator, outcome; PY = partial yes; RoB = risk of bias; RCTs = randomised controlled trials; Y = yes

[2] Did the report of the review contain an explicit statement that review methods were established prior to the conduct of the review and did report justify any significant deviations from protocol?
[4] Did the review authors use a comprehensive literature search strategy?
[7] Did the review authors provide a list of excluded studies and justify the exclusions?
[9] Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?
[11] If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?
[13] Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?
[15] If a quantitative synthesis was performed, did the review authors carry out adequate investigation of publication bias (small study bias) and discuss the likely impact on the results of the review?

Table 2h. AMSTAR 2 rating based on exercise modality, PICO: Effects of PA on cognition among PLWHA

Exercise modality	Study	No. of Studies No. of participants	QUALITY ASSESSMENT/AMSTAR 2 CRITICAL ITEMS							AMSTAR 2 Score	Summary of findings	Certainty
			Apriori Methods[2]	Lit Search Strategy[4]	Excluded Studies[7]	RoB Assessment[9]	Statistical Methods[11]	RoB Results[13]	Publication Bias[15]			
Aerobic Exercise	No systematic reviews identified											
Resistance Exercise	No systematic reviews identified											
Multimodal Exercise	No systematic reviews identified											

Abbreviations: PICO = population, intervention, comparator, outcome; RoB = risk of bias

[2] Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?
[4] Did the review authors use a comprehensive literature search strategy?
[7] Did the review authors provide a list of excluded studies and justify the exclusions?
[9] Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?
[11] If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?
[13] Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?
[15] If a quantitative synthesis was performed, did the review authors carry out adequate investigation of publication bias (small study bias) and discuss the likely impact on the results of the review?

Part 6. Abstracting and Grading the body of evidence

Evidence from all 24 full-text articles included were abstracted and these data are presented in Addendum 1. We utilized the GRADE (Grading of Recommendations Assessment, Development and Evaluation) process to develop "Evidence Profiles" tables, based on full-text narrative abstraction and AMSTAR 2 quality scoring of (Tables 3a-3h).

The GRADE criteria (Guyatt et al., 2008) used to rate the certainty of the evidence for each PICO were included the following: risk of bias, inconsistency, imprecision, Indirectedness and publication bias. Certainty regarding the extent to which the body of evidence represented a true estimate of effect for each outcome was reached based on the aforementioned criteria (Balshem et al., 2011). For each grade table, we provided an estimate of certainty or the strength of evidence (SOE, from high to very low) and a direction of effect (+ve, no effect, -ve). However, we ONLY provided a GRADE for studies scoring at least moderate for AMSTAR 2.

High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

GRADE TABLES

Table 3a. GRADE, PICO: Effects of PA on HRQOL among PLWHA

Exercise modality	Study	No. of Studies No. of participants	AMSTAR 2 Score	GRADE CRITERIA					Summary of findings	STRENGTH OF EVIDENCE
				Risk of Bias	Inconsistency	Imprecision	In-directedness	Publication Bias		
Aerobic Exercise	O'Brien, 2016	24 RCTs, N=1242	High	Y	N	N	N	Y	There is consistent evidence that aerobic exercise is effective in improving QoL. Main results show a statistically significant improvement in QoL. The two studies with 59 participants that were used to perform a meta-analysis for the eight sub-scales of the SF-36 questionnaire showed statistically significant and clinically relevant improvements (>10 point change) on subscales of mental health, role emotional and physical functioning, role physical, general health and energy/vitality sub-scale scores of the SF-36 questionnaire.	HIGH (+ve effect)
	O'Brien, 2010	14 RCTs, N=454	High	UC	N	N	N	N	There is consistent evidence amongst individual studies in the systematic review that aerobic exercise is effective in improving QoL. Stringer 1998 reported significant improvements in QoL for the exercise intervention groups compared to the non-exercising control groups. Baigis 2002 reported a non-significant trend that favoured those in the exercise group and significant improvements in the overall health subscale of the MOS-HIV questionnaire among exrcisers compared to non-exercisers. Mutimura 2008	HIGH (+ve effect)

									found significant improvements in QoL on the psychological, independence, social relationships, HIV and HAART-specific domains of QoL, and overall QoL for exercisers compared to non-exercisers.	
	Nixon, 2005	10 RCTs, N=276	High	Y	Y	N	Y	N	For aerobic exercise vs. no exercise, Stringer 1998 found significant improvements in QoL among those in the exercise group compared to no exercise. For moderate exercise vs. heavy exercise, no significant differences were found between groups by Stringer 1998.	LOW (+ve effect)
	O'Brien, 2004	10 RCTs, N=458 HIV+ only participants	high	Y	N	N	Y	UC	Meta-analysis was not possible due to the variety of outcomes used for psychological measures. Results of individual studies (Stringer 1998; Baigis, 2002), showed improvements in QoL in the exercise intervention groups.	MODERATE (+ve effect)
Resistance Exercise	O'Brien, 2017	20 RCTs, N=764	high	Y	Y	N	Y	N	The diversity of psychological outcomes did not allow for meta-analysis. Some individual studies found improvements in QoL and mood and life satisfaction scores among the exercise intervention groups (Agin 2001; Perez-Moreno 2007; Tiozzo 2011; Ogalha 2011). Bhasin (2000) found no change in HRQOL scores in either the testosterone or combined testosterone and exercise groups. Shevitz (2005) reported no significant change in QoL Adjusted Years within groups but reported the increase was greatest with combined progressive resistance exercise and nutrition compared with nutrition alone. The results are inconsistent.	LOW (inconclusive)
	O'Brien, 2008	10 RCTs, N=332	high	Y	Y	N	Y	N	The study reports mixed findings. Individual studies showed significant improvements in HRQOL in the exercise intervention group compared to the participants in the whey protein only and whey protein and PRE groups (Agin, 2001). On the other hand, Bhasin, 2000 found no association between changes in HRQOL measures between comparison groups. Shevitz, 2005 reported no significant change in QoL adjusted years within groups. However, the greatest increase was in the combined exercise and nutrition group.	VERY LOW (inconclusive)
Multimodal	Ibemene, 2019b	19 RCTs, N=661	high	Y	N	N	N	N	In a 6-month supervised exercise program, Mutimura 2008, found significant improvements	HIGH (+ve effect)

Exercise		participants included for QoL.							in the exercise group for psychological, independence and social relationships ($p < 0.001$) domains of QoL compared to the non-exercise group. Galantino 2005 also found an improvement in QoL for participants in the combined exercise group compared to the control group in the overall health perception subscale ($p=0.04$). Meta-analysis showed that in all domains of QoL, only role activity limitation due to physical health had a significant effect [5.04 point (95% CI:-8.49, -3.74, $p= 0.00001$)]. Both studies show a positive effect of combined aerobic and resistance exercise on PLWHA on HAART.	
	Nosrat, 2017	24 RCTs, N=1278	critically low	Y	N	N	N	N	Generally, among the studies that assessed QoL, there is consistent evidence that exercise is effective in improving QoL. Baigis 2002 reported significant improvement only in the health subscale of QoL in the exercise group compared to the control. Mutimura and Maharaj 2011 reported significant improvements in overall QoL domain in the exercise group compared to the control. Stringer reported significant improvement in QoL for both exercise groups compared to the control with no significant differences between the exercise groups (vigorous vs. moderate intensity). De Medeiros 2016 and Mnkandla 2016 reported significant improvements in QoL for the exercise group, while Hamid 2015 reported no significant differences in QoL between the two exercise groups. Galantino 2005, Fillipas 2006 and Rojas 2003 also reported improvement in QoL for the exercise group compared to the control group. Agin 2001 found that the progressive resistance exercise group showed significant improvement in subscales of PA, vitality, and general health perception of QoL and the combined resistance exercise and whey supplementation group significantly improved on the social functioning subscale of the QoL. Interestingly, there was a significant decline in the PA subscale of QoL for the whey protein supplementation group.	NO GRADE ASSIGNED (AMSTAR 2 score critically low)

	Gomes Neto, 2015	7 RCTs, N=386	high	Y	N	N	N	N	There is consistent evidence that exercise is effective in improving QoL. All studies that assessed QoL saw improvements in QoL in the exercise group compared to the control. Ogalha 2011 reported improvements in the general health and vitality domains of HRQOL in the exercise group compared to no exercise (p=0.05). Mutimura 2008 found that psychological independence, social relationships and HIV+HAART-specific domains of HRQOL improved in the exercise group compared to no exercise (p=0.05). Fillipas 2006 also found that the overall health and cognitive function domains of HRQOL improved in the exercise group compared to no exercise (p=0.05). Finally, Rojas 2003 reported improvements in health status, emotional well-being, energy, physical strength and global quality of life compared to no exercise (p=0.05).	HIGH (+ve effect)
	Gomes Neto, 2013a	29 RCTs + Clinical trials + Controlled trials, N=NR	critically low	Y	Y	N	N	N	Resistance exercise had little effect on quality of life (Agin 2001; Roubenoff 2001; Sattler 202; Shevitz 2005). Concurrent training showed a positive effect on QoL (Rojas 2003; Fillipas 2006; Mutimura 2008).	NO GRADE ASSIGNED (AMSTAR 2 score critically low)
	Gomes Neto, 2013b	8 RCTs, N=NR	low	Y	N	N	Y	N	All studies that assessed HRQOL reported significant improvements in HRQOL in the experimental group compared to the control group. Mutimura 2008 reported that psychological, independence, social relationships, HIV-HAART-specific and QoL domains significantly improved in the exercise group compared to no exercise. Perez-Moreno 2007, although statistical significance was not reached for the combined effect of group and time (p=0.09), QoL significantly increased (p<0.01) in the experimental group, whereas no change was observed in the controls. Fillipas 2006 reported an improvement in overall health and cognitive function subscales of QoL in the	NO GRADE ASSIGNED (AMSTAR 2 score low)

									experimental group. Rojas 2003 found better improvements in five subscales of QoL than in controls.	
	Bhatta, 2017	28 RCTs, N=4136	high	N	N	N	Y	N	Twenty-one studies reported improvements in QoL scores among the experimental group compared to the control group. Six studies reported an improvement in all the domains: two out of two domains (Berger 2008, Blank 2014, Brown 2014, McCain 2003), three out of three domains (Van Tam 2012), and four out of four domains (Wang 2010). The remaining studies reported that four out of five (Miles 2003, Mutimura), five out of nine (Cade 2010), five out of eight (Chhatre 2013) , seven out of 10 (Fillipas 2006), four out of 11 (Lechner 2003), two out of three (Li 2010), nine out of 10 (Maharaj 2011), two out of four (Molassiotis 2002), six out of eight (Ogalha 2011), and four out of six (Sikkema 2005), domains improved among the intervention group. Meta-analyses did not find any overall significant intervention effect in total QoL, social function, pain, energy/fatigue, role emotional, emotional well-being, and role physical domains of quality of life. Significant improvements were found in general health (overall effect: 0.37, 95% CI: 0.15, 0.60), mental health (0.70; 0.46, 0.93), environment (0.76; 0.44, 1.08) and physical function (0.58; 0.24, 0.91) domains of QoL among the intervention group.	HIGH (+ve effect)

	Lopez, 2015	28 RCTs + Quasi experimental studies, N=493	critically low	Y	N	N	Y	Y	The findings reveal a consistent evidence that exercise is effective in improving QoL. Stringer 1998 found significant changes in the aerobic training group on most items of the subset of a QoL questionnaire compared to the control group ($p<0.01$). Mutimura 2008 reported significant improvements in psychological, independence, social relationships, HIV+HAART-specific constructs and overall QoL ($p<0.0001$ for all) in the aerobic exercise arm compared to controls. Galantino 2005 found that combined aerobic and resistance exercise training (CARET) improves overall health perception in the exercise groups compared to the control group ($p=0.04$). Fillipas 2006 reported that the CARET group improved in overall health and cognitive functioning while the control slightly reduced their overall health and cognitive functioning with between group differences of 20.8 ($p=0.03$) and 14 ($p=0.04$) respectively. Tiozzo 2013 reported improved physical functioning (+11%, $p<0.03$) and mental health (+10%, $p<0.02$) in the CARET group compared to the control group. Gomes 2010 found improvements in Life Satisfaction in the CARET group ($p=0.002$) but the change in the exercise group was not significantly different from the control.	NO GRADE ASSIGNED (AMSTAR 2 score critically low)
	Pedro, 2017	5 RCTs, N=253	high	N	N	N	Y	N	Of the 5 studies that were included in the review, Mutimura 2008, reported a 3.2% increase in QoL in the aerobic exercise group compared to the control group.	MODERATE (+ve effect)
	Leyes, 2008	15 RCTs + 10 Open-label, N=1189	critically low	UC	N	UC	UC	UC	Exercise resulted in improvements in QoL (Shevitz 2005; Engelson 2006).	NO GRADE ASSIGNED (AMSTAR 2 score critically low)

Abbreviations: N = no; PICO = population, intervention, comparator, outcome; Y = yes; UC=unclear; RCTs = randomised controlled trials

1. Bhatta, 2017: First downgraded to moderate due to indirectness which may have been caused by heterogeneity due to differences in target population, exercise interventions, delivery persons, assessment tools, duration of intervention and follow up and study duration. This review also had low sample sizes. The moderate GRADE was then upgraded to high due to the evident dose-response relationship evident in the results.
2. Gomes Neto, 2015: First GRADED as moderate due to RoB because the risk to selective reporting was uncertain and none of the studies described blinding of therapists. This was later upgraded to high due to the evident dose-response relationship evident in the results.
3. Ibemene 2019b: First GRADED moderate due to RoB due to attrition. This was then upgraded to high due to the evident dose-response relationship.
4. Nixon, 2005: Downgraded to low due to (a) RoB due to attrition bias as a result of high withdrawal rates ranging from 4-76% (b) indirectness which may have been caused by the heterogeneity of outcome measures. There is also inconsistency in the findings.
5. O'Brien 2010: Not downgraded even if RoB is unclear.
6. O'Brien 2016: First, downgraded by the authors to low GRADE due to RoB due to performance bias and attrition bias (withdrawals of included studies were >15 %), publication bias was suspected, and due to variable heterogeneity on specific meta-analyses of sub scales ranging from (I^2 = 0 to 87 %). The low GRADE was later upgraded to high due to the evident dose-response relationship.
7. O'Brien, 2004: First downgraded to low because the authors report a possibility of publication bias, there was also attrition bias (20% drop out in 6 studies and more than 50% dropout in 2 studies), the review is also based on a small number of trials and participants. Heterogeneity may have occurred due to a variety of exercise interventions being used. The outcome was later upgraded to moderate due to the evident dose-response relationship.
8. O'Brien, 2008: Downgraded to very low because of a lot of variation among individual studies in the types of interventions, participants and outcomes, which may have led to heterogeneity and Indirectedness. Also, there is RoB due to attrition bias because of high withdrawal rates (>15%). There was also lack of blinding to the PRE intervention which may have resulted in the Hawthorn effect. The authors also report a possibility of performance bias due to increased levels of interaction between the investigators and participants in the exercise group resulting in more favourable outcomes for exercisers compared to non-exercisers. The review also used a small number of studies (n = 10) and there was total outcome data not available for 69 (17%) participants.
9. O'Brien, 2017: Low due to RoB because of high risk of performance and attrition bias; Inconsistency due to heterogeneity present due to participants' variability in ART, body composition, comorbidity, gender, type and location of intervention and methods of outcome measurement.
10. Pedro, 2017: Downgrade to moderate due to indirectness which might have been caused by different type of individuals in different studies, different types of exercise interventions and different types of assessment methods.

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Table 3b. GRADE, PICO: Effects of PA on body composition among PLWHA

Exercise modality	Study	No. of Studies No. of participants	AMSTAR 2 Score	GRADE CRITERIA					Summary of findings	STRENGTH OF EVIDENCE
				Risk of Bias	Inconsistency	Imprecision	Indirectedness	Publication Bias		
Aerobic Exercise	O'Brien, 2016	24 RCTs, N=1242	high	**Body mass index (BMI)**					Results showed no change in BMI of participants for four comparisons in the aerobic or combined aerobic and PRE group compared with non-exercising control; constant aerobic exercise compared with non-exercising control; combined aerobic and PRE exercise group compared with non-exercising control and combined aerobic exercise and diet/nutrition counselling group compared with diet/nutritional counselling group only.	HIGH (no effect)
				N	N	N	N	N		
				Lean body mass					Meta-analyses showed a significant increase in lean body mass of 1.75 kg for participants in the aerobic or combined aerobic and PRE group compared with participants in the non-exercising control group. No difference in lean body mass was reported for participants in the combined aerobic and PRE exercise group compared with non-exercising control group.	MODERATE (+ve effect)
				Y	N	N	N	N		
				Leg muscle area					A significant increase in change in leg muscle area of 4.79 cm2 among participants in the combined aerobic and PRE group compared with the non-exercising control group was reported.	MODERATE (+ve effect)
				Y	N	N	N	N		
				Percentage body fat					A significant decrease in percent body fat of 1.12 % for participants in the constant aerobic exercise group compared with participants in the non-exercising control	HIGH (+ve effect)

				Y	N	N	N	N	group was found and a significantly greater decrease in percent body fat of 2.35 % among participants in the combined aerobic exercise and diet or nutrition counselling group compared with diet or nutritional counselling group alone.	
				Fat mass					There was no difference in change in fat mass for two comparisons of participants in the aerobic or combined aerobic and PRE group compared with non-exercising control, and combined aerobic and PRE exercise group compared with non-exercising control.	MODERATE (no effect)
				Y	N	N	N	N		
				Waist and hip circumference and waist-to-hip ratio					No significant differences were found in change in waist circumference, hip circumference or waist-to-hip ratio for participants in the aerobic or combined aerobic and PRE group compared with non-exercising control; as well as participants in the constant aerobic versus exercise groups and combined aerobic and PRE exercise groups. Results found a slightly greater increase in waist to hip ratio of 0.02 (95 % CI: 0.01 to 0.03) for participants in the combined exercise and diet or nutrition counselling group compared with diet or nutritional counselling group only however these results were not clinically important.	MODERATE (inconclusive)
				Y	N	N	N	N		
	O'Brien, 2010	14 RCTS, N= 454	high	**BMI**					Results showed no difference in the change in BMI (WMD: 0.85kg/cm2, 95% CI: -0.62, 2.31, n=49, *P*=0.26) (Lox 1995, Perna 1999) for participants in the aerobic exercise group compared with participants in the non-exercising control group, and no difference in change in fat mass (WMD: 0.07 kg, 95% CI: -1.22, 1.36, n=60, *P*=0.92) (Grinspoon 2000, Dolan 2006) for participants in the combined aerobic and PRE group compared with the non-exercising control group.	HIGH (no effect)
				UC	N	N	N	N		
				Hip circumference					No difference in change in hip circumference (WMD: 0.11cm, 95% CI: -	HIGH (no effect)

				UC	N	N	N	N	0.63, 0.85, n=142, *P*=0.77) (Smith 2001, Mutimura 2008a) was reported for participants in the aerobic exercise group compared with participants in the non-exercising control group as well as participants in the constant aerobic exercise group compared with the non-exercising control group were also reported.	
				Waist circumference					Results showed no difference in change in waist circumference (WMD: -3.53cm, 95% CI: -10.25, 3.19, n=142, *P*=0.30) (Smith 2001, Mutimura 2008a) for participants in the aerobic exercise group compared with participants in the non-exercising control group as well as participants in the constant aerobic exercise group compared with the non-exercising control group were also reported.	HIGH (no effect)
				UC	N	N	N	N		
				Waist-to hip ratio (WHR)					No difference in change in waist-to-hip ratio (WMD: -0.51, 95% CI: -1.47, 0.45, n=142, *P*=0.30) (Smith 2001, Mutimura 2008a) reported for participants in the aerobic exercise group compared with participants in the non-exercising control group as well as participants in the constant aerobic exercise group compared with the non-exercising control group were also reported.	HIGH (no effect)
				UC	N	N	N	N		
				Percent body fat					Meta-analyses showed a significant decrease in percent body fat of 1.12% (95% CI: -2.18, -0.07, n=119, *P*=0.04) (Lox 1995, Mutimura 2008a) for participants in the aerobic exercise group compared with participants in the non-exercising control group.	HIGH (+ve effect)
				UC	N	N	N	N		
				Leg muscle area					Meta-analysis also showed a significant increase in change in leg muscle area of 4.79 cm2 among participants in the combined aerobic and PRE group compared with the non-exercising control group (95% CI: 2.04, 7.54, n=60, *P*=0.0007) (Grinspoon 2000, Dolan 2006).	HIGH (+ve effect)
				UC	N	N	N	N		

Resistance Exercise	O'Brien, 2017	20 RCTs, N=764	high	**BMI**					Sixteen meta-analyses were performed, each for body mass index, lean body mass, fat mass, arm and thigh girth, leg muscle area, and waist circumference. Results demonstrated no difference in change in body mass index for three comparisons of participants in the PRE or combined PRE and aerobic exercise group compared with non-exercising control; combined PRE and aerobic exercise group compared with non-exercising control and combined PRE (or combined PRE and aerobic exercise) and diet/nutrition counselling group compared with diet/nutritional counselling group only.	MODERATE (no effect)
				Y	N	N	Y	N			
				Lean body mass					Meta-analyses demonstrated no difference in change in lean body mass for three comparisons of participants in the PRE or combined PRE and aerobic exercise group compared with non-exercising control; combined PRE and aerobic exercise group compared with non-exercising control and combined PRE (or combined PRE and aerobic exercise) and testosterone group compared with the testosterone only group.	LOW (no effect)
				Y	N	N	Y	N			
				leg muscle area					Results for leg muscle area results demonstrated a significant increase in change in leg muscle area of 4.79 cm2 among participants in the combined PRE and aerobic exercise group compared with the non-exercising control group. No difference was found in leg muscle area for participants in the PRE (or combined PRE and aerobic exercise) and testosterone group compared with the testosterone only group.	LOW (+ve effect)
				Y	N	N	Y	N			
				Fat mass					Results demonstrated no difference in change in fat mass for three comparisons of participants in the PRE or combined PRE and aerobic exercise group compared with non-exercising control; combined PRE and aerobic exercise group compared with non-exercising control, and combined PRE (or	MODERATE (no effect)
				Y	N	N	Y	N			

									combined PRE and aerobic exercise) and testosterone group compared with the testosterone alone group.	
				waist circumference					No significant differences were found in change in waist circumference for participants in the combined PRE and aerobic exercise group compared with no exercise.	LOW (no effect)
				Y	N	N	Y	N		
				arm and thigh girth					Results demonstrated a significant increase in change in arm and thigh girth of 7.91 cm among participants in the PRE group compared with the aerobic exercise group. The point estimate is greater than 5 cm indicating a potential clinically important greater increase in girth among PRE versus aerobic exercisers. Heterogeneity was present in meta-analysis for arm and thigh girth.	MODERATE (+ve effect)
				Y	N	N	Y	N		
	O'Brien, 2008	10 RCTs, N=332	high	Y	N	N	Y	N	Nine of the 10 studies assessed weight and/or body composition. Six meta-analyses were performed for body composition. Meta-analysis showed a statistically significant and clinically important increase in arm and thigh girth of 7.91cm (95%CI: 2.18, 13.65; p0.007; n46) for participants in the PRE or combined PRE and aerobic exercise intervention group compared to the non-exercising control group. Given that many participants in the individual studies were diagnosed with AIDS-related wasting syndrome, increases in body composition may be interpreted as a favourable outcome. This meta-analysis was statistically significant for heterogeneity ($p = 0.08$; $I^2 = 67.4\%$) using a random effects model. Reasons for heterogeneity may be attributed to the different methods in which mean arm and thigh girth was measured between studies. The other five meta-analyses for body composition showed no difference among groups.	HIGH (+ve effect)

	Poton,2017	13 RCTs, N=291	moderate	UC	UC	UC	N	N	In general, the author found no change in lean body mass (LBM), with an overall effect size of 0.26 (−0.001 to 0.52; p = 0.051). In addition, there was low heterogeneity for trials investigating lean body mass (I^2 = 0.00; p = 0.88).	MODERATE (no effect)
Multimodal Exercise	Pedro, 2017	5 RCTs, N=253	high	N	N	N	Y	N	The authors found a decrease in body fat percentage in response to aerobic and concurrent training. There was also a reduction in trunk and limb fat and an increase in lean mass. Furthermore, one study showed that body fat percentage decreased after aerobic training. One of the limitation was that authors of this study did not conduct heterogeneity test among the studies together with small sample size. In summary, it might not be possible to conclude that physical training improves body composition; therefore, more studies are needed, using validated methods to investigate the effects of different types of training on body composition in individuals with HALS.	HIGH (+ve effect)
	Fillipas, 2010	9 RCTs, N=469	low	Y	N	N	Y	N	The results showed that compared to non-exercising controls, aerobic exercise (AE) resulted in decreased body mass index (weighted mean difference [WMD] −1.31; 95% CI, −2.59, −0.03; n=186), triceps skinfold thickness of subcutaneous fat (WMD −1.83 mm; 95% CI, −2.36, −1.30; n=144), total body fat (%) (standardised mean difference [SMD], −0.37; 95% CI, −0.74, −0.01; n=118), waist circumference (SMD −0.74 mm, 95% CI, −1.08, −0.39; n=142), and waist-hip ratio (SMD −0.94; 95% CI, −1.30, −0.58; n=142). Progressive resistive exercise (PRE) resulted in increased body weight (5.09 kg; 95% CI, 2.13, 8.05; n=46) and arm and thigh girth (SMD 1.08 cm; 95% CI, 0.35, 1.82; n=46). Aerobic exercise decreases adiposity and may improve certain lipid subsets. PRE increases body weight and limb girth.	NO GRADE ASSIGNED (AMSTAR 2 score low)

	Leyes, 2008	15 RCTs + 10 Open-label, N=1189	critically low	UC	Y	UC	UC	UC	One study (Dolan 2006) found no changes for body mass index (BMI), total body fat, subcutaneous adipose tissues (SAT), visceral adipose tissue (VAT). In another study (Roubenoff 1999a) found a significant reduction in body fat (-1.5 kg, 2%), especially for trunk fat (1.1 kg), but no improvements were found in lean body mass (LBM). Jones 2001 shows that a 10-week exercise training causes reduction in percent body fat and waist-to-hip ratio. One study (Yarasheki 2001) found that resistance exercise has a significant increase in LBM with various changes in fat mass. For example, there was an increase in LBM (+1.4 kg; 2%), with no reduction in whole body fat. One study (Roubenoff 1999b) also showed a significant increases in LBM (+1.7 kg; 3%) and reduction in fat (-0.9 kg; 4%).	NO GRADE ASSIGNED (AMSTAR 2 score critically low)
	Gomes Neto, 2013a	29 RCTs, N=1216	critically low	UC	N	N	Y	N	The findings of this study showed that resistance exercise training improved outcomes related to body composition. For example, there was increase in lean body mass, mid-thigh muscle area, bone mineral density, and reduction in body weight. As for aerobic exercise training, reduction was observed in body weight, total body fat and waist-to-hip ratio. Furthermore, concurrent training revealed significant increases in lean body mass, thigh muscle volume, mid-thigh muscle area, and a reduced thigh muscle adiposity, percent body fat and waist-to-hip ratio.	NO GRADE ASSIGNED (AMSTAR 2 score critically low)

Abbreviations: N = no; N/A = not applicable; PICO = population, intervention, comparator, outcome; PY = partial yes; RoB = risk of bias; Y = yes; UC=unclear; RCTs = randomised controlled trials

1. O'Brien, 2016

- BMI: The authors of the review did not downgrade BMI on the GRADE quality of evidence because this was an objective outcome of interest and publication bias was not suspected.
- Lean body mass: Downgraded to moderate due to attrition and performance bias reported in the review.
- Leg muscle area: Downgraded to moderate due to attrition and performance bias reported in the review.

- Percentage body fat: Upgraded from moderate to high due to large magnitude of effect.
- Fat mass: Downgraded to moderate due to attrition and performance bias reported in the review.
- Waist and hip circumference and waist-to-hip ratio: Downgraded to moderate due to attrition and performance bias reported in the review.

2. O'Brien, 2010

    - BMI; Hip circumference; waist circumference; waist-to hip ratio; percent body fat, fat mass, leg muscle area: not downgraded even if RoB was unclear.

3. O'Brien, 2008: Downgraded to low because of a lot of variation among individual studies in the types of interventions, participants and outcomes, which may have led to heterogeneity and Indirectedness. Also, there is RoB due to attrition bias because of high withdrawal rates (>15%). There was also lack of blinding to the PRE intervention which may have resulted in the Hawthorn effect. The authors also report a possibility of performance bias due to increased levels of interaction between the investigators and participants in the exercise group resulting in more favourable outcomes for exercisers compared to non-exercisers. The review also used a small number of studies (n = 10) and there was total outcome data not available for 69 (17%) participants. The low GRADE was then upgraded to high due to the evident dose-response relationship evident in the results.

4. O'Brien, 2017

    - BMI: Graded moderate because the authors of the review were moderately confident in the effect estimate of a non-significant increase of 0.40 kg/m^2 for body mass index comparing PRE (or combined PRE and aerobic exercise) with no exercise. The outcome was downgraded on the GRADE quality of evidence because publication bias was suspected and that withdrawal rates among the majority of included studies were <15%.
    - Lean body mass; Leg muscle are; Waist circumference: Downgraded to low because a high risk of performance bias existed across the included studies as 85% of them had a high risk of performance bias due to lack of participant blinding to the exercise intervention.
    - Fat mass: The authors of the review GRADED the outcome as moderate because they were moderately confident with the effect estimate of a non-significant increase of 0.36 kg in fat mass comparing PRE (or combined PRE and aerobic exercise) with non-exercising control. The outcome was downgraded on the GRADE quality of evidence due to incomplete outcome data (withdrawals of included studies were >15%).
    - Arm and thigh girth: First downgraded to very low because a high risk of performance bias existed across the included studies as 85% of them had a high risk of performance bias due to lack of participant blinding to the exercise intervention. Furthermore, heterogeneity was reported in the meta-analyses done for arm and thigh girth. The very low GRADE was then upgraded to moderate due to the evident dose-response relationship in the results.

5. Pedro, 2017: downgraded to moderate due to indirectness which might have been caused by different type of individual indifference studies, and different type of intervention and different type of assessment methods. The moderate GRADE was then upgraded to high due to the evident dose-response relationship evident in the results.

6. Poton 2017: Downgraded to moderate due to uncertainty in the status of RoB, inconsistency and imprecision as there is insufficient information in the review.

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Table 3c. GRADE, PICO: Effects of PA on anxiety/depression among PLWHA

Exercise modality	Study	No. of Studies No. of participants	AMSTAR 2 Score	GRADE CRITERIA					Summary of findings	STRENGTH OF EVIDENCE
				Risk of Bias	Inconsistency	Imprecision	Indirectedness	Publication Bias		
Aerobic Exercise	O'Brien, 2016	24 RCTs, N=1242	high	Y	N	N	N	N	One meta-analysis was performed and demonstrated a significant improvement in the depression-dejection sub scale of the Profile of Mood States Scale (POMS) by a	MODERATE (+ve effect)

									reduction of 7.68 points for participants in the aerobic exercise intervention group compared with the non-exercising control group. This represents a clinically important improvement in depression-dejection among exercisers compared to non-exercisers.	
	O'Brien, 2010	14 RCTs, N=454	high	UC	N	N	N	N	One meta-analysis was performed and showed a significant improvement in the depression-dejection subscale of the POMS by a reduction of 7.68 points (95% CI: -13.47, -1.90, n=65, *P*=0.009) for participants in the aerobic exercise intervention group compared with the non-exercising control group (LaPerriere 1990, Smith 2001). This represents a clinically important improvement in depression-dejection among exercisers compared to non-exercisers.	HIGH (+ve effect)
	Nixon, 2005	10 RCTs, N=276	high	Y	N	N	N	N	Meta-analysis demonstrated a significant improvement in the depression-dejection subscale of the POMS by a reduction of 7.68points (95% CI: -13.47, -1.90, n=65, p=0.009) for participants in the aerobic exercise intervention groups compared to the non-exercising control groups (LaPerriere 1990; Smith 2001). This represents a clinically important improvement in depression-dejection among exercisers compared to non-exercisers. LaPerriere 1990 found higher levels of anxiety and depression in non-exercising controls compared with exercisers. Smith 2001 (or Neidig 2003) found significant improvements in depression for exercisers compared to non-exercisers.	HIGH (+ve effect)
	O'Brien, 2004	10 RCTs, N=458 HIV+ only participants	high	Y	N	N	Y	UC	Meta-analysis was not possible for psychological status due to the variety of outcomes used. Results of psychological measures of individual studies show improvement in anxiety and depression (LaPerriere 1990).	LOW (+ve effect)

	Lofgren, 2018	7 RCTs + 2 Comparison trials + 6 Intervention trials +3 Cohort studies (1 study had 2 Cohorts) + 1 intervention, N=1966	critically low	UC	UC	UC	N	UC	A novel study used exercise to improve pulmonary function as well as mental health (Aweto 2016). They had 66% reduction in the depression symptoms and a net reduction of 49%.	Low (+ve effect)
Resistance Exercise	No systematic reviews identified									
Multimodal Exercise	Nosrat, 2017	24 RCTs, N=1278	critically low	Y	N	N	N	N	In one study, seropositive controls scored significantly higher in anxiety and depressive symptoms at the 1-week post HIV status notification when compared to the seropositive exercisers. Other researchers reported significant improvements in the depressive symptoms. However in two other studies, researchers reported no significant change in anxiety and depressive symptoms. One study reported a significant reduction in the depressive symptoms and mood disturbances in the resistance exercise group compared to non-exercisers.	Moderate
	Lopez, 2015	28 RCTs + Quasi experimental studies, N=493	critically low	Y	Y	N	Y	Y	The studies by Smith (2001), Galantino (2005), Neidig (2003), and Fillipas (2010) evaluated the effect of exercise on mental health. Smith 2001 and Neidig (2003) found that progressive aerobic training significantly improved depressive symptoms as measured by Center for Epidemiological Studies-Depression Scale ($p = 0.03$) and Profile of Mood States (POMS; $p = 0.011$), but not the Beck Depression Inventory. Galantino 2005 found that CARET had a significant main effect on tension anxiety on the POMS ($p < 0.005$).	NO GRADE ASSIGNED (AMSTAR 2 score critically low)

	Heissel, 2019	10 RCTs, N=479	low	Y	N	N	N	Y	Nine studies investigated depression (n = 194 in the exercise group, n = 201 in the control group). An overall standardized mean difference SMD = −0.84 (95% CI -1.57 to −0.11) in favour of the exercise group was found in the random-effect model for post-intervention values. There was a significant overall effect (Z = 2.27, p = 0.02) of exercise compared to the control group at post-treatment. Statistical heterogeneity was high (I2 = 91%, X2 = 87.82, df = 8, p < 0.001). Five studies investigated anxiety (n = 92 in the exercise group, n = 93 in the control group). An overall standardized mean difference SMD = −1.23 (95% CI -2.42 to −0.04) in favour of the exercise group was found in the random-effect model for post-intervention values. There was a significant overall effect (Z = 2.03, p = 0.04) of exercise compared to the control group at post-treatment. Pre-post analysis showed that the SMD difference in the depression post analysis (−0.84) and pre-post analysis (−0.91) was 0.07 favouring the pre-post analysis. A minimal difference in SMD post minus pre-post was found for anxiety (0.04) favouring the pre-post analyses. Therefore, no substantial differences between the results and heterogeneity between post and pre-post analyses exist.	NO GRADE ASSIGNED (AMSTAR 2 score low)

Abbreviations: N = no; N/A = not applicable; PICO = population, intervention, comparator, outcome; PY = partial yes; RoB = risk of bias; Y = yes; UC = unclear; RCTs = randomised controlled trials

1. O'Brien, 2016: Downgraded to moderate due to attrition and performance bias.
2. O'Brien, 2010: Not downgraded due to large effect size.
3. O'Brien, 2004: Downgraded to low because the authors report a possibility of publication bias, there was also attrition bias (20% drop out in 6 studies and more than 50% dropout in 2 studies), the review is also based on a small number of trials and participants. Heterogeneity may have occurred due to a variety of exercise interventions being used.
4. Lofgren, 2018: Downgraded to low because only one study reports on anxiety and depression and there is no clarity on RoB, inconsistency, imprecision and publication bias.
5. Nixon, 2005: Downgraded to moderate due to high withdrawal rates amongst the included studies. The low GRADE was then upgraded to high due to the evident dose-response relationship in the results.

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Table 3d. GRADE, PICO: Effects of PA on fitness and functional capacity among PLWHA

Exercise modality	Study	No. of Studies No. of participants	AMSTAR 2 Score	GRADE CRITERIA					Summary of findings	STRENGTH OF EVIDENCE
				Risk of Bias	Inconsistency	Imprecision	Indirectedness	Publication Bias		
Aerobic Exercise	O'Brien, 2016	24 RCTs, N=1242	high	**VO2max**					Six meta-analyses were performed for VO2max, five of which were significant favouring exercise compared with non-exercise. Meta-analyses showed a significant improvement in change of VO2max of 2.63 mL/kg/min for participants in the aerobic exercise intervention group compared with the non-exercising control group; significant improvement in change of VO2max of 2.40 ml/kg/min for participants in the constant aerobic exercise group compared with the non-exercising control group; significant improvement in VO2max of 3.71 ml/kg/min for participants in the combined aerobic and PRE group compared with the non-exercising control group; significant improvement of 2.87 ml/kg/min for participants in the aerobic or combined aerobic and PRE group compared with non-exercising control group and a significant trend towards a greater improvement in VO2max of 4.30 mL/kg/min for participants in the heavy-intensity exercise group compared with the moderate-intensity exercise group. No significant difference in change in VO2max was found for participants in the combined aerobic exercise and diet or nutrition counselling group compared with the diet or nutrition	VERY LOW (+ve effect)
				Y	N	N	N	N		

									counselling group only. All point estimates were greater than 2 mL/kg/min, which suggest a potential clinically important improvement in VO2max among exercisers and a greater improvement with heavy versus moderate-intensity exercise.	
				Maximum Heart Rate (HRmax)					Three meta-analyses performed showed a non-significant trend towards a decrease in HRmax of − 9.81 beats/min, 7.33 beats/min and 4.91 beats/min for participants in the aerobic exercise intervention group compared with the non-exercising control group; aerobic or combined aerobic and PRE group compared with the non-exercising control; and combined aerobic and PRE compared with non-exercising control respectively.	MODERATE (no effect)
				Y	N	N	N	N		
				Exercise time					The two meta-analyses that were performed showed significant increases in exercise time of 3.29 min for participants in the combined aerobic and PRE group compared with the non-exercising control group; and 2.66 min for participants in the aerobic or combined aerobic and PRE group compared with the non-exercising control group. Point estimates did not reach the 5 min threshold for clinical importance.	HIGH (+ve effect)
				Y	N	N	N	N		
				Strength					Meta-analyses showed significant improvements in upper and lower body	LOW (+ve effect)

				Y	N	N	N	N	strength as measured by increases in 1-repetition maximum for chest press, and knee flexion; and a non-significant improvement towards increases in 1-RM for leg press and knee extension for participants in the combined aerobic and PRE group versus non-exercising control group. Two meta-analyses were conducted comparing aerobic versus resistive exercise. Significantly, greater increases in strength were found among participants in the PRE group compared with participants in the aerobic exercise only group for upper and lower muscle groups. All six point estimates for upper and lower extremity strength are greater than 2 kg and 5 kg respectively indicating a clinically important greater increase in strength for resistive exercisers compared with aerobic exercise.	
	O'Brien, 2010	14 RCTs, N=454	high	**VO2max**					Three meta-analyses were performed for VO2max. Meta-analyses showed a significant improvement in change of VO2max of 2.63 mL/kg/min for participants in the aerobic exercise intervention group compared with the non-exercising control group (95% CI: 1.19, 4.07, n=276, *P*=0.0003) (Perna 1999; Smith 2001; Stringer 1998, Baigis 2002, Mutimura 2008a); significant improvement in change of VO2max of 2.40 ml/kg/min for participants in the constant aerobic exercise group compared with the non-exercising control group (95% CI: 0.82, 3.99, n=248, *P*=0.003) (Stringer 1998, Smith 2001, Baigis 2002, Mutimura 2008a); and a significant trend towards a greater improvement in VO2max of 4.30 mL/kg/min for participants in the heavy-intensity exercise group compared with the moderate-intensity exercise group (95% CI: 0.61,7.98, n=24, *P*=0.02) (Figure 13). All point estimates are greater than 2 mL/kg/min, which suggests a potential clinically important improvement in VO2max among exercisers and a greater	HIGH (+ve effect)
				UC	N	N	N	N		

									improvement with heavy- versus moderate-intensity exercise.	
				Maximum Heart Rate (HRmax)					One meta-analysis was performed and showed a non-significant decrease in HRmax of -9.81 beats/min (95% CI: -26.28, 6.67, n=49, *P*=0.24) for participants in the aerobic exercise intervention group compared with the non-exercising control group (Lox 1995, Perna 1999).	HIGH (+ve effect)
				UC	N	N	N	N		
				Exercise Time (minutes)					One meta-analysis was performed and showed a non-significant increase in exercise time of 3.92 minutes (95% CI: -0.63, 8.47, n=62, *P*=0.09) for participants in the combined aerobic and PRE group compared with the non-exercising control group (Rigsby 1992, Dolan 2006).	HIGH (+ve effect)
				UC	N	N	N	N		
				Strength					Six of the 14 included studies assessed muscle strength (Rigsby 1992, Lox 1995, Perna 1999, Grinspoon 2000, Driscoll 2004a, Dolan 2006). Meta-analysis could not be performed for strength due to differences in the types of strength outcomes assessed, types of interventions, types of comparison groups, and types of participants; however, individual studies suggested improvements in strength among exercisers compared with non-exercisers.	LOW (+ve effect)
				UC	N	N	Y	N		
	Nixon, 2005	10 RCTs, N=276	high	Y	N	N	Y	N	Nine of the 10 included studies reported cardiopulmonary outcomes, six of which compared constant or interval aerobic exercise to non-exercising controls (Baigis	MODERATE (+ve effect)

									2002; LaPerriere 1990; Lox 1995; Perna 1999; Smith 2001; Stringer 1998). Meta-analysis showed a non-significant improvement in VO2max of 1.8 ml/kg/min (95% CI: -0.5, 4.2, n=179, p=0.13) for participants in the aerobic exercise intervention groups compared to non-exercising control groups (Baigis 2002; Perna 1999; Smith 2001; Stringer 1998). The confidence interval demonstrates a positive trend towards improvements in VO2max in the exercise groups.	
	O'Brien, 2004	10 RCTs, N=458 HIV+ only participants	high	Y	N	N	Y	UC	Nine studies assessed cardiopulmonary status (Rigsby 1992; MacArthur 1993; Jadad 1996; Stringer 1998; Ledergerber 1999; Perna 1999; Terry 1999; Smith 2001; Baigis 2002). Significant improvements were found among individual trials of aerobic exercisers when compared with non-exercising controls, but meta-analysis could only be performed using VO2max due to varying outcomes reported. Three meta-analyses were performed, showing nonsignificant improvement in VO2max of 1.84 $mL \cdot kg^{-1} \cdot min^{-1}$ (95% CI:-0.53, 4.20, N 179) for participants in the aerobic exercise intervention group compared with non-exercising control group, non-significant improvement in VO2max of 1.56 $mL \cdot kg^{-1} \cdot min^{-1}$ (95% CI: -0.94, 4.07, N 151) for participants in the constant exercise group compared with the non-exercising control group, and statistically nonsignificant greater improvement in VO2max of 4.29 $mL \cdot kg^{-1} \cdot min^{-1}$ (95% CI: -1.23, 9.82, N 24) for participants in the heavy-intensity aerobic exercise group compared with participants in the moderate-intensity exercise group. This finding reached clinical importance but not statistical significance.	HIGH (+ve effect)
Resistance Exercise	Poton,2017	13 RCTs, N=291	moderate	UC	UC	UC	N	N	In general, the author found an improvement in muscular strength with resistance exercise with an overall effect size of 1.58 (1.46–1.70; $p < 0.01$; ~35.5%).	MODERATE (+ve effect)

									In addition, the I^2 statistic confirmed high heterogeneity for trials that investigated muscular strength (I^2 = 66.28; P < 0.001).	
	O'Brien, 2008	10 RCTs, N=332	high	Y	N	N	Y	N	Two studies evaluated sub maximum heartrate (Lox 1995; Rigsby 1992). Meta-analysis showed a non-significant reduction in heart rate of -13.02 beats/minute (95% CI: -26.67, 0.64; p = 0.06; n = 46) for participants in the PRE or combined PRE and aerobic exercise group compared to the non-exercising control group. The confidence interval indicated a trend towards a clinically important improvement in sub maximum heart rate among exercisers compared with non-exercisers (10 beats/min). This meta-analysis reported statistical significance for heterogeneity (p = 0.0005; I^2 = 91.8%) using a random effects model. Heterogeneity was likely attributed to the different exercise interventions between the studies. Two studies measured VO_{2max} (Dolan 2006; Lox 1995). Meta-analysis showed no difference in change in VO_{2max} among participants in the PRE or combined PRE and aerobic exercise group compared to the non-exercising control group (WMD: 81.99 ml/ kg/min; 95% CI: -155.34, 319.33; p = 0.50; n = 60). Two studies assessed exercise time (Dolan 2006; Rigsby 1992). Meta-analysis showed a non-significant increase in exercise time of 3.92 minutes (95% CI: -0.63, 8.47; p = 0.09; n = 62) for participants in the combined PRE and aerobic exercise group compared to the non-exercising control group. The confidence interval indicated a trend towards an improvement in exercise time among exercisers compared with non-exercisers. This meta-analysis reported statistical significance for heterogeneity (p < 0.00001; I^2 = 98.4%) using a random effects model. Heterogeneity was likely attributed to differences in the outcomes measured (total time to voluntary	HIGH (+ve effect)

									exhaustion versus exercise time). In terms of strength, all studies reported on strength outcomes but meta-analyses could not be performed due to differences in outcomes and participants; however, nine of the 10 studies suggested improvements in strength among exercisers compared to non-exercisers. Grinspoon 2000 found no significant differences in strength for participants in the combined aerobic and PRE exercise group compared with participants in the non-exercising control group.	
	O'Brien, 2017	20 RCTs, N=764	high	**VO2max**					Two meta-analyses were performed for VO2max, one of which included the same studies. Results showed a significant and potential clinically important improvement in change of VO2max of 3.71 mL/kg/min for participants in the aerobic exercise intervention group compared with the non-exercising control group. There was no statistical significance for heterogeneity.	MODERATE (+ve effect)
				Y	N	N	Y	N		
				HRmax					Two meta-analyses were performed and showed no significant difference in change in HRmax for participants in the PRE or combined PRE and aerobic exercise group compared with the non-exercising control; and combined PRE and aerobic exercise group compared with non-exercising control. Heterogeneity was present in both meta-analyses ($p < 0.1$).	LOW (no effect)
				Y	N	N	Y	N		
				Exercise time					Two meta-analyses were performed, one of which included the same studies. Meta-analysis demonstrated a significant increase in exercise time of 3.29 min for participants in the combined PRE and aerobic exercise group compared with the non-exercising control group. The point estimate did not reach the 5 min threshold for clinical importance. Meta-analyses were statistically significant for heterogeneity ($p < 0.1$).	HIGH (+ve effect)
				Y	N	N	Y	N		

				Strength					Ten meta-analyses were performed four strength outcomes, four of which included duplicate studies. improvements in upper and lower body strength as determined by increases in 1-repetition maximum for chest press, and knee flexion; and a non-significant trend towards improvement (increases) in 1-RM for leg press and knee extension for participants in the combined PRE and aerobic group versus non-exercising control group. Two more meta-analyses were conducted comparing combined exercise and testosterone compared with testosterone alone. Results indicated a non-significant trend towards greater increases in strength among participants in the combined exercise and testosterone group compared with participants in the testosterone alone group for knee flexion and extension. Five of the six point estimates for upper and lower extremity strength were greater than 2 kg and 5 kg respectively indicating a clinically important greater increase with exercise compared with non-exercise. Heterogeneity was present in five meta-analyses.	LOW (inconclusive)
				Y	N	N	Y	N		

Multimodal Exercise	Voigt, 2018	15 RCTs, N=537	moderate	UC	N	N	Y	N	For aerobic exercise training, Galantino (2005) revealed significant improvements in both cardiovascular (maximum oxygen consumption) and flexibility outcomes. Two studies (Agin 2001 and Strawford 1999) also reported significant improvements in strength outcomes in the intervention group compared to those in the control group using progressive resistance training interventions. Seven studies which uses combined aerobic and PRT interventions found significant improvement in overall strength, cardiovascular, and flexibility parameters. One study with a combined yoga and meditation, and another study with yoga alone found no changes in functional capacity. In another study that uses the tai chi exercise intervention revealed significant improvements in both flexibility and cardiovascular outcomes.	HIGH (+ve effect)
	Gomes Neto, 2013b	8 RCTs, N=NR	critically low	Y	N	N	Y	N	In terms of cardiopulmonary status, seven studies reported significant improvement in the concurrent training group compared to control group. For example, Mutimura 2008 used a Shuttle's test to evaluate the functional capacity to predict maximum oxygen uptake (VO2max). It was improved from 4.7 ± 3.9 to 0.5 ± 0.3 mL/kg per min in the intervention group compared to control ($P < 0.001$). One study did not compare the improvement intergroup, because they used a before and after evaluation (Rojas 2003).	NO GRADE ASSIGNED (AMSTAR 2 score critically low)
	Leyes, 2008	15 RCTs + 10 Open label, N=1189	critically low	UC	N	UC	UC	UC	One study reported that 16 weeks of supervised home-based aerobic and resistance in improved fitness and strength in the exercise group. In patients with lipoatrophy, 10 weeks of an exercise intervention resulted in muscle strength. Sixteen weeks of training have also resulted in muscular strength (Yarasheski, 2001). Eight weeks of resistance training produced significant increases in strength.	NO GRADE ASSIGNED (AMSTAR 2 score critically low)

	Lopez, 2015	28 RCTs + Quasi experimental studies, N=493	critically low	Y	Y	N	Y	Y	Fifteen studies from the present review reported the effects of exercise training on aerobic capacity and strength. One study showed that VO2max of PLWH increased significantly as a result of eight weeks of moderate exercise training, which was correlated with an increase in CD4+ T cell count and a de-crease in blood pressure; both of potential clinical relevance . One study revealed that VO2 max of PLWH increased significantly as a result of eight weeks of moderate exercise training, which was correlated with an increase in CD4+ T cell count and a decrease in blood pressure; both of potential clinical relevance (Ezema 2014). Five studies evaluated the effect of aerobic training on different measures of aerobic capacity including VO2 max, anaerobic threshold (VO2 threshold), respiratory equivalent (RE), lactic acid threshold (LAT), physical endurance, and/or heart rate. Thoni 2002 reported significant improvements in VO_2 max adjusted for body weight (measured during a progressive exercise test; $p = 0.005$), VO_2 threshold (measured using the Beaver method; $p = 0.004$), and RE for oxygen ($p = 0.04$) following an aerobic exercise intervention. Lindegaard 2008 reported a 14.4% improvement in VO2max ($p < 0.01$) following an endurance training intervention, in addition to a 7.8% increase in strength as measured by one-repetition maximum (1-RM) calculated from 3-RM. Stringer 1998 found that those in the heavy exercise group exhibited significant improvements in their peak work rate (i.e., endurance, $p < 0.05$), LAT (defined as the VO2 above which the VCO2 output increased faster than the VO2, $p < 0.05$) and VO2max ($p < 0.01$), when compared to the control group. Subjects in the moderate exercise group experienced improvements in LAT only ($p < 0.05$) compared to the	NO GRADE ASSIGNED (AMSTAR 2 score critically low)

									control group. In essence, the general trend was that exercise improved aerobic capacity and strength amongst exercisers compared to non- exercisers or the standard care group. Two RCTs that used CARET interventions found significant improvements in physical functioning in the intervention groups compared to the control groups. Galantino 2005 found significant interaction and main effects for both CARET and Tai Chi groups in functional reach ($p = 0.003$ and $p < 0.001$, respectively), sit and reach ($p = 0.003$ and $p < 0.001$, respectively), and sit up tests ($p = 0.001$) after 8 weeks. They also found significant interactions for climbing one flight of stairs ($p = 0.018$) and climbing 3 flights of stairs ($p = 0.018$). Dolan (2006) found that those in the exercise group had a significant improvement in the 6-minute walk test compared to the control group ($p = 0.009$).	
	Pedro 2017	5 RCTs, N=253	high	N	N	N	Y	N	Muscular strength increased in response to resistance and concurrent training in three studies (Lindegaard 2008; Dolan 2006; Mendes 2013). It also increased slightly in response to aerobic training (Lindegaard 2008). The $VO_{2\,max}$ increased in response to concurrent training (Dolan 2006; Mendes 2013) and aerobic training (Lindegaard 2008; Mendes 2013; Terry 2006), but did not increase in response to resistance training (Lindegaard 2008).	MODERATE (+ve effect)
	Chaparro , 2018	13 RCTs, N=NR	high	N	N	N	Y	Y	Two overall meta-analyses and 34 subgroup analyses were performed. The overall change after intervention on upper body strength in PLWH from baseline was 18 kg (95% CI: 11.2–24.8, $p< 0.001$) favouring the intervention group. Lower body strength also increased by 16.8 kg (95% CI: 13–20.6, $p< 0.001$) favouring the intervention group. Sub-analysis revealed a significant increase on lifted weight for each muscle group,	HIGH (+ve effect)

									favouring the intervention group. After long-term exercise, intervention group upper body strength showed a significant change 13.7 kg (95% CI: 6–21.5, p < 0.001). This was also true for intervention group lower-body strength with a mean change of 16 kg (95% CI: 11.6–20.4, p < 0.001), but significant changes were only for leg flexion and extension long-term exercise muscle groups.	
	Gomes Neto, 2013a	29 RCTs, N=1216	Critically low	UC	N	N	Y	N	Resistance exercise generated muscle strength gain. Aerobic exercise was also associated with increases in aerobic capacity, as measured by the VO2max/ peak or time on a treadmill (Smith 2001). Concurrent training was associated with significant increases in muscle strength, aerobic capacity, measured by the VO2max/ peak, exercise duration and the distance covered in 6 min walking test. Thus, in contrast to resistance and aerobic exercise performed in isolation, concurrent training showed improvement for all evaluated outcomes.	NO GRADE ASSIGNED (AMSTAR 2 score critically low)
	Gomes Neto, 2015	7 RCTs, N=386	high	Y	N	N	N	N	Two studies assessed muscle strength of the knee extensors and elbow flexors (Dolan 2006; Mendes 2013). A total of 118 patients were included in these 2 studies. Mendes 2013 and Dolan (2006) found significant improvements in muscle strength of the knee extensors and elbow flexors. A significant improvement in muscle strength of the knee extensors of 25.06 Kg (95% CI: 10.46, 39.66 N = 118) and of 4.44 Kg (95% CI: 1.22, 7.67 N = 118) for Elbow flexors were found for participants in the concurrent resistance and aerobic exercise group compared with no exercise group. Five studies (including 318 patients) assessed peak VO2 as outcome. In the study by Mutimura 2008, peak VO2 improved from 4.7 ± 3.9 vs 0.5 ± 0.3 ml / kg per min in the intervention group compared to control (p <0.001), while the	HIGH (+ve effect)

									study of Hand et al [27], detected an improvement of 21% in peak VO2 estimated in the exercise group versus no improvement in the control group (p <0.001). Similarly, Dolan 2006 observed an improvement (1.5 ± 0.8 vs -2.5 ± 1.6 mL/kgmin-1, p <0.001) in peak VO2 in the training group compared to control. However, Ogalha 2011, observed a non-significant improvement (0.6 ± 0.9 vs -0.2 ± 0.7 mL/kgmin-1, p <0.001) in peak VO2 in the training group compared to control. The mean peak VO2 in the analysed studies was 26.8 mL kg-1 min-1 at baseline, and it increased to 30.7 mL kg-1 min-1 at the end of the intervention. The meta-analyses showed a significant improvement in peak VO_2 of 4.48 mL kg-1 min-1 (95% CI: 2.95, 6.0, N = 318) for participants in the CARE group compared with no exercise group.	
	Zech, 2019	27 RCTs, N=1294	high	Y	N	N	N	UC	Seven main meta-analyses and 45 subgroup analyses were conducted. An overall SMD of 0.66 (p < .00001) was found in favour of the exercise group. Statistical heterogeneity was moderate (I^2 = 5 53%), indicating that there was relatively moderate variation in the effect sizes across trials. For the 6 minute walk test, an overall SMD = 0.59 in favour of the exercise group was found. There was a significant overall effect (p = .02) of exercise compared with the control group at post treatment. For maximum heart rate, an overall SMD = -0.38 in favour of the exercise group was found. There was no significant overall effect (p = .43) of exercise compared with the control group at post treatment. For resting heart rate, an overall SMD =- 0.29 was found in favour of the exercise group. There was no significant overall effect (p = .32) of exercise compared with the control group at post treatment. For systolic blood pressure, an overall SMD = -0.27 in favour of the exercise group was found. There was	MODERATE (+ve effect)

									no significant overall effect (p = .09) of exercise compared with the control group at post treatment. For diastolic blood pressure, an overall SMD = 0.01 in favour of the exercise group was found. There was no significant overall effect (p = .89) of exercise compared with the control group at post treatment. For maximum power output, ɑn overall SMD = 0.80 in favour of the exercise group was found. There was a significant overall effect (p 5 .009) of exercise compared with the control group at post treatment.	
	Ibemene, 2019a	23 RCTs, N=1073	High	y	Y	N	Y	N	The author found that there was a significant improvement (p = 0.0001; p = 0.001; p = < 0.01) in aerobic fitness/capacity in the study group. Eight studies reported statistically significant (p < 0.05) improvement in the peak/maximum oxygen uptake post-training period in the intervention group while two studies reported no significant (p > 0.05) improvement of the intervention on the stated outcomes. Two other trials reported a significant increase (p < 0.01) effect, respectively, in the mean of the forced expiratory volume (FEV_1) in the study group, compared to that of the control group. One other study (Farinatti 2010) observed a significant improvement (p < 0.05) in the slope/ intercept values for heart-Rate workload relationship. Furthermore, a total of 13 studies also reported a statistically significant improvement in the cardiopulmonary-related parameters while two other studies reported no significant improvement in the study group. The results of the meta-analysis revealed that there was an overall statistically significant (Z = 3.80, p < 0.0001) change in VO2max between comparison groups. Results demonstrated a statistically significant (Z = 2.62, p = 0.009) trend towards an increase in V02max in subjects	HIGH (+ve effect)

									in the aerobic exercises plus resistance exercises group compared with normal activities control group favouring the intervention. There was also a statistically significant (Z =6.29, p < 0.0001) trend towards an increase in VO2max in subjects in the aerobic exercises group compared with normal activities control group.	

Abbreviations: N = no; N/A = not applicable; PICO = population, intervention, comparator, outcome; PY = partial yes; RoB = risk of bias; Y = yes; UC=unclear; RCTs = randomised controlled trials

1. O'Brien, 2016
   - VO2max: Downgraded to very low by the authors of the review due to attrition (withdrawals of included studies >15 %), suspected publication bias, substantial heterogeneity (I2 = 67 %); and because the lower level of the confidence interval did not cross the estimated clinically important change in VO2max (despite the estimate surpassing the author's hypothesized clinically important change in VO2max of 2 ml/kg/min).
   - HRmax: Downgraded to moderate due to attrition and performance bias.
   - Exercise time: Downgraded to moderate due to attrition and performance bias. This was then upgraded to high due to the evident dose-response relationship in the findings.
   - Strength: The authors of the review downgraded the outcome from high to low due to incomplete outcome data (withdrawals of included studies were >15 %), publication bias suspected, and moderate heterogeneity (I2 = 46 %).
2. O'Brien, 2010
   - VO_{2max}: Moderate due to heterogeneity in the studies included. This was later upgraded to high due to the evident dose-response relationship in the findings.
   - Maximum Heart Rate (HRmax): High because there is no reason to downgrade even if RoB is unclear.
   - Exercise Time (minutes): High because there is no reason to downgrade even if RoB is unclear.
   - Strength: Downgraded to low due to a higher magnitude of indirectness.

3. O'Brien, 2004: Downgraded to low because the authors report a possibility of publication bias, there was also attrition bias (20% drop out in 6 studies and more than 50% dropout in 2 studies), the review is also based on a small number of trials and participants. Heterogeneity may have occurred due to a variety of exercise interventions being used. This low GRADE was then upgraded to high due to the evident dose-response relationship in the findings.
4. O'Brien, 2008: Downgraded to low because of a lot of variation among individual studies in the types of interventions, participants and outcomes, which may have led to heterogeneity and Indirectedness. Also, there is RoB due to attrition bias because of high withdrawal rates (>15%). There was also lack of blinding to the PRE intervention which may have resulted in the Hawthorn effect. The authors also report a possibility of performance bias due to increased levels of interaction between the investigators and participants in the exercise group resulting in more favourable outcomes for exercisers compared to non-exercisers. The review also used a small number of studies (n = 10) and there was total outcome data not available for 69 (17%) participants. This was then upgraded to high because of evidence of a dose-response relationship.
5. Nixon, 2005: Downgraded to low due to (a) RoB due to attrition bias as a result of high withdrawal rates ranging from 4-76% (b) indirectness which may have been caused by the heterogeneity of outcome measures. This was later upgraded to high due to the evident dose-response relationship in the findings.
6. O'Brien, 2017

- VO_{2max}: Graded moderate because the authors of the review were moderately confident in the effect estimate demonstrating a significant increase of 3.71 ml/kg/min for VO2max comparing PRE exercise (or combined PRE and aerobic exercise). The authors downgraded the outcome from high to moderate GRADE quality of evidence because the lower level of the confidence interval did not cross the estimated clinically important change in VO2max (despite the estimate surpassing their hypothesized clinically important change in VO2max of 2 ml/kg/min).
- HRmax: Downgraded to low because a high risk of performance bias existed across the included studies as 85% of them had a high risk of performance bias due to lack of participant blinding to the exercise intervention. Furthermore, Heterogeneity was present in both meta-analyses ($p < 0.1$) used for this outcome.
- Exercise time: Downgraded to very low because a high risk of performance bias existed across the included studies as 85% of them had a high risk of performance bias due to lack of participant blinding to the exercise intervention. Furthermore, Heterogeneity was present in both meta-analyses ($p < 0.1$) used for this outcome. This was then upgraded to high due to the presence of a dose-response relationship.
- Strength: The authors of the review GRADED the outcome as low because their confidence was limited in the effect estimate of a significant increase of 11.86 kg for 1-repetition maximum for chest press comparing PRE exercise (or combined PRE and aerobic exercise) with non-exercising control. The outcome was downgraded from high to low on the GRADE quality of evidence due to incomplete outcome data (withdrawals of included studies were >15%), publication bias suspected, and moderate heterogeneity (I^2=46%).

7. Pedro, 2017: Downgrade to moderate due to indirectness which might have been caused by different type of individuals in different studies, different types of exercise interventions and different types of assessment methods.
8. Chaparro, 2018: Graded low because there was publication bias on the systematic review and indirectness which could have been caused by the various differences among the included studies. This was then upgraded to high due to the presence of a dose-response relationship.
9. Gomes Neto, 2015: Moderate due to RoB because the risk to selective reporting was uncertain and none of the studies described blinding of therapists. This was then upgraded to high due to the presence of a dose-response relationship.
10. Zech, 2019: Downgraded to moderate because 9 of the 27 included studies showed a high risk of bias.
11. Poton 2017: Downgraded to moderate due to uncertainty in the status of RoB, inconsistency and imprecision as there is insufficient information in the review.
12. Voigt, 2018: downgraded to moderate due to uncertainty in the status of RoB and heterogeneity as a result of the different exercise intervention and small sample size. This was then upgraded to high due to the presence of a dose-response relationship.
13. Ibemene, 2019a: Downgraded to moderate due to RoB, inconsistency in the outcome measure and variability in the types of intervention used in the study. This was then upgraded to high due to the presence of a dose-response relationship.

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Table 3e. GRADE, PICO: Effects of PA on cardio metabolic markers among PLWHA

Exercise modality	Study	No. of Studies No. of participants	AMSTAR 2 Score	GRADE CRITERIA					Summary of findings	STRENGTH OF EVIDENCE
				Risk of Bias	Inconsistency	Imprecision	Indirectedness	Publication Bias		
Aerobic Exercise	No systematic reviews identified									
Resistance Exercise	No systematic reviews identified									
Multimodal Exercise	Leyes, 2008	15 RCTs + 10 Open-label, N=1189	critically low	UC	Y	UC	UC	UC	One study (Dolan 2006) revealed no improvement in plasma lipids, glucose tolerance and triglycerides. Although, for plasma cholesterol, one study (Jones 2001), a small pilot study which has not been reproduces in larger study found 18% reduction in plasma cholesterol levels.	NO GRADE ASSIGNED (AMSTAR 2 score critically low)
	Pedro, 2017	5 RCTs, N=253	high	N	Y	N	Y	N	Two studies found a reduction in total cholesterol after aerobic training. One of the studies did not found any reduction in total cholesterol. One study also found a reduction in triglyceride, after resistance training, a reduction in LDL-cholesterol after aerobic training and a reduction in FFA and an increase in HDL-cholesterol after aerobic or resistance training. No effects were established on insulin concentration or the HOMA Index. Glucose was lowered after aerobic training.	LOW (+ve effect)
	Fillipas, 2010	9 RCTs, N=469	low	Y	N	N	Y	N	Two studies (Fillipas 2006; Dolan 2006) examined the effects of combined training. One study found no effect on blood lipids or glucose nor on dual energy x-ray absorptiometry (DEXA) or computed tomography measures of fat (Dolan 2006) The other study demonstrated no effect on body weight (Fillipas 2006). One study compared the independent effects of aerobic exercise and PRE (Lindegaard 2008) Both exercise modalities improved insulin-mediated glucose uptake with no differences between groups. Decreases in	NO GRADE ASSIGNED (AMSTAR 2 score low)

									total cholesterol (TC) and low density lipoproteins (LDL) and increases in high density lipoproteins (HDL) were greater with aerobic exercise than with PRE, with large effect sizes.	
	Quiles, 2019	9 RCTs, N=638	low	Y	Y	N	N	N	Only one study investigated the effects of an AE intervention vs. no exercise (Roos 2014). The study showed an increase in HDL in the exercise group after a 12-month home-based physical activity program (+3.5 mg/dL, +6.3%; p = 0.01) (Roos 2014). In contrast, this same study showed decreases in blood glucose (−3.2 mg/dL, −3.5%; p < 0.05), TC (−8.1 mg/dL, −4.8%; p < 0.05) and LDL (−9.3 mg/dL, −9.5%; p < 0.05) for participants in the control group. Only one study investigated the effects of RE on lipid profile (Zanetti et al., 2016). The sole study reported decreases in TC (−29.2 mg/dL, −17%; p < 0.0001), LDL (−13.3 mg/dL, −14.3%; p = 0.049) and TG (−30.6 mg/dL, −20.4%; p < 0.0001), and increases in HDL (+14.0 mg/dL, +31.8%; p < 0.0001) after a 12-week RE program when compared to baseline. Four studies demonstrated positive effects on blood glucose, HDL, TG and TC (Grinspoon 2000; Mutimura 2008; Ogalha 2011; Tiozzo 2013). One study showed significant increases in HDL (+3 mg/dL, +7.3%; p < 0.01) and no changes in TC, LDL and TG after a 12-week placebo plus AE + RE intervention (Grinspoon 2000). Another 12-week combined AE + RE intervention reported significant decreases in blood glucose (−12 mg/dL, −12.9%; p < 0.048) in the exercise group, with no changes in HDL, LDL, TC and TGs (Tiozzo 2013). Similarly, a 24-week intervention showed significant decreases in blood glucose levels in the exercise group (−2.7 mg/dL, −3.0%; p < 0.04), but no changes in TC, LDL, HDL and TG levels (Ogalha 2011). Another study showed significant decreases in TG levels (−19.5 mg/dL, −16.5%; p < 0.05)	NO GRADE ASSIGNED (AMSTAR 2 score low)

									and blood glucose levels (−3.8 mg/dL, −4.4%; p < 0.0001), as well as decreases in TC levels (−1.2 mg/dL, −0.8%; p < 0.05) after a 24-week exercise intervention (Mutimura et al., 2008). No changes were observed in HDL and LDL in this study. Two studies reported no improvements in blood glucose levels or lipid profile with either a 16-week (Dolan 2006) or a 36-week (Jaggers 2016) combined AE + RE intervention. One of the studies reported increases in TC (+9.6 mg/dL, +5.5%; p = 0.03) in the AE + RE group, and in TC (+23.7 mg/dL, +15.7%; p = 0.004) and blood glucose levels (+12.2 mg/dL, +17%; p = 0.007) in the "playful exercise" group after a 12-week exercise intervention (Mangona 2015).	

Abbreviations: N = no; N/A = not applicable; PICO = population, intervention, comparator, outcome; PY = partial yes; RoB = risk of bias; Y = yes; UC=unclear; RCTs = randomised controlled trials

Pedro, 2017: downgraded to low due to indirectness which might have been caused by different type of individual indifference studies, and different type of intervention and different type of assessment methods. There is also inconsistencies in the findings of the study (Lindegaard 2008; Mutimura 2008 established reductions in total cholesterol after aerobic training. Whereas Terry 2006 did not showed reductions in total cholesterol).

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Table 3f. GRADE, PICO: Effects of PA on viral load and CD4+ cell count among PLWHA

Exercise modality	Study	No. of Studies No. of participants	AMSTAR 2 Score	GRADE CRITERIA					Summary of findings	STRENGTH OF EVIDENCE
				Risk of Bias	Inconsistency	Imprecision	Indirectedness	Publication Bias		
Aerobic Exercise	Nixon, 2005	10 RCTs, N=276	high	Y	N	N	Y	N	All ten included studies reported immunological/virological outcomes. Meta-analysis showed no difference in CD4 count for participants in the exercise intervention groups compared to the non-exercising control groups (Weighted Mean Difference: 14.3 cells/mm^3, 95% CI: -25.8, 54.5, n=209, p=0.48) (Baigis 2002; LaPerriere 1990; Lox 1995; Perna 1999; Smith 2001; Stringer 1998). Meta-analysis also showed no difference in CD4 percentage for participants in the exercise interventions groups compared to the non-exercising control groups (Weighted Mean Difference: -0.2%, 95% CI: -3.1, 2.7, n=118, p=0.90) (Baigis 2002; Smith 2001). Meta-analysis demonstrated no difference in viral load for participants in the exercise intervention groups compared to the non-exercising control groups (Weighted Mean Difference: 0.40 log10 copies, 95% CI: -0.3, 1.1, n=63, p=0.25) (Smith 2001; Stringer 1998).	LOW (no effect)

	O'Brien, 2004	10 RCTs, N=458 HIV+ only participants	high	Y	N	N	Y	UC	All 10 studies included used CD4 count as an outcome. Five meta-analyses were performed and showed no difference in CD4 count for participants in any type of aerobic exercise intervention group compared with the non-exercising control group (weighted mean difference: 14 cells·mm^{-3} , 95% CI: -26, 54, N= 209), no difference in CD4 count of participants in the constant aerobic exercise group compared with non-exercising control group (weighted mean difference: -4 cells·mm^{-3} , 95% CI: -50, 42, N 164) and nonsignificant improvement in CD4 count of 70 cells·mm^{-3} (95% CI: -11, 151, N 45) for participants in the interval aerobic exercise group compared with the non-exercising control group. Although not statistically significant, the point estimate is above 50 cells·mm^{-3}, which represents a possible clinically important increase in CD4 count. There was no difference in CD4 count in the moderate intensity aerobic exercise group compared with the heavy-intensity exercise group (weighted mean difference:-34, 95% CI: -156, 89, N 39) and no difference in CD4 count for participants in combined aerobic and progressive resistive exercise group compared with non-exercising control group (weighted mean difference: 6 cells·mm-3, 95% CI: -71, 83, N 46). Meta-analysis of three studies showed no difference in viral load for participants in the exercise intervention groups compared with the non-exercising control group (weighted mean difference: 0.40 log10 copies, 95% CI: -0.28, 1.07, N 63).	LOW (no effect)

	O'Brien, 2016	24 RCTs, N=1242	high	Y	N	N	N	Y	Seven meta-analyses were performed for CD4 count. Most (6 out of 7 meta-analyses) showed non-statistically significant changes in CD4 count between comparison groups. Results showed a non-significant trend towards an increase in change in CD4 count for participants in the aerobic or combined aerobic and PRE intervention group compared with the non-exercising control group; constant or PRE compared with no exercise; and significant increase in CD4 count for interval aerobic exercise compared with no exercise. The point estimate in the latter two meta-analyses was above 50 cells/mm3, which suggests a trend towards a potential clinically important improvement in CD4 count among exercisers compared with non-exercisers. Meta-analyses showed no difference in change in CD4 count for constant or interval aerobic exercise compared with no exercise; constant aerobic exercise compared with no exercise; as well as combined aerobic exercise and diet and/or nutrition counselling group compared with diet and/or nutrition counselling alone. No difference in change in CD4 count was found for participants exercising at moderate compared with heavy intensity. Four meta-analyses were performed for viral load, two of which included the same studies. Meta-analyses showed no difference in change in viral load for participants in the aerobic exercise intervention group compared with the non-exercising control group as well as the constant aerobic exercise group compared with the non-exercising control group; no difference in the combined aerobic and PRE group compared with the non-exercising control group; and no difference for participants in the aerobic or combined aerobic and PRE intervention group	MODERATE (no effect)

									compared with the non-exercising control group.	
	O'Brien, 2010	14 RCTs, N=454	high	**CD4⁺ cell count**					Five meta-analyses were performed. Generally, no significant changes in CD4 count were found between comparison groups.	MODERATE (no effect)
				UC	N	N	N	N		
				CD4 Percentage					Two meta-analyses were performed for CD4 percentage that included the same studies. Meta-analyses demonstrated no difference in change in CD4 percentage for participants in the exercise intervention group compared with the non-exercising control group as well as the constant aerobic exercise group compared with the non-exercising control (WMD: -0.33%, 95% CI: -1.98, 1.32, n=118, *P*=0.69) (Smith 2001, Baigis 2002).	High (no effect)
				UC	N	N	N	N		
				Viral Load					Three meta-analyses were performed for viral load, of which two included the same studies. Meta-analysis demonstrated no difference in change in viral load for participants in the exercise intervention group compared with the non-exercising control group as well as the constant	HIGH (no effect)

				UC	N	N	N	N	aerobic exercise group compared with the non-exercising control group (WMD: 0.40 log10copies, 95% CI: -0.28, 1.07, n=63, *P*=0.25) (Smith 2001; Stringer 1998), and no difference in the combined aerobic and PRE group compared with the non-exercising control group (WMD: 0.31 log10copies, 95% CI: -0.13, 0.74, n=60, *P*=0.17) (Grinspoon 2000, Dolan 2006).	
Resistance Exercise	Poton,2016	13 RCTs, N=291	moderate	UC	UC	UC	N	N	A slight increase in CD4 cell count occurred with an overall effect size of 0.37 (0.13–0.61; P = 0.003; ~26.1%).	MODERATE (+ve effect)
	O'Brien, 2017	20 RCTs, N=764	high	**CD4 count**					Four meta-analyses were performed for CD4 count. Two demonstrated no statistically significant changes in CD4 count between comparison groups, one demonstrated a significant increase in CD4 count favouring exercise and another demonstrated a significant decrease in CD4 count favouring testosterone alone. Point estimates were >50 cells/mm3 for two meta-analyses comparing exercise to control, which suggested a positive trend towards a potential clinically important improvement in CD4 count with exercise compared with no exercise.	VERY LOW (+ve effect)
				Y	N	N	Y	N		
				Viral load					Three meta-analyses were performed for viral load, one of which included the same studies. Meta-analyses demonstrated no difference in change in viral load for participants in the combined PRE and aerobic exercise intervention group compared with the non-exercising control group as well as the combined PRE and aerobic exercise group with diet and/or nutrition compared with the non-exercising diet and/or nutrition only group. None of the meta-analyses were significant for heterogeneity.	MODERATE (no effect)
				Y	N	N	Y	N		
	O'Brien, 2008	10 RCTs, N=332	high	Y	N	N	Y	N	For CD4 count, 3 meta-analyses were performed. Results showed no difference in change in CD4 count for participants in the combined aerobic and PRE group compared to the non-exercising control group (WMD:	LOW (no effect)

									24.83 cells/mm^3; 95% CI: -23.70, 73.36; p = 0.32; n = 84) and for participants in the PRE or combined PRE and aerobic exercise group compared to the non-exercising control group (WMD: 38.51 cells/mm$^{3;}$ 95% CI: -7.54, 84.56; p = 0.10; n = 106). A significant decrease in CD4 count was found in the combined PRE plus testosterone or combined PRE and aerobic exercise plus testosterone group compared with the testosterone only group (WMD: -32.13 cells/mm^3 ; 95% CI: -56.96, -7.30; p = 0.01; n = 51). These results did not reach the authors' pre-specified threshold for clinical importance (50 cells/mm^3). One meta-analysis was performed for viral load. Results demonstrated no difference in change in viral load among participants in the combined PRE and aerobic exercise group compared with the non-exercising control group (WMD: 0.31 log^{10} copies; 95% CI: -0.13; 0.74; p = 0.17; n = 60). Individual studies also showed no differences in changes in viral load among exercisers compared with non-exercisers.	
Multimodal Exercise	Ibemene, 2019b	19 RCTs, N=661 participants included for QoL.	high	Y	N	N	N	N	One study (Farinatti 2010) assessed immune function combined aerobic and resistance exercise among 27 HAART treated HIV-infected patients (age 45 ± 2 years). The exercise group (n = 19) were involved in aerobic training (cycle ergometer) for 30 min of moderate intensity, strengthening exercise (2 sets of 12 repetitions of 5 exercises at 60–80% 12 Repetition Maximum) for 50 min and flexibility exercise (2 sets of 30s at maximum range of motion of 8 exercises) while the control group (n = 8) received no treatment. Immune function (CD4 and CD4 %) were determined by specific monoclonal antibodies using fluorescein isothiocyanate and phycoerythrin monoclonal antibodies using a whole blood staining method. The study reported no significant change in the	MODERATE (no effect)

									CD4 T-cell count in either the exercise group or the control group (p = 0.19 for CD4 T-cells and p = 0.22 for CD4 %) .	
	Pedro, 2017	5 RCTs, N=253	high	N	N	N	Y	N	CD4 cell count was not influenced by physical training.	MODERATE (no effect)
	Lopez, 2015	28 RCTs, N=493	critically low	Y	Y	N	Y	Y	Of the studies that evaluated the effect of exercise on disease progression, seven of them reported no significant changes in CD4+ cell count, HIV RNA viral load, and/or both (Stringer 1998; Roubenoff 1999; Smith 2001; Neidig 2003; Dolan 2006; Fillipas 2006; Mutimura 2008; Mutimura 2008b; Gomes 2010). Ezema 2014 found that three weeks of moderate-intensity continuous exercise training increased VO2 max and CD4+ T cell count in PLWH. Changes in VO2max significantly correlated with changes in CD4+ T cell count ($r = 0.53$, $p < 0.05$). Tiozzo 2013 found a significant decrease in CD4+ T cell count (-16%, $p < 0.05$) in the control group, while the CARET group maintained a more stable count (-3%, $p = 0.39$). A positive effect of exercise training was also shown by Stringer 1998 who found that those who participated in moderate aerobic training program but not in heavy aerobic training, had an improvement in a skin test for *Candida albicans* antigen ($p < 0.05$), which is used to evaluate cellular immune response in those with reduced cellular hypersensitivity, when compared to the control group. Markers of disease progression remained unchanged after the interventions, so exercise training may be a safe therapeutic alternative for PLWH on ART.	NO GRADE ASSIGNED (AMSTAR 2 score critically low)
	Leyes,2008	15 RCTs+ 10 Open-label, N=1189	critically low	UC	N	UC	UC	UC	No changes in CD4+ cell count and viral load in relation to aerobic or resistance exercise were observed (Engelson 2006; Dolan 2006; Driscoll 2004; Strawford 1999).	NO GRADE ASSIGNED (AMSTAR 2 score critically low)

Abbreviations: N = no; N/A = not applicable; PICO = population, intervention, comparator, outcome; PY = partial yes; RoB = risk of bias; Y = yes; UC=unclear; RCTs = randomised controlled trials

1. O'Brien 2016: The authors reported a moderate GRADE for CD4+ cell count and did not report for viral load. CD4+ cell count was assigned a moderate GRADE due to incomplete outcome data (withdrawals of included studies were >15 %). We also assigned a moderate GRADE for viral load due to attrition bias and performance bias in the review.

2. O'Brien, 2010

   - CD4 cell count: Downgraded to moderate due to heterogeneity in the included studies.
   - CD4 Percentage: High, no reason to downgrade even if RoB is unclear.
   - Viral Load: High, no reason to downgrade even if RoB is unclear.

3. O'Brien, 2004: Downgraded to low because the authors report a possibility of publication bias, there was also attrition bias (20% drop out in 6 studies and more than 50% dropout in 2 studies), the review is also based on a small number of trials and participants. Heterogeneity may have occurred due to a variety of exercise interventions being used.

4. O'Brien, 2008: Downgraded to low because of a lot of variation among individual studies in the types of interventions, participants and outcomes, which may have led to heterogeneity and Indirectedness. Also, there is RoB due to attrition bias because of high withdrawal rates (>15%). There was also lack of blinding to the PRE intervention which may have resulted in the Hawthorn effect. The authors also report a possibility of performance bias due to increased levels of interaction between the investigators and participants in the exercise group resulting in more favourable outcomes for exercisers compared to non-exercisers. The review also used a small number of studies (n = 10) and there was total outcome data not available for 69 (17%) participants.

5. Nixon, 2005: Downgraded to low due to (a) RoB due to attrition bias as a result of high withdrawal rates ranging from 4-76% (b) indirectness which may have been caused by the heterogeneity of outcome measures.

6. O'Brien, 2017

   - CD4 count: First downgraded to low because RoB due to a high risk of performance bias existing across the included studies since 85% of them lacked participant blinding to the exercise intervention. There was also a high risk of attrition bias as 555 of the included studies reported rates of withdrawal greater than 15%. Indirectness could have been caused by heterogeneity as it was reported to be present in 47% of the meta-analyses due to participant variability in ART use, body composition, comorbidity, gender, type and location of intervention and method of outcome measurement. For CD4 count the "low" grade was further downgraded to very low because for CD4 count, 3 of the 4 meta-analyses that were done were statistically significant for heterogeneity.
   - Viral load: The authors of the review graded the result as moderate because they were moderately confident in the non-significant effect estimate of 0.12 log10copies demonstrating no difference in change in viral load comparing PRE exercise (or combined PRE and aerobic exercise). This outcome was downgraded from high to moderate GRADE quality of evidence due to incomplete outcome data (withdrawals of included studies were >15%).

7. Poton, 2017: Downgraded to moderate because we are uncertain about the status of RoB, inconsistency and imprecision as there insufficient information about these in the review.

8. Pedro, 2017: Downgraded to moderate due to indirectness which might have been caused by different type of individuals in different studies, different types of exercise interventions and different types of assessment methods.

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Table 3g. GRADE, PICO: Effects of PA on cognition among PLWHA

Exercise modality	Study	No. of Studies No. of participants	AMSTAR 2 Score	GRADE CRITERIA					Summary of findings	STRENGTH OF EVIDENCE
				Risk of Bias	Inconsistency	Imprecision	Indirectedness	Publication Bias		
Aerobic Exercise	No systematic reviews identified									
Resistance Exercise	No systematic reviews identified									
Multimodal Exercise	No systematic reviews identified									

Abbreviations: N = no; N/A = not applicable; PICO = population, intervention, comparator, outcome; PY = partial yes; RoB = risk of bias; Y = yes

ADDENDUM 1: DATA EXTRACTIONS

SYSTEMATIC REVIEW & META-ANALYSIS

Citation: Ibeneme SC, Omeje C, Myezwa H, Ezeofor SN, Anieto EM, Irem F, Nnamani AO, Ezenwankwo FE, Ibeneme GC. Effects of physical exercises on inflammatory biomarkers and cardiopulmonary function in patients living with HIV: a systematic review with meta-analysis. BMC Infectious Diseases. 2019 Dec; 19(1):359.

Purpose: To evaluate the effects of physical exercises on 1) inflammatory biomarkers and 2) cardiopulmonary function (VO_2 Max) in PLWH.

Timeframe: Variable start dates to January 2018

Total # studies included: 23

Other details (e.g. definitions used, exclusions etc)

Only randomized control trials investigating the effects of either aerobic or resistance or a combination of both exercise types with a control/other intervention(s) for a period of at least 4 weeks among adults living with HIV,

were included.

Outcomes addressed:

Cardio metabolic markers

Abstract:

Background: Pro-inflammatory cytokines expressed in human immune deficiency virus (HIV) infection, may induce oxidative stress that is likely to compromise the patency of the airways or damage the lung tissues/cardiac function. However, physical (aerobic and/or resistance) exercise-induced release of heat shock protein, immune function alteration or reduced tissue hypoxia, have been highlighted as possible mechanisms by which increasing physical activity may reduce plasma pro-inflammatory cytokines in uninfected individuals and should be appraised in the literature for evidence of similar benefits in people living with HIV (PLWH). Therefore, we evaluated the effects of physical exercises on 1) inflammatory biomarkers and 2) cardiopulmonary function (VO_2 Max) in PLWH.
Method: A systematic review was conducted using the Cochrane Collaboration protocol. Searching databases, up to January 2018. Only randomized control trials investigating the effects of either aerobic or resistance or a combination of both exercise types with a control/other intervention(s) for a period of at least 4 weeks among adults living with HIV, were included. Two independent reviewers determined the eligibility of the studies. Data were extracted and risk of bias (ROB) was assessed with the Cochrane Collaboration ROB tool. Meta-analyses were conducted with random effect models using the Review Manager (RevMan) computer software.
Result: Twenty-three studies met inclusion criteria (n = 1073 participants at study completion) comprising male and female with age range 18–65 years. Three meta-analyses across three sub-groups comparisons were performed. The result showed no significant change in biomarkers of inflammation (IL-6 and IL-1β) unlike a significant ($Z = 3.80$, $p < 0.0001$) improvement in VO_2 Max. Overall, the GRADE evidence for this review was of moderate quality.
Conclusion: There was evidence that engaging in either aerobic or resistance exercise, or a combination of both exercises, two to five times per week can lead to a significant improvement in cardiopulmonary function but not biomarkers of inflammation (IL-6 and IL-1β). However, this should not be interpreted as "No evidence of effect" because the individual trial studies did not attain sufficient power to detect treatment effects. The moderate grade evidence for this review suggests that further research may likely have an important impact on our confidence in the estimate of effects and may change the estimate.

SYSTEMATIC REVIEW & META-ANALYSIS

Citation: Ibeneme SC, Irem FO, Iloanusi NI, Ezuma AD, Ezenwankwo FE, Okere PC, Nnamani AO, Ezeofor SN, Dim NR, Fortwengel G. Impact of physical exercises on immune function, bone mineral density, and quality of life in people living with HIV/AIDS: a systematic review with meta-analysis. BMC Infectious Diseases. 2019 Dec;19(1):340.

Purpose: The main study objective was to evaluate the impact of physical (aerobic and resistance) exercises on CD_{4+} count, BMD and QoL in PLWHA.

Timeframe: Variable start dates to June 2017

Total # studies included: 19

Other details (e.g. definitions used, exclusions etc)

Outcomes addressed: HRQOL, Viral load/$CD4^+$ count

Abstract:

Background: Compromised immune function, associated with human immune deficiency virus (HIV) infection, is improved by antiretroviral therapy (ART) which also decreases bone mineral density (BMD), and possibly the quality of life (QoL). However, physical (aerobic/resistance) exercises, were reported to induce reverse effects in uninfected individuals and were appraised in the literature for evidence of similar benefits in people living with HIV/AIDS (PLWHA). The main study objective was to evaluate the impact of physical (aerobic and resistance) exercises on CD_{4+} count, BMD and QoL in PLWHA.
Methods: A systematic review was conducted using the Cochrane Collaboration protocol. Searching databases, up to June 2017, only randomized control trials investigating the effects of either aerobic, resistance or a combination of both exercise types with a control/other intervention(s) for a period of at least 4 weeks among adults living with HIV, were included. Two independent reviewers determined the eligibility of the studies. Data were extracted and risk of bias (ROB) was assessed with the Cochrane Collaboration ROB tool. Meta-analyses were conducted using random effect models using the Review Manager (RevMan) computer software.
Results: Nineteen studies met inclusion criteria (n = 491 participants at study completion) comprising male and female with age range 22–66 years. Two meta-analyses across 13 sub-group comparisons were performed. However, there were no RCTs on the impact of physical exercises on BMD in PLWHA. The result showed no significant change in CD_{4+} count unlike a significant effect of 5.04 point (95%CI:-8.49,-3.74, p = 0.00001) for role activity limitation due to physical health (QoL sub-domain). Overall, the GRADE evidence for this review was of moderate quality.
Conclusion: There was evidence that engaging in moderate intensity aerobic exercises (55–85% Maximum heart rate-MHR), for 30–60 min, two to five times/week for 6–24 weeks significantly improves role activity limitation due to physical health problems, otherwise physical(aerobic or/and resistance) exercises have no significant effects on $CD4_{+}$ count and other domains of QoL. Also, there is lack of evidence on the impact of exercises on BMD in PLWHA due to the paucity of RCTs. The moderate grade evidence for this review suggests that further research may likely have an important impact on our confidence in the estimate of effects and may change the estimate.

<table>
<tr><td colspan="2">SCI 1. SYSTEMATIC REVIEW
Citation: O'Brien KK, Tynan AM, Nixon SA, Glazier RH. Effectiveness of Progressive Resistive Exercise (PRE) in the context of HIV: systematic review and meta-analysis using the Cochrane Collaboration protocol. BMC Infectious Diseases. 2017 Dec;17(1):268.</td></tr>
<tr><td>Purpose: The study examined the safety and effectiveness of progressive resistive exercise (PRE) interventions on immunological, virological, cardiorespiratory, strength, weight, body composition, and psychological outcomes in adults living with HIV.</td><td rowspan="4">Abstract:

Background: HIV is increasingly considered a chronic illness. More individuals are living longer and aging with the health-related consequences associated with HIV and multi-morbidity. Exercise is a self-management approach that can promote health for people aging with HIV. We examined the safety and effectiveness of progressive resistive exercise (PRE) interventions on immunological, virological, cardiorespiratory, strength, weight, body composition, and psychological outcomes in adults living with HIV.
Methods: We conducted a systematic review using the Cochrane Collaboration protocol. Searching databases up to April 2013, we included randomized controlled trials that compared PRE with no exercise or another intervention performed at least three times per week for at least four weeks with adults living with HIV. Two reviewers independently determined study eligibility. We extracted data from included studies and assessed risk of bias using the Cochrane Collaboration risk of bias tool. Meta-analyses were conducted using random effects models with Review Manager (RevMan) computer software.
Results: Twenty studies met inclusion criteria (n = 764 participants at study completion); the majority of participants were men (77%) taking antiretroviral therapy (14/20 included studies). Exercise interventions included PRE alone (8 studies) or a combination of resistive and aerobic exercise (12 studies) ranging from 6 to 52 weeks in duration. Thirty-four meta-analyses were performed. Results demonstrated statistically significant improvements in cardiorespiratory status (maximum oxygen consumption, exercise time), strength (chest press, knee flexion), weight, and body composition (arm and thigh girth, leg muscle area) among exercisers versus non-exercisers. We found no significant differences in change in CD4 count and viral load. We were unable to perform meta-analyses for psychological outcomes however results from individual studies demonstrated improvements in health-related quality of life with exercisers compared with non-exercisers.
Conclusion: Performing progressive resistive exercise (PRE) or a combination of resistive and aerobic exercise at least three times per week for at least six weeks is safe and can lead to improvements in cardiorespiratory fitness, strength, weight, and body composition for adults with HIV. Exercise may be considered a safe and beneficial for enhancing the health of medically stable adults aging with HIV.</td></tr>
<tr><td>Timeframe: Variable start dates to April 2013.</td></tr>
<tr><td>Total # studies included: 20</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed: HRQOL, Body composition, Fitness and functional capacity, Cardio metabolic markers, Viral load/CD4$^+$ count.</td></tr>
</table>

<table>
<tr><td colspan="2">SCI 1. SYSTEMATIC REVIEW
Citation: O'Brien KK, Tynan AM, Nixon SA, Glazier RH. Effectiveness of aerobic exercise for adults living with HIV: systematic review and meta-analysis using the Cochrane Collaboration protocol. BMC Infectious Diseases. 2016 Dec;16(1):182.</td></tr>
<tr><td>Purpose: Our aim was to examine the safety and effectiveness of aerobic exercise interventions on immunological, virological, cardiorespiratory, strength, weight, body composition, and psychological outcomes in adults living with HIV.</td><td rowspan="5">Abstract:

Background: People with HIV are living longer with the health-related consequences of HIV, multi-morbidity, and aging. Exercise is a key strategy that may improve or sustain health for people living with HIV. Our aim was to examine the safety and effectiveness of aerobic exercise interventions on immunological, virological, cardiorespiratory, strength, weight, body composition, and psychological outcomes in adults living with HIV.
Methods: We conducted a systematic review using the Cochrane Collaboration protocol. We searched databases up to April 2013. We included randomized controlled trials comparing aerobic exercise with no exercise or another intervention performed at least three times per week for at least four weeks among adults living with HIV. Two reviewers independently determined study eligibility. Data were extracted from studies that met inclusion criteria using standardized forms. We assessed risk of bias using the Cochrane Collaboration's tool for assessing risk of bias. Outcomes were analyzed as continuous and meta-analyses conducted using random effects models with Review Manager (RevMan) computer software.
Results: Twenty-four studies met inclusion criteria (n = 936 participants at study completion); the majority of participants were men (73 %) and the majority were taking antiretroviral therapy (19/24 included studies). The exercise intervention included aerobic exercise alone (11 studies) or a combination of aerobic and resistive exercise (13 studies) ranging from 5 to 52 weeks. Fifty-eight meta-analyses were performed. Main results indicated statistically significant improvements in selected outcomes of cardiorespiratory status (maximum oxygen consumption, exercise time), strength (chest press, knee flexion), body composition (lean body mass, percent body fat, leg muscle area), depression symptoms, and quality of life (SF-36 questionnaire) among exercisers compared with non-exercisers. No significant differences in change in CD4 count and viral load were found.
Conclusions: Performing aerobic exercise or a combination of aerobic and resistive exercise at least three times per week for at least five weeks is safe and can lead to improvements in cardiorespiratory fitness, strength, body composition and quality of life for adults with HIV. Aerobic exercise is safe and beneficial for adults living with HIV who are medically stable.</td></tr>
<tr><td>Timeframe: Variable start dates to April 2013.</td></tr>
<tr><td>Total # studies included: 24</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed: HRQOL, body composition, anxiety/depression, fitness and functional capacity, viral load/CD4+ count</td></tr>
</table>

<table>
<tr><td colspan="2">SCI 1. SYSTEMATIC REVIEW
Citation: O'Brien K, Nixon S, Tynan AM, Glazier R. Aerobic exercise interventions for adults living with HIV/AIDS. Cochrane Database of Systematic Reviews. 2010(8).</td></tr>
<tr><td>Purpose: To examine the safety and effectiveness of aerobic exercise interventions on immunologic and virologic, cardiopulmonary, psychologic outcomes and strength, weight, and body composition in adults living with HIV.</td><td rowspan="4">Abstract:

Background: Access to combination antiretroviral therapy has turned HIV into a chronic and manageable disease for many. This increased chronicity has been mirrored by increased prevalence of health-related challenges experienced by people living with HIV (Rusch 2004). Exercise is a key strategy for people living with HIV and by rehabilitation professionals to address these disablements; however, knowledge about the effects of exercise among adults living with HIV still is emerging.
Objectives: To examine the safety and effectiveness of aerobic exercise interventions on immunologic and virologic, cardiopulmonary, psychologic outcomes and strength, weight, and body composition in adults living with HIV.
Search methods: Searches of MEDLINE, EMBASE, SCIENCE CITATION INDEX, CINAHL, HEALTHSTAR, PsycINFO, SPORTDISCUS and Cochrane Review Group Databases were conducted between 1980 and June 2009. Searches of published and unpublished abstracts and proceedings from major international and national HIV/AIDS conferences were conducted, as well as a hand search of reference lists and tables of contents of relevant journals and books.
Selection criteria: We included studies of randomised controlled trials (RCTs) comparing aerobic exercise interventions with no aerobic exercise interventions or another exercise or treatment modality, performed at least three times per week for at least four weeks among adults (18 years of age or older) living with HIV.
Data collection and analysis: Data on study design, participants, interventions, outcomes, and methodological quality were abstracted from included studies by two reviewers. Meta-analyses, using RevMan 5 computer software, were performed on outcomes when possible.
Results: A total of 14 studies met inclusion criteria for this review and 30 meta-analyses over several updates were performed. Main results indicated that performing constant or interval aerobic exercise, or a combination of constant aerobic exercise and progressive resistive exercise for at least 20 minutes at least three times per week for at least five weeks appears to be safe and may lead to significant improvements in selected outcomes of cardiopulmonary fitness (maximum oxygen consumption), body composition (leg muscle area, percent body fat), and psychological status (depression-dejection symptoms). These findings are limited to participants who continued to exercise and for whom there were adequate follow-up data.</td></tr>
<tr><td>Timeframe: Searches of papers from 1980 to June 2009.</td></tr>
<tr><td>Total # studies included: 14</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed: Viral load, Body composition, HRQOL, Fitness and functional capacity, Cardio metabolic markers, Anxiety/Depression</td></tr>
</table>

	Conclusion: Aerobic exercise appears to be safe and may be beneficial for adults living with HIV. These findings are limited by the small sample sizes and large withdrawal rates described in the studies. Future research would benefit from participant follow-up and intention-to-treat analysis. Further research is required to determine the optimal parameters in which aerobic exercise may be most beneficial for adults living with HIV.

SCI 1. SYSTEMATIC REVIEW **Citation:** Nixon S, O'Brien K, Glazier R, Tynan AM. Aerobic exercise interventions for adults living with HIV/AIDS. Cochrane Database of Systematic Reviews. 2005(2).	
Purpose: To examine the safety and eIectiveness of aerobic exercise interventions on immunological/virological, cardiopulmonary and psychological parameters in adults living with HIV/AIDS. **Timeframe:** From February 2001 to August 2003 **Total # studies included:** 10 **Other details (e.g. definitions used, exclusions etc)** **Outcomes addressed:** HRQOL, Anxiety/Depression, Fitness and Functional capacity, Viral load/CD4+ count	**Abstract:** **Background:** The profile of HIV infection is constantly changing. Although once viewed as an illness progressing to death, among those with access to antiretroviraltherapy, HIV can now present as a disease with an uncertain natural history, perhaps a chronic manageable disease for some. This increased chronicity of HIV infection has been mirrored by increased prevalence of disablement in the HIV-infected population (Rusch 2004). Thus, the needs of these individuals have increasingly included the management of impairments (problems with body function or structure as a significant deviation or loss, such as pain or weakness), activity limitations (diIiculties an individual may have in executing activities, such as inability to walk) and participation restrictions (problems an individual may experiences in involvement in life situations, such as inability to work) (WHO2001). Exercise is a key strategy employed by people living with HIV/AIDS and by rehabilitation professionals to address these issues. Exercise has been shown to improve strength, cardiovascular function and psychological status in seronegative populations (Bouchard 1993), but what are the elects of exercise for adults living with HIV? If the risks and benefits of exercise for people living withHIV are better understood, appropriate exercise may be undertaken by those living with HIV/AIDS and appropriate exercise prescription may be practiced by healthcare providers. If elective and safe, exercise may enhance the electiveness of HIV management, thus improving the overall outcome for adults living with HIV. **Objectives**: To examine the safety and eIectiveness of aerobic exercise interventions on immunological/virological, cardiopulmonary and psychological parameters in adults living with HIV/AIDS. **Search methods:** To identify the appropriate studies, we conducted a search using MEDLINE, EMBASE, SCIENCE CITATION INDEX, AIDSLINE, CINAHL, HEALTHSTAR, PSYCHLIT, SOCIOFILE, SCI, SSCI, ERIC and DAI. We also reviewed both published and unpublished

	abstracts and proceedings from major international and national HIV/AIDS conferences such as the Intersciences Conference on Antimicrobial Agents and Chemotherapy (ICAAC), the Conference on Retroviruses and Opportunistic Infections (CROI), the Infectious Diseases Society of America Conference (IDSA) and the International AIDS Conference (IAC). Reference lists from pertinent articles and books were reviewed and personal contacts with authors were used, as well as Collaborative Review Group databases. Targeted journals were hand searched for relevant articles. There were no language restrictions. Searches for the original review covered the period from 1980 to July 1999. The first update of this review included an additional search of the literature, followed by identification of included studies that met the inclusion criteria from August 1999 to January 2001. For the second update, we conducted a search to identify additional studies published from February 2001 to August 2003. **Selection criteria**: Studies were included if they were randomized controlled trials (RCTs) comparing aerobic exercise interventions with no aerobic exercise interventions or another exercise or treatment modality, performed at least three times per week for at least four weeks among adults (18 years of age or older) living with HIV/AIDS. **Data collection and analysis:** Data on study design, participants, interventions, outcomes and methodological quality were abstracted from studies that met the inclusion criteria onto specifically designed data collection forms by at least two reviewers. Meta-analysis was conducted using RevMan 4.2 computer soLware on outcomes whenever possible. **Main results:** A total of 10 studies (six from the original search, two from the first updated search and two from this second updated search) met the inclusion criteria for this review. Main results indicated that performing constant or interval aerobic exercise, or a combination of constant aerobic exercise and progressive resistive exercise for at least 20 minutes, at least three times per week for four weeks appears to be safe and may lead to significant reductions in depressive symptoms and potentially clinically important improvements in cardiopulmonary fitness. These findings are limited to those participants who continued to exercise and for whom there was adequate follow-up data. **Authors' conclusions**: Aerobic exercise appears to be safe and may be beneficial for adults living with HIV/AIDS. These findings are limited by the small sample sizes and large withdrawal rates of the included studies. Future research would benefit from an increased attention to participant follow-up and intention-to-treat analysis. Further research is required to determine the optimal parameters of aerobic exercise and stage of disease in which aerobic exercise may be most beneficial for adults living with HIV.

SCI 1. SYSTEMATIC REVIEW **Citation:** Bhatta DN, Liabsuetrakul T, McNeil EB. Social and behavioral interventions for improving quality of life of HIV infected people receiving antiretroviral therapy: a systematic review and meta-analysis. Health and Quality of Life Outcomes. 2017 Jan;15(1):80.	
Purpose: This review appraises the evidence for available interventions that focused on quality of life of HIV infected people receiving antiretroviral therapy (ART).	**Abstract:** **Background:** Improvement in quality of life is crucial for HIV infected people. Social and behavioral interventions have been implemented in different contexts to improve the quality of life among HIV infected people. This review appraises the evidence for available interventions that focused on quality of life of HIV infected people receiving antiretroviral therapy (ART). **Methods**: We searched electronic databases for randomized controlled trials of interventions to improve the quality of life of HIV infected people receiving ART. We searched PUBMED and the Cochrane Centre Register of Controlled Trials (CENTRAL) with the terms “social”, “behavioral”, “educational”, “quality of life”, “HIV”, and “RCT”. Searches were conducted for articles published from 1980 to December 16, 2015. Standardized data abstraction methods and searching steps were applied. **Results**: Twenty-eight studies reported the impact of social or behavioral interventions in quality of life among HIV
Timeframe: From 1980 to December 16, 2015.	
Total # studies included: 28	
Other details (e.g. definitions used, exclusions etc)	
Outcomes addressed: HRQOL	

	infected people, of which 15 were conducted in United States of America. A total of 4136 participants were enrolled. Of the 28 studies, four studies included females, two studies included males and remaining studies excluded both males and females. The overall reported methodological quality of the studies was subject to a high risk of bias and the study criteria were unclear in most studies. Twenty-one studies reported a significant intervention effect on at least one quality of life domain. Meta-analyses showed significant improvement in general health, mental health, physical function and environment domains of quality of life among intervention groups. However, the expected impact of the intervention was low to moderate because the rigorousness of the studies was low, information was limited, the sample sizes were small and other the quality of the study designs were poor. **Conclusions:** Although the available evidence suggests that existing social and behavioral interventions can improve some quality of life domains, the quality of evidence was insufficient to support the notion that these interventions can improve the overall quality of life of HIV infected people receiving ART. Well-designed and rigorous randomized controlled trials with high methodological quality are required.

SCI 1. SYSTEMATIC REVIEW **Citation:** Pedro RE, Guariglia DA, Peres SB, Moraes SM. Effects of physical training for people with HIV-associated lipodystrophy syndrome: a systematic review. The Journal of Sports Medicine and Physical Fitness. 2017 May;57(5):685-94.	
Purpose: The aim was systematically review the literature for physiological, metabolic, immunologic, and morphologic adaptations to aerobic, resistance, and concurrent training in people living with HALS. **Timeframe:** July 2013 and updated in July 2016	**Abstract:** **INTRODUCTION**: Human immunodeficiency virus-associated lipodystrophy syndrome (HALS) is a major problem among people living with HIV/aids. The exercise training has been used for its treatment; however, the knowledge about benefits and safety still is emerging. The aim was systematically review the literature for physiological, metabolic, immunologic, and morphologic adaptations to aerobic, resistance, and concurrent training in people living with HALS. **EVIDENCE ACQUISITION**: A search of the Medline, Embase, Cinahl, Lilacs, Scielo, Web of Science, the Cochrane Controlled Trials Register Library and PEDro was performed. The study selection was performed by two blinded researchers follow screening of titles, abstracts, and full-text articles. Therefore, only randomised clinical trials, which

Total # studies included: 5 **Other details (e.g. definitions used, exclusions etc)** **Outcomes addressed:** HRQOL, Body composition, Fitness and Functional capacity, Cardiometabolic markers, Viral load/CD4+ count	investigated the effects of physical training in people with HALS, were included in the present review. The risk of bias was assessed using a Jadad's scale. **EVIDENCE SYNTHESIS**: From the electronic and manual searches, 332 studies were selected by title, 139 abstracts were read and 95 were excluded, leaving 44 studies, which were read in full. After full text examination only five studies were included in the qualitative analyses. The limitations were: heterogeneity in training prescription, nutritional recommendations, and diagnosis of lipodystrophy, small sample size, utilization of methods with questionable validity for assessments. **CONCLUSIONS**: There is no effect of physical training on CD4 cell count. In addition, aerobic and concurrent training improve VO2max, likewise resistance and concurrent training improve muscular strength.

SCI 1. SYSTEMATIC REVIEW **Citation:** O Brien KE, Nixon S, Tynan AM, Glazier RH. Effectiveness of aerobic exercise in adults living with HIV/AIDS: systematic review. Medicine and science in sports and exercise. 2004 Oct 1;36:1659-66.	
Purpose: The objective of this systematic review was to examine the effectiveness and safety of aerobic exercise interventions on	**Abstract:** **Purpose:** The objective of this systematic review was to examine the effectiveness and safety of aerobic exercise interventions on immunological/virological, cardiopulmonary and psychological outcomes in adults living with

immunological/virological, cardiopulmonary and psychological outcomes in adults living with HIV/AIDS. **Timeframe:** From 1980 to November 2002. **Total # studies included:** 10 **Other details (e.g. definitions used, exclusions etc)** **Outcomes addressed:** HRQOL, Anxiety/Depression, Fitness and functional capacity, Viral load/CD4+ count	HIV/AIDS. **Methods:** Ten randomized trials of HIV-positive adults performing aerobic exercise three times per week for at least 4 wk were identified by searching 13 electronic databases, abstracts from conferences, reference lists, and personal contact with authors from 1980 to November 2002. At least two independent reviewers assessed articles for inclusion, extracted data, and assessed methodological quality. Random effects models were used for meta-analysis. **Results:** Main results indicated that aerobic exercise was associated with small non-significant changes in CD4 count (weighted mean difference: 14 cells-mm- 3, 95% CI: -26, 54), viral load (weighted mean difference: 0.40 log lO copies, 95% CI: -0.28, 1.07), and VO2. (weighted mean difference: 1.84 mL-kg-1, min-1, 95% CI: -0.53, 4.20). Individual studies suggested that aerobic exercise may improve psychological well-being for adults living with HIV/AIDS. These findings are limited to those participants who continued to exercise and for whom there was adequate follow-up. **Conclusion:** In conclusion, performing constant or interval aerobic exercise, or a combination of constant aerobic exercise and progressive resistive exercise for at least 20 min, at least three times per week for 4 wk may be beneficial and appears to be safe for adults living with HIV/AIDS. However, these findings should be interpreted cautiously due to small sample sizes and large dropout rates within the included studies. Future research would benefit from increased attention to participant follow-up and intention-to-treat analysis.

SCI 1. SYSTEMATIC REVIEW
Citation: O'brien K, Tynan AM, Nixon S, Glazier RH. Effects of progressive resistive exercise in adults living with HIV/AIDS: systematic review and meta-analysis of randomized trials. AIDS Care. 2008 Jul 1; 20(6):631-53.

Purpose: This systematic review examined the effectiveness and safety of progressive resistive exercise (PRE) interventions on immunological/virological, cardiopulmonary, weight, and body composition, strength and psychological outcomes in adults living with HIV. **Timeframe:** From 1980 to 2006 **Total # studies included:** 9 **Other details (e.g. definitions used, exclusions etc)** **Outcomes addressed:** HRQOL, Body composition, Fitness and functional capacity, Viral load/CD4+ count	**Abstract:** **Aim:** This systematic review examined the effectiveness and safety of progressive resistive exercise (PRE) interventions on immunological/virological, cardiopulmonary, weight, and body composition, strength and psychological outcomes in adults living with HIV. **Methods:** Using Cochrane Collaboration protocol, we included randomized controlled trials from 1980 to 2006 comparing PRE interventions with no PRE or another intervention. Ten studies met inclusion criteria. Seventeen meta-analyses were performed. **Results**: Results indicated that PRE or a combination of PRE and aerobic exercise may lead to statistically significant increases in weight (WMD: 2.68 kg; 95%CI: 0.40, 4.97) and arm and thigh girth (WMD: 7.91 cm; 95%CI: 2.18, 13.65) among exercisers versus non-exercisers. Trends toward improvement in submaximum heart rate and exercise time also were found. **Conclusions**: Individual studies suggested that PRE contributed to improved strength and psychological status. Findings are limited to participants who continued to exercise. Progressive resistive exercise appears to be safe and may be beneficial for medically-stable adults living with HIV.

<table>
<tr><td colspan="2">SCI 1. SYSTEMATIC REVIEW
Citation: Zech P, Pérez-Chaparro C, Schuch F, Wolfarth B, Rapp M, Heissel A. Effects of Aerobic and Resistance Exercise on Cardiovascular Parameters for People Living With HIV: A Meta-analysis. Journal of the Association of Nurses in AIDS Care. 2019 Mar 1; 30(2):186-205.</td></tr>
<tr><td>Purpose: The aim was to examine the effect of aerobic and resistance exercise alone and in combination on cardiovascular parameters.</td><td rowspan="4">Abstract:

Background: People living with HIV (PLWH) have limited exercise capacity because of anaemia, neuromuscular disorders, and pulmonary limitations.
Methods: We used a meta-analysis to examine the effect of aerobic and resistance exercise alone and in combination on cardiovascular parameters. Subgroup meta-analyses were conducted and long-term effects of exercise were investigated. A systematic literature search was conducted up to July/August 2017. The Physiotherapy Evidence Database-scale was used to rate quality and assess the risk of bias on the papers. Standardized mean differences (SMDs) were calculated to assess the effect of exercise.
Results: Post treatment comparison between the exercise and control groups revealed moderate and large effect sizes in favour of the intervention group for VO2max (SMD50.66, p,.0001) and the 6-minute walk test (SMD51.11, p5.0001). Exercise had a positive effect on cardiovascular parameters in PLWH.
Conclusion: Exercise can be a prevention factor for PLWH dealing with multiple comorbidities.</td></tr>
<tr><td>Timeframe: Up to August 2017</td></tr>
<tr><td>Total # studies included: 27</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed: Fitness and functional capacity</td></tr>
</table>

SCI 1. SYSTEMATIC REVIEW

Citation: Voigt N, Cho H, Schnall R. Supervised physical activity and improved functional capacity among adults living with HIV: A systematic review. Journal of the Association of Nurses in AIDS Care. 2018 Sep 1;29(5):667-80.

Purpose: The purpose of this review was to investigate whether supervised PA interventions improved functional capacity among adults living with HIV.

Timeframe: Not available

Total # studies included: 15

Other details (e.g. definitions used, exclusions etc)

Outcomes addressed: Fitness and Functional capacity

Abstract:

Background: Physical activity (PA) is an important strategy for healthy aging. Regular PA has been shown to be safe and combat the effects of inflammation, multi-morbidity, and long-term effects of antiretroviral therapy among people living with HIV. However, people living with HIV often fail to meet recommended guidelines for PA. It is recommended that people living with HIV engage in 20-40 minutes of combined aerobic and resistance training at least three times per week. Supervised PA interventions in the uninfected population have produced greater increases in muscular strength, cardiovascular fitness, and body composition compared to control study participants. The purpose of this review was to investigate whether supervised PA interventions improved functional capacity among adults living with HIV.

Methods: The Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines were followed for this review. Five databases were searched for randomized controlled trials in English, with adults aged 18 and over, where supervised PA was the intervention. Supervised PA was defined as a physical activity intervention that was supervised by a health care or allied health professional.

Results: The database literature search yielded 8,267 articles. After the title/abstract and full-text screening phases, 15 articles were included in the review. Using the Cochrane Collaboration's tool for assessing risk of bias, most studies fell in the 'low risk of bias' category within and across studies. Combined aerobic and progressive resistance training (PRT) improved strength, cardiovascular, and flexibility outcomes; three of four studies showed no significant improvements with aerobic interventions; PRT improved strength outcomes in all studies; yoga or combined yoga/meditation showed no difference between intervention and control groups; and, t'ai chi showed improvements in cardiovascular and flexibility outcomes.

Conclusions: Supervised PA interventions increase functional capacity among adults living with HIV. Combined aerobics and PRT showed improvements in strength, cardiovascular, and flexibility outcomes. Self-reported measures showed inconsistent results of functional capacity across studies.

<table>
<tr><td colspan="2">SCI 1. SYSTEMATIC REVIEW
Citation: Poton R, Polito M, Farinatti P. Effects of resistance training in HIV-infected patients: A meta-analysis of randomised controlled trials. Journal of sports sciences. 2017 Dec 17;35(24):2380-9.</td></tr>
<tr><td>Purpose: The purpose of this study was to perform a meta-analysis to determine the effects of RT upon muscle strength, muscle mass and CD4 cells count and to identify potential moderators of those outcomes in HIV-infected patients.</td><td rowspan="4">Abstract:

Background: The relative effects of resistance training (RT) upon muscle fitness and immune function among HIV infected patients are uncertain. The purpose of this study was to perform a meta-analysis to determine the effects of RT upon muscle strength, muscle mass and CD4 cells count and to identify potential moderators of those outcomes in HIV-infected patients.
Methods: Meta-analyses use random or fixed-effects model depending on the heterogeneity of effect sizes, complemented with Hedge’s g correction factor. Thirteen trials were meta-analysed.
Results: Overall, RT increased muscle strength (35.5%, P < 0.01) and CD4 cell count (26.1%, P = 0.003) versus controls (P < 0.03), but not muscle mass (P = 0.051). Meta-regression followed by subgroup moderator analysis showed that gains in muscle strength followed a dose– response pattern with largest increase detected among trials with longer (24 weeks; 49.3%) than shorter intervention (< 0.01).
Conclusions: RT appears to be efficacious to improve muscular strength (~35.5%) and CD4 cell count (~26.1%), but not muscle mass of HIV infected patients. Effects upon strength were greater in studies with higher quality and among trials with longer RT and HAART.</td></tr>
<tr><td>Timeframe: Up to June 2016</td></tr>
<tr><td>Total # studies included: 13</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed: Body composition, Fitness and functional capacity, Viral load/CD4 + count</td></tr>
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<table>
<tr><td colspan="2">SCI 1. SYSTEMATIC REVIEW
Citation: Gomes Neto M, Ogalha C, Andrade AM, Brites C. A systematic review of effects of concurrent strength and endurance training on the health-related quality of life and cardiopulmonary status in patients with HIV/AIDS. BioMed Research International. 2013b;2013.</td></tr>
<tr><td>Purpose: To determine the effects of concurrent strength and endurance training (concurrent training) on the Health-Related Quality of Life (HRQOL) and cardiopulmonary status among HIV-infected patients, using a systematic search strategy of randomized, controlled trials (RCTs).</td><td rowspan="4">Abstract:

Purpose: To determine the effects of concurrent strength and endurance training (concurrent training) on the Health-Related Quality of Life (HRQOL) and cardiopulmonary status among HIV-infected patients, using a systematic search strategy of randomized, controlled trials (RCTs).
Methods: A systematic review was performed by two independent reviewers using Cochrane Collaboration protocol. The sources used in this review were Cochrane Library, EMBASE, LILACS, MEDLINE, PEDro and Web of Science from1950 to August 2012.ThePEDro score was used to evaluate methodological quality.
Result: Individual studies suggested that concurrent training contributed to improved HRQOL and cardiovascular status. Concurrent training appears to be safe and may be beneficial for medically stable adults living with HIV. The rates of non adherence were of 16%.
Conclusion: Concurrent training improves the HRQOL and cardiopulmonary status. It may be an important intervention in the care and treatment of adults living with HIV. Further research is needed to determine the minimal and optimal duration, frequency, and intensity of exercise needed to produce beneficial changes in the HIV-infected population subgroups.</td></tr>
<tr><td>Timeframe: From1950 to August 2012.</td></tr>
<tr><td>Total # studies included: 8</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed: HRQOL, Fitness and functional capacity</td><td></td></tr>
</table>

SCI 1. SYSTEMATIC REVIEW **Citation:** Fillipas S, Cherry CL, Cicuttini F, Smirneos L, Holland AE. The effects of exercise training on metabolic and morphological outcomes for people living with HIV: a systematic review of randomised controlled trials. HIV Clinical Trials. 2010 Oct 1;11(5):270-82.	
Purpose: To determine the effects of exercise on metabolic and morphological outcomes among people with HIV using a systematic search strategy of randomized, controlled trials (RCTs). **Timeframe:** From 1980 to November 2009 **Total # studies included:** 9 **Other details (e.g. definitions used, exclusions etc)** **Outcomes addressed:** Body composition, Cardiometabolic markers	**Abstract:** **Purpose:** To determine the effects of exercise on metabolic and morphological outcomes among people with HIV using a systematic search strategy of randomized, controlled trials (RCTs). **Methods:** Two independent reviewers assessed studies using a predetermined protocol. **Results:** Nine RCTs (469 participants, 41% females) of moderate quality were included. Compared to non exercising controls, aerobic exercise (AE) resulted in decreased body mass index (weighted mean difference [WMD] −1.31; 95% CI, −2.59, −0.03; n=186), triceps skinfold thickness of subcutaneous fat (WMD −1.83 mm; 95% CI,−2.36, −1.30; n=144), total body fat (%) (standardised mean difference [SMD],−0.37; 95% CI, −0.74, −0.01; n=118), waist circumference (SMD −0.74 mm, 95% CI, −1.08, −0.39; n=142), and waist:hip ratio (SMD −0.94; 95% CI, −1.30, −0.58; n=142). Progressive resistive exercise (PRE) resulted in increased body weight (5.09 kg; 95% CI, 2.13, 8.05; n=46) and arm and thigh girth (SMD 1.08 cm; 95% CI, 0.35, 1.82; n=46). Few studies examined blood lipids, glucose, and bone density. **Conclusions:** Few RCTs exist and their quality varies. AE decreases adiposity and may improve certain lipid subsets. PRE increases body weight and limb girth. No additional effects of combining AE and PRE are evident. Larger, higher quality trials are needed to understand the effects of exercise on metabolic outcomes (eg, lipids, glucose, bone density) relevant to persons with chronic, treated HIV.

SCI 1. SYSTEMATIC REVIEW **Citation:** Heissel A, Zech P, Rapp MA, Schuch FB, Lawrence JB, Kangas M, Heinze S. Effects of exercise on depression and anxiety in persons living with HIV: A meta-analysis. Journal of Psychosomatic Research. 2019 Sep 2:109823.	
Purpose: The purpose of this systematic review and meta-analysis was to examine the effects of exercise on depression and anxiety in people living with HIV (PLWH), and to evaluate, through subgroup analysis, the effects of exercise type, frequency, supervision by exercise professionals, study quality, and control group conditions on these outcomes. **Timeframe:** Up to February 2019 **Total # studies included:** 10 **Other details (e.g. definitions used, exclusions etc)**	**Abstract:** **Objective:** The purpose of this systematic review and meta-analysis was to examine the effects of exercise on depression and anxiety in people living with HIV (PLWH), and to evaluate, through subgroup analysis, the effects of exercise type, frequency, supervision by exercise professionals, study quality, and control group conditions on these outcomes. **Method:** A literature search was conducted through four electronic databases from inception to February 2019. Considered for inclusion were randomized controlled trials (RCTs) investigating exercise interventions and depression or anxiety as outcomes in people living with HIV (≥ 18 years of age). Ten studies were included (n = 479 participants, 49.67% females at baseline), and the standardized mean difference (SMD) and heterogeneity were calculated using random-effect models. An additional pre-post meta-analysis was also conducted. **Results:** A large effect in favour of exercise when compared to controls was found for depression (SMD = −0.84, 95%CI = [−1.57, −0.11], p = 0.02) and anxiety (SMD = −1.23, 95%CI = [−2.42, −0.04], p = 0.04). Subgroup analyses for depression revealed large effects on depression for aerobic exercise only (SMD = −0.96, 95%CI = [−1.63, −0.30], p =

Outcomes addressed: Anxiety/Depression	0.004), a frequency of ≥3 exercise sessions per week (SMD = −1.39, 95%CI = [−2.24, −0.54], p < 0.001), professionally supervised exercise (SMD = −1.40, 95%CI = [−2.46, −0.17], p = 0.03]), and high-quality studies (SMD = −1.31, 95%CI = [−2.46, −0.17], p = 0.02). **Conclusion**: Exercise seems to decrease depressive symptoms and anxiety in PLWH, but other larger and high quality studies are needed to verify these effects.

SCI 1. SYSTEMATIC REVIEW **Citation:** Quiles NN, Piao L, Ortiz A. The effects of exercise on lipid profile and blood glucose levels in people living with HIV: A systematic review of randomized controlled trials. AIDS Care. 2019 Sep 14:1-8.	
Purpose: This systematic review was performed in order to examine the effects of exercise interventions on lipid profile and glucose levels on PLWH	**Abstract:** **Background:** Exercise is commonly prescribed to improve lipid profile and glucose levels in people living with HIV (PLWH). This systematic review was performed in order to examine the effects of exercise interventions on lipid profile and glucose levels on PLWH. **Methods**: Randomized controlled trials (RCTs) investigating the effects of exercise on blood glucose, triglycerides (TG), total cholesterol (TC), HDL and LDL published up to November 2017 were reviewed. Two reviewers assessed inclusion and exclusion criteria, methodological quality and extracted the data. The PEDro scale was used to assess the quality of
Timeframe: From January 1980 to November 2017	
Total # studies included: 9	

Other details (e.g. definitions used, exclusions etc)	the included studies. **Results**: Nine RCTs involving 638 PLWH met inclusion criteria. The median PEDro scale score was 5 out of 10. Three combined aerobic exercise + resistance exercise studies (AE+RE) showed improvements in blood glucose levels, one study showed improvements in HDL, one showed improvements in TG, and one showed improvements in TC. The AE only study reported improvements in HDL, while the RE only study reported improvements in TG, TC, HDL and LDL. **Conclusions:** Exercise can be effective for the improvement of some metabolic parameters, especially blood glucose and HDL. However, due to methodological issues, small number of studies and differences in exercise protocols, these findings should be interpreted with caution.
Outcomes addressed: Cardiometabolic markers	

SCI 1. SYSTEMATIC REVIEW **Citation:** Chaparro CG, Zech P, Schuch F, Wolfarth B, Rapp M, Heiβel A. Effects of aerobic and resistance exercise alone or combined on strength and hormone outcomes for people living with HIV. A meta-analysis. PloS One. 2018 Sep 4;13(9):e0203384.	
Purpose: To examine the effect of RT alone or combined with AE on strength parameters and hormones amongst PLWHA	**Abstract:** **Background:** Infection with human immunodeficiency virus (HIV) affects muscle mass, altering independent activities of people living with HIV (PLWH). Resistance training alone (RT) or combined with aerobic exercise (AE) is linked to improved muscle mass and strength maintenance in PLWH. These exercise benefits have been the focus of different meta-analyses, although only a limited number of studies have been identified up to the year 2013/4. An up-to-date systematic review and meta-analysis concerning the effect of RT alone or combined with AE on strength parameters
Timeframe: Up to December 2017	
Total # studies included: 13	

Other details (e.g. definitions used, exclusions etc)	and hormones is of high value, since more and recent studies dealing with these types of exercise in PLWH have been published. **Methods**: Randomized controlled trials evaluating the effects of RT alone, AE alone or the combination of both (AERT) on PLWH was performed through five web-databases up to December 2017. Risk of bias and study quality was attained using the PEDro scale. Weighted mean difference (WMD) from baseline to post-intervention changes was calculated. The I^2 statistics for heterogeneity was calculated. **Results:** Thirteen studies reported strength outcomes. Eight studies presented a low risk of bias. The overall change in upper body strength was 19.3 Kg (95% CI: 9.8–28.8, p< 0.001) after AERT and 17.5 Kg (95% CI: 16–19.1, p< 0.001) for RT. Lower body change was 29.4 Kg (95% CI: 18.1–40.8, p< 0.001) after RT and 10.2 Kg (95% CI: 6.7–13.8, p< 0.001) for AERT. Changes were higher after controlling for the risk of bias in upper and lower body strength and for supervised exercise in lower body strength. A significant change towards lower levels of IL-6 was found (-2.4 ng/dl (95% CI: -2.6, -2.1, p< 0.001). **Conclusion**: Both resistance training alone and combined with aerobic exercise showed a positive change when studies with low risk of bias and professional supervision were analyzed, improving upper and, more critically, lower body muscle strength. Also, this study found that exercise had a lowering effect on IL-6 levels in PLWH.
Outcomes addressed: Fitness and Functional capacity	

SCI 1. SYSTEMATIC REVIEW **Citation:** Nosrat S, Whitworth JW, Ciccolo JT. Exercise and mental health of people living with HIV: A systematic review. Chronic illness. 2017 Dec;13(4):299-319.	
Purpose: This study aimed to conduct a systematic literature review of the effects of exercise on mental health in people living with HIV.	**Abstract:** **Objective**: Mental illness is highly prevalent among people living with HIV. Poor mental health is linked to HIV disease progression, making the treatment of mental illness alongside HIV essential. While the benefits of exercise on the

Timeframe: Variable start dates to November 2016. **Total # studies included:** 24 **Other details (e.g. definitions used, exclusions etc)** **Outcomes addressed:** HRQOL, anxiety/depression	physical health of people living with HIV are well established, the effect of exercise on mental health in this population is less examined. Therefore, this study aimed to conduct a systematic literature review of the effects of exercise on mental health in people living with HIV. **Methods**: A search of electronic databases (PubMed, Web of Science, PsycINFO) through 30 November 2016 was completed. The methodological framework for scoping studies was used to conduct the review process. RISMA guidelines were used to report the results. **Results**: The search resulted in 2273 articles and 52 were determined to be relevant. After review of the full text of potentially relevant studies, 24 studies were included for the analysis. **Discussion**: Both aerobic and resistance exercise have independent and combined positive effects on various indicators of mental health in people living with HIV. Major limitations include high attrition rate, small sample size, and poor study designs. Higher quality studies with more diverse populations such as women, older adults, and transgender individuals are required.

SCI 1. SYSTEMATIC REVIEW
Citation: Gomes-Neto M, Conceicao CS, Carvalho VO, Brites C. A systematic review of the effects of different types of therapeutic exercise on physiologic and functional measurements in patients with HIV/AIDS. Clinics. 2013a;68(8):1157-67.

Purpose: The aim of this study was to determine the effects of different types of exercise on physiologic and functional measurements in patients with HIV using a systematic strategy for searching randomized controlled trials. **Timeframe:** Variable start dates to August 2012. **Total # studies included:** 29 **Other details (e.g. definitions used, exclusions etc)** **Outcomes addressed:** Body composition, HRQOL, Fitness and functional capacity	**Abstract:** **Background**: Several studies have reported the benefits of exercise training for adults with HIV, although there is no consensus regarding the most efficient modalities. The aim of this study was to determine the effects of different types of exercise on physiologic and functional measurements in patients with HIV using a systematic strategy for searching randomized controlled trials. **Methods**: The sources used in this review were the Cochrane Library, EMBASE, MEDLINE, and PEDro from 1950 to August 2012. We selected randomized controlled trials examining the effects of exercise on body composition, muscle strength, aerobic capacity, and/or quality of life in adults with HIV. Two independent reviewers screened the abstracts using the Cochrane Collaboration's protocol. The PEDro score was used to evaluate methodological quality. In total, 29 studies fulfilled the inclusion criteria. **Results**: Individual studies suggested that exercise training contributed to improvement of physiologic and functional parameters, but that the gains were specific to the type of exercise performed. Resistance exercise training improved outcomes related to body composition and muscle strength, with little impact on quality of life. Aerobic exercise training improved body composition and aerobic capacity. Concurrent training produced significant gains in all outcomes evaluated, although moderate intensity and a long duration were necessary. **Conclusion**: We concluded that exercise training was shown to be a safe and beneficial intervention in the treatment of patients with HIV.

SCI 1. SYSTEMATIC REVIEW

Citation: Lopez J, Richardson E, Tiozzo E, Lantigua L, Martinez C, Abreut G, Prendergast T, Atlas SE, Pangilinan AR, Ferris SM, Martinez AH. The effect of exercise training on disease progression, fitness, quality of life, and mental health in people living with HIV on antiretroviral therapy: a systematic review. Journal of Clinical and Translational Research. 2015 Dec 30;1(3):129.

Purpose: To summarizes the findings on the effects of aerobic or resistance training alone or combined aerobic and resistance exercise training (CARET) on disease progression, fitness, physical functioning, mental health, and quality of life (QOL) in PLWH receiving ART.

Timeframe: From 1996 to 2015.

Total # studies included: 18

Other details (e.g. definitions used, exclusions etc)

Outcomes addressed: HRQOL, Anxiety/Depression, Fitness and functional capacity, Viral load/CD4+ count

Abstract:

Background: Exercise has been associated with improvements in adverse physiological and psychological effects of long-term antiretroviral therapy (ART) in people living with HIV (PLWH).

Aim: To summarizes the findings on the effects of aerobic or resistance training alone or combined aerobic and resistance exercise training (CARET) on disease progression, fitness, physical functioning, mental health, and quality of life (QOL) in PLWH receiving ART. A systematic search of articles was performed in several databases, and 20 articles that met inclusion criteria were summarized.

Relevance for patients: Aerobic exercise was associated with improvements in aerobic capacity, QOL, and depressive symptoms, while resistance training improved strength. CARET was related to improved aerobic fitness, strength, physical functioning, QOL, and self-efficacy. At least one of the exercise interventions resulted in improvements in CD4+ cell count and HIV RNA viral load. Moreover, another study showed that HIV-specific biomarkers remained unchanged in the exercise intervention group, while they significantly worsened in the non-exercise group. In general, in spite of their well-known benefits, exercise programs have not been extensively utilized or widely recognized as viable therapeutic treatment options for this patient population. Knowing the possible health benefits of increasing physical activity level is important to better recommend exercise programs. However, the prescription must be done carefully and on an individual basis. Additional studies investigating the efficiency and effectiveness of different exercise training regimens for PLWH are needed.

SCI 1. SYSTEMATIC REVIEW **Citation:** Lofgren SM, Nakasujja N, Boulware DR. Systematic review of interventions for depression for people living with HIV in Africa. AIDS and Behavior. 2018 Jan 1;22(1):1-8.	
Purpose: To identify depression interventions for HIV-infected adults in Africa. **Timeframe:** Up to February 2017 **Total # studies included:** 18 **Other details (e.g. definitions used, exclusions etc)** **Outcomes addressed:** Anxiety/Depression	**Abstract:** **Background**: Depression interventions for individuals with HIV/AIDS in Africa are being increasingly evaluated. **Methods**: MEDLINE was searched using key terms: depression, Africa, and HIV, to identify depression interventions for HIV-infected adults in Africa. Perinatal women were excluded. Results were extracted and relative change in depression scores for interventions and net effect calculated. **Results:** The MEDLINE search yielded 18 articles. Six of seven studies evaluating feasibility were positive, and seven of seven studies evaluating acceptability were also positive. Three studies investigated the effect of psychotherapy (% relative decrease of depressive symptoms for intervention: %net decrease compared to controls) (73%:39% decrease). Four studies investigated task-shifting of psychotherapy (47%:34% decrease). Three studies evaluated antidepressants (79%:39% decrease). Three studies investigated task-shifting of antidepressant treatment (82%:65% decrease). An exercise intervention was evaluated (66%:49% decrease). One trial investigated minocycline with non-statistically significant results. Finally, three studies investigated other psychosocial interventions (44%:21% decrease). **Conclusions**: Overall, the results highlight the need for large, randomized trials to establish efficacy as well as implementation studies.

<table>
<tr><td colspan="2">SCI 1. SYSTEMATIC REVIEW
Citation: Leyes P, Martínez E, Forga MD. Use of diet, nutritional supplements and exercise in HIV-infected patients receiving combination antiretroviral therapies: a systematic review. Antiviral Therapy. 2008 Jan 1;13(2):149.</td></tr>
<tr><td>Purpose: To examine the the effects of diet, nutrition support and exercise on body composition and metabolic complications in patients receiving cART</td><td rowspan="4">Abstract:

Background: The use of combination of antiretroviral therapy (cART) has improved the prognosis of HIV infections, but it has also been linked to a spectrum of body composition changes and metabolic alterations known as lipodystrophy syndrome. Nutrition status could influence body composition changes.
Method: we performed a systematic search of published peer-reviewed data on the effect on the effects of diet, nutrition support and exercise on body composition and metabolic complications in patients receiving cART
Result: Few controlled studies, most of them with small sample size were found. Oral nutritional support increases protein and energy intake, and a results in body weight and fat mass gains. Resistance exercise, with or without aerobic component, increases lean mass and can improve insulin resistance. Low-fat diet or exercise can result in loss of fat mass, and they should be used with caution in subjects with lipoatrophy.
Conclusion: Nutritional support and exercise results in small but significant body composition changes and can be used as complementary intervention. There is a need for further research on nutritional intervention in HIV-infected patients receiving cART.</td></tr>
<tr><td>Timeframe: From 1996 onwards</td></tr>
<tr><td>Total # studies included: 9</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed: Body composition, Fitness and functional capacity, Viral load/CD4+ count</td><td></td></tr>
</table>

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