

Table E.1.4.d.1 Effects of physical activity on health-related quality of life among people living with HIV

Questions: What is the association between physical activity and health related quality of life (HRQOL)? Is there a dose response association (volume, duration, frequency, intensity)? Does the association vary by type or domain of PA?

Population: People living with HIV

Exposure: Greater volume, duration, frequency, or intensity of physical activity

Comparison: No physical activity or lesser volume, duration, frequency, or intensity of physical activity

Outcomes: Health-related quality of life (HRQOL)

Exercise modality	Study	No. of Studies No. of participants	AMSTAR2 Score	GRADE CRITERIA					Summary of findings	CERTAINTY
				Risk of Bias	Inconsistency	Imprecision	Indirectness	Publication Bias		
Aerobic Exercise	O'Brien, 2016 (67)	24 RCTs, N=936	High	Serious risk of bias	No serious inconsistency	No serious imprecision	No serious indirectness	No publication bias	This is the 4th updated systematic review by this group. The Cochrane Collaboration protocol was used to search databases up to April 2013. The review included 24 RCTs that compared aerobic exercise (performed at least 3 times per week for at least 20 min for at least 5 weeks) with no exercise or another intervention, among adults living with HIV. Majority of participants were male (73%), and receiving antiretroviral therapy (19/24). The exercise interventions in which HRQOL was measured (N=9) were all conducted 3 x weekly, at at least 50% VO ₂ max, or between 6 and 24 weeks, for at least 30 and up to 120 min. Of these, 7 showed statistically significant improvements in HRQOL, with one additional study showing a trend, in the intervention groups compared to control conditions. Two meta-analyses showed statistically significant changes on the subscales of mental health, role-emotional, and physical functioning, role physical, general health, and vitality) in quality of life among exercisers when compared with those who did not exercise. Attrition ranged between 5% and 38%.	HIGH (+ve effect)
	O'Brien, 2010 (69)	14 RCTs, N=454	High	Serious risk of bias	No serious inconsistency	No serious imprecision	No serious indirectness	No Serious publication bias	This study searched databases between 1980 and June 2009 and included only RCTs, that compared aerobic exercise interventions (at least 3 times per week, for at least 4 weeks, for at least 20 min) with no aerobic exercise interventions or alternative exercise or treatment modalities. Four studies specifically measured HRQOL (duration ranging from 6 to 24 wks) in exercising vs non-exercising groups and demonstrated significant improvements. No meta-analyses on HRQOL were conducted.	HIGH (+ve effect)
	Nixon, 2005 (70)	10 RCTs, N=276	High	Serious risk of bias	Serious inconsistency	No serious imprecision	Serious indirectness	No Serious publication bias	Four of the studies compared changes in HRQOL measured in persons undergoing interventions for aerobic exercise vs. no exercise (6- 15 wks) and demonstrated significant improvements. No meta-analyses on HRQOL were conducted..	LOW (+ve effect)
	O'Brien, 2004 (73)	10 RCTs, N=458 HIV+ only participants	high	Serious risk of bias	No Serious inconsistency	No serious imprecision	Serious indirectness	Serious publication bias	Meta-analysis was not possible due to the variety of outcomes used for psychological measures. Results of individual studies (Stringer 1998; Baigis, 2002, Lox et al., 1995), showed improvements in QoL in the exercise intervention groups.	MODERATE (+ve effect)

Resistance Exercise	O'Brien, 2017 (66)	20 RCTs, N=764	high	Serious risk of bias	Serious inconsistency	No serious imprecision	Serious indirectness	No Serious publication bias	Five 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 (74)	10 RCTs, N=332	high	Serious risk of bias	Serious inconsistency	No serious imprecision	Serious indirectness	No Serious publication bias	This study performed a systematic review and meta-analysis using the Cochrane Collaboration guidelines where 14 online databases were searched from 1980 to June 2006. Despite the mixed findings reported, individual studies showed significant enhancements 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 Exercise	Ibeneme, 2019b (65)	19 RCTs, N=661 participants included for QoL.	high	Serious risk of bias	No serious inconsistency	No serious imprecision	No Serious indirectness	No Serious Risk of Publication Bias	The study evaluates the impact of physical (aerobic and resistance) exercises on QoL in PLWHA by conducting a systematic review using the Cochrane Collaboration protocol. Databases were searched up to June 2017, only RCTs 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, comprising male and female with age range 22–66 years were included. Two meta-analyses across 13 sub-group comparisons were performed. 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. Overall, the GRADE evidence for this review was of moderate quality. There was evidence that engaging in moderate-intensity aerobic exercises (55–85% Maximum heart rate-MHR), for 30–60 min, 2-5 times/week for 6–24 weeks significantly improves role activity limitation. This corroborates Mutimura 2008 findings who found significant improvements in the exercise group for psychological, independence, and social relationships (p < 0.001) domains of QoL compared to the non-exercise group. Galantino	HIGH (+ve effect)

									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).	
	Gomes Neto, 2015 (68)	7 RCTs, N=386	high	Serious risk of bias	No serious inconsistency	No serious imprecision	No Serious indirectness	No serious publication bias	This study performed a meta-analysis to investigate the effects of a combination of aerobic and resistive exercise (CARE) in HIV-infected patients from the earliest date available to August 2014 for RCTs. There is consistent evidence that exercise is effective in improving QoL. All studies that assessed QoL showed 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, 2013b	8 RCTs, N=NR	low	Serious risk of bias	No serious inconsistency	No serious imprecision	Serious indirectness	No serious risk of publication bias	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 experimental group. Rojas 2003 found better improvements in five subscales of QoL than in controls.	MODERATE (+ve effect)
	Bhatta, 2017 (71)	28 RCTs, N=4136	high	Serious risk of bias	No serious inconsistency	No serious imprecision	Serious indirectness	No serious publication bias	Of the 28 included studies, only six utilised exercise interventions (Cade, 2010; Fillipas, 2006; Galantino, 2005; Maharaj, 2011; Mutimura, 2008; Ogalha, 2011). The intervention duration ranged from 8 (Galantino, 2005) to 24 weeks (Fillipas, 2006; Mutimura, 2008; Ogalha, 2011) and the follow-up period ranged from 2 (Galantino, 2005) to 6 months (Fillipas, 2006; Mutimura, 2008; Ogalha, 2011). The exercise sessions lasted from 1 hour (Fillipas, 2006; Galantino, 2005; Maharaj, 2011; Ogalha, 2011) to 1 hour and 40 minutes in Cade (2010). Where reported, the mean age ranged from	MODERATE (+ve effect)

										33.6 (Maharaj, 2011) to 45.0 years (Cade, 2010). Only three studies were included in the meta-analyses in the studies that used an exercise intervention (Cade, 2010; Maharaj, 2011; Ogalha, 2011). The studies reported different findings for the different domains of quality of life in the intervention group (QoL). Cade (2010) found no improvement in overall health-related QOL, except for emotional well-being. On the contrary, Fillipas (2006) found improvements in general health, as well as cognitive function and self-efficacy. Maharaj (2011) found significant improvements in the physical and mental components of QOL. Mutimura (2008), on the other hand, found improvements in psychological well-being and social interaction domains of QOL. Galantino (2005) reported some enhancements in the functional domain of QOL. Ogalha (2011) found an improvement in general health, vitality, and mental health domains. In summary, the results of the six studies show us that exercise can improve certain aspects of QOL but not others in PLWH. Thus the results are inconclusive
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Abbreviations: N = no; PICO = population, intervention, comparator, outcome; RCTs = randomised controlled trials

1. 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 %). It was later upgraded to HIGH due to the evident dose-response relationship.
2. O'Brien 2010: Not downgraded even if RoB is unclear.
3. 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.
4. 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.
5. 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.
6. 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 Indirectness. 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.
7. Ibeneme 2019b: First graded MODERATE due to RoB due to attrition. This was then upgraded to HIGH due to the evident dose-response relationship.
8. 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.
9. Bhatta, 2017: Graded to MODERATE due to serious risk of bias (since none of the included studies reported a strong internal or external validity and quality of evidence) and indirectness. There is also heterogeneity due to differences in target population, exercise interventions, delivery persons, assessment tools, duration of intervention and follow up and study duration. In all included studies, there is evidence of a dose-response relationship for selected QOL domains. The findings of the meta-analysis on the effects of exercise on QOL are also domain-specific (Cade, 2010; Maharaj, 2011; Ogalha, 2011), and overall these results are inconclusive, domain-specific mainly due to the fact that QOL is a multi-dimensional construct.