Table E.1.4.d.5: Effects of physical activity on cardio metabolic markers among people living with HIV

Questions: What is the association between physical activity and markers of cardiometabolic risk? 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
Outcome: Markers of cardiometabolic risk (blood lipids, glucose and insulin, blood pressure)

Exercise modality	Study	No. of Studies No. of participants	AMSTAR 2 Score	GRADE CRITERIA					Summary of findings	CERTAINTY
				Risk of Bias	Inconsis-tency	Imprecision	Indirectness	Publication Bias		
Aerobic Exercise	No systematic reviews identified									
Resistance Exercise	No systematic reviews identified									
	Pedro, 2017 (*72)*	5 RCTs, N=253	high	No serious risk of bias	Serious Inconsistency	No serious imprecision	Serious indirectness	No serious publication bias	This review focused on PLWHA and HIV-associated lipodystrophy syndrome (HALS) an important subset of PLWHA. Participants had HIV, HALS and had been on ARTs for longer than 3-months. The age of participants ranged between 18 -60 years. This review included studies of males only (Lindegaard ,2008), females only (Dolan, 2006) and mixed sex groups (Medes, 2013., Mutimura 2008, and Terry 2006). Aerobic training resulted in a reduction of total cholesterol in two studies (Lindegaard ,2008 and Mutimura 2008) and a reduction in LDL specifically in Lindegaards study, yet Terry 2006 demonstrating no decrease in total cholesterol under controlled dietary (mixed diet) conditions after aerobic intervention. With concurrent training total cholesterol dropped in Dolan 2006. Triglyceride levels were found by Lindegaard to improve after resistance training and that free fatty acids dropped, and HDL increased after either aerobic or resistance training. There was no effect demonstrated on HOMA or insulin concentrations by any exercise modality. Glucose levels reduced after aerobic training in only one study conclusively. Body fat percentage was reduced in response to all forms of training	LOW (+ve effect)

									(aerobic, resistance and concurrent) in all but one study. This is inconclusive however due to the poor methods of assessment used in all the studies barring Dolan 2006 and Lindegaard 2008. Only one study assessed inflammatory markers (which are important in the development of HALs) This study demonstrated that hs-CRP, TNF-α, IL-6 and IL-18 decreased after aerobic training and only IL-18 decreased after resistance training. There was no demonstrable effect on CD4 count in this population group indicating that training is safe in HALS patients. Aerobic and concurrent training improve VO2max while resistance training reduces fat mass and improves muscle strength. All of the above should improve the inflammatory and lipid profile but there is no true consensus/not enough evidence to support this.	
	Fillipas, 2006 *(80)*	9 RCTs, N=469	low	Serious Risk of Bias	No serious inconsistency	No serious imprecision	Serious indirectness	No serious publication bias	Of the 469 adult participants in this systematic review, 41% were female within RCTs where the interventions were either aerobic, progressive resistance exercises or a combination of the two. . The studies had to have a minimum intervention period of 4 weeks with a frequency of 2 sessions per week. The participants were at various stages of HIV with CD4 counts <100 to>1000 cells/mm^3. With 5 out of the 9 studies including participants who were on HAART (Fillipas 2006, Dolan 2006, Smith 2001, Lindegaard 2008 and Mutimura 2008), one study did not describe antiretroviral use (Terry 1999) and the others used non-HAART participants. No adverse events were attributable to training interventions although the dosage, intensity, frequency and type varied, all were safe. Aerobic exercise and resistance training are effective in improving BMI, fat mass(%) and WHR while resistance training increased body weight and muscle strength and was slightly better at reducing fat mass. Concurrent exercise studies included in this review were inconclusive. Where aerobic training (in one study of moderate effect size) had a small advantage over resistance training at reducing total cholesterol and LDL. Few studies examined blood lipids, glucose, and bone density which are important factors in participants with chronic HIV and HAART.	LOW (inconclusive)

	Quiles, 2019 *(82)*	9 RCTs, N=638	low	Serious Risk of Bias	Serious Inconsistency	No serious imprecision	No serious indirectness	No serious publication bias	This review aimed to investigate the effects of exercise on lipid profiles and blood glucose levels in adults >18 years living with HIV. The studies had to have a min intervention period of 4 weeks with a frequency of 2 sessions per week as with Fillipas, 2010. All studies included participants actively taking ART and 58.6% of the 638 participants were female. Aerobic activity alone caused an increase in HDL and a lack of activity to decrease blood glucose in one study given a homebased physical activity program (Roos 2014). Resistance training alone was also shown by only one study (Zanetti 2016) to decrease triglycerides, total cholesterol and LDL with a concomitant increase in HDL compared to baseline. Concurrent or combined aerobic and resistance training studies were inconsistent with some markers changing and others remaining as is. Those who indicated that glucose levels improve (from a 12-24week intervention) reported no changes in blood lipids (Ogalha 2011, Tiozzo 2013). While in a population with some body fat redistribution (Mutimura 2008) a drop in blood glucose saw slight improvements in total cholesterol and triglycerides but no improvements in LDL and HDL. Only one study indicated HDL improvements with concurrent training without any other lipid or glucose markers improving (Grinspoon 200) . Overall studies reported positive results for reductions in glucose levels and triglycerides with increases in HDL overall. Total cholesterol only slightly improved with the combined training. This suggests that inclusion of exercise can only help the metabolic profile of PLWH.	MODERATE (+ve effect)

Abbreviations: PICO = population, intervention, comparator, outcome; RoB = risk of bias; RCTs = randomised controlled trials

1. 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 were 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).
2. Fillipas 2006: Rated LOW because there is possible RoB, first due to the few studies that focused on the effects of exercise on cardiometabolic markers and because some trials were of short duration (4 wks). Heterogeneity and indirectness may have been due to differences in exercise interventions, outcome measures, and participants. Furthermore, dose-response is not evident and the results of the effects of exercise on cardiometabolic markers in these few studies are inconclusive
3. Quiles 2019: There is a possibility of RoB due to a limited number of studies investigating the effects of exercise on metabolic profile. Attrition rates were also relatively high in among some studies, with rates as high as 39% in one study (Roos et al., 2014). Also, the quality of the included RCTs as assessed by the PEDro scale was a median 5 out of a possible score of 10. Failure to do blinding of the participants and personnel to the exercise intervention, led to an overall high risk of the Hawthorne effect across all the included studies. Inconsistency

might have been caused by heterogeneity due to differences in exercise interventions, assessment protocols, outcomes and populations. There, we downgraded it to LOW. There is evidence of a dose-response relationship in most studies., and as result, we upgraded it to MODERATE.