

# Physical Activity Associated with HIV

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## Introduction

Sedentary behaviour, widely prevalent in developed countries is associated with a variety of diseases and with increased mortality [1]. However, physical activity clearly demonstrates beneficial effects on several health issues, including cardiovascular and all causes of mortality [2]. Among beneficial impacts of exercise we can identify a robust effect on cardiovascular outcomes inducing improvements in lipoproteins and body composition that are translated into reductions in risk of coronary disease, cardiac and probably stroke events [3], and cardiovascular deaths [1,4]. In this way, aerobic exercise improves insulin sensitivity, glycemic and blood pressure control, decreasing the risk of new onset diabetes, hypertension and obesity (with secondary beneficial effects). Besides this, a modest effect in prevention of breast, intestinal and pancreatic cancer [5,6] and an increment in bone mineral density (indeed reductions in hip fracture risks in patients with osteoporosis) have been established. Neurocognitive improvements (with reductions of stress, anxiety, depression and probably delays in cognitive decline and dementia development in older patients) [7,8] are well known and should also be considered.

With highly active antiretroviral therapy (HAART) introduction, we have witnessed a significant increase in survival and improvement in the quality of life of HIV infected patients in developed countries [9-11]. Consequently, common disease in general population (such as cardiovascular ones) [12] and side effects related to HAART (like lipodystrophy) have become a new focus of attention in these patients. In this way, physical activity has been recommended previously in HIV to induce favourable metabolic changes and reduce risk of cardiovascular disease [13-16]. Although its prevalence is really low in this population [17], according to its low cost probably regular physical activity interventions may be cost effective in HIV infected patients [18]. Indeed, aerobic exercise or a combination of aerobic and resistance progressive exercise (at least 30 min/day, 3 times a week for 4 weeks) may be safe [19] and beneficial in other parameters in HIV infected patients [18], such as psychological status, quality of life, anthropometric and metabolic cardiopulmonary and immunity function. Nevertheless, effectiveness of these interventions in HIV patients has not been well established, probably due to several limitations of most of the trials that has tried to investigate this point.

The objective of this review article is to assess the possible beneficial effects of programmed exercise on HIV infected patients and the security of these interventions.

## Effects of Physical Activity on HIV Infected Patients

### Effects of physical activity on lipodystrophy and anthropometric parameters

Lipodystrophy, which may be present in a range of 25% - 83% of HIV infected patients [20-22], is a stigmatizing condition that affects undoubtedly their quality of life [23-25], besides carrying an elevated cardiovascular risk.

Different guidelines on HIV people treatment [26,27] and reviews

about lipodystrophy management [21] mention physical exercise as an alternative in prevention and treatment of these conditions. Indeed, patients carrying out physical activity may have 79% less probability of developing lipodystrophy than patients who have a sedentary way of life [28]. Besides, few studies have evaluated its role in people infected by HIV, generally small and non prospective long term controlled trials which often did not specify the kind and intensity of exercise that may be indicated to obtain desired effects on lipodystrophy treatment. Isolated cases have reported beneficial effects [29,30] in programs of physical activity program including aerobic and resistance exercises reducing abdominal fat mass in HIV patients with lipodystrophy. A small series of two and a half months aerobic and resistance exercise in HIV people with lipodystrophy [31] agreed with the cases reported before [29,30]. Anyway decreases in subcutaneous fat mass and improvements in strength and muscular mass may not be extensive to HIV lipodystrophic patients on resistance exercise alone according to few series published [15,32].

Between anthropometric parameters in HIV patients with no lipodystrophy diagnosed, most of the individual studies [21,33-35] reported no significant changes in weight between exercise and non-exercise groups. While a significant increase of 2.12 kg in body weight for participants in resistive exercise groups compared to a decrease of 4.5 kg in the non-exercising controls have been reported [36], other authors found contradictory results [16], with decreases in weight in both types of exercise. As a matter of fact a recent metanalysis including most of the previous trials [37] found no difference in change in body weight for participants in the exercise groups compared with the non-exercising control group [16,21,34-36,38].

Similarly, body composition in HIV patients who undergo exercise interventions shows contradictory results. While significant decreases in body mass index, waist-to-hip ratio, and percentage of body fat in exercisers compared with controls have been reported [13,16,38], other authors found significant increases in body mass index [39] or no changes [35,36] in people ongoing exercise interventions. Metanalysis mentioned before [37] demonstrated a significant decrease in percent body fat of 1.12% (95% CI: -2.18, -0.07, n=119, P=0.04) for participants in the aerobic exercise group compared with participants in the non-exercising control group with no differences in change in waist circumference; hip circumference and waist-to-hip ratio. No difference in the change in body mass index for patients enrolled in the aerobic

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exercise group compared with participants in the non-exercising control group was reported [37].

In studies which assessed muscle strength, most of them have reported improvements among exercisers compared with non-exercisers [21,34-36,39,40].

Consequently body fat mass is probably reduced with aerobic exercise in HIV infected patients and this effect may be extended to those with lipodystrophy. While there is quite possibly a beneficial effect on muscle strength of HIV patients, other anthropometric parameters such as weight or waist to hip ratio show inconclusive results to date.

### Effects of physical activity on metabolic parameters

Several epidemiological studies in persons without HIV infection demonstrate that a high fitness level offers protection against cardiovascular diseases and premature mortality [41]. Morphological (lipodystrophy –see before) and metabolic abnormalities (including insulin resistance, dyslipidaemia and low-grade inflammation) associated, particularly with HAART, may contribute to an increased risk of cardiovascular diseases in HIV-infected patients.

Endurance training alone or combined with strength training decreases trunk and visceral fat in HIV-infected with lipodystrophy [36,42]. Both strength and endurance training improve peripheral insulin sensitivity in human immunodeficiency virus-infected patients with lipodystrophy [15], similar to HIV-negative individuals [43]. These studies [15,42] also demonstrate beneficial effects on lipid profiles on decreased total cholesterol, LDL-cholesterol, free fatty acids and HDL-cholesterol increased after endurance training, whereas triglycerides and free fatty acids decreased and HDL-cholesterol increased after strength trainings. Probably short term exercise interventions are able to produce significant reductions in lipid profile [32,44], preferably on hypertriglyceridemia [44], in HIV-infected men treated with HAART. A recent study from Brazil [18] suggests that the practice of regular exercise in individuals with HIV infection promoted significant modifications in body fat and hip circumference, increasing muscle mass and reducing fasting glucose and risk of diabetes. The authors also detected a decrease in low-density lipoprotein cholesterol and triglycerides. In conclusion regular exercising in HIV infected patients significantly improves the metabolic parameters.

### Immunological and virological effect of physical activity

Results of individual studies have found significant differences in CD4 counts of HIV infected patients in exercise groups compared with controls [36,39,45,46]. Indeed considerable averages of increment in CD4 count (60 cells/mm<sup>3</sup> [39] and 38 cells/mm<sup>3</sup> [46]) compared to a sensible decrease (39 cells/mm<sup>3</sup> [39] and 61 cells/mm<sup>3</sup> [46]) have been found. Less significant increments have been shown by other authors [36,45] in the exercise groups with averages of decrease of 78 and 4 cells/mm<sup>3</sup> in control groups. Nevertheless these results are inconclusive, attending to non significant changes or increases statistically non-significant that have been reported by others [13,21,33-35,38,40,47,48].

A recent metaanalysis that included most of the mentioned trials, found no difference in change in CD4 count for participants in the exercise intervention group compared with the non-exercising control group [37]. Although this metaanalysis may be quite heterogeneous because included trials comparing more versus less intensive aerobic exercise, aerobic exercise against no other intervention, aerobic exercise and another intervention such as metformin [34] or lipid lowering diet [16] against aerobic exercise alone...) a significant trend towards

an improvement in CD4 count of 69.58 cells/mm<sup>3</sup> for subanalysis exclusively of participants in the aerobic exercise trials compared with the non-exercising controls [37] was found. Besides that, the cutoff point estimated was above 50 cells/mm<sup>3</sup>, which suggests a potential clinically important increase in CD4 count for interval exercisers compared with non-exercisers.

On the other side, individual results have found non significant averages of decrease in viral load [47] in the exercise groups compared to no exercising controls, although co-interventions of exercise alone or with low lipid diet has been traduced on significant viral load values below 80 copies/mL [16]. No significant increase in viral load in people who underwent an exercise [35,38], program, or no differences in viral load [21,34] with respect to those who did not perform physical activity has not been reported either.

Consequently it is quite improbable the existence of a significant difference in the change of viral load for participants in the exercise intervention groups compared with the non-exercising controls, independently being aerobic or aerobic combined with resistance exercise [37].

### Cardiopulmonary effects of physical activity

Individual studies that measured cardiopulmonary status reported significant improvements in cardiopulmonary outcomes in exercisers versus non exercising controls. In this way significant improvements in maximum oxygen consumption (VO<sub>2</sub>max) [39,47], lactic acid threshold [47], and significant reductions in maximum heart rate [36,40] could be developed in people undergoing physical activity.

Aerobic exercise intervention groups can result in the most significant improvements in cardiopulmonary function, reaching changes in VO<sub>2</sub>max greater than 2 mL/kg/min, compared with the non-exercising controls [37]. Indeed a significant trend towards a greater improvement in VO<sub>2</sub>max of 4.30 mL/kg/min for participants in heavy-intensity exercise groups compared with the moderate-intensity exercise group has been reported [37]. These results suggest a potential clinically important improvement in cardiopulmonary function in aerobic HIV exercisers.

### Psychological effects of physical activity

Probably there is a significant improvement in the depression subscale of Profile of Mood States Scale (POMS) for participants in the exercise intervention group compared with the non-exercising control group [37]. Significant reduction of 7.68 points on physical active groups represents a clinically important improvement in depression-dejection among exercisers compared to non-exercisers.

No significant differences between the moderate-and high-intensity exercise groups for depression [39] or general health status [33,45] have been reported. Nevertheless, isolated authors have found significant improvements in general health [48] and quality of life questionnaire (QOL) [13,47] among exercisers, with lower levels of depression [38,46] and anxiety [46], higher mood and life satisfaction [36] and unspecified beneficial effects in psychological status [36,49,50].

According to these results it is quite possible that exercise (aerobic and maybe resistance activities as well) could give a beneficial outcome in psychological status in adults with HIV.

### Other effects of physical activity on HIV infected patients

**Effects on bone mineral metabolism:** Accelerated bone mineral loss in HIV infected patients receiving potent antiretroviral therapy

is clearly established [51], although it is probably that a short-term accelerated bone mineral loss develops in cohorts initiating HAART, probably followed by a longer period of stability [52]. Besides that, the difference in bone mineral density between HIV positive and HIV negative people may disappear after adjustment for weight [53]. Decreases in bone mineral density may increase fracture risk in HIV infected people [54]. In this way, it is quite possible that strength training reduces bone loss in HIV-infected patients, the same as happens in non HIV infected people. As a matter of fact, maintaining adequate weight and engaging in physical activity has been reported as a strategy that may help to preserve and perhaps improve bone mass density in HIV-infected patients [55].

In this way, thirty minutes of exercise (including jogging or walking) at least 3 days a week has been recently recommended [56] as a useful measure to prevent osteoporosis in HIV people. Nevertheless non double blind randomized controlled trials of exercise effects preventing osteoporosis in HIV infected patients have been performed.

**Effects on cancer:** The modest effect in prevention on several cancer [5,6] demonstrated by exercise interventions, and the probable reduction of all cancer mortality demonstrated in prospective studies in non HIV [57] people has not been investigated as far as we know in HIV infected people.

## Security of Physical Activity on HIV Infected Patients

Probable exercise interventions in HIV people are as safe as they are in general population. No adverse events or side effects [21], and no withdrawal signs due to illness or infection [38,47] has been mentioned in previous reports. As a matter of fact, a review considering joints, muscular, bone, nervous, vascular or immunity (decline in CD4 cell count or progression to AIDS) outcomes, as well as hospitalizations or deaths show no adverse effects in HIV infected patients who underwent exercise interventions [37]. Certainly, the only isolated adverse events related to exercise interventions reported before were an asthma exacerbation [35], a hospitalization [39] and a death case [40] (the latter, not attributed to the exercise intervention). According to this evidence, there is probably no formal contraindication in HIV patients as regards ongoing exercise activities.

## Limitations

Conclusions about the effect of exercise interventions in HIV infected patients are limited to few small trials that investigated this aim. Investigations have been performed predominately in men within a close range of ages [37], but a wide range of HIV infected patients (lipodystrophic and non-lipodystrophic, on HAART and untreated...). An important limitation too is the high rate of withdrawal in the trials [37], more than 25% in some of them. Besides that, several times intervention groups included a co-intervention, such as exercise and diet [16,29] or exercise and metformin [34], which makes difficult clarification of exercise effects alone. Body composition at the beginning of the trials has not always been reported, and the specification of the type of exercise and the level of supervision of this activity is infrequent. Consequently the above conclusions should be interpreted with caution.

## Conclusions

Progressive exercise interventions (aerobic and maybe resistance interventions too) report beneficial effects on outcomes in psychological status in HIV infected adults. There is quite possibly a benefit in muscle strength, body fat distribution and cardiopulmonary function (preferably with aerobic exercise), as well as better parameters of lipid

profile and insulin sensitivity compared with non exercising HIV people. These interventions are safe, probably with no change in viral load or CD4 count (or with little increase of these cells in HIV people ongoing aerobic exercise), and probably cost effective. In conclusion regular exercise should be extensively recommended in HIV infected people with no other general contraindication.

Future investigations should clarify possible differences between sexes or ethnics in order to standardize recommendations. Probably bigger trials with intention to treat analysis will collaborate to solve the problem of frequent withdrawals and the difficulty to obtain certain results.

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