**The influence of exercise on cardiovascular disease and metabolic disorders among people with HIV on HAART**

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**Abstract**

*Background:* People with human immunodeficiency virus (HIV) frequently experience metabolic impairments, are at an elevated risk of cardiovascular disease (CVD), and commonly lead sedentary lifestyles, with nearly half classified as sedentary. Although highly active antiretroviral therapy (HAART) may extend the lifespan of a person with HIV by 14-26 yr, it often compounds the metabolic impairments caused by the infection. This results in further health compromise with a higher risk of CVD and metabolic diseases. Few studies have investigated the influence of exercise on the cardiometabolic risk factor profile among people with HIV on HAART. Therefore, the objective of this review is to explore the effect of exercise on cardiovascular and metabolic parameters among people with HIV on HAART. *Methods:* PubMed, Scopus, and the Cochrane Library were used to obtain articles concerning either: 1) the cardiovascular and metabolic consequences of HIV and HAART, or 2) the effect of exercise on the cardiovascular and metabolic profiles of people with HIV taking HAART. For articles related to the cardiometabolic consequences of HIV and HAART, all medical subject headings related to “Anti-HIV Agents” were used in addition to key words appearing in the title (e.g., “cardiovascular”, “metabolic”, etc.). For articles related to exercise, the previous search term was used with the inclusion of additional title words such as “exercise”, “running”, “strength training”, etc. Articles were excluded if they did not characterize cardiovascular, metabolic, or anthropometric consequences of HIV and HAART, or quantify the effects of exercise on adults with HIV taking HAART. Only articles published in English in peer-reviewed journals were considered. *Overview:*This review provides information regarding the prevalence and pathophysiology of CVD and metabolic disease among people with HIV on HAART. It also discusses the impact of exercise on the cardiometabolic risk factor profile, evaluates the characteristics of exercise interventions where possible, and compares results across studies where appropriate.

**Introduction**

At least 34 million people are currently living with human immunodeficiency virus (HIV). Since the first cases were recognized in 1981 (*MMWR*, 1981), HIV infection has spread to every region of the world (Gottlieb et al., 1996; Faunci, 2006). The most recent data estimate annual HIV-related deaths to total more than 1.7 million, while 2.7 million new infections appear during that period (UNAIDS, 2012). Although these data are improving (at the end of 2006, there were 5.5 million more active cases, with 4.3 million new cases and 2.9 million deaths throughout the year; Karim et al., 2007), HIV remains a major public health concern both in the United States and abroad. At present, there over 1.1 million Americans (~0.4% of the population) who have HIV and approximately 56,000 new cases continue to appear annually (Lansky et al., 2010; UNAIDS, 2012; Karim et al., 2007).

Although HIV and acquired immunodeficiency syndrome (AIDS) have resulted in nearly 30 million deaths worldwide (UNAIDS, 2012), the introduction of antiretroviral medications in 1987, followed by highly active antiretroviral therapy (HAART) in 1996, has reduced the mortality rate by more than 70% (Lugassy, 2010; Palella et al., 1998). People with HIV can now be expected to live 14-26 years longer (Lugassy, 2010). Despite this increase in the *length* of life, HAART has not demonstrated a similar effect on the *quality* of life. The combination of HIV and HAART commonly results in the manifestation of anthropometric abnormalities (e.g., lipodystrophy, lipoatrophy, and lipomegaly), compromised metabolic functioning (e.g., muscle wasting, altered insulin action, dyslipidemia, and hepatic lipogenesis), and an increased risk of cardiovascular events such as myocardial infarctions (Anuurad et al., 2009; Fichtenbaum et al., 2010; Grinspoon & Carr, 2005; Jain et al., 2001).

Exercise is a possible strategy to manage the metabolic impairments, improve the anthropometric abnormalities, and mitigate the cardiovascular risks associated with HIV and HAART (Fillipas et al., 2010; Spierer et al., 2007; Robinson et al., 2007; Henricksen, 2002; Jones et al., 2001; Thoni et al., 2002). Despite these benefits, exercise has not become a standard component of therapeutic interventions for people with HIV who use HAART. Most interventions focus on awareness, diagnosis, and prevention.

On July 13th, 2010, the U.S. government presented a *National HIV/AIDS Strategy* (AIDS.gov, 2012) which outlines three primary goals to be accomplished by 2015:

1. *Reduce New HIV Infections*. By 2015, the goal is to reduce the annual number of new cases by 25% while increasing percentage of people with HIV who know their serostatus to 90%.
2. *Increase Access to Care and Improve Health Outcomes for People Living with HIV.* By 2015, the goal is to increase the proportion of HIV patients receiving clinical care from 65% to 85%.
3. *Reduce HIV-related health disparities.* By 2015, the goal is to increase the proportion of people living with HIV who have an undetectable viral load by 20%.

Less than five months after the *National HIV/AIDS Strategy* was announced, on December 2nd, 2010, the U.S. Department of Health and Human Services announced the *Healthy People 2020* initiative, listing HIV/AIDS as one of its major priorities. Eighteen specific objectives were disclosed, divided in four categories (U.S. Department of Health and Human Services, 2012a):

1. *Diagnosis of HIV Infection and AIDS.* Among the total population, the goal is to achieve an annual rate of 12.4 new cases per 100,000 people, down from 13.0 new cases in 2010. Additional goals have been established for subpopulations.
2. *Death, Survival, and Medical Healthcare After Diagnosis of HIV Infection and AIDS*. This includes increasing 3-year survival rate to 92.4% (from 84.0% in 2006) and reducing annual HIV-related deaths to 3.3 per 100,000 people. However, the goal of HIV-related deaths was met in 2008 and passed (3.0 per 100,000 people) in 2009.
3. *HIV Testing*. The overarching goals are to increase the percentage of adolescents and adults who get tested from 17.2% in 2010 to 18.9% in 2020, and increase the proportion of people with HIV who know their serostatus from 81.9% in 2009 to 90.0% in 2020.
4. *HIV Prevention*. This goal centers on the promotion of condom use in various populations (data are limited) and increasing the percentage of substance abuse treatment facilities with HIV/AIDS resources from 56.2% in 2010 to 59.8% in 2020.

Although the simultaneous implementation of two federal initiatives concerning HIV/AIDS illustrates its public health importance, neither initiative mentions the therapeutic potential of exercise or habitual physical activity (PA). Therefore, the purpose of this systematic review is to establish a case for exercise and PA as a supplement to HIV/AIDS treatment interventions. In doing so, this paper will explain the pathophysiology HIV/AIDS, examine comorbidities brought about by pharmacological interventions, assess the benefits of exercise, define appropriate exercise testing procedures, discuss the *F*requency, *I*ntensity, *T*ime, *T*ype, *V*olume, and *P*rogression (*FITT-VP*) of an ideal exercise prescription, and characterize the special considerations in developing an exercise prescription for adult men and women living with HIV who use HAART.

**Methods**

**Data Sources and Search Terms**

PubMed, Scopus, and the Cochrane Library were searched for articles related to 1) the cardiovascular and metabolic consequences of HIV and HAART, and 2) modes by which exercise can improve cardiovascular and metabolic profiles among people with HIV who take HAART.

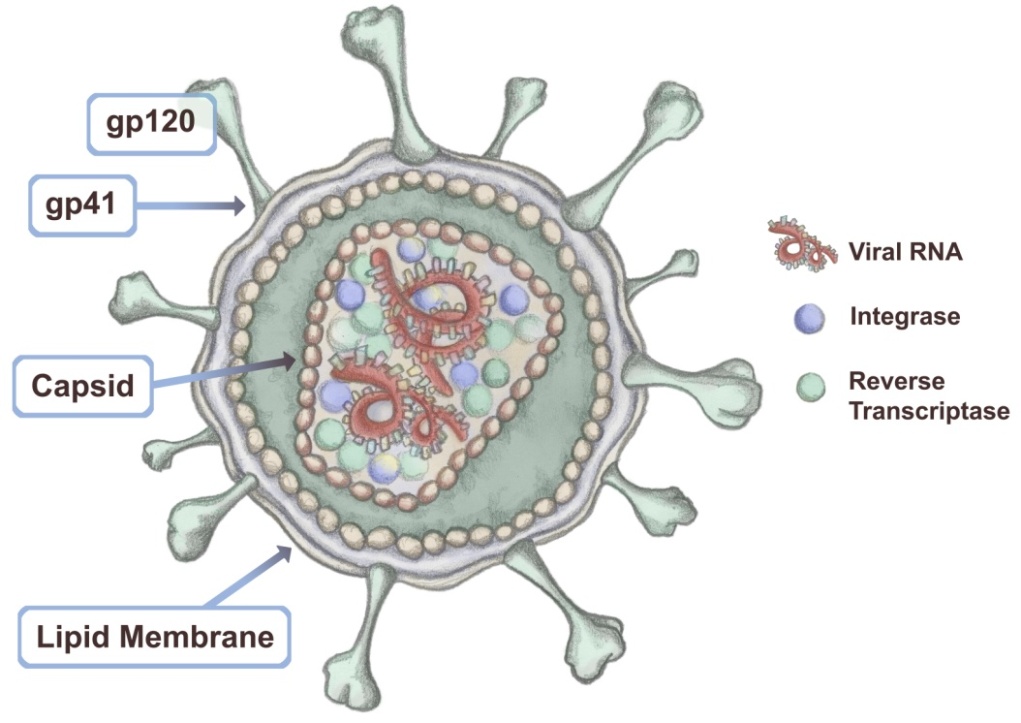
For articles related to the cardiovascular and metabolic consequences of HIV and HAART, the *PubMed* search term was: *("Anti-HIV Agents"[MAJR] OR haart[ti] OR "highly active antiretroviral therapy"[ti]) AND ("cardiovascular"[ti] OR hypertension[ti] OR hypertensive[ti] OR "blood pressure"[ti] OR smoking[ti] OR "tobacco use"[ti] OR diabetes[ti] OR "blood glucose"[ti] OR hyperglycemi\*[ti] OR "cholesterol"[ti] OR metabolic[ti] OR metabolism[ti] OR obesity[ti] OR overweight[ti] OR "body mass"[ti] OR "body composition"[ti] OR "body morphology"[ti] OR bmi[ti] OR weight[ti] OR diabetes[ti] OR lipid[ti] OR lipids[ti] OR lipodystroph\*[ti]) AND english[la] AND review[pt]*

For articles related to modes by which exercise can improve cardiovascular and metabolic profiles among people with HIV who take HAART, the *PubMed* search term was: *("Anti-HIV Agents"[MAJR] OR haart[ti] OR "antiretroviral therapy"[ti] OR "antiretroviral therapies"[ti] OR "HIV"[ti]) AND ("cardiovascular" OR hypertension OR hypertensive OR "blood pressure" OR smoking OR "tobacco use" OR diabetes OR "blood glucose" OR hyperglycemi\* OR "cholesterol" OR metabolic OR metabolism OR obesity OR overweight OR "body mass" OR "body composition" OR "body morphology" OR bmi OR weight OR diabetes OR lipid OR lipids OR lipodystroph\*) AND (exercise[ti] OR exercises[ti] OR "jogging"[ti] OR running[ti] OR running[mesh] OR treadmill[ti] OR treadmills[ti] OR "strength training"[ti] OR "weight lifting"[ti] OR "resistance training"[ti] OR "endurance training"[ti] OR "cardiovascular training"[ti] OR "speed training"[ti] OR plyometric[ti] OR plyometrics[ti] OR "agility training"[ti] OR "physical activity"[ti] OR "physical activities"[ti]) AND english[la]*

**Study Selection**

The searches resulted in 157 and 88 articles respectively. Articles were included if they characterized cardiovascular, metabolic, or anthropometric consequences of HIV and HAART (n=32) or quantified the effects of exercise on adults with HIV taking HAART (n=29). Investigations of other phenomena (e.g., mutagenesis, promotion of healthy nutrition, etc.) were excluded. Articles were excluded if the participants were children. Only articles published in English in peer-reviewed journals were considered.

**Disease Pathophysiology**

The International Committee on Taxonomy of Viruses (King et al., 2012) classifies HIV as a Group VI ribonucleic acid (RNA) virus, or a retrovirus. Retroviruses do not contain deoxyribonucleic acid (DNA) and thus replication must take place inside of a host cell (Klatt, 2012). HIV infection begins when the glycoprotein gp120 binds to a cluster of differentiation 4 (CD4) co-receptor on an immune system cell (most commonly T helper cells, which are referred to as CD4 cells). After gp120 is bound, gp41 facilitates the fusion of HIV to the immune cell membrane, opening a pore through which the viral core gains access to the host cell. A reverse transcriptase enzyme is bound to the HIV RNA, synthesizing a double-stranded cDNA, which functions as a template by which the enzyme integrase inserts it into host cell genomic DNA (Klatt, 2012). Once infected, there is a continuous replication of HIV virions and a progressive destruction of CD4 cells. A CD4 count below 200 is criteria for the diagnosis of AIDS (CDC, 2012). As HIV progresses toward AIDS, a variety of cardiometabolic abnormalities manifest. The mechanisms resulting in these changes are not well understood and likely to arise from a multitude of causes (Guardiola et al., 2006; Grunfeld, 1995; Glover, 2010).

**Etiology of HIV**

Untitled-1.jpgThe estimated risk of HIV contraction through injection drug use poses more risk than standard sexual intercourse and represents the primary mode of transmission (Mathers et al., 2008; EMCDDA, 2009; UNAIDS, 2011). Sexual intercourse with an HIV infected partner associates with typical transmission rates of 0.1% to 0.5%, although estimates can be as high as 1.7% per exposure depending on several variables (DeGruttola et al., 1989; Boily et al., 2009; Varghese et al., 2002). Intravenous drug use has a transmission probability of 0.7% per exposure, which translates to a 49% risk of infection after 100 exposures (Kaplan & Heimer, 1992; Kaplan & Heimer, 1995).

**Treatment recommendations**

The most successful and widely prescribed pharmaceutical treatments of HIV are anti-retroviral drugs. These are classified by the phase of the retroviral lifecycle they inhibit. Nucleoside (and nucleotide) reverse transcriptase inhibitors (NRTIs) inhibit reverse transcription via competitive inhibition. [Non-nucleoside reverse transcriptase inhibitors](http://en.wikipedia.org/wiki/Reverse_transcriptase_inhibitor) (NNRTIs) inhibit reverse transcription via non-competitive binding. [Protease inhibitors](http://en.wikipedia.org/wiki/Protease_inhibitor_(pharmacology)) (PIs) inhibit proteases, which are enzymes used by HIV in viral assembly. Entry (or fusion) inhibitors block several targets to inhibit entry of HIV into the host cell. CCR5 receptor antagonists bind to the CCR5 receptors on T-Cells, which is where most strains of HIV bind. Integrase inhibitors inhibit integrase, the enzyme that integrates viral DNA into the DNA of the infected cell. HAART is a combination of the above medications, targeting HIV replication at a variety of stages (U.S. Department of Health and Human Services, 2011b; Murphy, 1999; Wilson et al., 1993).

**Signs and symptoms**

HIV associates with a number of cardiometabolic and anthropometric abnormalities. Regarding anthropometric abnormalities, fat distribution changes such as lipoatrophy (selective fat loss; usually in the face) and lipomegaly (selective fat accumulation, usually in the abdominal area) are commonly experienced (Jain et al., 2001; Dube et al., 2011; Francielle et al., 2011; Terry et al., 2006). These changes frequently result in overall changes to body composition (Falutz et al., 2011; Engelson et al., 2006), which are compounded by the fact that a fifth of all patients with HIV experiencing muscle wasting (Yahiaoui et al., 2011). Regarding cardiometabolic changes, people with HIV commonly experience disruptions to their blood lipid profiles (e.g., (hypertriglyceridemia, hypercholesterolemia, altered low and high density lipoprotein cholesterol levels; Carpentier et al., 2005; Birk et al., 2002; Fillipas et al., 2010; Scevola et al., 2003), insulin resistance with altered glucose homeostasis (Mallewa et al., 2008; Driscoll et al., 2006; Yarasheki et al., 2011), and increased blood pressure (Spierer et al., 2007; Opravil et al., 1997). Owing to the summation of these health consequences, people with HIV experience an increased susceptibility to the metabolic syndrome (Samaras, 2007) and an elevated risk of CVD (Currier et al., 2003; Friis-Moller et al., 2003; Triant et al., 2007). Fisher et al. (2011) noted the presence of early atherosclerosis at autopsy in people with HIV, as well as coronary lesions in HIV-positive patients as young as 23.

The constellation of metabolic and morphological effects is broadened with the addition of HAART, resulting in additional compromise to one’s body composition and metabolic functioning while further elevating the risk of CVD (Anuurad et al., 2009; Caron-Debarle et al., 2010; Bozzette et al., 2003; Friis-Moller et al., 2007; Mary-Krause et al., 2003). Every year in which an HIV-infected patient stays on HAART (particularly protease inhibitors) increases the relative risk of a myocardial infarction by 26% (Friis-Moller et al., 2003). Consequently, CVD now accounts for 22% of all deaths among people with HIV, up from 8% in the pre-HAART era (Crum et al., 2006). There are a variety of explanations for this increase in CVD; one explanation involves lipids-lipoproteins. Riddler and colleagues (2003) found initiation of HAART increased total and LDL cholesterol while HDL cholesterol levels were maintained at approximately 10 mg/dl below pre-infection values. Another explanation for the compounding of risk of CVD is endothelial dysfunction. Wang et al. (2007) explain how this could arise through HAART’s role in the inhibition of nitric oxide, alteration of lipoprotein profiles, promotion of oxidative stress, and compromise to insulin function.

**Benefits of habitual physical activity**

Exercise is a possible strategy to mitigate the impairments to metabolism, morphological changes, and risk of CVD among people with HIV who take HAART. Exercise has been studied in this population, finding significant improvements in body composition (Engelson et al., 2006; Malita et al., 2005), fat redistribution changes (Florindo et al., 2007; Francielle et al., 2011; Terry et al., 2006), blood lipid profile (Birk et al., 2002; Fillipas et al., 2010; Scevola et al., 2003), pulmonary function (Dolan et al., 2006; Hand et al., 2008), hormone and cytokine profiles (Dudgeon et al., 2010), lactate kinetics (Bauer et al., 2004), blood pressure and autonomic regulation (Spierer et al., 2007), insulin action and glucose homeostasis (Driscoll et al., 2006; Yarasheki et al., 2011), and the risk of experiencing CVD (Ogalha et al., 2011). A variety of exercise prescriptions have been tested to achieve these benefits.

Mutimura and colleagues (2008a) tested the effect of a 6-month exercise program on anthropometric measures. Subjects were 100 adult men and women (aged 21-50) who were HIV-positive, living in Rwanda, on HAART for at least 6 months, and had experienced moderate to severe body fat redistribution after initiation of HAART. They randomized the subjects to an exercise group or a non-exercising control group. Those who were randomized to exercise completed 1.5 hour supervised sessions thrice weekly for six months. Each session involved a warm-up, 15 min brisk walking, 45-60 min of jogging, running, stair climbing, low-back and abdominal stabilization exercises, and resistance training, 15 min cool-down, and stretching. The intensity of the aerobic portion progressively increased from 45% age-predicted max HR for the first 3 weeks, 60% for the next six, and 75% for the remainder of the study. Intensity of the resistance training was not discussed.

They collected height, weight, skinfolds, and waist and hip circumferences. Following the 6-month exercise intervention, Mutimura and colleagues found significant differences between groups in the changes in overall body fat redistribution (p<0.0001), body mass index (BMI) (p<0.05), waist circumference (p>0.0001), waist to hip ratio (p<0.0001), body fat percent (p<0.0001), and all individual skinfold measurements (p≤0.0001).

In a subsequent publication, Mutimura and colleagues (2008b) reported metabolic indices (total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, fasting blood glucose, and insulin) from the same trial. After six months, no significant changes were found in levels of HDL or LDL cholesterol, but total cholesterol (p<0.05), fasting blood glucose (p<0.0001), and insulin (*p* <0.05) levels declined more in the exercise group than the non-exercise group.

Although there remains to be a trial in which people with HIV are assigned an exercise condition or non-exercise control condition and tracked until death (to test the association with CVD incidence), several authors have made projections based on the relationship between exercise and CVD risk factors. In a review by Scevola et al. (2003), they note that a combination of aerobic and anaerobic exercise, conducted at approximately 70% of one’s maximum heart rate may be expected to lower the risk of cardiovascular events owing to better control of metabolic changes.

**Appropriate exercise testing procedures**

Although the American College of Sports Medicine (ACSM) does not require people with HIV to undergo exercise testing prior to engaging in an exercise regimen, HIV and HAART do predispose an individual to cardiac dysfunction and increase risk of CVD (Crum et al., 2006; ACSM, 2013). Moreover, more than 40% of people with HIV are sedentary (Eidam et al., 2006; Ramirez-Marrero et al., 2008; Schuelter-Trevisol et al., 2010) and among people who were previously sedentary, CVD risk factors can be aggravated by acute exercise (Cobb & Weaver, 1986). Thus, a medical examination, although not required, may be useful. In addition to gaining information about CVD risk, it may provide the examiner with information relevant to the subsequent establishment of an exercise prescription (ACSM, 2013).

A variety of procedures may be used to assess physical fitness, including graded exercise tests (e.g., cycle ergometer test and 3-minute step test), measures of cardiometabolic health (e.g., resting BP, height, weight, and waist circumference), strength measures (e.g., curl-ups, push-ups, and isometric handgrip dynamometry), flexibility measures (e.g., sit-and-reach), and measures of mobility and physical functioning (e.g., floor transfer test) (ACSM, 2013).

**Unique considerations in exercise testing**

The day-to-day health is more variable among people with HIV than among those without (Peltzer & Phaswana-Mafuya, 2008). In the presence of an acute infection, testing should be postponed (ACSM, 2013). If the patient is asymptomatic on the day of testing, graded exercise tests showing a reduced exercise capacity is likely to suggest a sedentary lifestyle (ACSM, 2013); whereas if the patient is symptomatic, the exercise technician can expect to find limitations in exercise time, lactate kinetics, and ventilatory markers (Pothoff et al., 1991; Stringer, 2000). The presence of AIDS exacerbates these limitations dramatically, such that patients with AIDS are unlikely to achieve ventilatory threshold or peak oxygen consumption and may experience abnormal endocrine and nervous system responses (ACSM, 2013). In instances in which an acute infection is present, exercise testing should be postponed (ACSM, 2013). When exercise testing is conducted, measures should be taken to limit transmission of infection (e.g., sterilization of reusable instruments; Kendrick et al., 2003). Blood pressure and electrocardiogram should be evaluated periodically due to the high prevalence of cardiovascular impairments. There is also a high prevalence of peripheral neuropathies, which may impact testing capacity; tests should be adjusted accordingly in these situations (Nicholas et al., 2007).

**Exercise prescription**

The ACSM recommends individuals with HIV to engage in the following FITT-VP: Frequency: Aerobic exercise should be performed 3-5 times a week and resistance exercise 2-3 times a week. Intensity: Aerobic exercise should be conducted at 40%–<60% oxygen consumption reserve or heart rate reserve. For resistance exercise, the patient should complete 8-10 repetitions in each set at a load of approximately 60% one repetition max (1-RM). Time: The timing of aerobic exercise should reflect one’s capacity, beginning with 10 minute bouts and progressing to 30-60 minutes a day. For resistance exercise, the patient should complete 10-12 exercises, with 2-3 sets of each exercise, targeting all of the major muscle groups. It should take the patient approximately half an hour to complete. Type: The chosen mode of exercise must reflect the individual interests and capacities of the individual, taking into consideration physical limitations (e.g., peripheral neuropathies). Activities that promote flexibility should be incorporated into the exercise sessions 2-3 days a week for approximately 10 minutes. Volume: Initially, the volume (product of frequency, intensity, and time) may be met by more frequent bouts of moderate intensity exercise. As the patient becomes capable, increasing intensity can begin to account for a greater portion of volume. Progression: The progression toward a higher volume of exercise, especially in regard to the intensity component, is likely to occur much more slowly than could be expected by healthy populations. Despite this, the ultimate goal is to progress asymptomatic patients toward the ACSM FITT prescription for healthy adults. This progression must occur at a rate that can be tolerated by the individual.

Special considerations in exercise prescription

Feelings of fatigue are to be expected and should not preclude exercise participation, but if accompanied by dizziness, nausea, or swollen joints, exercise should be delayed (ACSM, 2013). If the patient is symptomatic, or has a diagnosis of one or more comorbidities, supervised exercise is recommended (ACSM, 2013). Due to the high day-to-day variability in health and exercise capacity, the components of the FITT principle should be adjusted based on acute state. For example, although Stringer (2000) reports better cardiovascular responses to vigorous (compared to moderate) intensity aerobic exercise, they note, based on symptoms, that it may be prudent to prescribe moderate intensity.

Contact or otherwise high-risk activities (e.g.,skateboarding, rock climbing) can be included with caution. According to the CDC (1996), with the exception of boxing, the risk of transmission during sport participation is very unlikely; one would have to participate in more than a million games. According to Kordi & Wallace (2004), there has yet to be a confirmed case of HIV transmission during sport. Despite this, it remains prudent to be cautious about including sports where bleeding is possible.

If osteopenia is present, weight-bearing activities should be a major focus (Tebas et al., 2000; Kelley et al., 2001). Due to the increased prevalence of cardiovascular impairment and dysfunction, markers for CVD risk should be periodically evaluated (Vittecoq et al., 2003).

The age of a patient may also impact exercise prescription. As HAART has elongated the expected lifespan of individuals with HIV, exercise for older populations has become a consideration. More than a quarter of all people in the U.S. who have HIV are 50 or older (Karpiak, Shippy, & Cantor, 2006). Although data on the effect of exercise on older individuals with HIV are limited (Evans et al., 1998; Oursler et al., 2006; Souza et al., 2008), Yahiaoui and colleagues (2011) summarized what data are available to establish a preliminary set of exercise recommendations for people living with HIV who are 50 or older. Their recommendations are that both resistance and aerobic exercise should be conducted at least 3 days a week as opposed to 3-5 days a week for AE and 2-3 days for RE. They recommend aerobic exercise be conducted in bouts of 20-40 minutes (as opposed to 30-60 minutes) with warm-ups preceding and cool-downs following each workout, and lasting 5-10 minutes. The intensity of AE should range from 50-90% of the estimated maximum heart rate (as opposed to 40-<60% of heart rate reserve). Although they advise beginning at a lower intensity and increasing in increments that can be tolerated, they note that higher intensities elicit the most beneficial outcomes. The authors suggest a goal of increasing intensity by 5% each week. Regarding RT, the authors recommend that patients begin by conducting 1-2 sets of each exercise (as opposed to 2-3 sets), incorporating all of the major muscle groups, completing 6-8 repetitions (as opposed to 8-10 repetitions) in each set at 60% 1-RM. As the patient is capable of tolerating an increased volume, they recommend a progression to 3 sets of 8-10 repetitions using 80-90% 1-RM.

Conclusion

HIV with concurrent use of HAART is associated with fat distribution changes, muscle wasting, worsening body composition, disruptions to the blood lipid profile, insulin resistance and impaired glucose homeostasis, increased blood pressure with autonomic dysregulation, compromised pulmonary function and pulmonary hypertension, an increased susceptibility to the metabolic syndrome, and an elevated risk of CVD. Each of these variables can be managed, either improving or mitigating further degeneration, by following an appropriate exercise prescription. For adult men and women who have HIV and take HAART, a combination of aerobic and resistance exercise at a moderate intensity, performed regularly, with modes that reflect the individual’s capacity, appears to be a safe and effective way to mitigate physiological deterioration, manage morphological changes, and reduce the risk of CVD.