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Evidence-Informed Practical Recommendations for Increasing Physical Activity among Persons Living with HIV

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Introduction

With the advent of effective antiretroviral therapy (ART), the care of persons living with HIV (PLWH) is shifting focus to the management of age-related chronic health conditions (e.g., metabolic syndrome and cardiovascular disease), syndromes of aging (e.g., dementia and frailty), and side effects related to ART. Non-ART polypharmacy is common among PLWH and associated with increasing risk of hospitalization and mortality [1]; thus, non-pharmacologic management of comorbidities is critical for PLWH who may experience an earlier onset and a greater burden of comorbidities. Routine engagement in health behaviors, including physical activity (PA), may help prevent and manage comorbid health conditions and syndromes of aging common among PLWH [2]. PA refers to any bodily movement produced by muscle contraction that causes energy expenditure, whereas exercise is a subset of PA that involves planned, repetitive body movement with the intent to increase well-being and energy level to allow for independent participation in physical activities [3]. The goal of this narrative review is to summarize key literature from the past 10 years examining the benefits of PA and to outline recommendations to prescribe and support PA engagement among PLWH.

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The second edition of PA Guidelines for Americans issued by the Department of Health and Human Services (HHS) [4] proposes that adults – even those with chronic conditions and disability – engage in at least 150 to 300 minutes of moderate-intensity or 75 to 150 minutes of vigorous-intensity aerobic PA per week, as well as muscle strengthening activities on two or more days a week. Balance training is additionally recommended as part of older adults' weekly PA to reduce fall risk. Importantly, HHS emphasizes that moving more and sitting less will benefit nearly everyone, with the most sedentary and least active individuals experiencing the greatest benefit from small PA increases [5]. Although some PLWH may have unique physical limitations that must be accommodated in order for them to safely engage in PA, the take-home recommendation is that PA participation is key to maximizing health and function. For additional information regarding PA recommendations and safety precautions for patients with combinations of cardiovascular disease risk factors (i.e., obesity, arterial hypertension, diabetes mellitus, and dyslipidemia), we refer the reader to an expert consensus statement on PA prescription [6].

Despite the well-established health benefits of PA (summarized in table 1), rates among PLWH remain low. A meta-analysis of 24 studies involving nearly 4000 PLWH found that only half of the individuals engaged in 150 minutes of moderate-intensity PA [7]. Among middle-aged PLWH, 26% reported no moderate, vigorous, or muscle strengthening PA, similar to rates in the U.S. general population [8]. These PA trends are consistent across settings: 32% of Vietnamese adults with HIV reported low or no PA [9, 10], with similar rates in the Swiss HIV Cohort study (41%) [11], Germany (39%) [12], and Brazil (44%) [13]. Despite limited engagement in PA, results of a qualitative study found that PLWH understood the health promotion benefits of PA and thought PA should be a greater priority in their life [14].

Alternative types of physical activity

In addition to traditional aerobic (e.g., walking, biking and swimming) and resistance exercises (Table 1), lower intensity PA such as yoga is associated with positive benefits among PLWH, including an improvement in quality of life [15], reduction of depressive symptoms [16], and reduction of blood pressure [16, 17]. Tai Chi was also associated with improved well-being and balance in PLWH [18]. The benefits of high-intensity exercise are similarly evident: Erlandson et al. recently demonstrated that among older PLWH, high-intensity aerobic and resistance exercise (based on target heart rate and resistance load) improved endurance and strength to a similar, if not greater, extent than moderate-intensity exercise [19]. Oursler et al. similarly demonstrated significant gains in endurance among older PLWH exercising at a higher compared to a more moderate-intensity aerobic program [20]. These studies of high-intensity exercise have indicated no reason to dissuade PLWH – young or old – from progressing to high-intensity exercise following several weeks of moderate-intensity training. More details about the effectiveness of various types of PA among PLWH can be found in a recent meta-analysis [21].

Barriers to physical activity among PLWH

Understanding barriers to PA specific to, or more pronounced among, PLWH is essential to developing effective, patient-centered PA recommendations. Across populations, PA is

affected by diverse factors, including intrapersonal, interpersonal and environmental barriers.

Intrapersonal barriers.—In a systematic review of 45 studies of PA in PLWH [22], lower engagement in PA was consistently associated with demographic (i.e., older age and fewer years of formal education), HIV-specific and biologic (i.e., being on ART, lower CD4 T-cell counts, lipodystrophy, lower cardiorespiratory fitness, and opportunistic infections), and psychological (i.e., lower motivation, depression, and worse self-perceived physical function) variables. Moreover, the experience of these physical and mental health challenges that hinder engagement in PA may be unpredictable and episodic for PLWH [23]. Many PLWH experience great symptom burden, including neuropathy [24], fatigue [25], and reduced cardiorespiratory fitness [26], with even greater impairments among older PLWH [27]. Reduced cardiorespiratory fitness among PLWH as indicated by impaired peripheral oxygen uptake [17], dysfunction of skeletal muscle mitochondria [28], reduction in mitochondrial DNA content [29], and/or limitations in lung function [30] (e.g., impaired carbon monoxide diffusion capacity [31]) may interfere with adaptation to PA. Aerobic and resistance exercise, however, may reduce symptoms such as HIV-related fatigue [32, 33]. Adherence to a moderate-intensity, home-based, aerobic exercise [33] or a supervised aerobic and resistance exercise intervention has shown reduced fatigue among PLWH, with increased benefit among those with high adherence [32].

Interpersonal barriers.—Social factors, including worries about HIV disclosure and stigma [34] and a lack of social support [35], can also hinder participation in PA. Interviews of PLWH who participated in a community-based exercise program, however, indicated that participants found the environment less stigmatizing than initially feared, suggesting the malleability of social determinants of PA engagement. Healthcare providers' recommendations can also play a key role in perceptions and engagement in PA among PLWH [36]. When providers only focus on HIV-related health outcomes and do not recommend routine PA, PLWH have less recognition of the health benefits of PA [36].

Environmental barriers.—Environmental barriers to PA may be more pronounced among PLWH, such as concern about physical safety [37]. While fitness centers may be ideal venues for engaging in PA, access may be limited by physical and financial accessibility [38, 39], and/or concerns regarding potential stigma related to body image [23]. Thus, when developing a PA plan, environmental barriers may need to be considered and solutions for overcoming these barriers may need to be identified (e.g., encouraging outdoor activity, access to indoor facilities such as a shopping mall, or short bouts of PA throughout the day that do not require gym access or equipment).

Collectively, this body of literature on barriers to PA among PLWH indicates an interplay of intrapersonal, interpersonal, and environmental factors. Considering potential barriers to PA and plausible solutions are essential components of a PA action plan for PLWH. PLWH may benefit from an individualized approach to promoting PA, such as a gradual increase in activity, a different type of PA or PA environment, additional social support, and/or a PA prescription that is tailored to the goals, abilities, and interests of the individual in order to

restore and achieve levels of cardiorespiratory fitness and physical function similar to HIV-uninfected peers.

Behavior change strategies for increasing engagement in physical activity

The American Heart Association recommends the routine assessment and promotion of PA as a "vital sign" with every patient at every visit [40]. Assessment and promotion of PA in the healthcare setting has been found to be so effective at improving patient outcomes that some healthcare systems have begun including PA as a vital sign in the electronic medical record [40]. The current extensive primary care guidelines for PLWH include detailed screening and management recommendations for hypertension, hyperlipidemia, and other common health conditions but do not mention PA assessment or counseling either routinely or in the management of comorbidities. The primary care guidelines for PLWH do recommend healthcare encounters every 3 to 6 months [41]: these frequent healthcare encounters provide excellent opportunities for healthcare providers to inquire about and promote PA among PLWH. A recent review confirms that assessment and promotion of PA by healthcare providers has a small to moderate positive effect on increasing PA levels, with larger effects observed when multiple behavior change strategies are implemented [42].

One simple, effective behavior change strategy is a PA prescription that is collaboratively developed by the patient and provider [43, 44]. We adapted the PA prescription from the "Exercise is Medicine" website [45] and included several behavior change strategies that can be personalized (Figure 1). The adapted PA prescription form allows healthcare providers to encourage patients to progress to higher levels of PA and/or work toward meeting the HHS recommendations by gradually increasing the amount of time, intensity, or number of times a week they are physically active. For sedentary or physically inactive PLWH, prescribing movement breaks or walking may be a practical initial strategy to increase PA as it does not require special skills or equipment [46].

Effective behavior change strategies that consider readiness to engage in PA in the context of living with a sometimes unpredictable and episodic illness are needed to optimally promote adherence to a PA prescription among PLWH [39]. Based on HIV-specific literature in combination with existing behavior change techniques recommended for all persons [47, 48], we recommend adoption of behavior change strategies, such as self-monitoring of PA; goal setting and action planning; prompts, cues or scheduling; and social support. Providing these strategies to patients may increase the likelihood of initiation and maintenance or sustained uptake of PA, ultimately leading to improved health and wellness in this population. We briefly summarize the benefits of these approaches:

Self-monitoring is a useful PA behavior change technique [48] that can include the use of wearable motion-sensing technologies (e.g., pedometers, Fitbit) [49], smartphone applications, and online tracking resources such as Go4Life from the National Institute on Aging [50]. Self-monitoring can also occur using low-technology strategies such as a pen and paper diary. Results from a scoping study indicated that wireless activity monitors are increasingly used among PLWH as an outcome measure of PA; however, evidence of their effectiveness to enhance PA among PLWH is scarce [51].

Goal setting and action planning are effective behavioral strategies for increasing engagement in PA [52]. Goal setting encourages specific behavioral resolution (e.g., engaging in more PA this week), while action planning involves detailed planning of what the person will do, when they will engage in the specified behavior, and for how long. Combining behavior change techniques, a person can self-monitor PA (e.g., steps per day) and then set a behavioral goal (e.g., increasing the number of steps by 10% per week). Action planning builds upon goal setting by linking behaviors to situational cues or an existing behavior (i.e., associative learning). For example, PA can be linked with the use of transportation (e.g., exiting one stop early on the subway or bus, parking at the outskirts of a parking lot, and taking the stairs), to establish a habit.

Prompts, cues and scheduling that remind PLWH to engage in PA may drive habit formation and improve long-term PA adherence. Pre-scheduled activity is more often adhered to than relying on impromptu self-motivation [53]. A calendar, alarms, and/or cell phone reminders to set aside a specific time for PA can support PA scheduling. An ongoing study is evaluating the effectiveness of a novel Short Message Service intervention (iSTEP) to increase moderate PA among PLWH [54, 55].

Social support is strongly linked to PA engagement. Recent data clearly describes the prominent role that healthcare providers have in integrating health promotion into routine HIV care [36]. Thus, providers can leverage their strong patient relationships to emphasize a holistic concept of well-being that includes PA [36]. Persons are more likely to engage in PA if they are linked to a similarly motivated person with whom they are able to engage in PA, creating a “buddy system” (e.g., making a “contract” with others to achieve specified levels of PA or participating in group exercise) [56]. Additionally, the social environment of group exercise can enhance motivation and adherence to PA among older PLWH [57].

Conclusion

Similar to the general population, approximately one-third of PLWH do not achieve the minimum PA guidelines despite the numerous health benefits across the life span. HIV providers have a responsibility to assess and promote PA in the routine healthcare of all PLWH. These evidence-based practice recommendations can be used as a tool to facilitate engagement in PA among PLWH.

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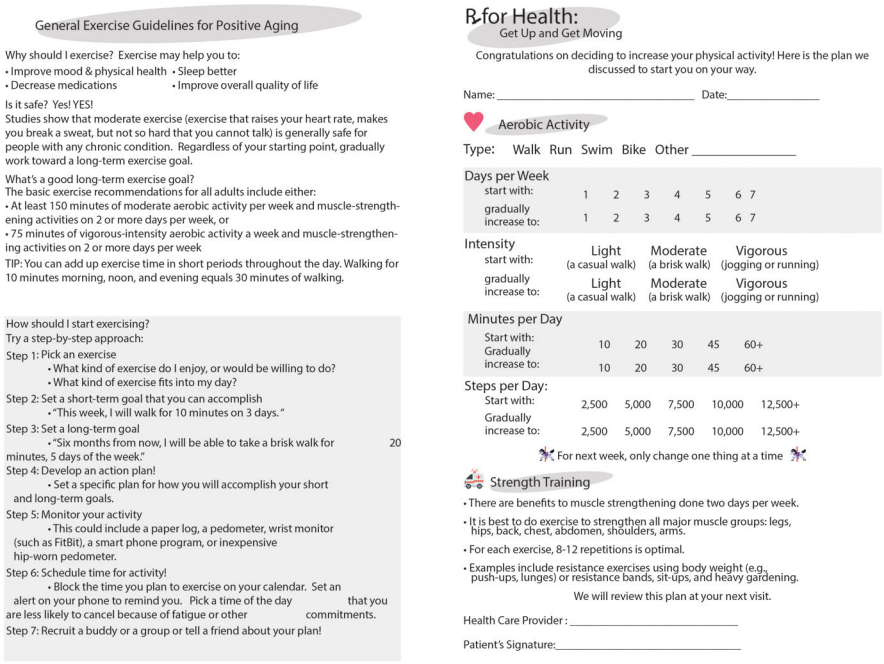

General Exercise Guidelines for Positive Aging

Why should I exercise? Exercise may help you to:
- Improve mood & physical health
- Sleep better
- Decrease medications
- Improve overall quality of life

Is it safe? Yes! YES!
Studies show that moderate exercise (exercise that raises your heart rate, makes you break a sweat, but not so hard that you cannot talk) is generally safe for people with any chronic condition. Regardless of your starting point, gradually work toward a long-term exercise goal.

What's a good long-term exercise goal?
The basic exercise recommendations for all adults include either:
- At least 150 minutes of moderate aerobic activity per week and muscle-strengthening activities on 2 or more days per week, or
- 75 minutes of vigorous-intensity aerobic activity a week and muscle-strengthening activities on 2 or more days per week

TIP: You can add up exercise time in short periods throughout the day. Walking for 10 minutes morning, noon, and evening equals 30 minutes of walking.

How should I start exercising?
Try a step-by-step approach:

Step 1: Pick an exercise
- What kind of exercise do I enjoy, or would be willing to do?
- What kind of exercise fits into my day?

Step 2: Set a short-term goal that you can accomplish
- "This week, I will walk for 10 minutes on 3 days."

Step 3: Set a long-term goal
- "Six months from now, I will be able to take a brisk walk for 20 minutes, 5 days of the week."

Step 4: Develop an action plan!
- Set a specific plan for how you will accomplish your short and long-term goals.

Step 5: Monitor your activity
- This could include a paper log, a pedometer, wrist monitor (such as FitBit), a smart phone program, or inexpensive hip-worn pedometer.

Step 6: Schedule time for activity!
- Block the time you plan to exercise on your calendar. Set an alert on your phone to remind you. Pick a time of the day that you are less likely to cancel because of fatigue or other commitments.

Step 7: Recruit a buddy or a group or tell a friend about your plan!

Rx for Health:
Get Up and Get Moving

Congratulations on deciding to increase your physical activity! Here is the plan we discussed to start you on your way.

Name: _____ Date: _____

Aerobic Activity

Type: Walk Run Swim Bike Other _____

Days per Week							
start with:	1	2	3	4	5	6	7
gradually increase to:	1	2	3	4	5	6	7

Intensity			
start with:	Light (a casual walk)	Moderate (a brisk walk)	Vigorous (jogging or running)
gradually increase to:	Light (a casual walk)	Moderate (a brisk walk)	Vigorous (jogging or running)

Minutes per Day					
Start with:	10	20	30	45	60+
Gradually increase to:	10	20	30	45	60+

Steps per Day:					
Start with:	2,500	5,000	7,500	10,000	12,500+
Gradually increase to:	2,500	5,000	7,500	10,000	12,500+

For next week, only change one thing at a time

Strength Training
- There are benefits to muscle strengthening done two days per week.
- It is best to do exercise to strengthen all major muscle groups: legs, hips, back, chest, abdomen, shoulders, arms.
- For each exercise, 8-12 repetitions is optimal.
- Examples include resistance exercises using body weight (e.g., push-ups, lunges) or resistance bands, sit-ups, and heavy gardening.

We will review this plan at your next visit.

Health Care Provider : _____

Patient's Signature: _____

Figure 1.
Physical activity rx contract

Table 1.

Summary of key findings from published studies (2009 – 2018) investigating the effects of physical activity on different body systems among adults living with HIV

Physical Activity	Brief Summary of Findings
Intervention (Training) Studies	
Aerobic + Resistance	
60 min aerobic + resistance 3x/week for 24 weeks (Ogalha, 2011) [32]	*Fatigue:* ↑ vitality *Anthropometry/body composition:* ↓ % body fat, HC, ↑ muscle mass, ↔ BMI, WC, WHR *Cardiometabolic profile:* ↓ resting HR, glucose, ↑ metabolic equivalent, ↔ hemoglobin, TC, HDL, LDL, TRIG, maximum oxygen consumption *Immunological profile:* ↑ $CD4^+$ T cell count *QOL / Mental Health:* ↑ QOL
40-60 min aerobic + resistance 4x/week for 12 weeks (Cutrono, 2016) [58]	*Anthropometry/body composition:* ↓ waist circumference, ↔ body weight, BMI *Cardiometabolic profile:* ↓ DBP, ↔ SBP, TRIG, TC, HDL, LDL, fasting glucose, % w/MetS *Inflammation:* ↔ hsCRP
Aerobic + resistance 3x/week for 24 weeks (Erlandson, 2018) [19]	*Physical function/frailty:* ↑ physical function
20 min aerobic + resistance 3x/weekly for 16 weeks (Pedro, 2017) [59]	*Inflammation:* ↓ IL-8, ↔ IL-4, IL-5, IL-6, IL-10, TNF-α, IFN-γ, GM-CSF
Aerobic and/or Resistance	
30 min aerobic exercise or progressive resistance 3x/week for 12 weeks (Maharaj, 2018) [60])	*Pain:* ↓ neuropathic pain
60 min brisk walking with or without 30 min circuit-training 3x/week for 12 weeks (Bonato, 2017) [61])	*Anthropometry/body composition:* ↓ body weight, BMI, WC, HC *Cardiometabolic profile:* ↓ TC, LDL *Inflammation:* ↓ hsCRP, IL-6, d-dimer, IL-18
Aerobic Alone	
High-intensity aerobic interval 3x/week for 12 weeks (Stoa, 2017) [62]	*Anthropometry/body composition:* ↓ Body weight, BMI, body fat %, WC, HC *Cardiometabolic profile:* ↓ HbA1c, DBP, ↔ HOMA-IR, SBP, TRIG, TC, HDL, LDL
45-60 min aerobic 5-7x/week for 12 weeks (Connick, 2017) [63]	*Cardiometabolic profile:* ↑ capacity of the endothelium to release t-PA
20-40 min light aerobic (walking or jogging) 3x/week for 12 weeks (Kocher, 2017) [64]	*Mitochondrial function:* ↑ Peripheral blood mononuclear cells mitochondrial respiratory capacity, spare respiratory capacity and nonmitochondrial respiration
30 min aerobic treadmill training 2x/week for 6 weeks (Hand, 2008) [65]	*Fatigue:* ↑ time to fatigue (measured by treadmill time), VO_2 max
Moderate-to-vigorous PA (≥2690 counts/min for ≥10 mins); accelerometry (Webel, 2018) [66]	*Anthropometry/body composition:* ↑ weight loss, ↔ BMI changes
Resistance Alone	
Circuit resistance 3x/week for 8 weeks (Ghayomzadeh, 2017) [67]	*Anthropometry/body composition:* ↓ fat mass, ↑ lean mass, ↔ body weight *Immunological profile:* ↑ $CD4^+$ T cell count
Resistance 3x/week for 6 weeks (Vingren, 2018) [68]	*Physical function/frailty:* ↑ strength, muscle mass, upper-arm & forearm circumference

Physical Activity	Brief Summary of Findings
	Inflammation: ↔ IFN-γ, IL-1β, IL-2, IL-4, IL-6, IL-10, TNF-α, VCAM-1, cortisol
Non-linear resistance 3x/week for 12 weeks (Zanetti, 2016) [69, 70]	*Anthropometry/body composition:* ↑ lean body mass, ↓ Body fat %, bod fat mass, ↔ body mass, BMI *Cardiometabolic profile:* ↑ HDL, ↓ TC, LDL, TRIG, CRP *Inflammation:* ↓ IL-1B, IL-6, IL-8, TNF-α, ↑ IL-10
Resistance 2x/week for 52 weeks (Souza, 2008) [71]	*Physical function/frailty:* ↑ muscular strength, ↔ bone mineral content *Anthropometry/body composition:* ↔ body weight, BMI, lean mass, fat mass *Immunological profile:* ↑ $CD4^+$ T cell count, CD4+/CD8+ ratio
Yoga	
6 days of training followed by daily home-based and 1x/week supervised yoga for 12 weeks (Mawar, 2015) [15]	*Anthropometry/body composition:* ↔ BMI *Immunological profile:* ↔ $CD4^+$ T cell count *QOL / Mental Health:* ↑ QOL
60 min yoga 6x/week for 4 weeks (Naoroibam, 2016) [16]	*Immunological profile:* ↑ $CD4^+$ T cell count *QOL / Mental Health:* ↓ depression symptoms
60 min yoga 2-3x/week for 20 weeks (Cade, 2010) [72]	*Anthropometry/body composition:* ↔ weight, fat mass *Cardiometabolic profile:* ↓ resting SBP, DBP, ↔ lipids, glucose tolerance *QOL / Mental Health:* ↔ QOL
60 min yoga 2x/week for 8 weeks (Agarwal, 2015) [73]	*QOL / Mental Health:* ↑ QOL (perceived stress and recent distress)
Observational Studies	
Step counts; accelerometry (Webel, 2018) [74]	*Cardiometabolic profile:* ↓ HOMA-IR, ↔ CAC score, SBP, DBP, TC *Inflammation:* ↓ IL-6 *Immunological profile:* ↔ $CD4^+$ T cell count
Moderate PA; accelerometry (Forde, 2018) [75]	*Cardiometabolic profile:* ↓ insulin resistance, TRIG
Moderate-vigorous activity (≥70 mins/day); SenseWear ® arm band (Wirth, 2015) [76]	*Inflammation:* ↓ CRP, ↔ IL-6
S-R >600 MET min/week relative to inactive; short-version IPAQ (Silveira, 2018) [13]	*Anthropometry/body composition:* ↓ WHR, ↔ % overweight, WC, body fat percentage *Cardiometabolic profile:* ↓ % hypertension, % diabetes
S-R of ≥3 days/week of moderate/high PA; IPAQ (Erlandson, 2017) [77]	*Physical function/frailty:* ↓ odds of frailty
S-R of ≥3 days/week of moderate/high PA; IPAQ (Johs, 2017) [78]	*Disability:* ↓ odds of impairment in activities of daily living
S-R of high PA (≥3 days/week of vigorous PA or ≥7 days combination of walking, moderate, and vigorous activity); IPAQ (Monroe, 2017) [79]	*Neurocognition:* ↓ odds of impairment in learning, memory, motor function
S-R of moderate PA; IPAQ (Fazeli, 2015) [80]	*Neurocognition:* ↓ odds of neurocognitive impairment, instrumental activities of daily living dependence
Moderate-vigorous PA (min); NIAID Adult AIDS Clinical Trials Group Physical Activity Assessment (Perazzo, 2018) [81]	*Bone:* ↑ BMD at the total hip and lumbar spine
S-R of PA; NIAID Adult AIDS Clinical Trials Group Physical Activity Assessment (Dirajlal-Fargo, 2016) [82]	*Anthropometry/body composition:* ↔ BMI *Cardiometabolic profile:* ↓ leptin, hyperemic VTI, ↔ HDL, LDL, TRIG, HOMA-IR, carotid distensibility, pericardial fat, flow mediated dilation, mean-mean IMT *Inflammation:* ↓ IL-6, hsCRP, ↔ sCD163, sCD14, % CD14+ CD16+ monocytes, % CD14dimCD16+ monocytes
S-R of home-based exercise (min); 7-day diary (Webel, 2016) [33]	*Fatigue:* ↓ fatigue

Physical Activity	Brief Summary of Findings
S-R of >4 hours/week of PA, relative to <4 hours/week or no PA (Erlandson, 2018) [83]	*Bone:* ↑ BMD
S-R moderate-high PA, relative to low PA (Kazooba, 2017) [84]	*Anthropometry/body composition:* ↓ waist circumference, ↔ waist/hip ratio, BMI *Cardiometabolic profile:* ↓ SBP, DBP, Framingham risk score
S-R of PA in last 72 hrs (Dufour, 2018) [85]	*Neurocognition:* ↑ neurocognitive functioning (higher baseline and maintenance of neurocognitive function over time)
S-R of PA in last 72 hrs (Dufour, 2013) [86]	*Neurocognition:* ↓ rates of global neurocognitive impairment, driven by ↓ rates of impairment in working memory and speed of information processing

Note: ↑ denotes increase/improvement; ↓ denotes decrease/decline; ↔ denotes no significant change/difference

BMD = body mineral density; BMI = body mass index; BP = blood pressure; CAC = coronary artery calcium; DBP = diastolic blood pressure; GM-CSF = Granulocyte-macrophage colony-stimulating factor; HbA1c = hemoglobin A1c; HC = hip circumference; HDL = high-density lipoprotein cholesterol; HOMA-IR = hemostatic model assessment of insulin resistance; HR = heart rate; hsCRP = high sensitivity C-reactive protein; IFN-γ = *Interferon gamma;* IL = interleukin; IPAQ = International Physical Activity Questionnaire; LDL = low-density lipoprotein cholesterol; MetS = metabolic syndrome; QOL = quality of life; SBP = systolic blood pressure; sCD14 = soluble cluster of differentiation 14; sCD163 = soluble cluster of Differentiation 163; S-R = self-report; TC = total cholesterol; TNF-α = Tumor necrosis factor-alpha; t-PA = tissue-type plasminogen activator; TRIG = triglycerides; VCAM-1 = Vascular cell adhesion protein 1; WC = waist circumference; WHR = waist-to-hip ratio