



# The impacts of exercise on pediatric obesity

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Over the last few decades, the rates of pediatric obesity have more than doubled regardless of sociodemographic categorization, and despite these rates plateauing in recent years there continues to be an increase in the severity of obesity in children and adolescents. This review will discuss the pediatric obesity mediated cardiovascular disease (CVD) risk factors such as attenuated levels of satiety and energy metabolism hormones, insulin resistance, vascular endothelial dysfunction, and arterial stiffness. Additionally, early intervention to combat pediatric obesity is critical as obesity has been suggested to track into adulthood, and these obese children and adolescents are at an increased risk of early mortality. Current suggested strategies to combat pediatric obesity are modifying diet, limiting sedentary behavior, and increasing physical activity. The effects of exercise intervention on metabolic hormones such as leptin and adiponectin, insulin sensitivity/resistance, and body fat in obese children and adolescents will be discussed along with the exercise modality, intensity, and duration. Specifically, this review will focus on the differential effects of aerobic exercise, resistance training, and combined exercise on the cardiovascular risks in pediatric obesity. This review outlines the evidence that exercise intervention is a beneficial therapeutic strategy to reduce the risk factors for CVD and the ideal exercise prescription to combat pediatric obesity should contain both muscle strengthening and aerobic components with an emphasis on fat mass reduction and long-term adherence.

**Key words:** Pediatric obesity, Cardiovascular disease, Metabolic disease, Exercise

## Key message

Pediatric obesity contributes to the development of vascular dysfunction and metabolic and cardiovascular diseases which have all been shown to track into adulthood, increasing the risk of early mortality. Early exercise intervention is critical for combating obesity-related comorbidities and the optimal exercise prescription has yet to be well documented. Exercise prescriptions to combat pediatric obesity should incorporate both aerobic and muscle-strengthening exercises with an emphasis on long-term adherence.

## Introduction

In 2013 approximately 2.1 billion individuals were considered overweight or obese which was defined as a body mass index (BMI) greater than 25 kg/m<sup>2</sup>.<sup>1)</sup> Over the last few decades the obesity rates in more than 70 countries have doubled,<sup>2,3)</sup> while the rate of this increase in obesity is higher in children than in adults regardless of sociodemographic categorization.<sup>2)</sup> Additionally, epidemiological data indicate that the proportion of children and adolescents with obesity appears to be plateauing in recent years but the rate of more severe obesity cases continues to rise.<sup>4,5)</sup> Although the development of pediatric obesity is a multifaceted process that involves genetic, behavioral, and environmental influences,<sup>6,7)</sup> the lifestyle behaviors during childhood and adolescence might have the greatest influence on the development of obesity.<sup>8,9)</sup>

Obesity is characterized by an energy imbalance that is affected by lifestyle behaviors such as poor dietary habits<sup>10-13)</sup> and inadequate physical activity time<sup>14)</sup> which are both strongly associated with the development of obesity. More specifically, sedentary behaviors such as increased video gaming, television watching, and computer screen time<sup>15,16)</sup> are highly associated with the development of obesity.<sup>17)</sup> The development of obesity often influences the onset of several cardiovascular disease (CVD) risk factors.<sup>18)</sup> Additionally, the relative risk for CVDs such as hypertension, stroke, and heart disease is 1.5- to 5.1-times higher in obese children when compared to children with normal body composition.<sup>19)</sup> Combating pediatric obesity is critical as there is a strong connection between pediatric obesity and adult obesity.<sup>4,20)</sup> A previous meta-analysis identified that when compared to normal-weight children, obese children are 5 times more likely to be obese in adulthood,<sup>21)</sup> and about 80% of obese adolescents remain obese in adulthood.<sup>22)</sup>

Physical inactivity and sedentary behaviors are significant contributors to the development of pediatric obesity.<sup>14,23,24)</sup> Physical activity and exercise have been suggested as powerful treatments to help prevent obesity as well as improve obesity-related risk factors in children and adolescents.<sup>25-27)</sup> For every one hour of moderate-to-vigorous activity there is a 10% decrease in the risk of developing obesity.<sup>14)</sup> Additionally, regular exercise is

considered an effective treatment for reducing inflammation,<sup>28)</sup> obesity-related risk factors, and the development of comorbidities.<sup>29)</sup> Therefore, this review will focus on the health risks associated with pediatric obesity and further discuss optimal exercise strategies, specifically, aerobic exercise (AE) such as running, cycling, or jump rope, resistance training (RT) such as free weights, cable machines, or resistance bands, and combined aerobic and resistance exercise (CRAE) such as the combination of running and free weights, to combat pediatric obesity and the associated risk factors and comorbidities (Table 1).

## Pediatric obesity

The prevalence of pediatric obesity continues to increase around the world<sup>1)</sup> and obesity is expected to affect 91 million children by the year 2025.<sup>2)</sup> Obesity is a multifactorial condition that can be affected by genetic, psychological, lifestyle, environmental, behavioral, and hormonal factors.<sup>3)</sup> It is well-accepted that there is no single cause of pediatric obesity, however, obesity is characterized by the accumulation of excess fat mass which develops when caloric intake exceeds total energy expenditure.<sup>4)</sup> The neuroendocrine regulation of fat stores is a complex system based on circulating hormones, which send signals to specialized neurons in the hypothalamus to indicate the status of body fat (BF) stores in the body, which in turn induces the appropriate response necessary to maintain these fat stores.<sup>5)</sup> Amidst other important functions, the hypothalamus is the control center for feelings of hunger and satiety. An individual's susceptibility to the development of obesity can in part be explained by mechanisms that may negatively affect hypothalamic neurons, leading to an improper hunger/satiety balance, and genetic and environmental modulators such as leptin and insulin resistance (IR).<sup>5)</sup> Both leptin resistance and IR are associated with feeding behavior and weight gain. Pediatric obesity also negatively effects cardiovascular health and is also accompanied by a host of other comorbidities and associated risk factors.<sup>8)</sup>

### 1. Health risks associated with obesity

Pediatric obesity is associated with a myriad of CVD risk factors including increased IR,<sup>9)</sup> impaired glucose tolerance, dyslipidemia,<sup>10,11)</sup> impaired microvascular function,<sup>12)</sup> systemic low-grade inflammation,<sup>13)</sup> increased artery wall thickness,<sup>14)</sup> and elevated blood pressure (BP).<sup>9)</sup> In addition to an increased risk of CVD, pediatric obesity is also associated with the development of nonalcoholic fatty liver disease,<sup>9)</sup> cancer, pulmonary disease, asthma, sleep apnea, orthopedic problems, and depression<sup>15-17)</sup> and has also been identified as an independent risk factor for the development of insulin-resistant type 2 diabetes (T2D).<sup>18-21)</sup> Furthermore, the severity of these obesity-related risk factors and comorbidities significantly increases with the severity of obesity.<sup>17,18,22,23)</sup> Combating obesity early in childhood is critical as even mild reductions in body mass before the onset of puberty has been shown to decrease the risk of CVD and other obesity-

related risk factors such as hypertension, dyslipidemia, T2D, and coronary heart disease later in life if normal bodyweight is maintained.<sup>22-25)</sup> If pediatric obesity cannot be treated appropriately, obese children and adolescents will be at an increased risk of premature death<sup>26)</sup> and a significantly increased risk for CVD and CVD-related mortality in adulthood.<sup>27)</sup>

### 2. Pediatric obesity and health risks track into adulthood

In 2015, there were approximately 4 million international obesity-related deaths with 70% of these deaths being attributed to CVD.<sup>28,29)</sup> Pediatric obesity has been known as a significant contributor to the current obesity and CVD epidemics in adults.<sup>27)</sup> Individuals who are obese during childhood are more likely to become obese as adults<sup>30-33)</sup> and there is compelling evidence suggesting that obesity-associated CVD risk factors, such as dyslipidemia, IR, and elevated BP, track from childhood into adulthood.<sup>18,27,34,35)</sup> Obese children who were tracked from childhood to adulthood were more likely to suffer from CVD, digestive disease, metabolic diseases, and cancer as an adult when compared to children of normal weight.<sup>8,16)</sup> Additionally, obesity in childhood is strongly associated with a 3.5-times higher risk of CVD mortality in adulthood and is projected to account for as much as 25% of all adult CVD-related deaths.<sup>27)</sup> The manifestation of obesity-related CVD risk factors can appear in as early as the third year of life,<sup>15,20)</sup> and the duration of obesity during childhood and adolescence is associated with increased risk of developing obesity-related comorbidities and CVD-related mortality in adulthood.<sup>18,19,23)</sup> In fact, pediatric obesity is a well-established predictor of CVD and premature mortality in adulthood<sup>26,36,37)</sup> thereby highlighting the importance of early intervention to prevent the development of obesity. These types of interventions should serve to target improvements in several metabolic, hormonal, and cardiovascular parameters to better protect young populations from future CVD complications, as well as instilling a healthy lifestyle that can be maintained throughout adulthood.

## Metabolic syndrome and adipokines

Metabolic syndrome (MetS) is defined as a cluster of conditions including high central adiposity, dyslipidemia, and high fasting blood glucose, all of which contribute to an increased risk of CVD.<sup>30)</sup> Obesity has been identified as a major contributor to the development of MetS<sup>30)</sup> and obesity-associated MetS risk factors have been shown to track from childhood into adulthood.<sup>31,32)</sup> Obesity is characterized by an increase in adipose tissue which is considered an active metabolic endocrine organ and a source of inflammation through the production of inflammatory cytokines.<sup>33,34)</sup> Adipose tissue-derived cytokines are referred to as, adipokines, and 2 of the most prominent adipokines are leptin and adiponectin which are negatively affected by obesity.<sup>35,36)</sup> Additionally, T2D is the most common comorbidity associated with pediatric obesity.<sup>37)</sup> T2D development, whether

**Table 1. Characteristics of exercise studies investigating the effects of exercise in pediatric obesity**

Study	Exercise modality	Intensity	Frequency	Duration (min)	Total time per week (min)	Intervention duration (wk)	Outcomes
Karacabey <sup>52)</sup>	Aerobic exercise (walking/jogging)	Moderate	3x/wk	25-55	75-165	12	↓ BMI, ↓ LDL, ↓ cortisol, ↓ leptin, ↓ insulin
Lee et al. <sup>141)</sup>	Aerobic exercise (jump rope)	Moderate	4x/wk	40-50	120-150	12	↓ Plasma Visfatin, ↓ insulin resistance
Kim et al. <sup>70)</sup>	Aerobic exercise (jump rope)	Moderate	5x/wk	50	250	12	↓ WC, ↓ SBP, ↓ glucose, ↓ insulin, ↓ HOMA-IR
Nascimento et al. <sup>27)</sup>	Aerobic exercise (indoor sports)	Low	3x/wk	100	300	8	↓ BMI, ↓ BF%, ↓ CRP, ↓ TNF-alpha, ↑ adiponectin
Seabra et al. <sup>57)</sup>	Aerobic exercise (soccer)	Moderate	3x/wk	60-90	180-270	26	↓ BF%, ↓ WC, ↓ TC
Park et al. <sup>58)</sup>	Aerobic exercise (walking)	Moderate	6x/wk	30-40	180-240	12	↓ BF%, ↓ BMI, ↓ WC, ↓ waist-hip ratio
Kim et al. <sup>61)</sup>	Aerobic exercise (jump rope)	Moderate	5x/wk	40	200	6	↓ BF%, ↑ insulin sensitivity, ↑ adiponectin
Nassis et al. <sup>65)</sup>	Aerobic exercise (indoor sports)	Moderate	3x/wk	40	120	12	↑ Insulin sensitivity, ↓ BF%, ↓ IL-6, ↑ adiponectin, ↓ CRP
Sung et al. <sup>142)</sup>	Aerobic exercise (jump rope)	Moderate	5x/wk	50	250	12	↓ BF%, ↓ WC, ↓ SBP, ↓ baPWV, ↓ CRP, ↑ nitrate/nitrite levels
Watts et al. <sup>88)</sup>	Aerobic exercise (cycle ergometer)	Moderate	3x/wk	60	180	8	↑ FMD
Racil et al. <sup>63)</sup>	Aerobic exercise (MIIT/HIIT)	Moderate - High	2x/wk	12-16	24-32	12	↓ BMI, ↓ BF%, ↓ LDL, ↑ HDL, ↑ adiponectin, ↓ WC, ↓ TC, ↓ HOMA-IR, ↑ insulin sensitivity
Lee et al. <sup>150)</sup>	Aerobic exercise (treadmill/elliptical)	Moderate	3x/wk	60	180	12	↓ BF%, ↓ intrahepatic lipid, ↑ insulin sensitivity
Lee et al. <sup>159)</sup>	Resistance training (cable machines)	Moderate	3x/wk	60	180	≥6	↓ BF%, ↓ insulin resistance
Shaibi et al. <sup>71)</sup>	Resistance training (free weights)	Moderate	2x/wk	-	-	16	↓ BF%, ↑ insulin sensitivity, ↑ adiponectin, ↑ upper body strength
Van Der Heijden et al. <sup>72)</sup>	Resistance training (free weights)	Moderate	2x/wk	60	120	12	↑ Strength, ↑ BW, ↑ lean body mass, ↑ insulin sensitivity, ↓ GPR
Lee et al. <sup>149)</sup>	Resistance training (whole body training)	Moderate	3x/wk	60	180	12	↓ Visceral fat, ↓ intrahepatic lipid, ↑ insulin sensitivity
Watts et al. <sup>89)</sup>	CRAE Training (RT/Cycling)	High	3x/wk	60	180	8	↓ Abdominal/trunk fat mass, ↑ strength, ↑ FMD
Bharath et al. <sup>76)</sup>	CRAE training (resistant band/treadmill)	Moderate	5x/wk	50	250	12	↓ BW, ↓ BMI, ↓ WC, ↓ plasma glucose, ↓ insulin, ↓ leptin, ↑ adiponectin
Son et al. <sup>42)</sup>	CRAE training (plyometrics/jump rope)	Moderate	3x/wk	60	180	12	↓ BF%, ↓ WC, ↓ BP, ↓ baPWV, ↓ HOMA-IR, ↓ ET-1, ↑ nitrate/nitrite levels
Lee et al. <sup>159)</sup>	CRAE training (free weights/running)	Moderate	3x/wk	60	180	≥6	↓ BF%, ↓ BMI, ↓ LDL
Lopes et al. <sup>41)</sup>	CRAE training (free weights/running)	Moderate - High	3x/wk	60	180	12	↓ BF%, ↓ CRP, ↓ leptin, ↑ VO <sub>2</sub> peak, ↓ insulin resistance, ↑ fat-free mass, ↑ 1RM for leg press
Wong et al. <sup>62)</sup>	CRAE training (resistant band/treadmill)	Moderate	3x/wk	50	150	12	↑ Nitrate/nitrite levels, ↑ adiponectin/leptin ratio, ↓ arterial stiffness, ↓ CRP, ↓ glucose, ↓ insulin, ↓ BF%
Jeon et al. <sup>40)</sup>	CRAE training (free weights/running)	Moderate	2x/wk	40	80	18	↓ BMI, ↓ BF%, ↓ WC, ↓ SBP, ↓ HOMA-IR, ↑ lean body mass
Damaso et al. <sup>56)</sup>	AE training (free weights/running)	Moderate	3x/wk	60	180	52	↓ BF%, ↓ LDL, ↑ lean body mass

BMI, body mass index; LDL, low-density lipoprotein; WC, waist circumference; SBP, systolic blood pressure; HOMA-IR, homeostatic model assessment of insulin resistance; BF%, body fat percentage; CRP, C-reactive protein; baPWV, brachial-to-ankle pulse wave velocity; ET-1, endothelin-1; 1RM, 1 repetition maximum; VO<sub>2</sub>peak, peak oxygen uptake; TNF-alpha, tumor necrosis factor alpha; IL-6, interleukin 6; TC, total cholesterol; FMD, flow-mediated dilation; MIIT/HIIT, moderate-intensity interval training/high-intensity interval training; HDL, high density lipoprotein; BW, body weight; GPR, glucose production rate; CRAE, combined resistance and aerobic exercise; RT, resistance training.

in childhood or adulthood, may be partially explained by the adverse effect of obesity on the dysregulation of leptin and adiponectin levels which play a crucial role in homeostatic status of IR/sensitivity.<sup>38,39</sup> Previous research suggests levels of these adipokines and insulin sensitivity may be positively affected by exercise in obese children and adolescents.<sup>27,40-42</sup> Therefore, exercise therapy use in children may support intact homeostatic regulation of leptin and adiponectin levels, which may reduce the likelihood of IR and T2D development in this population.

### 1. Leptin

Leptin's primary function is to promote body mass reduction through sympathetic-driven appetite reduction,<sup>43,44</sup> improved lipid metabolism, and increased energy expenditure<sup>39</sup> in a healthy, nonobese individual. However, leptin is considered one of the primary hormone markers for obesity.<sup>45</sup> Leptin levels are paradoxically increased in obesity,<sup>46,47</sup> indicating that obesity is associated with a state of leptin resistance and disturbed leptin bioactivity. Furthermore, increased levels of leptin are strongly correlated with IR and increased inflammation in adolescents<sup>48,49</sup> and also contributes to obesity-related hypertension through increased sympathetic tone.<sup>43,44</sup>

Available literature indicates that exercise interventions have been shown to positively impact leptin levels when there is also a significant decrease in BF.<sup>36,50</sup> Many individual studies indicate that AE interventions improve body composition and leptin levels in obese children and adolescents.<sup>51-53</sup> However, previously completed pooled-analyses indicate that there was no significant affect of AE on leptin levels in obese children and adolescents.<sup>36</sup> It is important to note by using nonrandomized control trials, Garcia-Hermoso et al.<sup>36</sup> did conclude that AE interventions resulted in significantly reduced leptin levels in obese children and adolescents. To our knowledge, only a single previous study investigates the effects of RT on leptin levels in pediatric obesity. Shultz et al.<sup>54</sup> found that following a 16-week RT intervention leptin levels were not significantly changed in obese adolescents. Interestingly, they did find that participants that had significantly increased aerobic capacity also had significantly decrease leptin levels following RT. Additionally, Racil et al.<sup>55</sup> showed that following 12 weeks of high-intensity interval training (HIIT) there were significant improvements in body composition and reductions in leptin levels in obese adolescents. In the same study, they showed that obese adolescents could gain even greater benefits if they performed CRAE training. Utilizing the same protocol with an additional plyometric component, obese adolescents had significantly greater improvements in body compositions and leptin levels.<sup>55</sup> Dâmaso et al.<sup>56</sup> also showed that when compared to AE, CRAE training resulted in greater improvements in body composition and leptin levels in obese adolescents. Overall, previous data show that exercise interventions reduce leptin levels in obese adolescents<sup>25</sup> and also indicate that the improvements in leptin levels are likely mediated by concomitant reductions in BF due to increased energy expenditure<sup>27,41,50,53,57,58</sup> which may be accomplished

through exercise interventions of greater frequency, intensity, or duration.

### 2. Adiponectin

Adiponectin is an adipokine with antiatherogenic and anti-inflammatory properties<sup>59</sup> and is an important regulator of glucose homeostasis and insulin sensitivity<sup>38</sup> that helps protect against obesity-related MetS.<sup>46</sup> Adiponectin levels are often decreased in obesity.<sup>60</sup> However, in pediatric obesity, adiponectin levels may be increased with exercise training, and like leptin, significant improvements in adiponectin levels are strongly associated with decreases in BF and this relationship has been highlighted by many previous exercise training studies with obese adolescents.<sup>27,36,61</sup> Dâmaso et al.<sup>56</sup> found that after 1 year of an exercise program consisting of RT and AE obese adolescents experienced significant improvements in adiponectin/leptin ratio and body composition. Additionally, our group has shown that CRAE 3 days per week, for 12 weeks significantly improved body composition and adiponectin/leptin ratio in obese adolescent girls.<sup>62</sup> These results are supported by another previous study utilizing CRAE training that observed significant improvements in body composition and adiponectin levels in obese adolescents.<sup>41</sup> Additionally, the effects of HIIT highlight the relationship between decreased BF and improved adiponectin levels as Racil et al.<sup>63</sup> showed that 12 weeks of moderate-intensity interval training (MIIT) and HIIT both improved BF percentage (BF%), blood lipids, and adiponectin, but HIIT results in significantly greater improvements in these measures in addition to significantly reducing waist circumference (WC). It is important to note that a previous study has shown that combined resistance as CRAE training may positively impact body composition and insulin sensitivity without altering adiponectin levels in obese adolescents.<sup>40</sup> In this study, there were no changes in adiponectin levels following a 12-week exercise program in obese adolescents, however, there were significant improvements in BF, lean body mass, and insulin sensitivity. Similar results have been observed in other studies examining the impacts of AE<sup>64,65</sup> and it was suggested that the improvements in insulin sensitivity were due to improved glucose uptake and utilization by skeletal muscle in response to exercise.<sup>66</sup> The exact exercise-induced mechanisms and training volume and duration implicit in improved adiponectin levels in obese children and adolescents requires further investigation.

### 3. Insulin resistance

T2D is characterized by reduced insulin sensitivity leading to excess blood glucose levels which can contribute to a host of other complications including, CVD, cancer, and diabetic neuropathy, nephropathy, and retinopathy.<sup>67</sup> In recent years T2D has increased dramatically in children and adolescents throughout the world<sup>68</sup> and there is a strong relationship between the increase in pediatric obesity and rising incidence of T2D.<sup>69</sup> It is well established that increased physical activity and exercise are the most comprehensive treatment for the IR associated with

pediatric obesity.<sup>26</sup> IR in pediatric obesity has previously been shown to be improved by a variety of types of exercise including AE,<sup>40,70</sup> RT,<sup>71,72</sup> MIIT,<sup>63</sup> and HIIT.<sup>55,63</sup> It is important to note that previous studies have also shown that exercise interventions do not always result in improvements in IR in obese children and adolescents.<sup>73,74</sup> A meta-analysis completed by Marson et al.<sup>74</sup> compared the effects of AE, RT, and CRAE training on IR, fasting glucose, and insulin levels in overweight and obese children and adolescents. The analysis concluded that exercise training in general was not associated with a reduction in fasting glucose, however, AE does result in improvements in fasting insulin levels and IR. Additionally, Marson et al.<sup>74</sup> concluded that the efficacy of RT and CRAE training as interventions to improve IR in pediatric obesity could not be determined due to limited available literature. CRAE training is of particular interest as it has been shown to provide greater benefits than AE or RT alone.<sup>75</sup> Our group has shown in multiple studies that CRAE training improves fasting glucose<sup>62,70,76</sup> and insulin levels<sup>62,70,76</sup> as well as IR<sup>42,70</sup> in obese adolescents. Nonetheless, increasing physical activity in the obese pediatric population is of paramount importance as sedentary behaviors and physical inactivity have been identified as significant contributors to the development of obesity and MetS.<sup>14,23,24</sup>

## Vascular function

Obesity during adolescence is a well-established marker for increased arterial stiffness, coronary artery calcification, hypertension, and atherosclerosis in adulthood,<sup>77</sup> with some atherosclerotic lesions appearing as early as the teenage years.<sup>78</sup> Pediatric obesity is associated with an increase in a plethora of proatherogenic and proinflammatory factors<sup>59,79-86</sup> which contribute to impaired vascular function<sup>87-90</sup> and the development of atherosclerosis.<sup>91</sup> Obesity-associated IR and leptin resistance as well as increased adipokine secretion promote inflammation and endothelial dysfunction.<sup>92-95</sup> Intact endothelial function is widely considered a critical component of a healthy vascular system<sup>96</sup> and endothelial dysfunction is highly predictive of cardiovascular mortality and morbidity.<sup>96-99</sup> Impaired endothelial function has also been identified as an important prerequisite to the development of atherosclerosis<sup>96,100</sup> and hypertension.<sup>101</sup> Early intervention to prevent atherosclerosis may be essential due to the progressive nature of atherosclerotic development.<sup>91</sup> Interventions that enhance vascular function and endothelial function, such as exercise,<sup>102-104</sup> may reduce CVD risks for obese children and adolescents as well as protect against cardiovascular mortality and morbidity later in life.

### 1. Endothelial function and exercise

Early intervention to improve vascular function in obese adolescents is of paramount importance, as it may reduce the risk of CVD later in life through a reduction in global CVD risk.<sup>105</sup> Flow-mediated dilation (FMD) is a well-established

assessment of vascular endothelial function<sup>96</sup> and CVD risk<sup>106-108</sup> in children and adolescents and a decrease in FMD of 1% results in a 13% increase in future cardiovascular event risk.<sup>97</sup> Previous research has established that pediatric obesity is associated with attenuated vasodilator function through endothelium-dependent mechanisms.<sup>88,109,110</sup> Watts et al.<sup>88,89</sup> has shown that when compared to lean age-matched control participants, obese adolescent FMD is significantly attenuated,  $12.32\% \pm 3.14\%$  versus  $6.00\% \pm 0.69\%$ ,<sup>88</sup> and  $8.9\% \pm 1.5\%$  versus  $5.3\% \pm 0.9\%$ .<sup>89</sup> Additionally, this group has shown that following exercise training FMD was significantly improved (from  $6.00\% \pm 0.69\%$  to  $7.35\% \pm 0.99\%$ ,<sup>88</sup> from  $5.3\% \pm 0.9\%$  to  $8.8\% \pm 0.8\%$ <sup>89</sup>). Dias et al.<sup>111</sup> confirmed these results in a 2015 meta-analysis that concluded that obese adolescents had significantly impaired FMD compared to age-matched control participants and that following exercise training the obese adolescent FMD values were restored to the level of the nonobese age-matched counterparts. Furthermore, the effects of exercise training are not specific to the vasculature of the working muscles used during exercise but exercise results in global/systemic improvements in endothelial function.<sup>102,104</sup> It is important to note that endothelial function is often improved following exercise regardless of changes in body composition, BP, or glycemic control<sup>89,112</sup> which indicates that the improvements in endothelial function following exercise may be mediated through alterations in hemodynamic factors such as shear stress acting on the vessel wall.<sup>113,114</sup> Finally, following periods of detraining the improvements in FMD observed in obese adolescents do not persist.<sup>89</sup> These results are in agreement with the loss of endothelial function improvement observed in adults following the cessation of exercise.<sup>102,104</sup> This indicates the vascular benefits of exercise are reversible if a physically active lifestyle is not maintained, which therefore supports the incorporation of exercise as a lifestyle change to maintain intact endothelial function. All together the available literature suggests that exercise training is an efficacious therapy to reverse the attenuated endothelial and vascular function associated with pediatric obesity.

### 2. Arterial stiffness

Arterial stiffness indicates vascular compliance and distensibility and is a key player in vascular reactivity and vascular health.<sup>115</sup> Pulse wave velocity (PWV) is used as the gold standard measurement for small and larger arterial stiffness,<sup>116,117</sup> with increased values corresponding to increased stiffness and decreased compliance and distensibility.<sup>118</sup> Considering the relationship between obesity with hypertension and atherosclerosis, it is reasonable to assume that obesity would be associated with increased arterial stiffness which has been shown to be true in obese adults.<sup>119</sup> Contradictory to this intuitive conclusion, Charakida et al.<sup>120</sup> found that arterial stiffness assessed by PWV was significantly lower in obese adolescents when compared to lean age-matched controls,  $6.99 \pm 1.01$  m/sec and  $7.65 \pm 1.23$  m/sec ( $P < 0.05$ ) respectively, with various other studies confirming

these results.<sup>121-123</sup> The PWV values measured by Charakida et al. in obese adolescents are considered normal and healthy and the difference between groups does not meet the clinically significant threshold of 1.0 m/sec.<sup>124</sup> It is important to note that another group, Cote et al.,<sup>93</sup> found that obese children and adolescents had significantly greater carotid and aortic PWV values when compared to age-matched nonobese controls. Nonetheless, these results indicate that pediatric obesity may affect vascular structure (stiffness) and function (FMD) differently. The relationship between exercise and arterial stiffness in pediatric obesity is unknown. In adults, measures of arterial stiffness are improved with exercise<sup>125</sup> and are significantly lower in adults with greater cardiorespiratory fitness.<sup>126</sup> Our group has shown that arterial stiffness was either significantly reduced<sup>42,62</sup> or unchanged<sup>76</sup> in obese adolescents following 12 weeks of CRAE training. However, the reduced arterial stiffness observed was likely due to an improved nitric oxide (NO) and endothelin-1 (ET-1) ratio and increased vasodilatory<sup>62</sup> capacity as arterial stiffness is a measurement of a vessel's structural elasticity which tends to change with time.<sup>127,128</sup> It is also important to note that in response to exercise previous studies suggest that shear stress, or the force of blood flowing on the endothelial surface, mediates complimentary adaptations in artery function and structure with changes in function preceding changes in structure.<sup>114,129</sup> Future research should adopt long-term assessments utilizing multiple time points to determine the vascular adaptations associated with pediatric obesity and the effects of exercise over time on arterial stiffness.

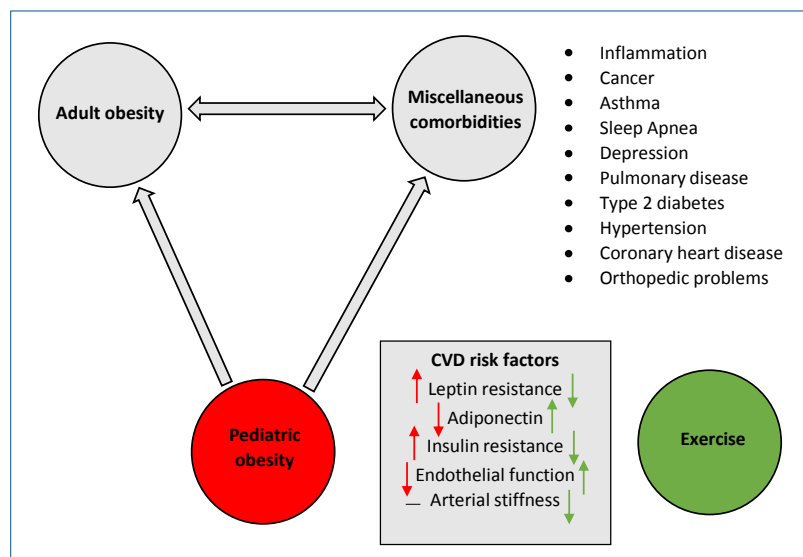
## Exercise modality and prescription

It is widely accepted that obesity is caused by an imbalance

between energy intake and energy expenditure, specifically when energy intake exceeds energy expenditure resulting in increased adipose tissue accumulation. Dietary habits, levels of physical activity, and sedentary behaviors all affect an individual's energy balance.<sup>130</sup> Interestingly, modern trends for physical activity reveal that in general, there is a significant increase in the frequency of sedentary behaviors, such as screen time and watching television, during childhood.<sup>131</sup> Increased frequency of sedentary behaviors and decreased physical activity time are significant contributors to the development of pediatric obesity as previous research has shown that decreased levels of physical activity are associated with increased BMI<sup>132</sup> and fat mass<sup>133</sup> and obesity.<sup>14,134</sup> Various obesity-related comorbidities and CVD risk factors can be attributed to the accumulation of excess fat mass.<sup>30-32</sup> Previous studies utilizing exercise interventions have shown that exercise improves body composition and has a positive impact on blood lipid profiles and BP as well as blood levels of metabolic hormones in obese children and adolescents (Fig. 1).<sup>135,136</sup> However, the effects of exercise may be dependent on the modality of exercise (AE, RT, and CRAE) as each modality may lead to distinct results.

### 1. Aerobic exercise

Obesity is associated with an increased risk of all-cause morbidity and mortality<sup>34,137</sup> which can be reduced through improved cardiorespiratory fitness.<sup>138</sup> It is well established that in children, adolescents, and adults, AE is an effective means of improving cardiorespiratory fitness. In fact, AE training may be the most researched modality of exercise intervention in the pediatric population. AE is generally performed as a moderate-intensity physical exercise such as running, cycling, or jump rope for a sustained period of time, approximately 30–60 minutes per exercise bout, with the purpose of improving the body's ability



**Fig. 1.** Obesity is associated with a number of comorbidities as well as increased risk factors for cardiovascular disease. In pediatric obesity, these conditions manifest early in life and have been shown to track into adulthood. Exercise has been shown to be an efficacious therapeutic strategy to combat pediatric obesity.

to transport and utilize oxygen in the skeletal muscle and the heart. Previous meta-analyses suggest that AE interventions are effective for reducing fasting insulin levels, IR,<sup>74,135</sup> and BF%<sup>139</sup> as well as improving blood lipid levels<sup>140</sup> in obese adolescents. Additionally, previous studies have shown that AE training can lower overall body weight, BMI, low-density lipoprotein,<sup>52</sup> as well as improve blood levels of leptin, cortisol<sup>52</sup> and visfatin.<sup>141</sup> Previous studies generally prescribe AE for 30 to 90 minutes at a moderate or moderate-to-vigorous intensity for 3 to 5 days a week. These interventions prescribe progressively more intense AE over the duration of the interventions which range from 8 weeks to 48 weeks and utilize a variety of modalities including water activities, walking, jogging, and recreational sport.<sup>74</sup> Our group has previously utilized the same jump rope exercise protocol in 2 separate studies to investigate the effects of exercise on cardiovascular and metabolic parameters in obese adolescents.<sup>70,142</sup> The 12-week jump rope exercise program consisted of a 5-minute warm-up, 40 minutes of jump rope which increased in intensity every 4 weeks (weeks 1–4 at 40%–50% heart rate reserve [HRR], weeks 5–8 at 50%–60% HRR, and weeks 9–12 at 60%–70% HRR), and a 5-minute cool-down, which was completed 5 days a week for 12 weeks. The 12-week jump rope program resulted in improved body composition, BP, resting levels of NO, ET-1, insulin, and glucose, and reduced markers of inflammation and IR.<sup>70,142</sup> AE is more commonly prescribed to adolescents as AE training modalities such as jump rope, play, dancing, and sport may often be considered more fun and enjoyable which is an important factor for motivation, participation, and long-term adherence.<sup>143,144</sup> AE induces a multitude of positive effects; however, AE alone may not be the most efficacious exercise modality to combat pediatric obesity.

## 2. Resistance training

RT exercises utilize external loads in the form of free weights, resistance bands, cable machines, or body weight to apply resistance against the contraction of a skeletal muscle with the purpose of increasing muscular strength, power, hypertrophy, and/or endurance. RT is generally performed 1 to 3 times per week while the number of repetitions and sets as well as the duration and intensity of a bout of RT is dependent on the focus of the RT program, muscular strength, power, hypertrophy, or endurance. RT has traditionally been reserved for adult athletes as the primary purpose of RT is to improve muscular performance and it was believed children and adolescents did not experience the same benefits of RT as adults. However, more recent studies suggest that adolescents can improve physical performance, muscle size, and strength through RT.<sup>145</sup> Additionally, it is generally accepted that AE is optimal for reducing BF while RT is optimal for increasing lean body mass.<sup>146</sup> This may explain why AE is more commonly prescribed for weight management as reducing fat mass is commonly the primary focus of an exercise prescription for obese individuals due to the negative metabolic and inflammatory effects of excess

adipose tissue.<sup>33-36</sup> However, AE alone may only minimally affect muscular strength and lean body mass in adults, children, and adolescents. In obese adults, RT has been shown to reduce fat mass and improve blood lipid levels and IR<sup>147,148</sup> but there is limited research focused on investigating the effects of RT on body composition and cardiovascular and metabolic parameters in obese adolescents. Lee et al.<sup>149</sup> found that abdominal adiposity was significantly reduced following 3 months of RT or AE in obese adolescent boys but only the RT group's adiposity loss was associated with significant improvements in IR. However, in a follow-up study, the same group found that following 13 weeks of AE or RT, BF% was significantly reduced in obese adolescent girls but only AE resulted in improved insulin sensitivity which was believed to be attributed to greater reductions in BF in response to the AE modality.<sup>150</sup> These results indicate that there may be differential responses to RT between sexes in obese adolescents. Previous meta-analyses have identified that RT alone is not associated with significant decreases in fat mass or improvements in metabolic parameters and CVD risk factors in obese children and adolescents.<sup>74,151</sup> It was suggested that this may be due to the insufficient literature available and the variations of the study designs and methodologies. In the studies analyzed most prescribed RT interventions were similar to American College of Sports Medicine guidelines (1 to 2 sets of 10 to 15 repetitions of upper body and lower body multi-joint exercises, 2 to 3 times per week) but variance between age, sex, and adherence was present. Even so, current physical activity guidelines for the pediatric population suggest performing AE and muscle-strengthening activities 3 times per week<sup>152</sup> as muscular strength has been shown to be an important factor for protecting against chronic diseases and all-cause mortality.<sup>153,154</sup>

## 3. CRAE training

As previously discussed, AE and RT interventions may have different effects on body composition and cardiovascular and metabolic parameters in pediatric obesity. CRAE training is a unique training modality that utilizes both AE and RT components in a single exercise protocol to provide the benefits of each modality, which may potentially be more beneficial for metabolic parameters, vascular function, and CVD risk factors than AE or RT alone. CRAE training generally involves completing a bout of RT, one set of 8–20 repetitions of multiple upper body and lower body resistance exercises, followed by a bout of AE, 20–30 minutes at a moderate intensity, during a single exercise session. CRAE training has been shown to improve both cardiorespiratory fitness and muscular strength<sup>76,155</sup> and previous reviews suggest that in adults, CRAE training is more effective for reducing BF%,<sup>156</sup> WC, BP,<sup>76</sup> levels of blood lipids, and improving glycemic control<sup>157</sup> when compared to AE or RT alone. One CRAE training protocol our group has previously developed consisted of a 5-minute warm-up, 20 minutes of RT (one set of 15–20 repetitions of 5 upper body and 3 lower body exercises), 30 minutes of walking or jogging at 60%–70% HRR, and a 5-minute cool-down performed 5 times

a week for 12 weeks. Our group has shown in obese adolescents that CRAE training improves anthropometric measurements (BF%, WC),<sup>42,76)</sup> reduces BP, arterial stiffness, IR, markers of inflammation, levels of ET-1, and increases NO bioavailability.<sup>44)</sup> Our findings are supported by previously completed reviews that indicate CRAE training improves body composition, blood lipid profiles, blood levels of adipokines,<sup>151,158)</sup> and insulin sensitivity.<sup>151,159)</sup> These reviews also conclude AE alone and CRAE training are more effective than RT for improving fat mass, lipid profiles, fasting insulin, fasting glucose, and IR but do not provide significantly different benefits.<sup>151,159)</sup> However, Dâmaso et al.<sup>56)</sup> found that following 1 year of CRAE training obese adolescents experienced significantly greater improvements in BF mass, blood lipid levels, lean body mass, blood levels of leptin and adiponectin, and leptin/adiponectin ratio when compared to obese adolescents that completed 1 year of AE. Further research is required to confirm the efficacy of CRAE training over AE and RT. Nonetheless, it is important that obese children and adolescents perform both AE and RT, or CRAE training, which is may be more beneficial than AE or RT alone to prevent the development of obesity-related metabolic diseases and CVD. Additionally, adherence rate of the exercise training is crucial to have positive effects of exercise training for obese children and adolescents. Although there is no study that has directly compared the exercise training adherence rates in AE, RT, and CRAE, our recent studies suggest that CRAE training may have greater exercise training adherence rates compared to AE and RT. Since CRAE training is able to combine multiple different exercise modalities, it may be more enjoyable and less demanding in these young individuals compared to AE or RT alone. This notion can be supported by previous studies that reported adolescents of various backgrounds have stated that they would be more inclined to engage in exercise if it is perceived as fun and enjoyable.<sup>143,144,160)</sup> Studies about specific exercise modality, and adherence rate are warranted to develop optimal exercise modalities for pediatric populations.

## Conclusion

Obesity is one of the most prominent public health concerns of modern times with the potential to place a substantial burden on healthcare systems. Pediatric obesity is a well-established risk factor for the development of MetS, T2D, CVD, cancer, and early mortality in adulthood. Although the exact cause of pediatric obesity is multifaceted, it is a condition that can be improved with effective and maintainable lifestyle changes. Exercise has proven to be an efficacious intervention to combat pediatric obesity and its related risk factors and comorbidities. While RT provides benefits, AE and CRAE training appear to be the most effective exercise modalities to reduce BF and combat pediatric obesity. Based off of previous research we suggest that the most appropriate exercise prescription to improve pediatric obesity would be a CRAE training protocol, which contains both

muscle strengthening (RT) and aerobic components (AE), that places emphasis on reducing fat mass and long-term adherence.

## Conflicts of interest

No potential conflict of interest relevant to this article was reported.

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