The Effect of Childhood- versus Adult-Onset Obesity on Cardiorespiratory Fitness, Handgrip Strength, Resting Metabolic Rate and Substrate Oxidation in Adults

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complies with the regulations of the University and meets the accepted standards with respect to originality and quality.

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Abstract

The Effect of Childhood-versus Adult-Onset Obesity on Cardiorespiratory Fitness, Handgrip Strength, Resting Metabolic Rate and Substrate Oxidation in Adults

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BACKGROUND: Obesity is associated with a variety of cardiovascular, pulmonary, and skeletal muscle aberrations that negatively affect physical fitness and other metabolic parameters. However, it is unclear whether these impairments are exacerbated in lifelong obesity. **OBJECTIVE**: We aimed to examine how age of obesity onset (childhood versus adult) affects cardiorespiratory fitness (CRF), handgrip strength, resting metabolic rate (RMR), and substrate oxidation in adults. **METHODS**: We recruited 31 adults (BMI 29.5 to 39.4 kg/m^2) who had either developed obesity before puberty (childhood-onset [CO]; n=13) or after the age of 18 (adult-onset [AO]; n=18). CRF was measured using the YMCA submaximal bike test and handgrip strength was measured using handgrip dynamometry. RMR and substrate oxidation was measured using indirect calorimetry. **RESULTS**: Mean handgrip strength (±SD) was lower in adults with childhood- versus adult-onset obesity (CO: 56 ± 10 vs. AO: 72 ± 20 kg; $p = 0.01$). Fat oxidation was also lower in the childhood-onset group (CO: 51.07 ± 18.39 vs. AO: 67.55 ± 23.83 mg/min; $p = 0.04$), while CRF, RMR and carbohydrate oxidation were not different between groups ($p > 0.05$). These results persisted when adjusting for age, sex, and body composition. **CONCLUSION**: Our results show that persistent obesity since childhood impairs muscle strength and fat oxidation, but not RMR and CRF, compared to adult-onset obesity. These results suggest that maintaining a healthy body weight early in life may delay the loss of muscle strength and impairment in fat oxidation in later life and help prevent future disease.

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Abbreviations

BMI	Body mass index
CHD	Coronary heart disease
CHO OX	Carbohydrate oxidation
CRF	Cardiorespiratory fitness
CVD	Cardiovascular disease
DXA	Dual x-ray absorptiometry
Fat OX	Fat oxidation
FFM	Fat-free mass
FM	Fat mass
HR	Heart rate
LBM	Lean body mass
MET	Metabolic equivalents
RER	Resting exchange ratio
RMR	Resting metabolic rate
VO_2max	Maximal oxygen uptake

Background and literature review

1. Introduction

Obesity is defined as an excessive accumulation of body fat that negatively impacts health[1]. Operationally, the World Health Organization (WHO) defines obesity as a body mass index (BMI) of greater than or equal to 30 kg/m^2[1]. In Canada, obesity in the adult population (aged ≥18) has increased steadily from 6.1% in 1985 to 18.1% in 2011[2]. It is estimated that obesity prevalence in Canadian adults will increase to 21.2% by 2019, causing an annual economic burden between $4.6 and $7.1 billion[3]. Obesity is linked to an increased risk of developing chronic diseases, such as cardiovascular disease (CVD), type 2 diabetes, and stroke[4,5]. Furthermore, obesity has been associated with increased incidences of breast, colon, and prostate cancer among other co-morbidities[6]. However, not all individuals with obesity have the same disease risk profile. One factor that might explain this variability is the age at which an individual develops obesity. Numerous studies have shown that adults with childhood-onset obesity have higher risk of various chronic illnesses in adulthood, including cardiovascular, musculoskeletal and metabolic diseases, compared to those with adult-onset obesity [7-11]. Given that higher CRF and muscle strength are associated with reduced comorbidities in obesity, it is possible that there are differences in these fitness components, as well as other metabolic factors, in individuals with childhood-onset and adult-onset obesity[12-14,15]. At the present time, there are limited data available regarding the impact and implications of the timing of obesity onset on cardiorespiratory fitness (CRF), skeletal muscle strength, resting metabolic rate (RMR) and substrate oxidation.

2. The significance of age of obesity onset

Children who develop obesity under the age of eight and continue to have obesity throughout adulthood are at an increased risk of developing CVD, type 2 diabetes, musculoskeletal disorders, and cancer (Figure 1)[7]. Longitudinal studies that have tracked cohorts of children into adulthood observed that not only is overweight/obesity in childhood a risk factor for adulthood overweight/obesity, but is also associated with higher rates of morbidity and mortality[10,16,17]. One explanation for the observed discrepancy in disease risk between childhood-onset and adult-onset obesity arises from known differences in adipose tissue form and function. Age of obesity onset affects the number and size of adipocytes in obese and overweight

adults[18,19]. Adults who developed obesity in childhood increase their adipose tissue by hyperplasia (increased number) and /or hypertrophy (increased size). However, adults who develop obesity later in life increase adipose tissue by hypertrophy[19]. A study conducted by Brook et al[18] investigated the relationship between age of obesity onset and number of adipocytes. The total number of adipocytes was significantly increased in children who had obesity by the age of one year, as well as in adults who dated their obesity to childhood. A recent study showed that the number of adipocytes increases in childhood and adolescence, while the number remains constant in adulthood in both lean and obese individuals[19]. Both hyperplasia (number) and hypertrophy (size) contribute to adipose tissue remodeling[19]. In the obese state, adipose tissue remodeling is associated with many metabolic disease risk factors such as cell death, inflammation, altered adipokine profile, and hypoxia[20]. Furthermore, another study found a strong association between increased adipocyte size and insulin resistance that was already apparent in childhood[21].

Apart from differences in adipocytes, several studies found that obese children and adults had higher resting cardiac output and stroke volume, causing significant stress to the cardiovascular system[22]. This eventually leads to functional and structural changes in the heart[23,24], especially in individuals with a BMI above 40 kg/m^2 who had obesity for more than 10 years[25]. In addition, childhood obesity is associated with left ventricular hypertrophy, elevated levels of C-reactive protein and other risk factors for coronary heart disease (CHD)[26]. In summary, certain changes in the heart and adiposity during growth can work together to impact health status in childhood and adolescence, and potentially influence future disease risk in adulthood (see Figure1)[10,17].

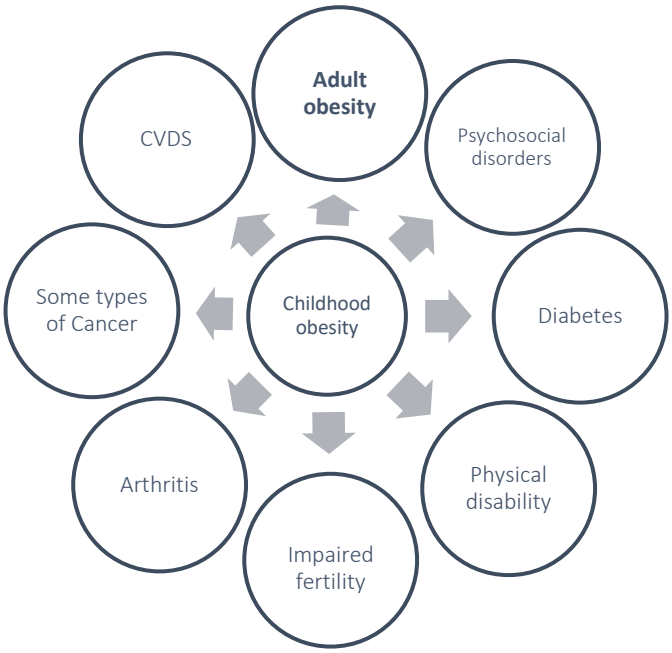

Figure1. Schematic diagram summarizing the complications of childhood obesity (adapted and redrawn from Lakshman) [7].

3. Cardiorespiratory fitness

Cardiorespiratory fitness (CRF) is a health-related component of physical fitness and an important marker of cardiovascular health[27,28]. CRF can be defined as the ability of the circulatory and respiratory systems to deliver oxygen to the muscular system, and for the muscles to efficiently utilize oxygen during sustained physical activity[29,30]. CRF can be expressed in metabolic equivalents (METs) or maximal oxygen uptake (VO_2max) and measured as an absolute value or scaled to an individual on the basis of body weight[29,31]. The latter approach may be more appropriate, as it gives the ability to compare people with different sizes and allows for safer exercise prescription in individuals with obesity[32-34]. Several studies found that doing the equivalent amount of absolute work is not the same in terms of the oxygen consumption for individuals with obesity compared to normal weight population, especially with weight bearing activity[33,35,36]. A study by Mattson et al[33] found that normal-weight individuals had lower relative oxygen costs (36% of VO_2max) when compared to individuals with obesity (56% of VO_2max) when walking at a comfortable speed[33,34].

It is well known that obesity and low CRF are associated with high risk of CVD and all-cause mortality[14]. In general, studies have shown that individuals with obesity have reduced CRF[37,38]. However, the risk of mortality and morbidity have been found to be reduced by higher CRF regardless of whether an individual is of normal weight or has overweight or obesity[12-14]. In addition, a meta-analysis found that a 1 MET (3.5 $ml \cdot kg^{-1} \cdot min^{-1}$) improvement in CRF equates to a 13% and 15% decrease in all-cause mortality and cardiovascular events, respectively[28]. Furthermore, increased CRF helps improve muscle insulin sensitivity, which facilitates the transport of glucose from blood to muscle[39]. It can also increase lipoprotein lipase activity in skeletal muscle which can in turn, improve clearance rates of plasma triglycerides and increase transport of lipids and lipoproteins from the peripheral circulation and tissues to the liver[40]

3.1 Factors limiting VO_2max consumption

VO2max can be limited through three primary physiological factors: 1) the pulmonary diffusing capacity, 2) cardiac output, and 3) blood volume and flow[41].

Pulmonary diffusing capacity is defined as the ability to transfer (diffuse) oxygen and carbon dioxide between the lungs and the blood. Pulmonary diffusion may become a limiting factor when a high increase in cardiac output shortens the time during which the blood can take the oxygen from the lungs, possibly leading to lower blood oxygen saturation levels[42,43].

Cardiac output is the amount of blood pumped by each ventricle in one minute; it is the stroke volume multiplied by heart rate (HR)[44]. Therefore, an increase in either HR or stroke volume increases cardiac output. Cardiac output normally ranges from 4.5 to 5.5 L/min in adults in the resting state and can increase up to 20-30 L/min during maximal exertion[44].

Stroke volume is the amount of blood pumped in one beat. Stroke volume is the product of end of diastolic volume subtracted from the end systolic volume, which is the blood that remains in the ventricle after contraction. There are three factors that effect stroke volume: contractility, preload, and afterload. Contractility is defined by the force of the contraction of the heart muscle. Preload is the stretch of the left ventricle of the heart to allow for blood filling and can be measured by the end diastolic volume. Then, afterload is the pressure that the ventricle needs to overcome to eject blood. However, not all blood is ejected from the ventricle in each beat; the percentage ejected is called the ejection fraction, and a healthier heart has a higher value.[44].

With regard to blood volume and flow, we know that the working muscle needs more oxygen and nutrients than other muscle. Enhanced blood flow achieved by reducing blood's viscosity, can overcome this limitation and improve oxygen delivery to the working muscle[45].

3.2 Measurement of cardiorespiratory fitness

The VO_2max test, the direct measurement of maximal oxygen consumption, is considered the gold standard for assessing CRF[29,46-48]. Limitations of using the VO_2max method include cost, need for highly trained personnel, specialized equipment[49]. In comparison, submaximal testing provides an alternative for assessing CRF in obese or otherwise unhealthy individuals[33,34,48]. Various submaximal tests have been developed to assess CRF, including the Astrand-Rhyming test[50], Canadian aerobic fitness test[51], YMCA cycle ergometer test[52], and a single-stage submaximal treadmill walking test[53].

The YMCA test is a commonly used submaximal fitness test with a multistage protocol that progressively increases the workload based on the participant's heart rate[52,54]. A study by Carter et al[55] compared the treadmill VO_2max test to the submaximal YMCA protocol and found that the YMCA test underestimated VO_2max by approximately 5-10%. This might be due to different factors including reduced muscle mass engagement and biomechanical inefficiencies during cycling. As the protocol relies on the relationship between heart rate and oxygen consumption, decreased biomechanical efficiency may result in an under-prediction of aerobic capacity[54]. However, previous research has confirmed the validity of using the submaximal cycle ergometer test to predict VO_2max. A study by George et al[56] compared the cycle ergometer test to the maximal graded exercise test on a treadmill for assessing VO_2max using a larger sample size (n=156). The VO_2max results derived from both these tests showed a significant positive relationship in women (r = 0.90) and men (r = 0.74). Selected participants in this study (n=34) performed the submaximal test twice over a 5-day period to confirm intra-class reliability (r = 0.93). These results were supported in a separate cross-validation study by Beekley et al[52]. This study found no statistically significant difference between the YMCA predicted VO_2max and the standard measure of VO_2max (mean difference = 1.3 $ml \cdot kg^{-1} \cdot min^{-1}$), suggesting that the YMCA stationary bike test is effective in predicting VO_2max. These results were further supported by a moderately high correlation between the predicted and measured values (r = 0.79).

3.3 Implications of obesity on cardiorespiratory fitness

The increased mass of adipose tissue in obesity could affect CRF by putting stress on the heart and increasing the overall metabolic demand of the body[25]. This can also lead to a larger blood volume and resulting increases in left ventricle preload and afterload which in turn, can cause left ventricular hypertrophy[22,57]. Abnormalities in left ventricular diastolic filling have been found in 50% of individuals with obesity[57]. Abnormal myocardial function during exercise is evidenced by a decrease in stroke volume, lower maximal cardiac output as well as a decrease in other markers of diastolic and systolic function[58]. Studies show that individuals with obesity demonstrate suppression of ventricular function at rest and decrease of myocardial performance during exercise[59-61]. A study by Alpert et al[62] illustrated that during exercise alterations in left ventricle ejection fraction were more related to heart mass in individuals with class III obesity BMI (> 40 kg/m^2). In individuals with a heart mass around 150-200 grams, a normal response was observed (+20-30%), whereas in individual with a heart mass > 350 grams, the ejection fraction fell with exercise. Furthermore, Licata et al[63] found that percent change in ejection fraction at peak exercise negatively correlated with the duration of obesity (r =-0.59). Ejection fraction was only increased in individuals who had obesity for less than 10 years.

With respect to performance-based CRF, obesity has been shown to be detrimental. A study conducted by Drinkard et al[64] observed a negative correlation (r = - 0.82) between the BMI and distance on a 12-minute walk/run test. A separate study conducted by Rowland et al[65] concluded that the increased effort required by individuals with obesity to move their additional body mass may explain 32% of the variance in finishing times during a one-mile run.

Studies in adults and children consistently find that VO_2max, a marker of CRF, is lower in obese compared to lean individuals[37,66,67]. Despite studies that show greater CRF in people with obesity (expressed in L/min), when adjustment for weight is made, the opposite is true[68]. A study by Hulens et al[36] found that obese subjects had lower VO_2max compared to lean subjects (12.3 ± 1.8 ml·kg^{-1}·min^{-1} and 17.7 ± 2.4 ml·kg^{-1}·min^{-1}, respectively). Another study by Vinet et al[69] that compared two groups of men, obese adult to normal weight, also found that the obese group had a significantly lower mean VO_2max (27.9 ± 1.7 ml·kg^{-1}·min^{-1})vs 38.6 ± 1.2 ml·kg^{-1}·min^{-1}). Loftin et al[70] reported that the average VO_2max for preadolescent girls with normal weight was significantly higher (45.8 ± 7.2 ml·kg^{-1}·min^{-1}) compared to preadolescent girls with

obesity (22.8 ± 7.3 ml/kg/min). Thus, lower CRF in individuals with obesity is more likely due to a higher body weight that inflates the size-normalizing factor ('per kg').

Despite the well-documented effects of obesity on CRF, there is limited data available that specifically identifies the effects of age of obesity onset. To our knowledge, only a single study by Rupp et al[71], has examined this relationship. In their study, there were differences between groups with childhood-onset obesity and adult-onset obesity. The childhood-onset group had significantly higher CRF. However, limitations of this study include a wide BMI range (25-40 kg/m^2), a retrospective classification of participants into the childhood-onset and adult-onset groups, and differences in age between the two groups; the childhood-onset group was significantly younger. Therefore, more research is required to further assess the real impact of obesity onset on the CRF.

4. Muscle strength

The requirement of good CRF for optimal health maintenance has been well-established[28,72]. In addition to CRF, muscle strength is also considered a critical element to sustain overall health and fitness and perform day-to-day activities[73,74]. Muscle strength is defined as a maximal, voluntary, isometric force. In other words, it is the ability to produce a force against a resistance[75]. Muscle strength is determined by neural, mechanical, and muscular factors[76]. It can be assessed as isometric (i.e. static) or isokinetic (i.e. dynamic) strength [77]. For isometric measurements, handgrip dynamometers, and cable tensiometers are used. This type of measurement limits results to the muscle group and joint angle involved in testing. Despite the limitation of handgrip strength to a specific muscle group, the handgrip strength measurement has been shown to predict mortality and functional status of adult individuals[78,79]. A study by Ling et al[80] found that there was an increase in risk for all-cause mortality (hazard ratio 1.06, CI 1.01-1.12, $p = 0.033$) for each 5-kg decrease in handgrip strength. In another large cohort study by Ortega et al[15], researchers followed more than one million adolescent participants for 24 years and found that participants with higher strength had 20-30% decrease in all cause mortality.

4.1 Implications of obesity on muscle strength

There are several perspectives on how obesity affects muscle strength. One view is that obesity can positively affect muscle strength as a consequence of increased effort to move their

additional body mass, especially in the lower body. This mimics a training effect[81]. Hulens et al[82] was one of the first to investigate the effect of obesity on muscle strength in adults and found that those with obesity have higher absolute strength in the lower body compared to normal weight subjects, whereas no differences were found in handgrip strength. The greater absolute knee extension and trunk extension strength were linked to the training effect of weight bearing in individuals with obesity. However, when all the strength results were adjusted for fat-free mass, the results were significantly lower for individuals with obesity (6 %)[82]. Other researchers have found that obesity is linked to reduced muscle strength, mass and quality[83].

Lower skeletal muscle strength in obesity may be caused by a number of factors. As obesity is associated with lower protein synthesis in skeletal muscle, this may result in a significantly reduced positive adaptation triggered from the weight bearing effects[84]. In addition, muscle strength has been observed to be negatively affected by intramuscular fat which is accumulated with increasing BMI/adiposity and has been associated with poorer muscle strength[85]. Furthermore, obesity is associated with impaired regulation of glucose metabolism and increased advanced glycation end-products in the blood. As muscle mass is the main site for glucose uptake, any impairment in glucose regulation might contribute to low muscle strength[86]. In addition, muscle stiffness and poorer physical function have been linked to increased advanced glycation end products. Individuals with obesity can encounter functional challenges in muscular performance as well postural balance limitations, reduce strength, and impaired mobility[87,88].

Only one study has investigated the effect of age of onset of obesity on muscle strength in older adults (> 55 years)[89]. They found that handgrip strength was lower in individuals who developed obesity as early as 20 years of age versus later in life. Furthermore, several studies have found that obesity negatively affects muscle strength in older adults[90,91], young adults[82,87] and adolescents[92,93], yet little is known about the specific muscle adaptations in individual who acquire adiposity early in life.

5. Resting metabolic rate and substrate oxidation

Total energy expenditure consists of three components: 1) resting metabolic rate (RMR), 2) diet-induced thermogenesis, and 3) physical activity. RMR in sedentary individuals accounts for approximately 50-75% of their total energy expenditure[94]. RMR is defined by the amount of

energy required by an individual at rest[95]. Thus, measurement of RMR is fundamental in understanding the metabolism of an individual[96]. The relationship between RMR and body composition is a critical factor to consider when examining obesity[97]. RMR can be measured through indirect calorimetry which is a non-invasive technique based on the measurement of O_2 consumption and CO_2 production. Accordingly, RMR can be estimated in the absence of a direct measurement of heat production[98].

Indirect calorimetry is based on several principles. One principle is that the oxidation of macronutrients reflects the O_2 uptake and there is no substantial reservation of O_2 in the body[99]. Another principle is that all chemical energy created in the body comes from the oxidation of macronutrients: carbohydrate, fat, and protein. A third principle is that the ratio of O_2 consumption and CO_2 production from oxidation of these substrates are fixed[99]. By collecting the amount of oxygen consumption and carbon dioxide production, the calculation of RMR can be estimated using the Weir equation[100].

Several factors have been found to influence RMR. For example, studies have shown differences in RMR between men and women[101,102]. A study by Arciero et al[101] found that absolute RMR was 23% lower in women (1,348 +/- 125 kcal/day) than in men (1,740 +/- 194 kcal/day)[101], and this result persisted after adjusting for FFM. Age also plays a role in RMR; young adults have higher RMRs than older adults (over 70 years of age). In addition, previous studies in adults have shown an age-related reduction in RMR[103,104]. This was also consistent in children as they have an inverse relationship between age and RMR[105,106]. A longitudinal study by Keys et al[107] found that changes in body composition are a precursor to the decline in age-related metabolic rate. However, it is still debatable whether these changes in the RMR are solely due to changes in body composition or active cellular mass[108,109].

The resting exchange ratio (RER) is calculated as the ratio of carbon dioxide production to oxygen consumption, and can provide information about which substrate (fat or carbohydrate) is being utilized as the main fuel[110,111]. Proteins contribute 5-15 % to energy production at rest as their main role is to build muscle tissue and organs and provide essential enzymes and hormones[112].

Several validated equations such as the Livesey&Elia equations[113] have also been developed to quantify rates of substrate oxidation. Substrate oxidation is defined as the ability of the body to oxidize carbohydrate, fat, and protein at rest in the fasted state. Under normal

conditions, healthy individuals have the ability to utilize both fats and carbohydrates, and switch between them based on the availability of these substrates[114]. This ability can be defined as metabolic flexibility[115]. However, the impairment of substrate oxidation, through either a declining fat utilization rate or a shift toward glucose oxidation can be defined as metabolic inflexibility[115]. Furthermore, metabolic inflexibility has been observed in chronic conditions such as diabetes, insulin resistance, non-alcoholic fatty liver disease,and obesity[116,117]. In combination with RMR, RER and substrate oxidation rates can provide valuable information about an individual's metabolism[118].

5.1 Implications of obesity on resting metabolic rate

Metabolic variables like RMR is are highly dependent on body size. Fat-free mass (FFM) is the major contributor to RMR[119,120] with some studies finding an additional contribution of fat mass (FM)[121,122]. Several studies found that RMR was significantly lower (360 kcal/d) in individuals with normal weight compared to individuals with obesity[123-128]; however, others found no differences[129,130]. These inconsistent findings may be because the comparison groups in the latter studies[129,130] had similar amounts of FFM. Based on a review published in 2016 by Carneiro et al[131] there a was positive association between RMR and higher weight[125,128,132]. In comparative studies between different obese classifications and normal weight, the largest difference was found between individuals with class III obesity and normal weight. Class III obese had (540 kcal/d) higher RMR than normal weight and individuals with class1 obese had (240 kcal/d) higer than normal weight individuals[123,127,128]. Moreover, another cohort study by Weijs and Vansant[133] found a higher difference by 800 kcal/d (p<0.001) as they compare individual with a BMI>50 (RMR =2157 kcal/d) with non-obese individuals (RMR=1331 kcal/d). Hence, RMR is commonly expressed per body mass or FFM to allow the comparison between groups with difference body sizes(though statistical adjustment for body mass or FFM is more accurate). It has been shown that, RMR per body mass is lower in individuals with obesity if we compare those with obesity to those with normal weight[134]. However, it has been observed that if the two individuals with obesity and normal weight have identical FFM then RMR per FFM would be equal[135].

The role of age of obesity onset on RMR, however, remains unclear. Only one study by Blair & Buskirk[136] in 1987, examined the effect of time of obesity onset on RMR. They found that adult and child-onset did not differ. However, their study had a serious limitation as they conducted the RMR measurement for only 5-10 minutes. For an accurate measurement, researchers often eliminate the first 5-10 minutes to make sure participants are in a steady state and past the acclimatization phase[137].

5.2 Implications of obesity on substrate oxidation

Decreased fat oxidation has been associated with obesity[138,139]. In individuals with obesity, the capacity to mobilize fatty acids from adipose tissue for oxidation in skeletal muscle has been reported to be impaired[140,141]. There are several factors that can affect this abnormality such as the availability of fatty acids[142], skeletal muscle characteristics, muscle glycolytic flux, and hormonal and neural abnormalities[143]. In addition, decreased activity of some enzymes involved in the process of fat utilization may also contribute to the reduction of fat oxidation in individuals with obesity[144]. Activity of carnitine palmitoyl transferase, citrate synthase, and cytochrome *c* oxidase were found in a study conducted by Simoneau et al[144] to be significantly lower in skeletal muscle samples that were collected from individuals with obesity compared to individuals with normal weight. Their findings were remarkable as they proposed some deficiencies in important key regulatory stages of fat oxidation, for instance fat transfer into the mitochondria carnitine palmitoyl transferase, enzymes of the Krebs cycle and the electron transport chain[144]. These finding were supported by several other studies that found a reduction in carnitine palmitoyl transferase, citrate synthase, and cytochrome c oxidase in the skeletal muscle of individuals with obesity[141,145,146]. Besides the decline of the activity of theses enzymes, there are also abnormalities in mitochondria morphology in individuals with obesity. In a study by Kirkwood et al[147], they found a reduced size of skeletal muscle mitochondria in individuals with obesity compared to lean individuals by 35%. The reduced size of skeletal muscle mitochondria can lead to fat accumulation which might be a direct or indirect factor in the impairment of fat oxidation[148]. Taking these alterations together may provide information on the underlying mechanisms of the impairment of fat oxidation in individuals with obesity. However, to our knowledge, no one has studied the effect of obesity onset on substrate oxidation.

6. Rationale

Obesity, in general, is associated with unwanted consequences such as inflammation and increased metabolic disease risk[149]. Moreover, adults with obesity who dated their obesity to childhood have a greater risk of developing CVD and type 2 diabetes than those who were normal weight in childhood [5,150,151]. Despite our understanding of the pathophysiology underpinning obesity, there is limited data to explain the long-term effects of obesity in the adult population. Childhood-onset obesity not only prolongs the duration of obesity, but is also associated with alterations in adipose tissue growth and function that has been hypothesized to lead to earlier presentation of cardiovascular, musculoskeletal and metabolic diseases[10,11,150,152]. However, the risk of mortality and morbidity has been found to be reduced by higher CRF in individuals with obesity[12-14], and higher muscle strength has been found to reduce mortality by 20-30%[15]. Hence, it is worth exploring whether there are differences in CRF, handgrip strength as well as resting metabolism between individuals with childhood-onset versus adult-onset obesity. An increased understanding of how the timing of obesity onset affects these parameters will shape our ability to create therapeutic programs for this growing sub-population and may even help prevent future diseases.

7. Study objectives

The objective of this study is to determine the effect of age of obesity onset (childhood versus adulthood) on CRF, handgrip strength, RMR, and substrate oxidation in adults with obesity.

8. Hypothesis

We hypothesize that adults with obesity who developed obesity in childhood will have lower CRF compared to adults with obesity who developed obesity later in life. This is opposite to the finding of Rupp at el[71], the only study to test this hypothesis, due to the study's limitations mentioned above.

We also hypothesize that adults with obesity who developed obesity in childhood will have lower handgrip strength, RMR, and fat oxidation compared to adults with obesity who developed obesity later in life.

9. Methods

9.1 Study participants

Adult volunteers (male and female) were recruited through radio, poster, newspaper and online advertisements. In total, we recruited 31 sedentary participants aged 25-40 years old with a BMI of 29.5-39.4 kg/m^2. Participants had either childhood-onset or adult-onset obesity. Childhood-onset obesity was defined as obesity acquired pre- or peri-puberty as previously described by Lakshman et al[7]. Adulthood-onset obesity was defined as obesity acquired after the age of 18. Participants were asked to provide pictures of themselves as children and adolescents to assess their onset of obesity. In addition, all participants answered questions using body rating scales to confirm their age of obesity onset. The Collins scale[153] (Appendix A), consisting of seven pictures for boys and girls ranging from underweight to obese, was used to assess weight status during childhood and adolescence. The Stunkard body rating scale[154] (Appendix A), containing nine different pictures of men and women ranging from very thin to very obese, was used to assess weight status during adulthood.

Eligibility of candidates to participate in the study was initially assessed through a telephone screening questionnaire. Suitable candidates were then interviewed in person about their weight, medical history, and dietary habits and physical activity. Individuals with certain cardiovascular diseases (i.e. heart attack and stroke), cancer, chronic respiratory diseases (i.e. chronic obstructive pulmonary disease), diabetes, autoimmune disease, mental illnesses or eating disorders were excluded. Individuals with hypothyroidism were eligible if their thyroid stimulating hormone concentrations were stable for at least one year. In addition, pregnant or breastfeeding women and individuals who used nicotine-containing products were not eligible for this study. Selected participants provided written in formed consent (Appendix B) and completed the physical activity readiness questionnaire (PAR-Q) (Appendix C)[155]. Resting blood pressure was measured using an electronic blood pressure monitor (AccutorrV). Participants had a fasted blood draw for measurement of serum lipid profile and plasma glucose concentration. The blood was analyzed at the Montreal General Hospital- Clinical Laboratory Unit.

9.2 Anthropometric and body composition assessments

Participants had their height and weight recorded in light clothing without shoes. A fixed-wall stadiometer (Seca 216, Seca Corp., Chino, CA) was used to measure height to the nearest 0.1 cm. Weight was obtained to the nearest 0.1 kg using a calibrated scale (DIN 2, AmCells Corp, Vista, CA). BMI was calculated as weight (kg) divided by height-squared (m^2). Also, a calibrated dual X-ray absorptiometry (DXA) scanner (GE Healthcare Lunar Prodigy Advance™) was used to measure total FM, FFM and LBM, as well as forearm LBM.

9.3 Cardiorespiratory fitness

Participants underwent a submaximal bike test using the YMCA protocol to estimate their VO_2max[52]. The test was divided into 2-4 stages, with each stage at least 3 minutes in duration. The test assumes a linear relationship between an individual's heart rate and VO_2max, which occurs when the heart rate is >110 beats/min[77]. Each participant pedaled on a stationary bike (150 kpm/min, 0.5 KP or 25 watts at 50 rpm) with a gradual increase in resistance based on his or her heart rate during the first stage (see Figure 2).

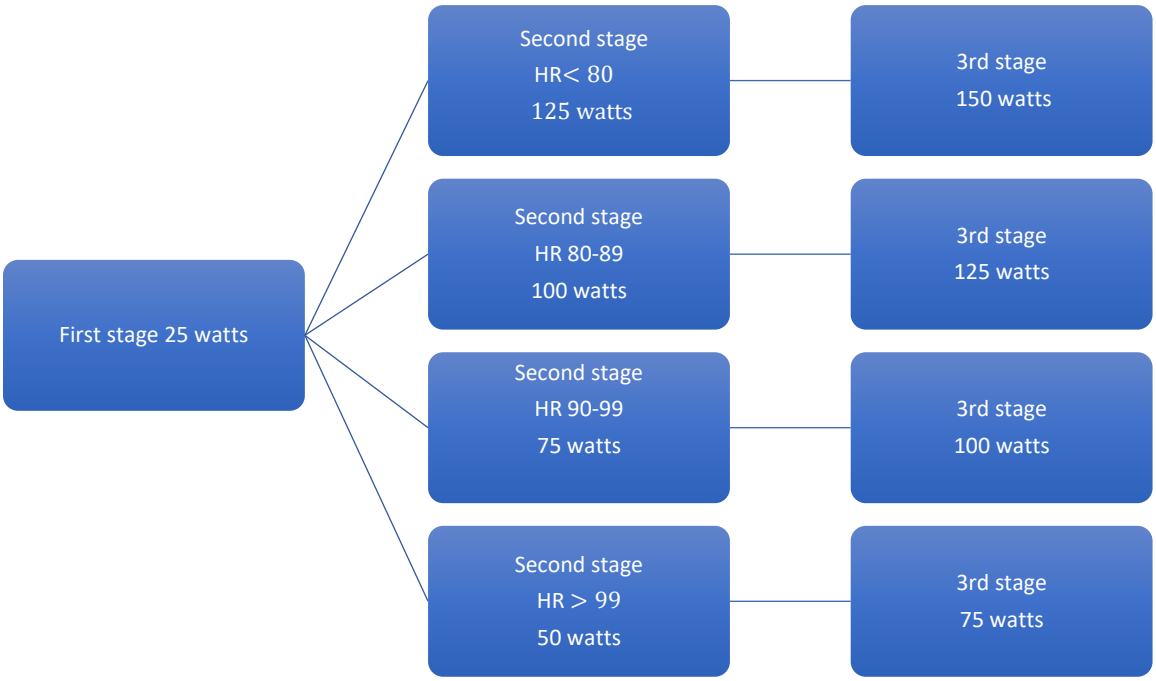

Figure 2. YMCA bike test stages

As shown in Figure 2, the heart rate response in Stage 1 determined the workload in Stage 2. After that, the workload increased by 25 watts in all subsequent stages until the

participant reaches 85% of their age-predicted maximum heart rate (HRmax). Heart rate was recorded every minute. If the participant's heart rate varied by >5 beats between the last two minutes of each stage, an additional minute was added to that stage until heart rate for the last two minutes was within ±5 beats/minute. If the participant's heart rate did not plateau, or if the participant did not maintain cadence, the test was considered invalid. Blood pressure was taken and recorded between the 2nd and 3rd minute of each stage. Participants were then asked about their rating of perceived exertion[156] before the end of each stage.

The test is designed to have a minimum of three stages: a 0.5 KP warm-up stage, followed by two additional submaximal stages based on the heart's response to the first stage. An optional fourth stage was added if the participant's heart rate did not exceed the required 110 beats/min. The workloads and heart rate values calculated in the final two stages of the protocol were used to estimate VO_2max. We used the following formula to calculate sub-maximal VO_2 at second-last workload (SM1) and submaximal VO_2 at last workload (SM2): [(workload in watts/weight in Kg) * 10.8] + 7.0. Next, we calculated the slope (b) by using a second formula: (SM2-SM1)/(HR2-HR1). Here, HR1= average of last two heart rates from the second-last stage, while HR2= average of last two heart rates from the last stage. Finally, we estimated VO_2max (ml/kg/min) by using the following formula: VO_2max (ml/kg/min) = SM2+[b(HRmax-HR2)].

9.4 Handgrip strength

A hand dynamometer was used to assess handgrip strength. For this assessment, the participant holds the handgrip dynamometer in the hand to be tested, inline with the forearm at the level of the thigh slightly away from the body. The handle of the dynamometer was adjusted, if required, for the grip size in order for the participant to feel comfortable while squeezing. When ready the subject squeezed the dynamometer with maximum isometric effort, which is maintained for about 5 seconds. Encouragement was given to help participants achieve maximum effort. There are two trials for each hand and the highest scores of each trial was combined to quantify the overall strength of the participant.

9.5 Resting metabolic rate and substrate oxidation

Participants arrived at the testing location at 0800 am fasted for at least 8 hours. Their height and weight were measured, after which subjects were required to lie supine on a bed in a

dark environment and remain there resting for 90 minutes. A calibrated indirect calorimetry system (Sable Systems International) was used to measure the volume of O_2 uptake (VO_2) and CO_2 production (VCO_2) simultaneously with a hood canopy. Participants were instructed to remain awake and still throughout the measurement for 35 minutes. The system was set to record the fractional amount of O_2 and CO_2, mixing chamber temperature, water vapour pressure, barometric pressure, subsample flow rate, and mass flow rate in a negative pressure design.

Calculations

The indirect calorimetry data were truncated by 10 min for acclimatization with the ventilated hood. Data (VO_2 and VCO_2) were then included in the calculation of substrate oxidation (CHOox) and lipid (FATox) according to the following formulae[113]:

CHOox (g/min) = $4.59V_{CO2}$ (l/min) - $3.23V_{O2}$ (l/min)

FATox (g/min) = $-1.70V_{CO2}$ (l/min) + 1.70_{VO2} (l/min)

9.6 Statistical analysis

Statistical software SPSS (version 22.0) was used to analyze the data. Differences in CRF, handgrip strength, RMR and substrate oxidation between childhood-onset and adult-onset obesity were assessed using an independent samples *t*-test. The two-group distributions were sufficiently normal for the purpose of conducting a t-test (i.e., skew < (2.0) and kurtosis < (9.0)[157]. Furthermore, the assumption for homogeneity of variances was tested and satisfied via Levene's *F* test. Cohen's *d* was calculated based on the *t* test value for a between subjects *t* test and the degrees of freedom using the following formula ($2t/\sqrt{(df)}$) with a value of 0.8 or higher indicating a large effect size based on Cohen's (1992) guidelines[158]. We used a multiple linear regression to test the effect of age of onset of obesity on CRF, hand grip strength, RMR and substrate oxidation adjusting for age and sex, and where relevant, body composition. Also, we computed Pearson correlation coefficients to assess the linear relationship between variables.

10. Results

10.1 Characteristics of study participants

There were 31 participants included in this study: 18 with adult-onset obesity and 13 with childhood-onset obesity (Table 1). The two groups were similar in mean age and sex distribution. Weight and body mass index were also similar between groups as was body composition. Percent body fat was 41.5 ± 6.4% in the adult-onset group and 43.7 ± 4.7% in the childhood-onset group. Blood samples were taken and assessed from all participants and no differences were found in total high-density lipoprotein and low-density lipoprotein cholesterol, and triglyceride concentrations between groups.

10.2 Handgrip strength and cardiorespiratory fitness

Mean handgrip strength based on the highest value for both hands combined was significantly lower in adults with childhood-onset obesity versus adult-onset obesity (CO: 56 ± 10 vs. AO: 72 ± 20 kg; $p = 0.01$) (Figure 4). This was also the case when handgrip strength was based on the best value from the dominant hand only (CO: 28 ± 6 vs. AO: 35 ± 10 kg; $p = 0.02$) (Table 2). Cohen's *d* was estimated at 1.10, which is indicated a large effect size. These differences persisted when adjustments for forearm lean mass, age, and sex were made. Also, total grip strength and forearm lean mass were strongly correlated ($r = 0.805$, $p < 0.001$). In addition, a multiple linear regression analysis (Table 4) showed that both age of obesity onset and total forearm lean mass were significant predictors for both total and dominant handgrip strength independent of age and sex.

We found no differences in CRF between groups (CO: 32 ± 6 vs. AO: 31 ± 5 $ml \cdot kg^{-1} \cdot min^{-1}$; $p = 0.38$) (Figure 5; Table 2) even when adjusting for age, sex (Table 5). Results were similar when expressing VO_2max per LBM or FFM. In the multiple linear regression, sex was a predicter of CRF VO_2max ($ml \cdot kg^{-1} \cdot min^{-1}$) independent of age and obesity onset (Table 5).

10.3 Resting metabolic rate & substrate oxidation results

RMR was not significantly different ($p = 0.66$) between groups (Table 6). Resting rates of fat oxidation were lower ($p = 0.04$) in the childhood-onset group compared to the adult-onset group (CO: 51.07 ± 18.39 vs. AO: 67.55 ± 23.83 mg/min) (Figure 7). Results persisted when

expressing fat oxidation per body weight. In contrast, there were no differences ($p = 0.18$) in rates of resting carbohydrate oxidation between groups (Figure 8). The differences in fat oxidation and similarities in carbohydrate oxidation in childhood- and adult-onset obesity persisted when age, sex, and body composition were adjusted for.

Figure 3. Subject participation overview

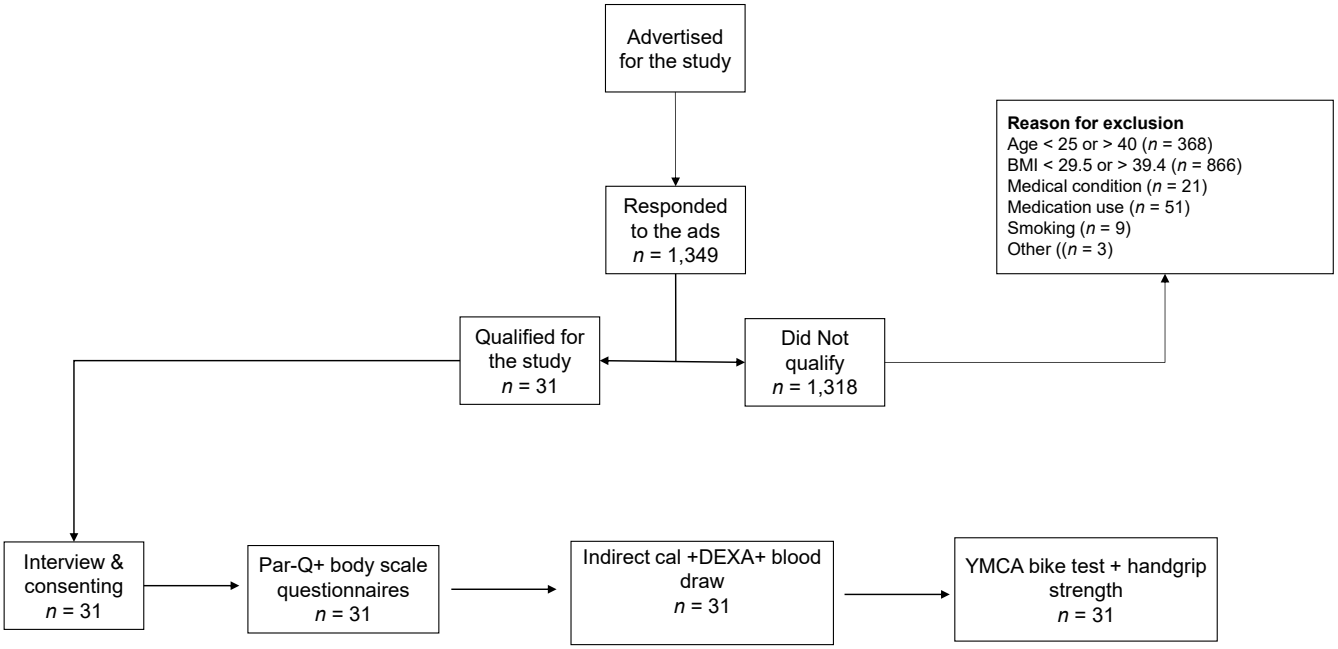

Table 1. Subject characteristics

Parameters	Adult-onset (*n*=18)	Childhood-onset (*n*=13)	*p*-value
Age (Years)	30 ± 3	30 ± 3	0.79
Sex *n* (%) Men	6 (33.3)	3 (23.1)	0.55
Women	12 (66.7)	10 (76.9)	
Weight (kg)	95.4 ± 9.8	94.7 ± 11.9	0.87
Height (cm)	171 ± 8	166 ± 5	0.10
Body mass index (kg/m^2)	32 ± 3	33 ± 3	0.22
Body fat (%)	41.5 ± 6.4	43.7 ± 4.7	0.29
Total fat mass (kg)	39.6 ± 7.6	41.3 ± 6.7	0.52
Total lean mass (kg)	52.3 ± 7.4	50.0 ± 8.5	0.45
Fat free mass (kg)	55.2 ± 7.7	52.8 ± 9.0	0.43
Glucose (mmol/L)	4.76 ± 0.41	4.75 ± 0.58	0.99
Total Cholesterol (mmol/L)	4.46 ± 0.97	4.50 ± 0.84	0.89
High-density lipoprotein (mmol/L)	1.17 ± 0.23	1.23 ± 0.23	0.56
Low-density lipoprotein (mmol/L)	2.73 ± 0.81	2.73 ± 0.70	0.99
Triglyceride (mmol/L)	1.33 ± 0.49	1.19 ± 0.51	0.48

Values are mean ± SD. *p*-value between Childhood-onset and Adult-onset obesity groups

Table 2. Cardiorespiratory fitness and grip strength

Parameters	Childhood-onset (*n*=13)	Adult-onset (*n*=18)	*p*-value	*Cohen's d*
Predicted Vo2max ($ml \cdot min^{-1}$)	3.08 ± 0.80	3.02 ± 0.57	0.83	0.08
Predicted Vo2max ($ml \cdot kg^{-1} \cdot min^{-1}$)	32 ± 6	31 ± 5	0.84	0.07
Heart rate (rest) (bpm)	87 ± 16	85 ± 9	0.64	0.17
Systolic (rest)bp (mmHg)	115 ± 13	114 ± 10	0.84	0.07
Diastolic (rest) bp (mmHg)	76 ± 10	76 ± 7	0.91	0.04
Heart rate (2 min recovery) (bpm)	125 ± 10	127 ± 7	0.51	0.28
Systolic (2min recovery) (mmHg)	125 ± 13	138 ± 15	0.02	0.92
Diastolic (2min recovery) (mmHg)	63 ± 13	65 ± 11	0.65	0.18
Handgrip strength total (kg)	56 ± 10	72 ± 20	0.01	1.10
Dominant hand grip strength (kg)	28 ± 6	35 ± 10	0.02	0.90

Values are mean ± SD. *p*-value between Childhood-onset and Adult-onset obesity groups

Table 3. Resting metabolic rate and substrate oxidation.

Parameters	Childhood-onset (*n*= 13)	Adult-onset (*n*=18)	*P*-value	*Cohen's d*
RMR (kcal • d^{-1})	1830 ± 321	1873 ± 216	0.66	0.18
RER (VCO_2 • VO_2^{-1})	0.88 ± 0.41	0.85 ± 0.42	0.06	0.77
Fat oxidation (mg• min^{-1})	51.07 ± 18.39	67.55 ± 23.83	0.04	1.09
Carbohydrate oxidation(mg• min^{-1})	212.8 ± 70.72	180.1 ± 57.9	0.18	0.01

Values are mean ± SD. *p*-value between Childhood-onset and Adult-onset obesity groups.

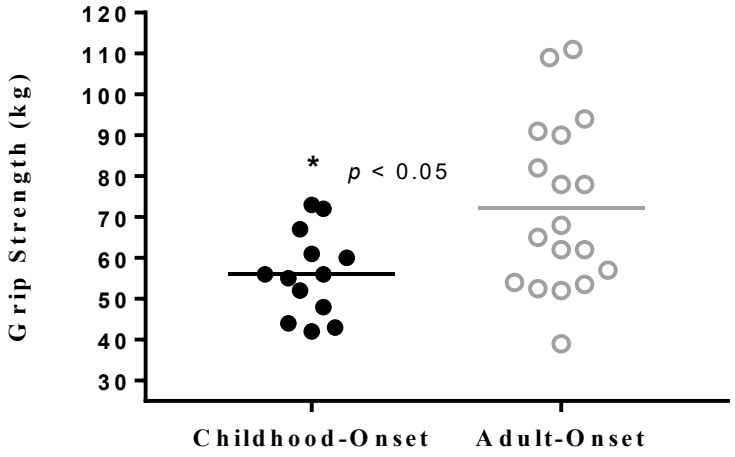

Figure 4. Handgrip strength by obesity-onset.

A graphical representation of the individual participant data and means.

Table 4. Pearson correlation between total hand grip strength, dominant handgrip strength and total forearm lean mass and dominant hand forearm lean mass.

Model		Handgrip strength	Dominant hand S
Total forearm lean mass (kg)	r	0.80**	0.79**
	p-value	0.00	0.00
Dominant forearm lean mass (kg)	r	0.79**	0.78**
	p-value	0.00	0.001

Table 5. A multiple linear regression on handgrip strength.

Model	*B* (kg)	95% Confidence Interval	*p*-value
Intercept	-18.076	(-67.612 , 31.460)	0.46
Age (years)	0.499	(-0.733 , 1.731)	0.41
Sex (men vs. women)	1.397	(-12.921 , 15.715)	0.84
Total forearm lean mass (kg)	30.614	(17.333 , 43.896)	0.00
Obesity-onset (adult vs. childhood)	10.841	(3.022 , 18.659)	0.01

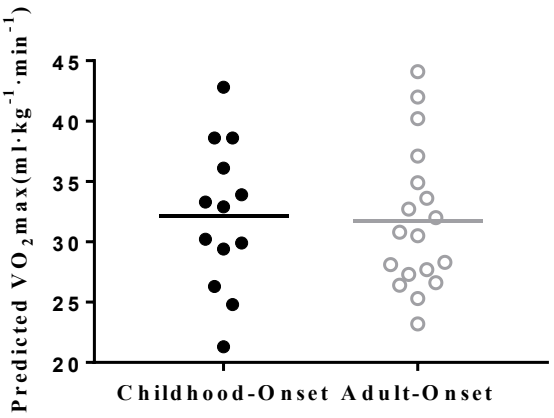

Figure 5. Cardiorespiratory fitness by obesity-onset.

A graphical representation of the individual participant data and means.

Table 6. A multiple linear regression on CRF VO_2max(ml·kg-1·min-1).

Model	*B(ml·kg^{-1}·min^{-1})*	95% Confidence Interval	*p*-value
Intercept	35.178	(15.709, 54.648)	0.00
Age (years)	0.014	(-0.651, 0.679)	0.96
Sex (men vs. women)	-5.838	(-10.653, -1.022)	0.02
Obesity Onset (adult vs. childhood)	1.033	(-3.133, 5.200)	0.62

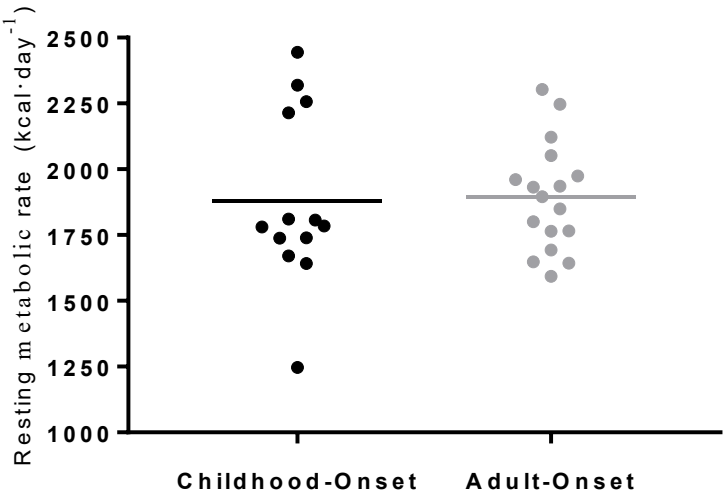

Figure 6. Resting metabolic rate by obesity-onset.

A graphical representation of the individual participant data and means.

Table 7. A multiple linear regression on resting metabolic rate (kcal · d^{-1}).

Model	*B* (*(kcal · d^{-1})*	95% Confidence Interval	*p*-value
Intercept	1317.909	(512.544, 2123.273)	0.00
Age (years)	25.5	(-2.048 ,52.973)	0.07
Sex (men vs. women)	-323.556	(-522.749, -124.364)	0.00
Obesity Onset (adult vs. childhood)	-17.723	(-190.076 ,154.630)	0.83

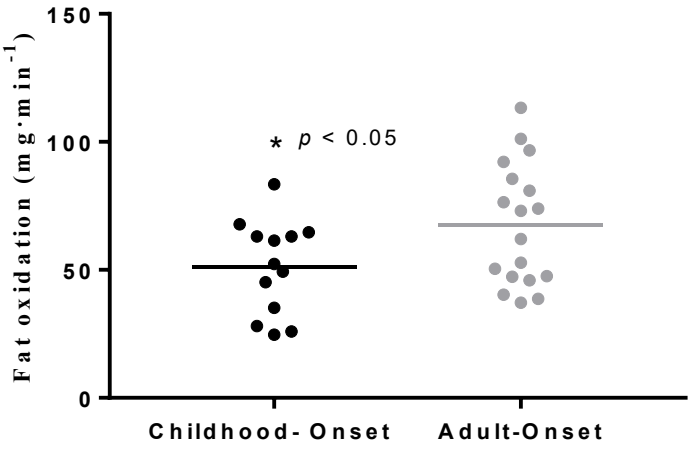

Figure 7. Fat oxidation by obesity-onset.

A graphical representation of the individual participant data and means.

Table 8. A multiple linear regression on fat oxidation.

Model	*B* ($mg \cdot min^{-1}$)	95% Confidence Interval	*p*-value
Intercept	39.05	(-39.17 ,117.29)	0.31
Age (years)	1.01	(-1.65, 3.68)	0.44
Sex (men vs. women)	-3.28	(-22.63, 16.06)	0.73
Obesity onset (adult vs. childhood)	-16.48	(-33.22, 0.26)	0.05

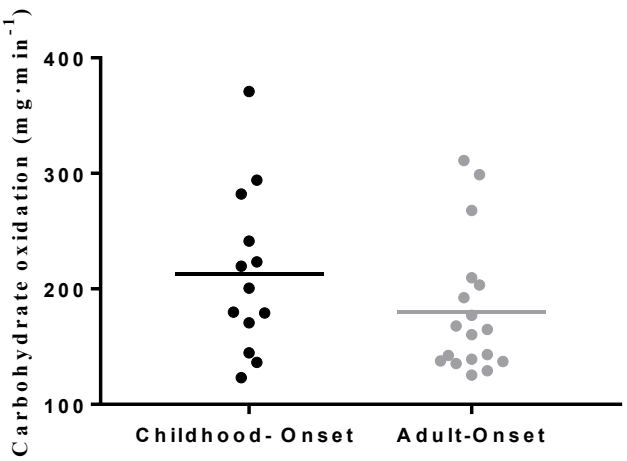

Figure 8. Carbohydrate oxidation by obesity-onset.

A graphical representation of the individual participant data and means.

Table 9. A multiple linear regression on carbohydrate oxidation ($mg \cdot min^{-1}$).

Model	*B* ($mg \cdot min^{-1}$)	95% Confidence Interval	*p*-value
Intercept	148.44	(-66.94, 363.83)	0.16
Age (years)	2.205	(-5.15, 9.56)	0.54
Sex (men vs. women)	-52.57	(-105.84, 0.70)	0.05
Obesity Onset (adult vs. childhood)	37.27	(-8.82, 83.36)	0.10

11. Discussion

This study examines whether obesity onset in childhood versus adulthood affects handgrip strength, CRF, RMR and substrate oxidation. To our knowledge, we are the first to investigate the effect of obesity onset on substrate oxidation and handgrip strength in young adults. Our overall findings indicate that those with obesity onset during childhood have lower handgrip strength and fat oxidation compared to those with adult-onset obesity. Furthermore, we found no differences in CRF between the two groups, though the majority of individuals had a poor rating. For example, for a 32-year-old male, a predicted VO_2max less than 33.7 ($ml \cdot kg^{-1} \cdot min^{-1}$) is considered poor.

11.1 Handgrip strength

Muscle strength is known as an important aspect of fitness and overall health; several studies have shown that handgrip strength can predict morbidity and mortality[15,79,159,160]. However, we know little about the effect of obesity onset on handgrip strength. In our study, we observed that individuals with childhood-onset obesity had lower handgrip strength. More importantly, we found that both obesity-onset and forearm lean mass were predictors of handgrip strength independent of age and sex. This indicates that age of obesity onset could be an important factor in affecting muscle strength and quality in adulthood.

The only other study to examine the effect of obesity onset on handgrip strength was conducted by Stenholm et al[89]. Their findings indicate that individuals with early-onset obesity have lower muscle strength compared to those with late-onset obesity. This is consistent with our findings. However, though our results are similar, it is important to note that our participants were considerably younger than those of Stenholm et al[89]. The average age in the Stenholm study was 67 years, which is considered an older adult. In addition, they defined early-onset obesity to describe people who were considered obese as early as 20 years of age; based on our definition, this is still acquiring obesity as adult. Also, it is well known that aging is often accompanied with sarcopenia and dynapenia, the loss of muscle mass and strength respectively[161]. As their participants were older adults, an important question therefore arises: are their results the effect of aging, obesity or both? Furthermore, the duration of obesity might play an important role in the transition of muscle fiber types from slow twitch to fast twitch, and in turn, affect muscle

strength and function (see review[162]). The Stenholm study also used BMI alone to classify obesity, an approach that has several limitations, such as not distinguishing between fat mass and muscle mass. We were able to confirm our BMI definition of obesity with DXA. Our findings are also unique in terms of the age groups and the definition of childhood-onset obesity used in the study.

Our result suggests that the effect of obesity onset on muscle strength may have more to do with muscle function than mass as no difference in total or forearm LBM were found between the two-groups measured by DXA. Several cohort and cross-sectional studies have associated declining grip strength with higher fasting insulin, which may indicate that poor muscle strength precedes the development of insulin resistance[163-165].

Other possible explanations for the poor strength in adults with childhood-onset obesity have been suggested, including the view that it is a consequence of having obesity-associated systemic inflammation and insulin resistance[165-168]. Several studies have found that prolonged obesity is a risk factor for both insulin resistance and type 2 diabetes[169-171] Other well-documented factors such as increased fat mass and physical inactivity can lead to increased muscle fat infiltration resulting in decreased muscle quality, increased inflammation and insulin resistance[172]. Though our groups had similar fat mass and physical activity levels, we do not know if they had differences in inter- and intra-muscular fat content.

11.2 Cardiorespiratory fitness

It is well known that higher CRF can attenuate disease risk factors that accompany obesity[173]. In obese individuals, lower CRF has been observed compared to lean individual[36,37]. Thus far, only one study has investigated the effect of obesity onset on CRF. In 2016, Rupp et al[71] found that individuals with childhood-onset obesity had higher CRF results than those with late onset obesity[71]. In our study, however, we found no difference between groups. The lack of agreement between the results of the two studies may be due to different factors. In Rupp's study, the mean age of the early onset group was significantly younger than the mean age of the late onset group by 7 years. CRF has been shown to decrease with aging, and their results did not adjust for age[174]. Also, participant weight history was determined through self-report, which can be influenced by participant perceptions. No additional evidence was used to verify the participants' age of obesity onset. In our study, both pictures, the Stunkard and Collin scales

were used to obtain more accurate weight histories. In addition, in Rupp et al[71] there was a wide range of BMIs among participants (25- 40 kg/m^2), and the BMI was significantly higher in the childhood-onset group.

Another difference between the Rupp study and ours is that Rupp used a treadmill test, which is a weight-bearing test, while we used a YMCA bike test, which is a non-weight bearing test. As previously reported by Mattson et al[33], during normal walking, obese individuals used 57 % of their VO_2max compared to individuals of normal weight, who used only 36% of their VO_2max. This may explain why individuals with obesity found walking difficult, even at low intensity. Therefore, a non-weight-bearing test may be a more appropriate measure, especially for individuals with obesity. Combined with handgrip strength, our findings indicate that early adiposity, influences strength but not CRF.

11.3 Resting metabolic rate

No difference in RMR was found between the two groups. This finding was consistent with a previous study by Blair & Elsworth[136], which explored the effect of obesity onset on RMR. Our results expanded on the findings of this study, which had a small sample size and used a different protocol to measure RMR. They used a 5-10 minutes measurements period, whereas, we used a 35-minute period. This is a serious limitation in their protocol as continuous measurement of indirect calorimetry less than 30 minutes is considered an insufficient duration and might result in a failure to reach steady state (physiologically)[175]. The two groups showed no differences in term of their age, sex, body composition, and weight. Based on these and our findings, it appears that age of obesity onset is not as important of a factor in determining RMR relative to other more major factors, such as age, sex, and body composition, especially FFM as it is a more metabolically active tissue. As expected, FFM and RMR were highly correlated for all groups, which is consistent with other studies[120].

11.4 Substrate oxidation

This is the first study to examine how age of obesity onset affects substrate oxidation. Though there were no differences in RMR between our two groups, rates of fat oxidation were 27% lower in the childhood- than in the adult-onset obesity group. Furthermore, the childhood-onset group had a 16.5 mg/min lower fat oxidation rate than the adult-onset group independent of

age and sex (Table 8). There may be different reasons for this finding, such as obesity associated with increased insulin, which could prevent the transfer of fat across the muscle membrane and /or the mitochondrial membranes[176]. It has been found that childhood obesity predicts insulin resistance in young adulthood[177]. The role of insulin is to not only promote fat storage by process called lipogenesis, but also to prevent the body from using fat as fuel in another process called lipolysis[178]. Though not measured in our study, it is possible that greater insulin resistance in our childhood onset group could contribute towards impairment of fat oxidation at rest as insulin resistance decreases the rate of fat utilization in skeletal muscle and increase the appearance of free fatty acids. This causes accumulation of intracellular fatty acid metabolites that inhibit the insulin signaling pathway[179].

Since RMR and CHO oxidation were not different between the groups, and fat oxidation was higher in the adult-onset group, this might suggest that proteins oxidation could be higher in the childhood-onset group. This suggestion should be a topic for a future research.

12. Limitations

We were not able to gather medically measured weight histories. However, we did ask the participants to provide childhood pictures and used Stunkard and Collins scales in order to determine age of obesity onset to partially overcome this limitation. These scales have been validated by Must et al[180] to assess long term recall of body size. They observed high correlations (r = 0.70 - 0.75) between recalled body size and measured BMI at ages 10 and 15. Also, there was a lack of control in terms of individuals' diet composition (fat and CHO) before the measurement, which has been found to have an effect on substrate oxidation. A study by Bisschop et al[181], studied three different diet compositions for 11 days prior to each measurement ranging from no fat (0%) to moderate (42%) to high fat (83%). When participants had a high fat diet (83%) as opposed to a mixed diet, the fat oxidation increased significantly (p <0.05) compared to other diets. However, in our study based on 24 h dietary recalls, the majority of our participants consumed a mixed diet. Also, it is worth noting that we did not calculate protein oxidation because of the minor role of protein as a fuel especially in the resting state and because most participant who are weight stable are in nitrogen balance. This still might lead to small error or overestimations of fuel from other substrates[182].

Another limitation of the study is that we did not measure the participant's insulin levels, so we are unsure if participants were insulin sensitive or insulin resistant. Even though our participants did not have diabetes and had normal fasting plasma glucose concentration, they could still have hyperinsulinemia which is often characteristic of insulin resistance[183]. Finally, we did not calculate the duration of obesity in our outcomes as that might has an effect in our outcomes.

As this study is cross-sectional in nature, cause and effect could not be determined. However, it would only be possible to confirm this if we were able to follow participants from childhood to adulthood, which is outside the scope of this study.

13. Strengths

DXA is the gold standard for measuring body composition and was used to measure participant body fat percentage, FFM and lean mass. As we found similarities in body composition between the two groups, other mechanisms or factors, besides body composition, may explain the observed difference in strength and fat metabolism. Our groups were also similar in age, and our age range was fairly narrow. This strengthens our results, as we know that FFM and VO^2max decline with aging. Also, we used indirect calorimetry, the gold standard to measure RMR and substrate oxidation, instead of relying on predictive equations. Several studies have shown that some equations may not be accurate or appropriate for metabolic rate prediction in certain body weight categories[184].

Summary

Findings from our study suggest that there are differences in metabolism and muscle strength between those who have had obesity from childhood and those who only developed obesity in adulthood. Though CRF was not affected by obesity onset, those who developed obesity in childhood had decreased muscle strength despite similar muscle mass, which might indicate poor muscle quality and function. Moreover, though RMR was similar between the groups, those who had obesity since childhood also had impaired fat oxidation. This finding suggests that fat loss may be more difficult in these individuals as this might indicate a preference for fat storage rather than utilization.

14. Future direction

Further studies are necessary to investigate whether there are differences in inter-and intra-muscular fat in these individuals that may affect grip strength. It may be also worthwhile to investigate the effect of diet composition on substrate oxidation prior to indirect calorimetry measurement[181]. Finally, these findings require replication through studies of participants with both childhood- and adult-onset obesity that include medical and fitness histories to also identify the real effect of the duration of obesity. Furthermore, measurement of additional variables, such as insulin sensitivity and C-reactive protein would further our understanding of how the timing of obesity onset affects metabolism, fitness and overall health.

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Appendix A: Body Rating Scales

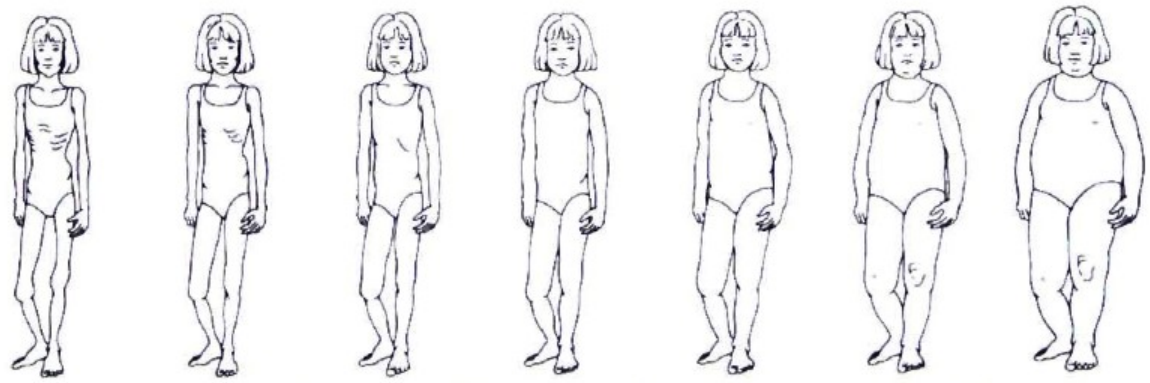
Body Rating Chart

Participants will be asked to report how their body status at 5 years old, 10 years old, puberty, 20 years old and present compares to the figure drawings in the age- and sex-specific body rating scales below.

	Figure number								
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**
Age 5	☐	☐	☐	☐	☐	☐	☐		
Age 10	☐	☐	☐	☐	☐	☐	☐		
Puberty (Age _____)	☐	☐	☐	☐	☐	☐	☐		
Age 20	☐	☐	☐	☐	☐	☐	☐	☐	☐
Currently (Age _____)	☐	☐	☐	☐	☐	☐	☐	☐	☐

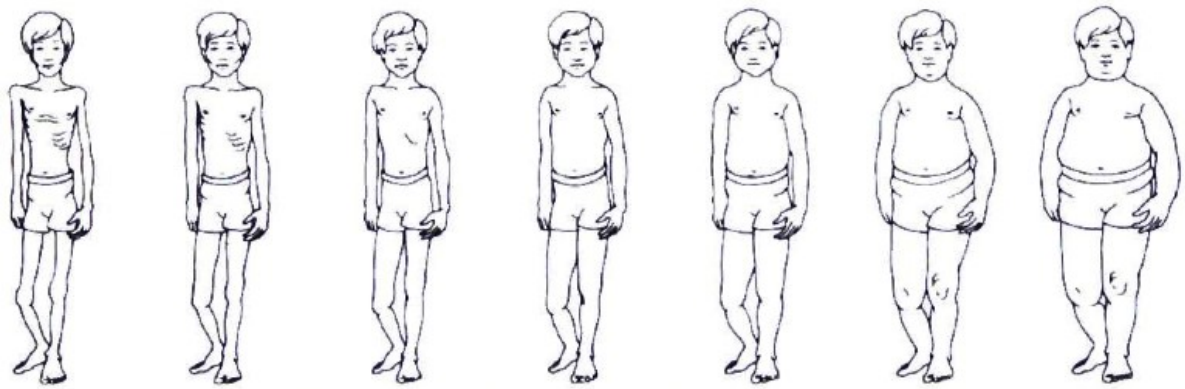
Childhood Body Rating Scale: Collins[153]' Figure Drawings

Girls



1 2 3 4 5 6 7

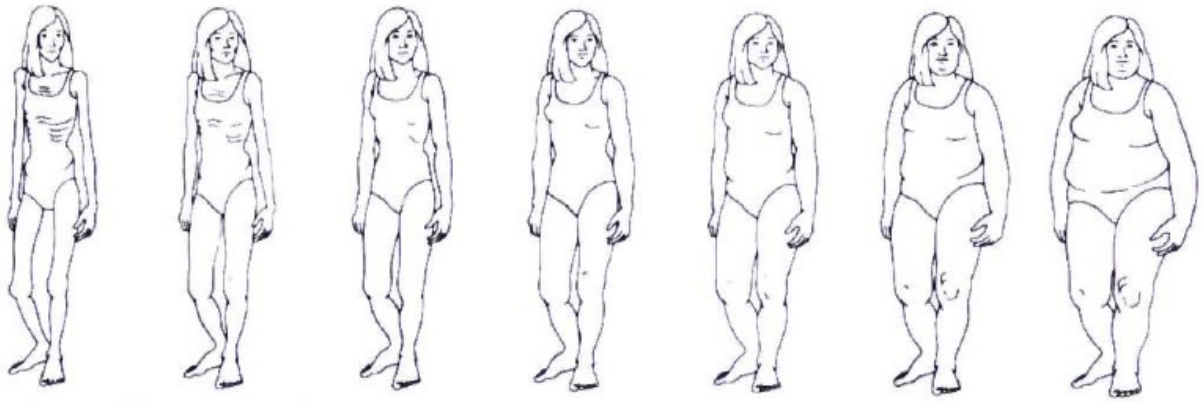
Boys



1 2 3 4 5 6 7

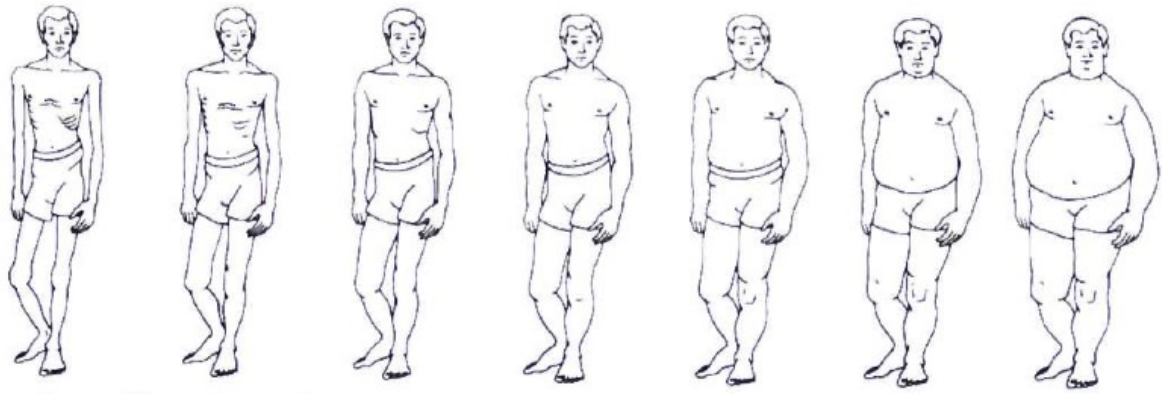
Adolescent Body Rating Scale: Collins[153]' Figure Drawings

Girls



1 2 3 4 5 6 7

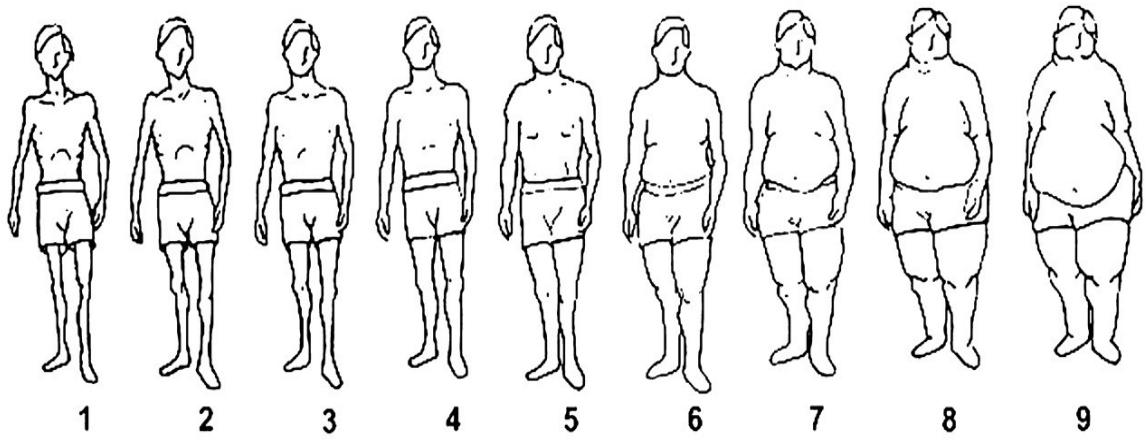
Boys



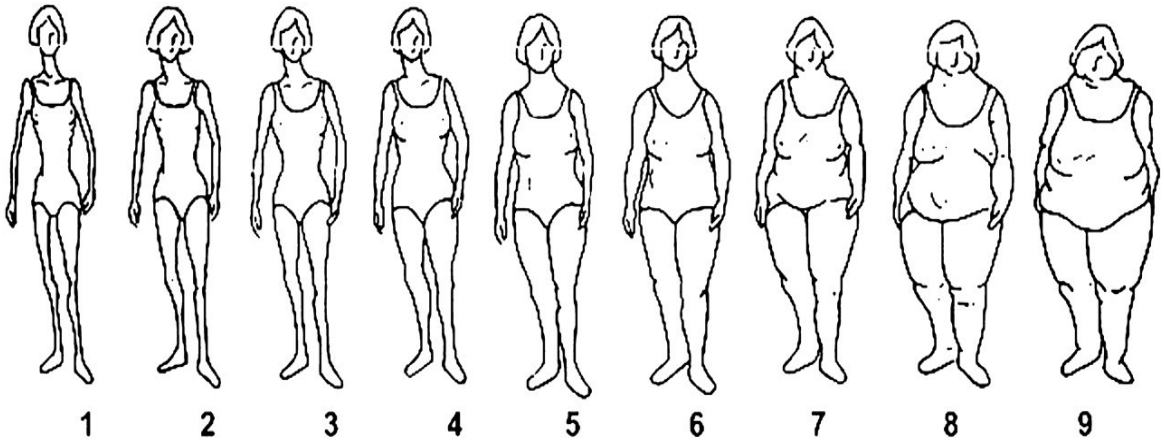
1 2 3 4 5 6 7

Adulthood Body Rating Scale: Stunkard[185] Body Rating Scale

Men



Women



Appendix B: Consent form.

INFORMATION AND CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Study Title:

Acute and Chronic Effects of Obesity

Researcher:

Sylvia Santosa, PhD

Assistant Professor

Department of Exercise Science

Researcher's Contact Information:

Science Pavilion165.21

Concordia University

7141 Sherbrooke Street West

Montreal, QC H4B 1R6

514.848.2424 ex. 5841

s.santosa@concordia.ca

Source of funding for the study:

Heart and Stroke Foundation of Canada

You are being invited to participate in the research study mentioned above. This form provides information about what participating would mean. Please read it carefully before deciding if you want to participate or not. If there is anything you do not understand, or if you want more information, please ask the researcher.

A.**PURPOSE**

You have been invited to take part in a study on aging, fat tissue risk factors for disease, and weight loss. By participating, you will help us to better understand whether weight loss changes disease risk differently depending on the age when a person becomes overweight.

B.**PROCEDURES**

Your involvement in the study will last about 6 months or shortly after you lose around 10% of your starting body weight. The description below provides a general outline of the study protocol. Please note that there may be times where assessments and sample collection (e.g. a blood draw) occur outside of the usual timeline for reasons such as scheduling conflicts.

Screening

□*Maximum of 2 visits of up to 1.5 hours each*

The screening process will determine whether you are eligible for the study and will provide information for designing your weight loss protocol.

Information Session. You will meet with members of the research staff to discuss the study and have your questions answered. If you agree to enter the study, you will sign the consent form and provide a picture and medical records of height and weight from childhood. You will also be asked to review and sign a behavioural contract agreeing to do your best to engage fully in the research project.

Interview and Health Assessment. You will be asked to arrive after an overnight fast (no food for at least 8 hours before visit; water only). You will be interviewed about your medical history, weight history and diet. The health assessment will include a fasted blood draw, urine collection, and measurement of blood pressure, heart rate, weight and height. Please note that the health assessment will be repeated during the post-weight loss stabilization period.

Questionnaires. You will be asked to complete questionnaires about your health, eating behaviour, and quality of life. Please note that these questionnaires will be repeated during the post-weight loss stabilization period.

Pre- and Post-Weight Loss Stabilization Periods

At least 4 visits of 5-10 minutes each over 2 weeks

You will be instructed to follow your usual diet to maintain a stable weight for 2 weeks both before and after the weight loss protocol. To ensure that you are weight stable, you will be weighed after fasting for at least 8 hours at least twice a week. You will also record your food intake for 3 days (2 weekdays and 1 weekend day).

Weight Loss Protocol

Several visits a week for approximately 5 months

During this period you will lose weight by diet and exercise. You will be instructed on how to decrease the amount of calories you eat in your diet by 20 % and increase the number of calories you burn by 10 % through moderate intensity exercise. You will be required to keep a paper-based record of your daily diet. You will also be required to wear a small physical activity monitor, similar to a step counter, periodically throughout the study. All exercise will be performed on cardio equipment at the study site at a self-selected frequency (2-4 visits) that will meet your weekly target. In addition, your weight will be measured and your weight loss progress will be monitored on a weekly basis. Monthly educational or support group sessions will also be conducted. *You will follow the weight loss protocol until you lose around 10 % of your starting body weight, which is estimated to take approximately 5 months.*

Assessments

Approximately 3-4 morning visits per time point

You will have assessments at the following 3 time points:

(1) Towards the end/after pre-weight loss stabilization period

(2) 12-weeks after starting weight loss protocol

(3) Towards the end/after post-weight loss stabilization period

The following assessments will be conducted at time points (1), (2) and (3):

Fitness Assessment. The fitness assessment will involve 3 tests.

You will undergo a submaximal fitness test. You will pedal on a stationary bike for approximately 15 minutes. Throughout this time, the resistance will be gradually increased, and your heart rate and blood pressure will be periodically assessed.

You will perform a shuttle run/walk test. You will run/walk back and forth between two lines in time with an audio 'beep'. The period of time required to reach the line will get progressively shorter. The test will end when you can no longer continue or when you do not reach the line before the 'beep' on 2 consecutive occasions.

You will perform a handgrip test. You will squeeze your fist for 10-15 seconds around a device that measures your strength. The test will be repeated 3 times per hand with at least 30 seconds rest between each test.

Body Composition Assessment *by Dual Energy X-ray Absorptiometry (DEXA).* For the DEXA scan you will be positioned on the table and be asked to lie still as the DEXA arm passes over you. Total scan time is usually about 15 minutes.

Circumference Measurements. The circumferences of different parts of your body (e.g. waist, hip, chest, arm, thigh) will be measured with a measuring tape.

Energy Expenditure Assessment *by Indirect Calorimetry.* You will arrive after an overnight fast of at least 8 hours and will rest comfortably for 2 hours before the test. You will breathe normally under a clear, plastic canopy for around 30 minutes while lying down. This will allow us to measure the rate at which your body burns calories (your energy expenditure). Information from this assessment will help us determine how many calories you need to maintain weight or to lose weight at a certain rate.

Blood Draw. Your blood will be drawn after an overnight fast of at least 8 hours.

The following assessments will be conducted at time points (1) and (3) only:

Body Composition Assessment by Computed Tomography (CT). If you are female, a urine pregnancy test will be conducted prior to this test to ensure you are not pregnant. During this test, you will lie on a table that will be passed through a large, open circular tube. The CT

machine will take pictures of your abdomen. The scan takes approximately 5-10 minutes to complete.

Arterial Measurement. The hardening of your arteries will be measured while you are resting using a pen-like pressure sensor that will be placed on your skin on top of your pulse at three sites (wrist, neck, and crease of the leg).

Biopsies. You will be asked to arrive after an overnight fast (water only after midnight). You will also be asked to not consume caffeine or alcohol for at least 24 hours prior to this visit. Strenuous exercise should also be avoided for at least 24 hours before the procedure.

Fat. A sample will be taken from the fat in your stomach and thigh region. The procedure involves cleaning the skin to remove any germs, numbing the skin by injecting a local anesthesia (to freeze the area) with a thin needle, making a small nick incision and then removing the fat just below the skin. To remove the fat, a small hollow tube attached to a syringe will be used to suction out a small amount of fat tissue underneath your skin. The procedure will not require stitches, as the incisions are small; the physician will simply place sterile tape to close the incision. After the biopsies are done, post-biopsy care will be explained and you will be provided with written instructions.

Muscle. A sample will be taken from the muscle on the outside side of your thigh. The procedure involves cleaning the skin to remove any germs, numbing the skin by injecting a local anesthesia (to freeze the area) with a thin needle, and making a small incision. A needle (hollow tube) will be inserted to remove a small piece of muscle. The procedure will not require stitches, as the incisions are small; the physician will simply place sterile tape to close the incision. Firm pressure will be applied to the area for 10 minutes to prevent bruising. After the biopsy is done, post-biopsy care will be explained and you will be provided with written instructions.

C. RISKS AND BENEFITS

The risks involved in the research tests are considered to be minimal. The risks are listed below:

Blood Draws. There is a risk of discomfort, pain, fainting, bruising or infection (rare) from the blood draw. The amount of blood drawn at each time point will vary. Total blood drawn throughout the study will not exceed 2 cups (~500 mL). It is recommended that you avoid taking aspirin 3 days before and after the blood draws, and that you don't donate blood for up to 8 weeks following your participation in the study.

- ***Fat and Muscle Biopsies***. The most common risks of fat and muscle biopsies include pain, a small dent or bump and bruising at the site where the sample was taken. The bruising may last one to two weeks. Less common risks of biopsies include bleeding, infection, a small scar, and numbness of the skin around the biopsy site. The chance of these risks is less than 1% (1 in 100). There is also a chance of an allergic reaction to the lidocaine used for local anaesthesia. Care will be taken to reduce the chances of these risks. Aspirin should be avoided 3 days before and after the biopsies. It is not advised to participate in any vigorous activities for 3 days before and after the biopsies. Exposure to water for prolonged periods should be avoided (e.g bathtubs, hot tubs or swimming) for 5 days after the biopsies. Showering is permitted, however band-aids must be changed afterwards. Normal daily activities will not be affected.

- ***Indirect Calorimetry***. There is a slight risk of discomfort and hyperventilation from claustrophobia when under the clear, plastic hood. Staff will be present and the hood is easily removable.

- ***DEXA and CT Scans***. You will be exposed to some radiation with the DEXA and CT scan. The amount of radiation used is considered too low to cause any harmful side effects. Radiation exposure from the DEXA scan is similar to the amount you would receive from sun exposure on a sunny day ($1/10^{th}$ that of a chest x-ray). The amount of radiation you are exposed to from the CT scan is less than your exposure from one return transatlantic plane flight (about 2-3 chest x-rays). The radiation does not remain in the body after the scan. Should you have any concerns, the research team will be happy to address them with you.

- ***Fitness Test and Exercise***. You may experience some discomfort from physical exertion during the fitness test and the exercise component of the weight loss protocol.

Your assessments will be supervised by experienced research staff who will make every effort to keep you comfortable during the study.

Although the assessments conducted as part of this protocol are not expected to provide you with any direct benefits, the results will tell you more about your health and metabolism and you may see positive changes in your health during weight loss.

D. **CONFIDENTIALITY**

We will gather the following information as part of this research: demographic information, contact information, and the results of all study procedures described above.

We will not allow anyone to access the information, except people directly involved in conducting the research, and except as described in this form. We will only use the information for the purposes of the research described in this form.

To verify that the research is being conducted properly, regulatory authorities such as Health Canada might examine the information gathered. By participating, you agree to let these authorities have access to the information.

The information gathered will be coded. That means that the information will be identified by a code. The researcher will have a list that links the code to your name.

All of your paper-based information will be kept in a filing cabinet in a secure and private research office. All of your electronic information will be stored on a password-protected research computer. The urine, blood, fat and muscle samples will be coded and safely stored for analyses at Concordia University.

We intend to publish the results of the research. However, it will not be possible to identify you in the published results.

E. **BIOLOGICAL SAMPLES**

You will be asked to provide the following biological samples as part of the research: urine, blood, fat and muscle.

Taking these specimens involves urinating into a plastic container, blood draws, and fat and muscle biopsies as described in the procedures section above.

We will use your urine sample to assess your overall health with a standard urinalysis, and to do a pregnancy test for female participants. We will use your blood samples to measure things like sugar, cholesterol and inflammatory markers. We will use the biopsy samples to assess the

health of your fat and muscle. This includes things like the size of your fat cells, the amount and type of inflammatory markers in your fat, and how well your muscle uses energy.

We will keep the specimens for up to 25 years after the end of the study. After that, they will be destroyed.

If we find anything that might be relevant to your health, we will contact you and direct you to the appropriate service.

F.**CONDITIONS OF PARTICIPATION**

You do not have to participate in this research. It is purely your decision. If you do participate, you can stop at any time. In addition, the research team may withdraw you from the study if you are not compliant.

As a compensatory indemnity for participating in this research, you will receive $500. If you withdraw before the end of the research, you will receive an amount proportional to the time you spent in the study, as assessed by the research team. To make sure that research money is being spent properly, auditors from Concordia or outside will have access to a coded list of participants. It will not be possible to identify you from this list.

We will tell you if we learn of anything that could affect your decision to stay in the research.

There are no negative consequences for not participating, stopping in the middle, or asking us not to use your information.

We will not be able to offer you compensation if you are injured in this research. However, you are not waiving any legal right to compensation by signing this form.

G. **PARTICIPANT'S DECLARATION**

I have read and understood this form. I have had the chance to ask questions and any questions have been answered. I agree to participate in this research under the conditions described.

NAME (please print) _____

SIGNATURE _____

DATE _____

If you have questions about the scientific or scholarly aspects of this research, please contact the researcher. Their contact information is on page 1.

If you have concerns about ethical issues in this research, please contact the Manager, Research Ethics, Concordia University, 514.848.2424 ex. 7481 or oor.ethics@concordia.ca.

Appendix C: Par-Q Questionnaire

Physical Activity Readiness Questionnaire - PAR-Q (revised 2002)

PAR-Q & YOU

(A Questionnaire for People Aged 15 to 69)

Regular physical activity is fun and healthy, and increasingly more people are starting to become more active every day. Being more active is very safe for most people. However, some people should check with their doctor before they start becoming much more physically active.

If you are planning to become much more physically active than you are now, start by answering the seven questions in the box below. If you are between the ages of 15 and 69, the PAR-Q will tell you if you should check with your doctor before you start. If you are over 69 years of age, and you are not used to being very active, check with your doctor.

Common sense is your best guide when you answer these questions. Please read the questions carefully and answer each one honestly: check YES or NO.

YES	NO	
☐	☐	1. **Has your doctor ever said that you have a heart condition and that you should only do physical activity recommended by a doctor?**
☐	☐	2. **Do you feel pain in your chest when you do physical activity?**
☐	☐	3. **In the past month, have you had chest pain when you were not doing physical activity?**
☐	☐	4. **Do you lose your balance because of dizziness or do you ever lose consciousness?**
☐	☐	5. **Do you have a bone or joint problem (for example, back, knee or hip) that could be made worse by a change in your physical activity?**
☐	☐	6. **Is your doctor currently prescribing drugs (for example, water pills) for your blood pressure or heart condition?**
☐	☐	7. **Do you know of any other reason why you should not do physical activity?**

If you answered

YES to one or more questions

Talk with your doctor by phone or in person BEFORE you start becoming much more physically active or BEFORE you have a fitness appraisal. Tell your doctor about the PAR-Q and which questions you answered YES.

- You may be able to do any activity you want — as long as you start slowly and build up gradually. Or, you may need to restrict your activities to those which are safe for you. Talk with your doctor about the kinds of activities you wish to participate in and follow his/her advice.
- Find out which community programs are safe and helpful for you.

NO to all questions

If you answered NO honestly to all PAR-Q questions, you can be reasonably sure that you can:

- start becoming much more physically active – begin slowly and build up gradually. This is the safest and easiest way to go.
- take part in a fitness appraisal – this is an excellent way to determine your basic fitness so that you can plan the best way for you to live actively. It is also highly recommended that you have your blood pressure evaluated. If your reading is over 144/94, talk with your doctor before you start becoming much more physically active.

DELAY BECOMING MUCH MORE ACTIVE:

- if you are not feeling well because of a temporary illness such as a cold or a fever – wait until you feel better; or
- if you are or may be pregnant – talk to your doctor before you start becoming more active.

PLEASE NOTE: If your health changes so that you then answer YES to any of the above questions, tell your fitness or health professional. Ask whether you should change your physical activity plan.

Informed Use of the PAR-Q: The Canadian Society for Exercise Physiology, Health Canada, and their agents assume no liability for persons who undertake physical activity, and if in doubt after completing this questionnaire, consult your doctor prior to physical activity.

No changes permitted. You are encouraged to photocopy the PAR-Q but only if you use the entire form.

NOTE: If the PAR-Q is being given to a person before he or she participates in a physical activity program or a fitness appraisal, this section may be used for legal or administrative purposes.

"I have read, understood and completed this questionnaire. Any questions I had were answered to my full satisfaction."

NAME _____

SIGNATURE _____ DATE _____

SIGNATURE OF PARENT or GUARDIAN (for participants under the age of majority) _____ WITNESS _____

Note: This physical activity clearance is valid for a maximum of 12 months from the date it is completed and becomes invalid if your condition changes so that you would answer YES to any of the seven questions.

Supported by: Health Canada Santé Canada

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Appendix D: Normative table for YMCA bike test.

HEART RATE AND LOADING SEQUENCE FOR THE CYCLE ERGOMETER TEST

1st workload (3 minutes)	150 kpm·minute^{-1} (0.5 kp or 25W)			
	Heart Rate for the last minute of the 1st workload determines subsequent workloads			
	HR<80 bp	*HR = 80-89 bpm*	*HR = 90-100 bpm*	*HR>100 bpm*
2nd workload	750 kpm·min^{-1} (2.5 kp or 125W)	600 kpm·min^{-1} (2.0 kp or 100W)	450 kpm·min^{-1} (1.5 kp or 75W)	300 kpm·min^{-1} (1.0 kp or 50W)
3rd workload	900 kpm·min^{-1} (3.0 kp or 150W)	750 kpm·min^{-1} (2.5 kp or 100W)	600 kpm·min^{-1} (2.0 kp or 100W)	450 kpm·min^{-1} (1.5 kp or 75W)
4th workload	1050 kpm·min^{-1} (3.5 kp or 175W)	900 kpm·min^{-1} (3.0 kp or 150W)	750 kpm·min^{-1} (2.5 kp or 125W)	600 kpm·min^{-1} (2.0 kp or 100W)
Additional workloads	*If additional workloads are required to achieve within 10 bpm of 85%HRmax, add 150 kpm·min^{-1} (0.5 kp or 25W) to the previous workload*			

ESTIMATED VO_2MAX - HEALTH BENEFIT RATING

Select the appropriate age and gender column to locate the client's score and record the associated Health Benefit Rating on the Client Information Sheet for discussion in Step 3.

Age	Zone	Male	Female	Age	Zone	Male	Female
15-19	Excellent	57.4+	49.0+	40-49	Excellent	47.0+	40.0+
	Very Good	52.4-57.3	43.7-48.9		Very Good	42.7-46.9	35.1-39.9
	Good	48.8-57.3	39.5-43.6		Good	35.5-42.6	31.9-35.0
	Fair	43.6-48.7	36.8-39.4		Fair	31.9-35.4	27.1-31.8
	Poor	<43.6	<36.8		Poor	<31.9	<27.1
20-29	Excellent	55.6+	47.2+	50-59	Excellent	41.8+	36.6+
	Very Good	50.6-55.5	42.0-47.1		Very Good	36.5-41.7	34.0-36.5
	Good	47.2-50.5	37.8-41.9		Good	30.1-36.4	31.0-33.9
	Fair	41.6-47.1	35.0-37.7		Fair	26.0-30.0	24.6-30.9
	Poor	<41.6	<35.0		Poor	<26.0	<24.6
30-39	Excellent	48.8+	45.4+	60-69	Excellent	38.4+	35.8+
	Very Good	45.4-48.7	40.1-45.3		Very Good	32.8-38.3	32.8-35.7
	Good	40.1-45.3	36.0-40.0		Good	28.7-32.7	29.6-32.7
	Fair	33.7-40.0	33.0-35.9		Fair	23.5-28.6	23.5-29.5
	Poor	<33.7	<33.0		Poor	<23.5	<23.5

Appendix E: Normative table for Hand grip strength.

Grip Strength

Hand grip is a measure of isometric strength and is a widely used indicator of total body strength. It has been shown to be predictive of functional limitations and disability later in life. Good muscle strength in midlife may protect people from old age disability by providing a greater safety margin above the threshold of disability. *(Rantanen et al., 1999)*

EQUIPMENT

- ☐ Hand Dynamometer

INSTRUCTIONS

Ask the client to grasp the grip between the fingers and palm at the base of the thumb.

Adjust the grip so the second joint of the fingers fits snugly under the handle and takes the weight of the instrument. Lock the grip in place.

Have the client hold the dynamometer in-line with the forearm at the level of the thigh, away from the body. (See illustration.)

Place a marker on the wall and ask the client to concentrate on it as they squeeze maximally on the hand dynamometer to exert maximal force. Have the client exhale while squeezing (to avoid build-up of intrathoracic pressure).

Neither the hand nor the dynamometer should touch the body or any other object.

Measure each hand twice, alternating hands. Record the maximum scores for each hand to the nearest kilogram.

SCORING AND RECORDING

Combine the maximum scores from each of the left and right hands.

Record the result and associated Health Benefit Rating (from the table below) on the Client Information Sheet.

CONVERTING THE GRIP STRENGTH SCORE (KILOGRAMS) TO A HEALTH BENEFIT RATING

AGE	ZONE	MALE	FEMALE	AGE	ZONE	MALE	FEMALE
15-19	Excellent	≥108	≥68	40-49	Excellent	≥108	≥69
	Very Good	98-107	60-67		Very Good	97-107	61-68
	Good	90-97	53-59		Good	88-96	54-60
	Fair	79-89	48-52		Fair	80-87	49-53
	Poor	≤78	<47		Poor	≤79	≤48
20-29	Excellent	>115	≥70	50-59	Excellent	≥101	≥61
	Very Good	104-114	63-69		Very Good	92-100	54-60
	Good	95-103	58-62		Good	84-91	49-53
	Fair	84-94	52-57		Fair	76-83	45-48
	Poor	<83	<51		Poor	<75	≤44
30-39	Excellent	≥115	≥71	60-69	Excellent	≥100	>54
	Very Good	104-114	63-70		Very Good	91-99	48-53
	Good	95-103	58-62		Good	84-90	45-47
	Fir	84-94	51-57		Fair	73-83	41-44
	Poor	≤83	≤50		Poor	≤72	≤40