

**THE IMPORTANCE OF RISK STRATIFICATION AND  
CARDIORESPIRATORY FITNESS IN PEDIATRIC OBESITY**

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## Abstract

*Ninety-four children (age 8-17 yrs; BMI  $\geq$  95<sup>th</sup> percentile) were staged according to their risk profile in manuscript one by the Edmonton Obesity Staging System for Pediatrics (EOSS-P) based on metabolic, mechanical, mental and/or family risk factors. Children completed a maximal treadmill test yielding  $VO_2$ peak data (mlO<sub>2</sub>/kg/min). Children were stratified into three groups: (Stage 1 n=28; Stage 2 n=47; Stage 3 n=19).  $VO_2$ peak was significantly lower in Stage 3 ( $p = 0.02$ ) compared to Stages 1 and 2. Children were re-stratified into three groups for manuscript two without the family category of the EOSS-P applied: Low Risk (LR) (n=40); Elevated Risk (ER) (n=45); and High Risk (HR) (n=9).  $VO_2$ peak was significantly lower in the HR group ( $p = 0.04$ ) compared to the LR group. Stage 3/HR children (highest risk category) in both manuscripts displayed the lowest levels of cardiorespiratory fitness, suggesting an increased risk for complications associated with pediatric obesity.*

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## Co-Authorship

This thesis presents the work of Mr. Kevin Belanger in collaboration with his Thesis Supervisor, Dr. Kristi B. Adamo, and contributions from the following co-authors: Dr. Katherine Baldwin; Dr. Geoff D.C. Ball; Dr. Annick Buchholz; Dr. Stasia Hadjiyannakis; and Ms. Jane Rutherford.

**Manuscript 1:** *Children's cardiorespiratory fitness varies between stages of the Edmonton Obesity Staging System for Pediatrics (EOSS-P).* Dr. Adamo, Kevin Belanger and all aforementioned authors were responsible for the initialization and conceptualization of this project. The fitness testing, statistical analysis, interpretation of results, and writing of the manuscript were performed by Kevin Belanger. All authors reviewed and agreed to the finalized content of this manuscript. This manuscript has been formatted and will be submitted to the *International Journal of Obesity*.

**Manuscript 2:** *Identifying influential categories of the Edmonton Obesity Staging System for Pediatrics and their relationship with cardiorespiratory fitness in children with obesity.* Dr. Adamo, Kevin Belanger, Dr. Hadjiyannakis and Ms. Rutherford were responsible for the initialization and conceptualization of this project. The fitness testing, statistical analysis, interpretation of results, and writing of the manuscript were performed by Kevin Belanger. All authors reviewed and agreed to the finalized content of this manuscript. This manuscript has been formatted and will be submitted to the journal *BMC Pediatrics*.

The Introduction, Literature Review, General Discussion and Appendices were completed by Kevin Belanger. The final content of this thesis was complemented by suggestions and editorial comments from Dr. Adamo.

## **Statement of Originality**

I hereby certify that all of the work described within this thesis is the original work of the author. Any published (or unpublished) ideas and/or techniques from the work of others are fully acknowledged in accordance with the standard referencing practices.

Kevin Belanger

January, 2014

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## **Thesis Organization and Presentation**

The following Master of Science conforms to the regulations provided by the University of Ottawa, Faculty of Health Sciences, School of Human Kinetics. This thesis commences in Chapter 1 with a general overview of pediatric obesity. Chapter 2 provides a current review of the literature for topic areas related to this thesis (Pediatric Obesity, Body Mass Index, Cardiorespiratory Fitness), followed by the objectives and hypotheses for this thesis. Chapter 3 presents the first prepared manuscript entitled, “Children’s cardiorespiratory fitness varies between stages of the Edmonton Obesity Staging System for Pediatrics (EOSS-P).” This manuscript will be submitted to the *International Journal of Obesity* and has been formatted to the journal’s requirements. Chapter 4 contains the second prepared manuscript entitled, “Identifying influential categories of the Edmonton Obesity Staging System for Pediatrics and their relationship with cardiorespiratory fitness in children with obesity.” This manuscript will be submitted to the journal *BMC Pediatrics* and has been formatted to the journal’s requirements. Chapter 5 provides the reader with a global discussion of the findings obtained from the two projects, suggests possible implications from the research performed, and conclusions from the research and topic areas. This thesis will finish with Chapter 6, which outlines the contribution from the lead author of this thesis and aforementioned projects, as well as contributions from co-authors involved in both projects.

## **Ethical Considerations and Safety Issues**

There was little to no risk for the children who participated in the two projects. Children who participated in the maximal cardiorespiratory fitness test may have benefited from the objective feedback surrounding their aerobic fitness levels. In the unlikely event that children would experience an injury or encounter a medical/psychological crisis during the fitness test, a safety protocol was in place that alerts emergency response support from the hospital. All fitness tests were performed at the Children's Hospital of Eastern Ontario under the supervision of two certified exercise physiologists with up to date CPR and First Aid certifications. There was no risk for the application of the EOSS-P staging tool, as it was a retrospective medical chart review performed by two clinicians. The retrospective chart review for projects one and two were approved by the Children's Hospital of Eastern Ontario's Research Ethics Board and the University of Ottawa Research Ethics Board respectively.

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## **List of Abbreviations**

BMI: Body Mass Index

CDC: Centers for Disease Control and Prevention

CHAL: Centre for Healthy Active Living

CHEO: Children's Hospital of Eastern Ontario

CRF: Cardiorespiratory fitness

ER: Elevated Risk Group

EOSS: Edmonton Obesity Staging System

EOSS-P: Edmonton Obesity Staging System for Pediatrics

HR: High Risk Group

IOTF: International Obesity Task Force

LR: Low Risk Group

WHO: World Health Organization

# Chapter 1

## Introduction

### *Overview*

Childhood obesity has solidified itself as a major health concern in both the developed and developing world (1, 2). High prevalence rates of obesity have been identified in Canada amongst children & youth of all ages (3, 4). Recent data has demonstrated that 15.1% of male and 8.0% of female school-aged children are obese in Canada (5). More importantly, the prevalence of childhood obesity has more than doubled in Canadian children from 1979-1980 to Canadian children in 2008 (6).

If untreated, obesity-related risk factors such as sleep apnea (7), cardiovascular disease (8) and type 2 diabetes (9) can develop in children. Furthermore, children struggling with obesity are very likely to carry their excess adiposity into adulthood (10). Non-existent programming or inability to access obesity treatment programs can result in a significant burden on health care costs. Health care costs for children with obesity in Canada are, on average, 21 percent higher than those for children of normal weight (11). Additionally, children with obesity in Canada visit their pediatrician more often than those of healthy weight (11). One potential method to reduce this economic burden would be to have a 'triage' system that would allow clinicians to treat those obese children who are at greatest risk of obesity-related risk factors more aggressively, instead of treating all those who present with a Body Mass Index (BMI) indicative of obesity, a tool known to be less reliable for risk stratification (for more information on BMI limitations, see pg. 11). Thus, it is crucial for clinicians to employ an accurate and detailed form of risk

assessment in children who are screened for obesity and subsequently provide appropriate options for reducing risk and improving health outcomes.

Cardiorespiratory fitness has been shown to be both a key and modifiable health indicator in children and adolescence (14), and there is data to suggest that obese children have poorer physical fitness, more specifically cardiorespiratory fitness, than their normal weight peers (12, 13). Regular physical activity in pediatric populations can serve as a form of protection against chronic diseases (15) and higher levels of cardiorespiratory fitness have been correlated with healthier metabolic profiles in children (16). Therefore, the promotion of cardiorespiratory fitness in obese children can serve as a vital component for the improvement and maintenance of healthy growth and development in youth.

To triage, and ultimately mitigate, the growing trends related to childhood obesity, a more thorough evaluation or screening process is required to identify which children may require clinical care (and to what extent) for their obesity. Prior to expensive and time consuming forms of clinical treatment, health care practitioners should promote regular physical activity to improve or maintain cardiorespiratory fitness in everyone, regardless of body size, in hopes of reducing the likelihood of developing severe medical complications.

## **Chapter 2**

### **Literature Review**

#### *Obesity*

Obesity is characterized by an increase in adiposity over time, and is classified in adults by an individual's BMI (in kg/m<sup>2</sup>) surpassing 30.0 (17, 18). The BMI tool provides an estimation of adiposity through the comparison of an individual's mass in kilograms, divided by his or her height in metres squared (19). Obesity typically stems from a positive energy balance, whereby more calories are consumed than expended (20). Children are also susceptible to obesity, and there are many contributing factors that can lead to its development. For instance, living with an obese parent, having a parent who smokes, and physical inactivity are just some of the many factors associated with pediatric obesity (21).

In nearly half a century, there has been a continuous global rise in prevalence rates of obesity. Obesity in Canadian adults has increased by 70 percent between 1978-2004 (22). This increase in obesity has manifested itself in both male and female Canadian adults, which equates to approximately 23 percent of each sex currently struggling with this disease (23). Moreover, increasing obesity trends have been identified globally, such that approximately 30 percent of American adults are now classified as obese (24). Additional developed countries such as Australia (25), Finland (26), and Portugal (27) have experienced recent marked obesity prevalence increases in both male and female adult populations.

Coupled with the global increase in obesity prevalence is the number of bariatric surgeries performed. In 2004, the number of bariatric surgeries in the United States peaked at 64 operations per 100,000 U.S. citizens (28). The increase in the amount of

bariatric procedures performed over time suggests, and potentially reinforces, that more individuals are attaining higher classifications of obesity. Individuals receiving bariatric surgery have a greater risk of developing obesity-related co-morbidities (29), which demonstrates the tremendous threat that obesity can pose on population health and wellness.

From a clinical standpoint, obesity is directly related to numerous risk factors and co-morbidities that can threaten the human body. For instance, developing obesity increases the diagnostic risk of cardiovascular disease (8, 30), Type 2 Diabetes (9, 30-32), hypertension (33-35), sleep apnea (7, 36), lipid disorders (37-39), and numerous types of cancer (40), notably breast, colon, rectum and prostate cancer (41). Obesity can also harm an individual's musculoskeletal system. Obese individuals can experience fractures of the acetabulum (42), tibia (43), and slipped capital femoral epiphyses (44) from carrying excess weight. Additionally, obesity can threaten the psychological well-being of an individual. For example, in comparison to the non-obese population, adults with obesity display higher levels of depression (45-47), diminished quality of life (48-50), and lower self-esteem (51, 52). In 1999, it was estimated that obesity was responsible for 280,000-325,000 deaths per year in the United States (53). The aforementioned co-morbidities, diseases and risk factors are just some of the conditions that can reduce the life expectancy of obese adults.

In a public health care system, such as in Canada, preventable diseases, like obesity, put a tremendous strain on much needed health care resources. Total direct costs of obesity in 1997 were estimated to be over 1.8 billion dollars (54). Just recently, Katzmarzyk and Janssen (55) published an analytical review on the economic burden that

obesity has on Canada. It was reported that, in 2001, obesity constituted 4.3 billion dollars in health care expenditures (1.6 billion in direct costs; 2.7 billion in indirect costs) in Canada (55). Obesity, in turn, equated to 2.2% of total health care costs in Canada at this time (54). Furthermore, as it has been shown that obesity is associated with multiple risk factors and chronic diseases, it is no surprise that coronary artery disease, hypertension and osteoarthritis accounted for 1.3 billion, 979 million and 881 million dollars respectively in obesity related treatment (55). Additionally, obesity is estimated to comprise 2-7% of total health care costs in countries around the world (56), supporting the trends seen in Canada.

Despite the ever growing attention that obesity receives from scientific, medical and social communities worldwide, it is important to recognize that poor lifestyle habits are suggested to be the major driving forces behind obesity's increased prevalence. The current obesogenic environment is in desperate need of modification to promote healthier lifestyle habits in order to combat high obesity rates.

## *Pediatric Obesity*

While obesity is well established as a significant health concern in adult populations, pediatric obesity has also been referred to as a global epidemic. The World Health Organization has reported that pediatric obesity is the most prevalent, non-communicable disease in developed countries (57). Consistent with adulthood obesity, children struggling with pediatric obesity are prone to obesity-related risk factors and chronic diseases at crucial periods of development (58). Pediatric obesity is of utmost importance for clinicians, health policy makers and government officials as it is probable that obese children will continue to carry extra weight through their developmental stages and progress into obese adults (10).

Despite its status as a well-developed country, Canada is not immune to the global rises in pediatric obesity and has some of the world's highest pediatric obesity rates (59-63). Currently, it is estimated that 15.1% of male and 8.0% of female school-aged children in Canada meet WHO criteria for obesity (5). Similarly, in 2002 it was estimated that 16 percent of American children were classified as obese according to CDC criteria (64). Internationally, England (65), Italy (66) and Australia (67) have reported recent increases in the prevalence of pediatric obesity using IOTF guidelines for obesity.

Although there are a plethora of factors contributing to the development of pediatric obesity, poor lifestyle tendencies, namely high levels of sedentary behaviour and unhealthy nutritional habits, may be more notable and modifiable contributors. For instance in 2010, 88% of Canadian children, did not engage in enough physical activity to receive health benefits (60 min. physical activity/day) (59). In 2012, this percentage increased with 93% of children failing to meet Canadian physical activity guidelines (60).

Habitual decreases in energy expenditure, combined with increases in energy intake, can lead to undesired weight gain, and even obesity (61, 62). Albeit not the only determinants, these modifiable contributors are the proverbial ‘low hanging fruit’ and the most notable targets for reducing the growing prevalence of obesity.

Comparable with adulthood obesity, pediatric obesity is highly associated with numerous risk factors and health conditions (68, 69). Children with obesity are more prone to developing type 2 diabetes (70-74), sleep apnea (75), lipid disorders (76-78), hypertension (79), and musculoskeletal impairments (80). Without intervention, these risk factors can be further compounded by progressing into additional chronic disease, such as cardiovascular disease (81-83) and various forms of cancer (84). Moreover, there are numerous psychological issues that can further complicate pediatric obesity treatment and intervention. Obese children are more commonly affected by depression (85, 86), low self-esteem (51, 52) and reduced quality of life (87, 88) than their lean counterparts. Furthermore, it is reported that obese children are stigmatized and bullied more frequently than their normal weight peers (89-91). These physiological and psychological risk factors may elicit serious consequences on children that are at a crucial stage of development, and can potentially lead to a maladjusted adulthood.

Congruent with adulthood obesity, pediatric obesity has also taken its toll on Canada’s health care system (54, 55). Considering that children and adolescents with obesity typically continue their high level of adiposity into adulthood (92), the financial strain on Canada’s public health care system becomes even more amplified. It is thus imperative that children with weight management issues are accurately screened for

severity and complications in order to appropriately triage those resources allocated for pediatric obesity.

### ***Body Mass Index and its Limitations in Classifying Pediatric Obesity***

Body Mass Index (BMI) is the most universally accepted measure used to classify obesity (93). BMI is a measure of weight relative to height; however, it is not a direct measure of adiposity (94). The relationship between BMI and adiposity varies by age, sex, race and ethnicity and therefore risk related cut-offs may also vary. While BMI tends to correlate with percent body fat, it is also associated with muscle and lean mass as well as height within age groupings (95).

In adults, obesity is defined as a BMI greater than or equal to  $30 \text{ kg/m}^2$  (17, 18), a value that epidemiological evidence has related to health risk (96). For children BMI varies with age and sex and therefore must be compared with reference values that are age and sex specific. A BMI Z-score or a BMI percentile represents a measure of weight, adjusted for height, sex and age relative to a smoothed reference distribution. Pediatric obesity is defined as a BMI for age and sex  $\geq 95^{\text{th}}$ % of the Centers for Disease Control and Prevention (CDC) reference population (97) or a Z-score of  $> 3$  based on the World Health Organization (WHO) reference population (98). Similarly, the International Obesity Task Force (IOTF) has provided cut-off values for defining obesity; however, the IOTF used an international sample whereby the goal was to provide a harmonized definition of pediatric obesity so descriptive comparisons could be made by researchers and policy makers around the globe (99). Despite its popularity in clinical practice, these cut-points are statistically based; therefore, it is possible for children with a BMI over these cut-points to have an absence of clinical complications or health risks related to

their weight. Therefore, solely using body mass index to screen for obesity-related risk factors in overweight children may not prove to be feasible.

### ***Edmonton Obesity Staging System***

Anthropometric measures do not reflect the presence of underlying obesity related co-morbidity, quality of life or functional limitations (100). The Canadian health practitioner community has identified that more comprehensive criterion must be considered in order to adequately screen for health risks associated with obesity and have subsequently proposed the development of a clinically applicable tool to assist in this screening

The recently developed Edmonton Obesity Staging System (EOSS) is a clinical staging system that ranks obese adults on a 5-point ordinal scale that incorporates obesity related co-morbidities and functional status into the assessment (see Appendix 1). EOSS scores were a strong predictor of mortality in adults, independent of BMI with clear separation of survival curves according to score (101, 102). Individuals with EOSS stage 0 and 1 had no difference in all-cause mortality risk when compared with normal weight individuals. Individuals with EOSS stage 2 and 3 had higher relative risk for all-cause mortality, whereas an individual with an EOSS stage of 4 would require intensive treatment (101). Although the EOSS does not provide a direct measure of adiposity, it does provide a more detailed assessment of the obese individual, which can help clinicians with their prognosis. An EOSS stage of 0 and 1 would typically delineate weight maintenance and promotion of health behaviours, rather than weight loss. EOSS scores of 2, 3 and 4 would require more medical intervention, as there are more obesity-related risk factors and chronic disease present. This staging system, in turn, can help to

ration health care resources, as Stage 0 and 1 individuals would not require as many follow-up evaluations due to a subsequent lower risk level.

***Proposed Functional and Disease Related Staging for Obesity: Edmonton Obesity Staging System for Pediatrics***

Using anthropometric measurements exclusively to classify obesity poses more limitations in children than in adults. Therefore, a staging system similar to the EOSS could provide information and guide clinicians in their evaluation and management of pediatric obesity.

This proposed pediatric staging system (see Appendix 2), like the EOSS, is based on simple clinical assessments that include a medical, mental health, functional and social history as well as routine diagnostic evaluations that are easily and widely available (103). Unique in this pediatric staging system is an assessment of family functioning in order to provide additional information on the obese child's health status (104). The thorough use of this proposed staging system, the Edmonton Obesity Staging System for Pediatrics (EOSS-P), could aid clinicians in their appraisal of obese children. This tool could appropriately stratify obese children based on either an absence (Stage 0) or presence of obesity-related risk factors (Stages 1-3), and ultimately yield more detailed treatment options. However, the EOSS-P differs from the adult form of this tool, since mortality is not a typical primary outcome in a pediatric population. Other markers of health, such as cardiorespiratory fitness, may be more appropriate for children.

### *The Importance of Cardiorespiratory Fitness in Children and Adolescents*

Cardiorespiratory fitness (CRF), also known as aerobic fitness or cardiovascular fitness, is defined as the maximum ability of the human body to transport and consume oxygen ( $\text{VO}_2\text{max}$ ) during sustained aerobic work (105). A comprehensive review by Ortega et al. (106) demonstrated that CRF is a valuable health indicator in children and adolescents. Children with a higher level of CRF were found to have lower total adiposity (107), an association also identified in children who were overweight or obese (108) - illustrating the importance of CRF independent of body mass index status. Furthermore, numerous studies on children and adolescents (109, 110) have found an inverse association between CRF and cardiovascular disease risk. Improvement in CRF has also been associated with better mental health and well-being in children and adolescents, namely self-esteem and depression status (111). Thus, CRF is a modifiable health indicator that can serve as a strong surrogate of health in children and adolescents.

Given that obesity is characterized by a greater than average increase in adiposity over time (18), it is critical for this population to engage in healthy living behaviours, namely regular physical activity and a reduction in sedentary behaviours, in order to modify obesity-related risk factors. Regular bouts of moderate to vigorous physical activity in youth are associated with improved levels of cardiorespiratory fitness (112). Addressing and improving cardiorespiratory fitness in children with pediatric obesity may lead to the development of healthy habits and consequently healthier tendencies as these individuals continue into adulthood. Ultimately, the importance of cardiorespiratory fitness as a modifiable risk factor requires more emphasis when addressing the epidemic of pediatric obesity.

### *Cardiorespiratory Fitness in Children with Obesity*

The evaluation of cardiorespiratory fitness as a health indicator is gradually gaining acceptance as an important component in pediatric obesity assessment and management. However, measuring cardiorespiratory fitness in a population of obese children may be challenging for exercise physiologists unfamiliar with the complexities of obesity. It has been widely demonstrated that obese children have poorer maximal fitness levels than their normal weight peers, given the increased effort required to move a larger mass (113). Maximal aerobic exertion ( $VO_{2max}$ ) is seldom attained in untrained individuals, thus,  $VO_{2peak}$  is commonly used as a default.  $VO_{2peak}$  is the highest observed amount of oxygen consumed by the body during exercise; however, it is not the individual's true maximum as oxygen consumption does not plateau when at a maximal workload (114) (Figure 1). Recently, Breithaupt et al. (115) found that only 18 in a sample of 62 children with obesity were able to attain a true  $VO_{2max}$ . Furthermore, compared to a lean population obese individuals demonstrate lower levels of muscular endurance and power related movements (116). It has also been suggested that obese children may perceive various intensities of physical exertion differently than their normal weight counterparts (17, 51, 117). Marinov et al. (118) illustrated that obese children rated their perceived exertion, on a standard workload, significantly higher than their normal weight controls.

While children with obesity often present lower fitness levels than desirable, this should be a primary focus for this population as CRF is modifiable and cost-effective. Goran et al. (119) demonstrated that obese children do not have lower maximal aerobic capacity of their fat-free mass compared to their lean counterparts; therefore, children

with obesity are not limited by their musculature when performing exercise. Furthermore, obese children with higher CRF display lower central and total adiposity compared to unfit obese children in the same BMI category (120). While certain factors may limit the efficacy of a maximal fitness test in obese children, the importance of cardiorespiratory fitness should be routinely promoted by health care professionals specializing in obesity.

## *Objectives and Hypotheses*

While pediatric obesity continues to be a major health concern worldwide, there is a growing need in the clinical community for more effective forms of obesity screening and evaluation. In addition to the more traditional use of anthropometric measures to classify pediatric obesity (i.e., BMI, BMI percentiles, BMI z-scores), this thesis contends that other important variables, such as cardiorespiratory fitness (CRF), should be considered for inclusion in the assessment of children with obesity. Furthermore, it may be more feasible to categorize children with obesity according to their respective risk profile in order to effectively administer care plans and/or interventions. The objectives of the two projects within this thesis were to:

- 1) Categorize children and youth with obesity according to the newly developed Edmonton Obesity Staging System for Pediatrics (EOSS-P), and examine levels of CRF across the range of stages according to the EOSS-P. We hypothesized that there would be an inverse relationship between CRF and EOSS-P stage.
- 2) Examine if a child's EOSS-P stage score would change if future health indicators (family category) of the tool were not applied; how this re-staging approach affects the relationship between CRF and stage group in the children; and finally to identify which category of the EOSS-P is more influential for deciding final stage score. It is hypothesized that there will be a difference in EOSS-P stage distribution after re-staging the children without the family-arm of the EOSS-P. It is also hypothesized that children staged in the highest EOSS-P group will have the lowest levels of CRF.

## Chapter 3

### **Thesis Manuscript #1: Children's cardiorespiratory fitness varies between stages of the Edmonton Obesity Staging System for Pediatrics**

#### **Children's cardiorespiratory fitness varies between stages of the Edmonton Obesity Staging System for Pediatrics (EOSS-P)**

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**Keywords:** obesity, cardiorespiratory fitness, children, exercise, health, Canada

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## ABSTRACT

**BACKGROUND:** The traditional definition of childhood obesity using body mass index (BMI) percentiles has significant limitations. Specifically, it does not accurately and reliably identify children with obesity related health risks or co-morbidities.

**OBJECTIVE:** The objectives of this study were to: 1) categorize children and youth with obesity with a newly developed pediatric obesity staging tool, and 2) examine cardiorespiratory fitness levels, as a surrogate marker of health, across the different categories as defined by the tool

**METHODS:** Ninety-four children and youth with obesity were retrospectively assigned to one of four possible stages (0-3) from the Edmonton Obesity Staging System for Pediatrics (EOSS-P). Children were assigned to an EOSS-P stage based on metabolic, mechanical, mental and/or family milieu obesity-related risk factors. Each individual completed a maximal-graded treadmill cardiorespiratory fitness test to yield  $VO_2$ peak (mlO<sub>2</sub>/kg/min).

**RESULTS:** Children and youth were stratified into three stage groups: (EOSS-P Stage 0  $n = 0$ ; EOSS-P Stage 1  $n = 28$ ; EOSS-P Stage 2  $n = 47$ ; EOSS-P Stage 3  $n = 19$ ).  $VO_2$ peak was significantly lower in the EOSS-P Stage 3 group ( $p = 0.02$ ) compared to EOSS-P Stages 1 and 2.

**CONCLUSION:** Cardiorespiratory fitness has been identified as a sensitive marker of overall health risk. Children with stage 3 obesity based on the EOSS-P classification system had the lowest level of cardiorespiratory fitness, suggesting that these children have the greatest health risk.

## INTRODUCTION

Childhood obesity remains a significant global health concern and is associated with numerous co-morbidities, namely cardiovascular disease,<sup>1-3</sup> type two diabetes,<sup>4-6</sup> and sleep apnea.<sup>7,8</sup> Furthermore, children and youth with obesity are likely to remain obese as adults.<sup>9-11</sup> The impact of obesity on health and well-being, however, can vary considerably between individuals based on independent and synergistic genetic, biologic, developmental, and psychosocial influences.<sup>1</sup> It is clear that some individuals are disproportionately burdened by co-morbidities linked with obesity,<sup>2-6</sup> and these differences appear to be independent of the degree of obesity. Observations such as these reinforce the complexity of obesity and lend support to the long-standing position that there are different types of obesity (*obesities*) with varying etiologies and health consequences.<sup>7</sup> Given this heterogeneity, it can be argued that obesity should not only be defined according to degree of adiposity or excess weight, but on the basis of overall health and well-being.

The body mass index (BMI) is the most widely accepted anthropometric measure used to classify obesity. However, among its limitations<sup>13,14</sup> BMI can vary substantially between children of different ages and sex; therefore, reference values that are age and sex-specific must be applied. While several definitions of childhood obesity are available,<sup>15-17</sup> children with a high BMI may be classified as obese but otherwise healthy (i.e. have no obesity-related co-morbidities). As a more health-specific measure, it has been suggested recently<sup>18</sup> that childhood obesity screening should be performed by applying an evidence-based staging tool, similar to a recently developed adult-tool. The Edmonton Obesity Staging System<sup>19</sup> (EOSS) is a five category tool (Stages 0-4) that

stratifies adults with obesity according to the severity of obesity-related risk factors. A score of '0' delineates an absence of obesity-related risk factors (i.e., metabolically healthy obese), whereas a score of '4' represents severe disability from obesity-related chronic diseases and severe impairment of wellbeing. In the EOSS evaluation study mortality served as the primary outcome for adults, and it was found that EOSS scores of 2 and 3 were associated with increased mortality compared to scores of 0 and 1, despite adjusting for BMI and metabolic syndrome.<sup>19</sup> A newly-developed pediatric version of this tool has been proposed to stratify children and youth with obesity;<sup>20</sup> however, mortality is not an appropriate outcome to be used for evaluation of this tool in this population. Other surrogate markers of health, such as cardiorespiratory fitness, may be a more appropriate health indicator in a pediatric population.

There is evidence to suggest that cardiorespiratory fitness (CRF) can help to mitigate weight-related co-morbidities in individuals with obesity. For instance, central and total adiposity were found to be lower in obese children who had a high level of CRF<sup>21</sup>. Additionally, high levels of CRF are associated with healthier metabolic profiles,<sup>22,23</sup> improved liver function<sup>24</sup> and decreased cardiovascular disease risk in children with obesity.<sup>25,26</sup> Moreover, interventions designed to increase CRF can lead to concomitant improvements in mental health and general well-being.<sup>27</sup>

The objectives of this study were to: (1) categorize children and youth with obesity according to the EOSS-P and (2) examine levels of CRF in individuals who were categorized across the range of stages according to the EOSS-P.<sup>20</sup> It was hypothesized that CRF would be inversely associated with EOSS-P stage.

## METHODS

### Study design and population

This study was a cross-sectional retrospective medical record review of children and youth with obesity. All individuals visited the Children's Hospital of Eastern Ontario's Centre for Healthy Active Living (CHAL) after being referred by a health care provider. Each individual underwent a comprehensive baseline health assessment that was completed by a multi-disciplinary team of clinicians (e.g., pediatric endocrinologist, clinical psychologist, registered nurse, registered dietitian, and exercise specialist). Inclusion criteria for this study were: i) 8 – 17 years old with a sex- and age-specific BMI  $\geq 95^{\text{th}}$  percentile (plus weight related co-morbidity) or BMI  $\geq 99^{\text{th}}$  percentile<sup>15</sup> and ii) successful completion of a maximal cardiorespiratory fitness test in the HALO Research Laboratory. All eligible children and youth who were assessed through the CHAL program and completed the maximal CRF test were retrospectively staged using the EOSS-P tool. This study was approved by the Children's Hospital of Eastern Ontario's Research Ethics Board.

### *Staging Tool: Edmonton Obesity Staging System for Pediatrics*

The Edmonton Obesity Staging System for Pediatrics (EOSS-P), modified from the Edmonton Obesity Staging System for adults,<sup>19</sup> is a four-category pediatric obesity clinical staging tool that consists of metabolic, mechanical, mental, and family milieu obesity-related factors (see **Table 1**).<sup>20</sup> An individual was assigned to one of four possible stages, based on that stage's criteria, by the same clinician (SH or KB) that the individual was treated by in the CHAL program. Dictation for each child's psychological profile was always performed by the same psychologists for consistency. The final EOSS-P

stage assigned to an individual was determined by the highest score in one of the four categories. For example, if a child received a score of '1' for metabolic and mechanical stages, but a score of '2' for mental and family milieu stages, the final score assigned to that child would be '2'. The EOSS-P stage score was assigned after the clinician revisited each child's medical record, which contained dictations from the clinicians as well as lab analysis from blood work.

### Cardiorespiratory fitness assessment

All children completed a graded-treadmill maximal CRF test according to the protocol and termination criteria developed by Gutin et al.<sup>28</sup> CRF data, namely  $VO_{2peak}$  expressed as  $mlO_2/kg/min$ , was collected breath-by-breath with a MedGraphics Ultima metabolic cart (MedicalGraphics Corporation, St. Paul, Minn., USA). Maximal aerobic exertion ( $VO_{2max}$ ) is rarely attained in untrained individuals and children<sup>29</sup>, thus,  $VO_{2peak}$  is more appropriate to report in this study. Individuals began the fitness test with a self-selected walking speed that was maintained as a 4-minute warm-up. Depending on the individual's age and self-selected walking speed, treadmill speed increased for the first 2 minute stage to 2.0, 2.5, 3.0 or 3.5 miles per hour (mph) at a grade of 0%. Treadmill speed increased by 0.5 mph in the second 2 minute stage and was maintained for the entire duration of the test, while treadmill grade remained at 0%. Beginning at the third 2 minute stage, treadmill grade increased by 2.0% and continued to increase after each 2 minute stage was completed. The test was terminated when the child signaled that they could no longer continue. A minimum of a 2 minute cool-down period was provided for each subject to normalize their heart rate. Each CRF test was conducted under the supervision of two certified exercise physiologists.

## Statistical Analysis

Descriptive statistics were used to summarize children and youth's anthropometric and physical variables. A Kruskal-Wallis test was performed to test for differences in sex distribution between EOSS-P stages. A one-way analysis of variance (ANOVA) was used to test for significant differences between EOSS-P stages for anthropometric and CRF variables. A Tukey post-hoc test was performed to identify specific between-group differences. Additionally, effect sizes were examined for CRF between the EOSS-P stage score groups using Cohen's *d* method. All analyses were performed using SPSS version 20.0 (SPSS, Chicago, IL) with significance set at  $P < 0.05$ .

## RESULTS

Ninety-four children and youth with obesity participated in this study (43 males). Baseline characteristics and EOSS-P stage score stratification are displayed in Table 2. No children were staged by the EOSS-P as a score of 0. There were no significant differences in sex distribution between the three EOSS-P stages. There were no significant differences between EOSS-P stages according to age or height; however, body mass ( $F(2, 91) = 4.77, p < 0.01$ ) and BMI ( $F(2, 91) = 5.37, p < 0.01$ ) differed between stages 1, 2 and 3. Post-hoc analyses showed that body mass and BMI (both  $p < 0.01$ ) were lower in EOSS-P Stage 1 compared to EOSS-P Stage 3. There were no differences in weight or BMI between EOSS-P Stage 1 and Stage 2.

Differences were also observed across EOSS-P stages according to  $VO_2$ peak values ( $F(2, 91) = 4.16, p = 0.02$ ). Post-hoc comparisons revealed differences in  $VO_2$ peak values between EOSS-P Stages 1 and 3 ( $p = 0.04$ ) and EOSS-P Stages 2 and 3

( $p = 0.02$ ) (Figure 1). There were no differences in  $VO_2$ peak values between EOSS-P Stages 1 and 2. The effect size was moderate for  $VO_2$ peak value comparisons between both EOSS-P Stage 1 and 3 (Cohen's  $d$  value: 0.70) and EOSS-P Stage 2 and 3 (Cohen's  $d$  value: 0.74) (Table 3). The effect size for  $VO_2$ peak values between EOSS-P Stage 1 and 2 was negligible.

## **DISCUSSION**

The main finding of the present study, which supported the stated hypothesis, was that cardiorespiratory fitness (CRF) levels were significantly different between children with obesity stratified by the Edmonton Obesity Staging System for Pediatrics (EOSS-P). Children with obesity in EOSS-P Stage 1 and Stage 2 had significantly higher CRF levels compared to EOSS-P Stage 3 children. This is the first study to examine differences in CRF levels in a population of children and youth with obesity stratified by a pediatric obesity staging tool. A strength of this study was the assessment of CRF using a maximal graded treadmill test, complemented with breath-by-breath capture of gas exchange, which is the exercise test mode considered to produce the highest values of oxygen consumption.<sup>30</sup>

After using the EOSS-P to stage children with obesity, the majority of this sample was categorized into EOSS-P Stage 2 ( $n = 48/94$ ). There were no children or adolescents assigned a stage score of 0 from this sample. This may be explained by the fact that this sample was obtained from a program that specializes in complex severe obesity, and that those participating in the treatment program likely have at least one obesity-related risk factor. Additionally, the results indicated that EOSS-P Stage 1 and 2 had very similar CRF levels. It was hypothesized that CRF levels would be highest in Stage 1 and

subsequently decrease as EOSS-P stage score increased. This hypothesis was partially supported by the results; however, it was anticipated that EOSS-P Stage 2 would have lower, and not similar, CRF scores than EOSS-P Stage 1. This could be due to the application of the EOSS-P tool (see limitations). Additionally, body mass and BMI were significantly higher in EOSS-P Stage 3 ( $p < 0.01$  for both weight and BMI) compared to EOSS-P Stage 1. Similar findings have been observed in adult-based studies, where metabolically unhealthy obese individuals had significantly higher BMI, body fat percentage and waist circumference compared to metabolically healthy obese individuals.<sup>31</sup>

Previous literature has identified a metabolically healthy but obese phenotype,<sup>32-</sup><sup>34</sup> which suggests that different *obesities* could exist in a given population. Although this has been typically documented in adults, a healthy obese phenotype corresponds most with an EOSS-P stage score of 0 (complete absence of obesity-related risk factors). It has been demonstrated that metabolically healthy obese individuals are not at an increased risk of cardiovascular disease compared to their metabolically healthy non-obese counterparts.<sup>35</sup> Additionally, it has been suggested that the metabolically healthy but obese phenotype may be protected from obesity-related risk factors due to higher levels of CRF.<sup>32</sup> Conversely, obese individuals with low levels of CRF may be at a higher risk of obesity-related co-morbidities. The results in this study show that the highest EOSS-P stage score of 3, which indicates the presence of *established* chronic diseases related to obesity, had significantly lower CRF levels ( $p < 0.05$ ) compared to EOSS-P Stages 1 and 2. This association may be similar to findings observed in adults, whereby metabolically unhealthy obese individuals with low CRF levels had increased risk of all-cause

mortality, cancer mortality and both non-fatal and fatal cardiovascular disease.<sup>32</sup> Although differences in CRF between groups were observed, higher body mass may have affected EOSS-P Stage 3 CRF levels, as  $VO_{2peak}$  values were divided by mass in kilograms. Yet, children in EOSS-P Stage 1 and Stage 2 had similar levels of CRF, despite body mass not being identical between groups. Overall, children in this study had relatively low levels of CRF fitness compared to recent reference values for children.<sup>36</sup> However, the  $VO_{2peak}$  values presented in this study were baseline values obtained upon entering the CHAL treatment program; therefore, similar CRF levels compared to reference populations were not anticipated in these children.

There were, however, limitations that existed during the execution of this study. The EOSS-P is a newly developed tool, and this is the first occasion in which it has been applied to a population of children and youth with obesity. Certain modifications may be made in the future to the tool upon its evaluation (i.e., removing a category, providing a weighted score per category, etc.), and may slightly alter the EOSS-P from the methodology used in this study. Also, since the EOSS-P accounts for family obesity-related risk factors, it is possible for children or youth with obesity to be assigned a high stage score (i.e., 2 or 3) from family-related criteria, despite having a normal metabolic, mechanical and psychological profile. Consequently, this could inflate a particular stage score's distribution without the presence of physiological co-morbidities related to obesity. Additionally, fat mass was not objectively calculated for each child in this study, which limited the amount of controlling for certain statistical analyses.

This study suggests that cardiorespiratory fitness levels differ between EOSS-P stages. The highest EOSS-P stage score group (3), which is reflective of established

chronic disease in pediatric obesity, displayed significantly lower cardiorespiratory fitness levels compared to EOSS-P Stage 1 and 2. This may be of concern, as a higher level cardiorespiratory fitness has been suggested to limit the severity of obesity-related risk factors. Future research should examine the construct validity of the EOSS-P, investigate whether the stage score changes if the family category of the tool is excluded, and objectively measure fat mass in the children staged (i.e., DXA scan). Globally, the application of the EOSS-P may serve as a method to better indicate which individuals with pediatric obesity require immediate forms of intervention (i.e., Stage 3), versus those who may need less intensive forms of clinical care (i.e., Stage 1). Ultimately, the evaluation of CRF as a health indicator in pediatric obesity may provide additional information when assessing overall health and well-being.

## **CONFLICT OF INTEREST**

The authors declare no conflict of interest.

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## **AUTHOR CONTRIBUTIONS**

Study design (KB, SH, AB, GDCB, KBA), data collection (KB, JR), data analyses (KB), discussion of data and writing of the manuscript (KB), revisions and editorial comments of final manuscript (all authors).

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**Table 3.1** Summary of criteria for the Edmonton Obesity Staging System for Pediatrics

<b>Stage 0</b>	No metabolic, mechanical, mental/cognitive, or family obesity-related risk factors apparent.
<b>Stage 1</b>	Presence of metabolic (e.g. elevated cholesterol, impaired fasting glucose levels), mechanical (e.g. <b>mild</b> OSA, <b>minor</b> musculoskeletal pain, dyspnea with P.A. only), mental (e.g. ADHD, <b>mild</b> depression/anxiety, <b>mild</b> quality of life impairment) and/or family (e.g. <b>minor</b> relationship issues with family members, parents may require support in parenting skills) subclinical obesity-related risk factors.
<b>Stage 2</b>	Presence of metabolic (e.g. T2D without diabetes-related complications, hypertension, severe fatty infiltration of liver), mechanical (e.g. OSA requiring BiPAP or CPAP, <b>moderate</b> MSK pain limiting P.A and daily activities), mental (e.g. <b>major</b> depression or anxiety disorder, <b>moderate</b> developmental delay, <b>significant</b> body image disturbance), and/or family (parents have medical/physical problems that interfere with parenting, children having <b>moderate</b> problems with parents and/or family) obesity-related chronic diseases and associated health issues.
<b>Stage 3</b>	Presence of metabolic (e.g. cardiomegaly, gall bladder disease/stones, T2D with diabetes-related complications), mechanical (e.g. pulmonary hypertension, peripheral edema, Blount’s Disease, Osteoarthritis), mental (e.g. <b>uncontrolled</b> psychopathology, <b>severe</b> binge eating, self/physical loathing), and/or family (parents unable to monitor/discipline child, <b>dangerous</b> home environment) established chronic diseases and associated health issues.

**Table 3.2** Demographic and anthropometric characteristics for study participants

	EOSS-P Stage 1	EOSS-P Stage 2	EOSS-P Stage 3
Variable			
<i>n</i>	28 (11M/17F)	47 (24M/23F)	19 (9M/10F)
Age (y)	13.0 ± 2.69	14.0 ± 2.57	14.6 ± 2.32
Height (cm)	161.3 ± 10.2	165.8 ± 12.9	166.3 ± 8.89
Body Mass (kg)	92.0 ± 24.0	102.8 ± 22.4	115.3 ± 33.4*
BMI (kg/m <sup>2</sup> )	34.8 ± 5.69	37.0 ± 5.18	41.5 ± 11.0*

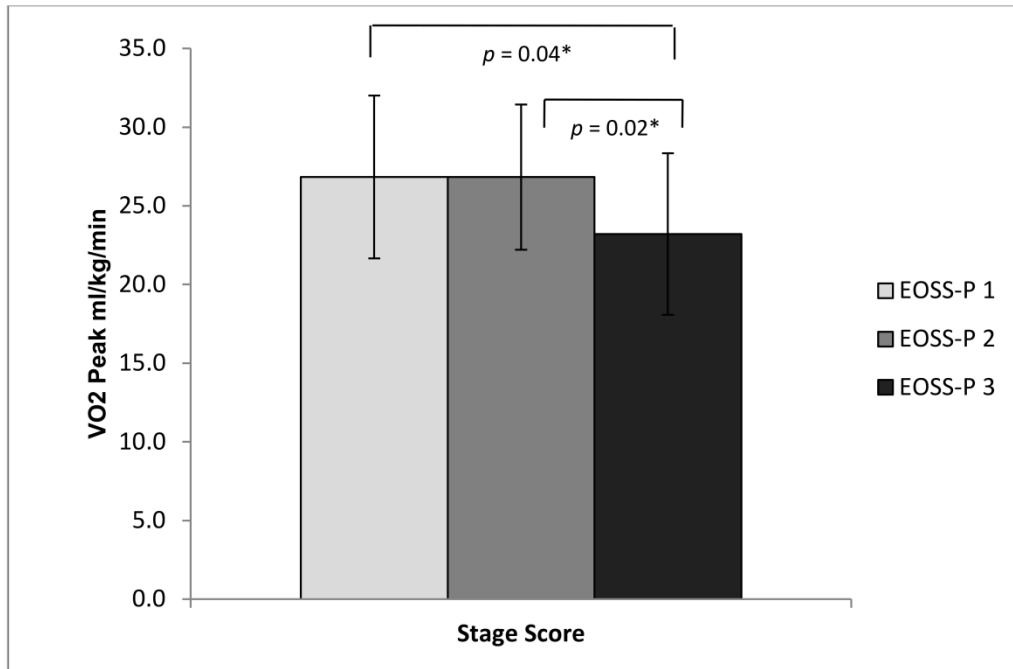
Values are means ± SD.; M=male; F=female BMI=body mass index. \* *P* <0.01 compared to EOSS-P Stage 1 as reference value.

**Table 3.3** Effect size for cardiorespiratory fitness comparisons between EOSS-P groups

Comparison	Effect Size
EOSS-P Stage 1 vs. EOSS-P Stage 2	0.00
EOSS-P Stage 1 vs. EOSS-P Stage 3	0.70
EOSS-P Stage 2 vs. EOSS-P Stage 3	0.74

Effect sizes were considered negligible if  $< 0.2$ , small if between 0.2-0.5, moderate if between 0.5-0.8, and important if  $> 0.8$ .

**Figure 3.1** Children’s mean ( $\pm$ SD) cardiorespiratory fitness levels across EOSS-P stages, measured in mlO<sub>2</sub>/kg/min. \* $P < 0.05$



## **Chapter 4**

### **Thesis Manuscript #2: Identifying influential categories of the Edmonton Obesity Staging System for Pediatrics and their relationship with cardiorespiratory fitness in children with obesity**

#### **Identifying influential categories of the Edmonton Obesity Staging System for Pediatrics and their relationship with cardiorespiratory fitness in children with obesity**

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**Keywords:** obesity, cardiorespiratory fitness, children, exercise, health

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## **Abstract**

**Background:** The objectives of this study were to: 1) examine if children previously categorized by the Edmonton Obesity Staging System for Pediatrics (EOSS-P) would have an altered stage score if the family-arm of the tool was withdrawn; 2) identify if there were differences in cardiorespiratory fitness between groups after the children were re-staged; and 3) determine which category of the EOSS-P is more influential for determining final stage score.

**Methods:** Ninety-four children and youth with obesity were retrospectively assigned to one of three groups (Low Risk: Stage 0-1; Elevated Risk: Stage 2; High Risk: Stage 3) after being staged without the family category of the EOSS-P. Children were staged based on metabolic, mechanical and mental criteria of the EOSS-P. Each individual completed a maximal-graded treadmill cardiorespiratory fitness test to yield  $VO_{2peak}$  ( $mlO_2/kg/min$ ).

**Results:** Children and youth were stratified into three stage groups: Low Risk group ( $n = 40$ ); Elevated Risk group ( $n = 45$ ); and High Risk group ( $n = 9$ ).  $VO_{2peak}$  was significantly lower in the High Risk group ( $p = 0.04$ ) compared to the Low Risk group. Furthermore, significant differences in distribution were observed between the Low Risk group and the Elevated Risk group ( $p < 0.01$ ) in the categories of the EOSS-P that determined final stage score.

**Conclusions:** When children were re-staged without the family category of the EOSS-P, 22% ( $n=21$ ) were re-stratified to a lower risk group. Children in the High Risk group displayed the lowest level of cardiorespiratory fitness, suggesting that their health profile warrants serious clinical care. Children in Elevated and High Risk categories tended to be staged by a singular EOSS-P category, with more severe obesity-related risk factors present.

## Background

The worldwide prevalence of childhood obesity has escalated to alarming rates. Childhood obesity has been linked to both acute [1-5] and chronic health concerns [6-9], consequently earning the description as a *complex disease*. Despite these descriptions, not all children classified as obese by traditional anthropometric methods (i.e., Body Mass Index (BMI), BMI percentiles, BMI z-scores) are at risk for developing obesity-related co-morbidities. Other methods and variables, such as staging tools that take into account multiple factors outside of BMI and cardiorespiratory fitness (CRF) respectively, may be more suitable when evaluating overall health in children with obesity. High CRF has been shown to reduce obesity-related risk factors by improving central and total adiposity [10], metabolic profiles [11,12], and reducing cardiovascular disease risk [13,14]. Conversely, children with low CRF and elevated adiposity are at increased risk of developing cardiovascular disease [15]. Recently, differences in CRF ( $\text{VO}_2\text{peak ml O}_2/\text{kg}/\text{min}$ ) were observed between groups staged using the Edmonton Obesity Staging System for Pediatrics [16,17]. Children that were categorized as an EOSS-P Stage 3, which indicated the presence of established obesity-related disease(s), displayed significantly lower levels of CRF compared to children in EOSS-P Stage 1 and 2. This finding suggested that EOSS-P Stage 3 children were at a greater health risk compared to the other children from their cohort. The initial evaluative work, however, noted the possibility that a child's EOSS-P stage score could be increased to a more serious level (i.e., Stage 2-3) by the family category of the tool, despite having only subclinical obesity-related health complications.

The family component of the EOSS-P is reflective of the family environment of the child or youth living with obesity. It is a measure of external supports or barriers to weight management and as such an important predictor of success in obesity management, future weight trajectory and subsequently health. While recognizing that the family component plays a major role in a child's social, physical and psychological development [18], its presence in an obesity staging tool may not be a direct indicator of current physical health as represented through the CRF measurement. Other health indicators, namely the metabolic, mechanical and mental categories of the EOSS-P, may be more related to current CRF as a surrogate marker of overall health in children.

Therefore, the objectives of this study were to: 1) examine if a child's EOSS-P stage score would change if the family-arm of the tool was not applied; 2) identify differences between groups in cardiorespiratory fitness after the children were re-staged; and 3) determine which category of the EOSS-P is most influential in deciding final stage score. It was hypothesized that there would be a difference in EOSS-P stage distribution after re-staging the children without the family-arm of the EOSS-P. It was also hypothesized that children staged in the highest EOSS-P group would have the lowest levels of CRF.

## **Methods**

### **Study Design and Setting**

Ninety-four children and adolescents with obesity (sex and age-specific BMI  $\geq 95^{\text{th}}$  percentile and weight related co-morbidity or BMI  $\geq 99^{\text{th}}$  percentile [19]) from the Children's Hospital of Eastern Ontario's Centre for Healthy Active Living (CHAL), ages 8-17 years, were staged with the Edmonton Obesity Staging System for Pediatrics [16] via a cross-sectional retrospective medical record review [17]. To be included in this

study, the children were required to be previously staged by the EOSS-P and have successfully completed a graded-maximal cardiorespiratory fitness test on a treadmill. For this study, the same physicians (SH and KB) who initially staged the children revisited each child's medical file and re-categorized the children without the family category of the EOSS-P. This study was approved by the Children's Hospital of Eastern Ontario's Research Ethics Board.

### **Staging Tool: Edmonton Obesity Staging System for Pediatrics (EOSS-P)**

The EOSS-P is a comprehensive staging system that stratifies children with obesity according to criteria outlined in the tool's four categories (metabolic, mechanical, mental and family-milieu) [16]. The final stage score is assigned based on the criteria met in the highest stage category. For example, a child could meet Stage 1 criteria for metabolic, mechanical and family milieu categories; however, if the child meets Stage 2 criteria for the mental health category then his or her final stage score is 2. Additional information and criteria outlined in the EOSS-P are available [16,17]. However, since the family category was removed for this study, children could only be staged by the metabolic, mechanical and/or mental categories of the EOSS-P.

To examine which category of the EOSS-P determined final stage score, frequencies were assigned to 5 possible groups: mental only; metabolic only; mechanical only; Any 2 categories; All 3 categories.

### **Cardiorespiratory Fitness Assessment**

Children staged by the EOSS-P previously completed a maximal CRF protocol created by Gutin et al. [20]. The test was performed on a treadmill and data ( $\text{VO}_2$  peak in ml/kg/min) were collected breath-by-breath with a MedGraphics Ultima metabolic cart

(MedicalGraphics Corporation, St. Paul, Minn., USA) in the HALO Research Laboratory. Children began the fitness test with a self-selected walking speed that was maintained as a 4-minute warm-up. Depending on the child's age and self-selected walking speed, treadmill speed increased for the first 2 minute stage to 2.0, 2.5, 3.0 or 3.5 miles per hour (mph) at a grade of 0%. Treadmill speed increased for the last time by 0.5 mph in the second 2 minute stage, while treadmill grade was maintained at 0%. Beginning at the third 2 minute stage, treadmill grade increased by 2.0% and continued to increase after each 2 minute stage was completed. The test was terminated when the child signaled that they could no longer continue. A minimum of a 2 minute cool-down period was provided for each child to normalize heart rate.

### **Statistical Analysis**

Descriptive statistics were used to summarize children and youth's anthropometric and physical variables. A Kruskal-Wallis test was performed to test for differences in sex distribution between EOSS-P stage groups, and for distribution differences between stage groups in the categories of the EOSS-P (i.e., metabolic, mechanical, mental) that determined a child's final stage score. A Bonferroni post-hoc correction was performed to account for the three post-hoc tests, whereby significance threshold level was defined as  $p < 0.017$ . A one-way analysis of variance (ANOVA) was used to test for significant differences between EOSS-P stage groups for anthropometric and CRF variables. A Tukey post-hoc test was performed to identify specific between-group differences in anthropometrics and CRF. Effect sizes were calculated for CRF between the EOSS-P stage score groups using Cohen's  $d$  method. All analyses were performed using SPSS version 21.0 (SPSS, Chicago, IL) with significance set at  $p < 0.05$ .

## Results

Ninety-four children (43 males, 51 females) with obesity participated in this study. Children were stratified by the EOSS-P into one of three groups: Low Risk (LR) (Stage 0-1) ( $n = 40$ ); Elevated Risk (ER) (Stage 2) ( $n = 45$ ); and High Risk (HR) (Stage 3) ( $n = 9$ ). Baseline characteristics by EOSS-P group stratification are displayed in Table 1. There were no significant differences in sex-based distribution between the three groups. There were significant differences between the groups in body mass ( $F(2, 91) = 5.28, p < 0.01$ ) and BMI ( $F(2, 91) = 4.58, p = 0.01$ ). Post-hoc analyses revealed significantly higher body mass ( $p = 0.01$ ) and BMI ( $p = 0.02$ ) in the HR group compared to the LR group. No differences were observed in baseline characteristics between the LR and ER group, or for the ER group and HR group. Additionally, 22% ( $n = 21/94$ ) of the children had their EOSS-P stage score decrease when staged without the family category of the tool (Figure 1). 10 children had their EOSS-P score decrease from Stage 2 to Stage 1, 9 children decreased from Stage 3 to Stage 2, and 2 children decrease from Stage 3 to Stage 1.

Differences were also observed between the three groups after examining  $VO_{2peak}$  values ( $F(2, 91) = 3.52, p = 0.03$ ) (Figure 2). Post-hoc analyses showed  $VO_{2peak}$  was significantly lower in the HR group ( $p = 0.04$ ) compared to the LR group. There were no differences in  $VO_{2peak}$  values between the LR and ER group, or the ER and HR group. Effect size for  $VO_{2peak}$  was considered important (Cohen's  $d$  value: 0.90) between the LR and HR group, moderate (Cohen's  $d$  value: 0.57) between the ER and HR group, and small between the LR and ER group (Cohen's  $d$  value: 0.39) (Table 2).

There was a significant difference in the distribution of the EOSS-P categories (mental, mechanical, metabolic) that determined the children's final stage score ( $X^2 = 9.96$ ,  $df = 2$ ,  $p < 0.01$ ) (Figure 3). Specifically, this difference was observed between the LR group and the ER group ( $p < 0.01$ ). No differences in distribution were observed between the LR and HR group, or the ER and HR group.

## **Discussion**

The main findings of this study were the following: nearly a quarter of the children ( $n = 21/94$ ) had their stage score decrease when the family category of the EOSS-P was withdrawn; CRF was significantly lower in the HR group compared to the LR group; and, the LR group had a significantly different distribution in the EOSS-P categories that determined final stage score compared to the ER group.

After re-staging the children without the family category of the EOSS-P, 21 of the 94 children (Figure 1) displayed a lower stage score compared to their initial staging [17]. As a result, the majority of this sample was re-stratified into the LR group (Stage 0-1,  $n = 40$ ) and ER group (Stage 2,  $n = 45$ ), with only a small number of children remaining in the HR group (Stage 3,  $n = 9$ ). This redistribution supported the stated hypothesis, as one of the limitations of the EOSS-P tool was that future health indicators and criteria (i.e., family category) may increase a child's overall stage score. While the family category of the staging tool may be more reflective of future risk, it appears to be less reflective of current morbidity.

Moreover, the HR group had significantly lower levels of fitness compared to the LR group ( $p = 0.04$ ; Cohen's  $d$  value: 0.90) (Figure 2); thus, this finding supported the second hypothesis. This is consistent with findings from the initial staging of this sample

[17], whereby Stage 3 children displayed the lowest levels of CRF within the sample. Low levels of CRF may be troublesome for children in the HR group, as a decrease in peak VO<sub>2</sub> has been associated with an increase in cardiovascular disease risk [21]. There were no differences between the LR and ER group in CRF levels in this study, which was also similar to previous findings [17]. However, there was a significant difference in distribution between the LR and ER group in the categories of the EOSS-P that determined final stage score ( $p < 0.01$ ) (Figure 3). The majority of children staged in the LR group had a combination of 2 categories of the EOSS-P determine their final stage score. This may be explained by the *subclinical* obesity-related risk factors listed in EOSS-P Stage 1 [16], which could allow a child in the LR group to meet several criteria across different categories of the tool. Conversely, the majority of children staged in the ER and HR group had one category of the EOSS-P determine their final stage score. This suggests that a singular, but more severe, obesity-related disease/health issue determined their stage score. Furthermore, of the three isolated categories (mental, metabolic, or mechanical) the mental category of the EOSS-P displayed the highest frequency for determining stage score for the LR and ER group. This finding may not be unusual, as children with obesity have been found to report lower quality of life [22], decreased self-esteem [23], and encounter weight-related teasing that can affect emotional well-being [24,25]. This finding reinforces the importance of evaluating the psychological profile of children with obesity during health assessments.

Stressful family environments have been linked to childhood obesity [26]. Of more importance, however, may be the role family environments play on dictating future health risk in children with obesity. Although family environments may not always be

indicative of current health risk, they can represent barriers and factors that can significantly complicate weight management – leading to future health disparity in children with obesity.

## **Strengths and Limitations**

Strengths of this study were testing CRF using a maximal graded treadmill protocol, with breath by breath capture of gas exchange, as well as having a well phenotyped clinical population. The recent inception and application of the EOSS-P may be viewed as a limitation of this study; thus, evaluation and feedback on the tool will be warranted from health experts. Also, the sample size for this study was relatively small ( $n = 94$ ); therefore, future research should augment the sample size to perform more robust statistical analyses. Additionally, future studies should examine how certain variables (i.e., Quality of Life) correlate with the categories of the EOSS-P.

## **Conclusions**

The results derived from this study suggest that future health-related criteria (i.e., family category) listed in the Edmonton Obesity Staging System for Pediatrics has the potential to increase the stage score in children staged by the tool. The results presented here indicate that children categorized in the High Risk group have significantly lower cardiorespiratory fitness levels compared to the Low Risk group. Finally, most children stratified in the Low Risk group had their final stage score determined by a combination of 2 categories of the EOSS-P; however, final stage score in the Elevated Risk and High Risk group tended to be determined by only one category of the EOSS-P, which may suggest that obesity-related risk factors and/or diseases are progressing in these children.

**Abbreviations**

ANOVA: Analysis of Variance; BMI: Body Mass Index; CRF: cardiorespiratory fitness; EOSS-P: Edmonton Obesity Staging System for Pediatrics; ER: Elevated Risk group; HR: High Risk group; LR: Low Risk group

**Competing Interests**

The authors declare no competing interests

**Author Contributions**

KBA, KB1, SH and JR were responsible for the initialization and conceptualization of this project. SH and KB2 staged the children with the EOSS-P tool. The fitness testing, statistical analysis, interpretation of results, and writing of the manuscript were performed by KB1. All authors reviewed and agreed to the finalized content of this manuscript.

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**Table 4.1 Demographic and anthropometric characteristics for study participants**

	Low Risk (Stage 0-1)	Elevated Risk (Stage 2)	High Risk (Stage 3)
Variable			
<i>n</i>	40 (17M/23F)	45 (22M/23F)	9 (5M/4F)
Age (y)	13.3 ± 2.74	14.1 ± 2.39	14.7 ± 2.74
Height (cm)	162.2 ± 10.9	165.6 ± 12.03	170.0 ± 9.52
Body Mass (kg)	94.1 ± 23.7	105.6 ± 26.0	123.3 ± 29.0*
BMI (kg/m <sup>2</sup> )	35.2 ± 5.47	38.2 ± 7.66	42.6 ± 9.14*

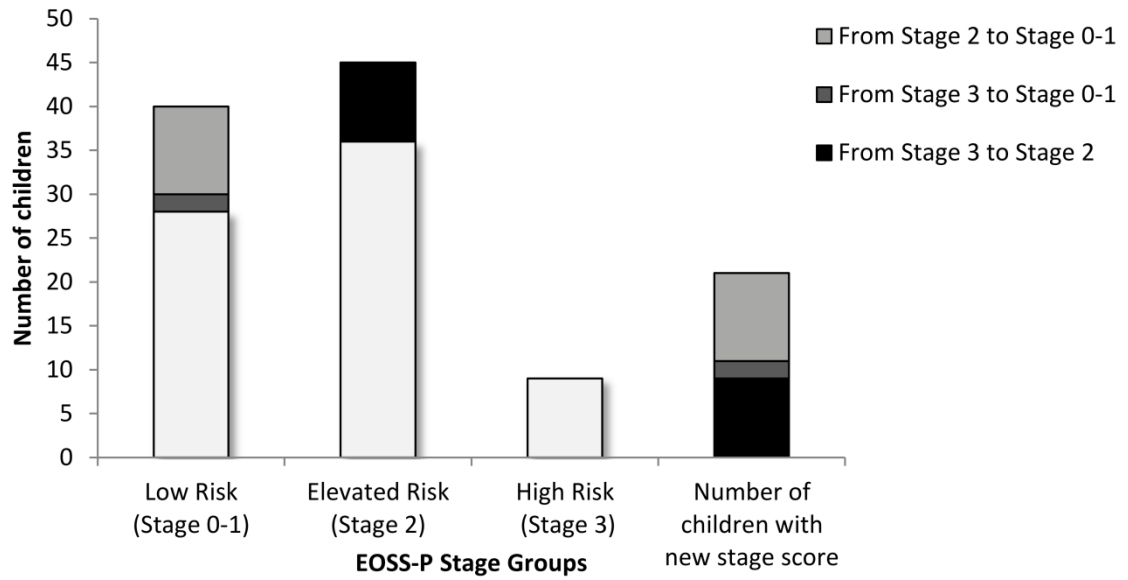
Values are means ± SD.; M=male; F=female BMI=body mass index.\**P* <0.05 compared to Low Risk group as reference value.

**Table 4.2 Effect size for cardiorespiratory fitness between EOSS-P groups**

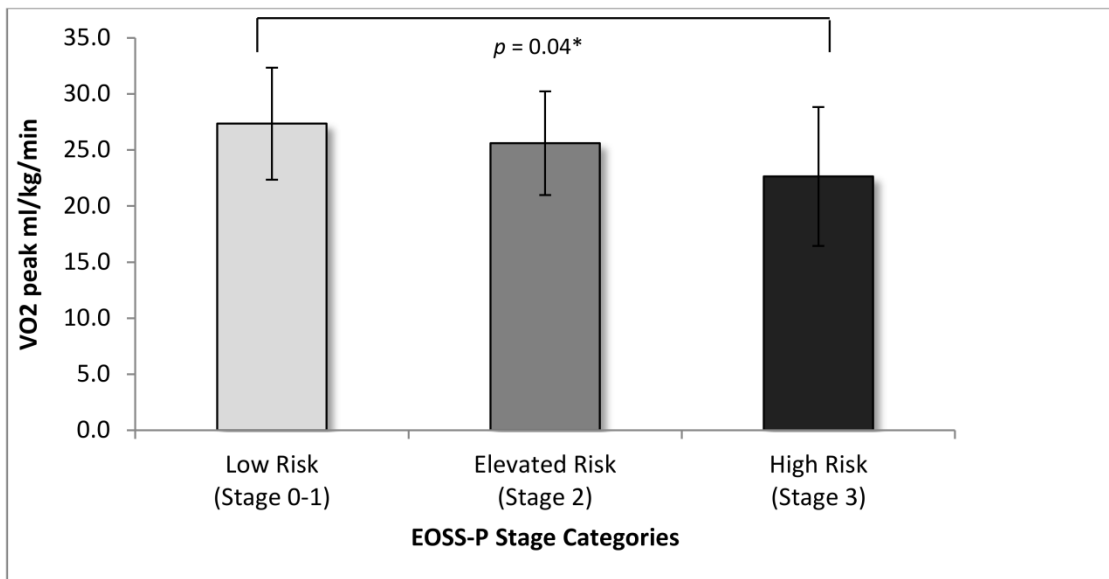
Comparison	Effect Size
Low Risk vs. Elevated Risk	0.39
Low Risk vs. High Risk	0.90*
Elevated Risk vs. High Risk	0.57

Effect sizes were considered negligible if < 0.2, small if between 0.2-0.5, moderate if between 0.5-0.8, and important if > 0.8\*

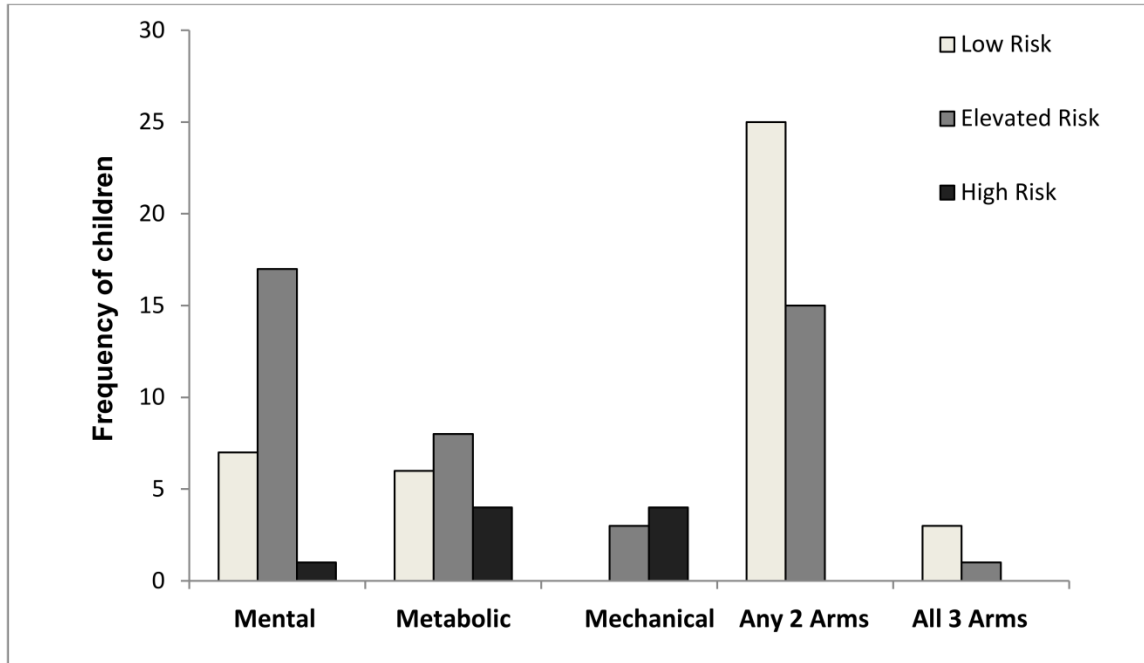
**Figure 4.1 Frequency and categorization of children re-staged without family category of EOSS-P included.**



**Figure 4.2 Children's mean ( $\pm$ SD) cardiorespiratory fitness levels across different EOSS-P stage groups, measured in  $\text{mlO}_2/\text{kg}/\text{min}$ . \* $P < 0.05$ .**



**Figure 4.3 Frequency comparisons of EOSS-P categories that determined final stage score between groups.**



Significant difference in the distribution of the EOSS-P categories that determined the children's final stage score was found ( $X^2 = 9.96$ ,  $df = 2$ ,  $p < 0.01$ ). This difference was observed between the LR group and the ER group ( $p < 0.01$ ). No differences in distribution were observed between the LR and HR group, or the ER and HR group.

## Chapter 5

### General Discussion and Conclusions

#### *Summary of Results*

The overall objective of this thesis was to stage children with obesity using the newly developed Edmonton Obesity Staging System for Pediatrics (EOSS-P) tool and evaluate cardiorespiratory fitness (CRF) levels after being categorized by the EOSS-P.

The first manuscript presented in this thesis sought to categorize a sample of children with obesity ( $n = 94$ ) with the EOSS-P. After being stratified into the four possible EOSS-P stages (Stages 0-3), children's CRF levels, expressed in  $\text{mlO}_2/\text{kg}/\text{min}$ , were examined between groups. Significant body mass (kg) and BMI differences were identified between Stage 1 and Stage 3 groups. No differences in anthropometrics were found comparing Stage 1 and Stage 2, or for Stage 2 and Stage 3. Significant differences in  $\text{VO}_2\text{peak}$  were found in the different stage groups (Stage 1, Stage 2 and Stage 3), and a post-hoc test revealed that differences in  $\text{VO}_2\text{peak}$  existed between Stage 1 and Stage 3, and also between Stage 2 and Stage 3; there were no differences in  $\text{VO}_2\text{peak}$  between Stage 1 and Stage 2. Additionally, moderate effect size values comparing  $\text{VO}_2\text{peak}$  levels were observed between Stage 1 and Stage 3, as well as between Stage 2 and Stage 3. This finding supported the hypothesis that CRF levels would decrease as EOSS-P stage score increased. A limitation in this study's design was that future health criteria (family category) of the EOSS-P may have increased a child's stage score to a more serious and current level of obesity. These results also suggested, not surprisingly, that EOSS-P Stage 3 children were at the greatest health risk, due to low levels of functional capacity and a presence of established obesity-related disease(s). Thus, the application of the EOSS-P, in

conjunction with measuring CRF, served as a useful method to categorize children with obesity and evaluate their risk profile.

The second manuscript within this thesis aimed to re-stage the same sample of children minus the family category of the tool and evaluate CRF levels in these newly redistributed groups. In addition, this study explored which category, or which combination of categories, of the EOSS-P (metabolic, mechanical, mental) determined final stage score across the three groups: Low Risk Group (LR) (EOSS-P Stage 0-1); Elevated Risk Group (ER) (EOSS-P Stage 2); and High Risk Group (HR) (EOSS-P Stage 3). Twenty-one of the 94 children had their stage score decrease after being re-staged without including the family-arm of the tool. Similar to the EOSS-P stage groups in the first manuscript, body mass (kg) and BMI were significantly higher in the HR group compared to the LR group.  $VO_{2peak}$  values were also significantly lower in the HR group compared to the LR group; there were no observed differences in CRF between the LR and the ER group, or the ER and HR group. Moreover, an *important* effect size value ( $> 0.8$ ) was found comparing  $VO_{2peak}$  between the LR and the HR group. There was also a significant difference between the LR and ER group in the distribution of EOSS-P categories (mental, metabolic, mechanical) that determined final stage score. The majority of children in the LR group had their final stage score determined by a combination of any 2 categories of the EOSS-P; whereas, the majority of the ER group had one category decide final EOSS-P stage score. Moreover, of the three isolated categories (mental, metabolic, or mechanical) the mental category of the EOSS-P displayed the highest frequency for determining final stage score. A limitation of this

study, however, was the small sample size ( $n = 94$ ), which future studies should aim to increase..

### ***Clinical and Broader Implications***

Based on the results provided in the two aforementioned manuscripts, there are many implications that have the potential to improve pediatric obesity screening and assessment in clinical settings. The Edmonton Obesity Staging System for Pediatrics (EOSS-P) could be used as an effective tool to triage children with obesity according to their respective risk profile. In turn, not all children defined as obese by traditional BMI measures (percentiles, z-scores, etc.) would require comprehensive and invasive screening tests (i.e., blood samples, liver ultrasounds, oral glucose tolerance tests). Furthermore, the EOSS-P could help diminish forms of weight bias targeted at children with obesity; this more comprehensive form of screening will preclude individuals from making health assumptions based solely on a child's BMI. On a broader level, Canada's public health care system could also benefit from the adoption of the EOSS-P, as the finite health care resources could be allocated to those children who require more intensive care. Conversely, children with obesity who possess minimal or no obesity-related risk factors could be directed towards other forms of intervention; for instance, interacting and using community resources rather than tertiary care facilities.

Pediatric obesity assessments could also benefit from incorporating a measure of cardiorespiratory fitness (CRF) when evaluating the health of children with obesity. Evaluating CRF (i.e.,  $VO_{2peak}$ ) can provide clinical teams with more information on cardiovascular function and health-related physical fitness (121). In turn, this can help exercise specialists design and prescribe appropriate physical activity and exercise

recommendations based a child's functional capacity. A strength of using CRF, specifically  $VO_{2peak}$ , as a baseline measurement for physical fitness would be its accuracy, as it would objectively inform exercise specialists and health care practitioners the current and/or baseline fitness level of the child. However, certain weaknesses exist for measuring CRF: access to facilities with expensive and technical equipment; trained and certified staff; and staff experienced in testing children with obesity. Despite these limitations, there is mounting evidence suggesting the importance of measuring CRF as a surrogate marker of health in children with obesity (122). Therefore, it can be contended the inclusion of CRF in a pediatric obesity assessment is warranted.

### ***Future Research Directions***

Though there has been considerable growth in the amount of research and health care focus on addressing pediatric obesity, high rates of obesity in children persist globally (59-63). This is troublesome as pediatric obesity is associated with a plethora of physiological comorbidities (70-76) that have the potential to track into adulthood as well (10). Given the complexities surrounding pediatric obesity, it is vital for these children to be effectively screened and evaluated so that health care resources are rationed appropriately. Thus, it is paramount for future research to continue its progress in determining effective screening, management and evaluation strategies in this specific pediatric population.

Regarding future research surrounding the use of the EOSS-P, studies should evaluate the construct validity of the tool, as well as inter-rater reliability between clinicians who apply the EOSS-P. Future research should also aim to increase the sample size of children staged by the EOSS-P in order to perform more robust statistical analyses. Moreover, future research should objectively determine adiposity (i.e., fat mass) and lean muscle mass (i.e., fat-free mass) to control for statistical comparisons. Additionally, other outcome variables, such as quality of life, should be explored across the stages of the EOSS-P given the influence of the mental category in determining final stage score.

## *Conclusions*

The research in this thesis has introduced a more comprehensive method of screening children with obesity, whereby children were categorized by a pediatric staging tool according to a pre-determined set of criteria designed to represent risk status. The primary outcome variable that was used to compare children across stages of risk was cardiorespiratory fitness ( $VO_2$ peak), a surrogate marker of health and functional capacity. The two projects within this thesis were also the first to successfully apply this newly developed staging system (EOSS-P), and examine differences between groups of children stratified by obesity-related health risk.

Although childhood obesity has been labeled as a modern health epidemic, it is vital that health experts consider the growing notion that different obesity phenotypes may exist in a given population of children. Solely using traditional screening methods for pediatric obesity (i.e., BMI, BMI percentile, BMI z-score, etc.) without considering other health indicators, namely metabolic, mechanical, mental and family parameters, may overestimate the number of children requiring clinical care for obesity. With more comprehensive forms of screening (i.e., EOSS-P) and baseline measurements, such as CRF, health care experts could have access to a more accurate number of children struggling with obesity. Theoretically, this approach could potentially reduce unnecessary health care expenditures (i.e., EOSS-P Stage 0 child), and focus the finite health care resources on children that require more intensive forms of treatment (i.e., EOSS-P Stage 2 & 3). Though not an immediate solution to the obesity crisis, considering these methods, specifically the EOSS-P and measuring CRF, may serve as a preferable approach for health experts involved in assessing children for pediatric obesity.

## Chapter 6

### Statement of Contribution from Collaborators

- Mr. Kevin Belanger performed all of the CRF testing of the study participants, formulated and performed all of the statistical analyses and was the primary contributor to the research papers within this thesis.
- Dr. Kristi B. Adamo, in addition to her role as Thesis Supervisor, aided in the research project design, and reviewed and revised the two thesis manuscripts.
- Dr. Katherine Baldwin staged the children with Edmonton Obesity Staging System, aided in the research project design, and reviewed and revised the two thesis manuscripts.
- Dr. Geoff D.C. Ball, aided in the research project design, and reviewed and revised the two thesis manuscripts.
- Dr. Annick Buccholz aided in the research project design, and reviewed and revised the two thesis manuscripts.
- Dr. Stasia Hadjiyannakis, Medical Director of the CHAL program, staged the children with Edmonton Obesity Staging System, aided in the research project design, and reviewed and revised the two thesis manuscripts.
- Ms. Jane Rutherford aided Kevin Belanger in performing the maximal cardiorespiratory fitness tests on the children, aided in the research project design, and reviewed and revised the two thesis manuscripts.

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## Appendix A

### Criteria for the Edmonton Obesity Staging System for Pediatrics

#### Stage 0: No obesity-related risk factors:

- Metabolic: No metabolic or biochemical abnormalities
- Mechanical: No functional limitations
- Mental: No abnormal psychopathology
- Family: No parental, familial, or social environment concerns

#### Stage 1: Presence of subclinical obesity-related risk factors

- Metabolic:
  - Acanthosis Nigricans
  - Pre-hypertension: Systolic or diastolic BP 90-95<sup>th</sup> %
  - Fasting blood glucose 5.6 – 6.9 mmol/L
  - 2-hour blood sugar (OGTT) 7.8 – 11.0 mmol/L (IGT)
  - LDL-C or Non-HDL-cholesterol 4.2 – 4.8 mmol/L
  - HDL-Cholesterol 0.8 – 1.03 mmol/L
  - Triglycerides 1.7 – 3.5 mmol/L
  - ALT 1.5 – 2x normal
- Mechanical:
  - Mild OSA not requiring BiPAP or CPAP
  - Mild musculoskeletal pain that does not interfere with activities of daily living
  - Dyspnea with physical activity that does not interfere with activities of daily living
- Mental:
  - ADHD and/or learning disability
  - Mild depression or anxiety that does not interfere with functioning
  - Mild body image preoccupation/concern
  - Mild emotional/binge eating (occasional)
  - Occasional bullying at school or at home
  - Mild impairment in quality of life
  - Mild developmental delay
- Family:
  - There are minor problems in the relationships of the child/youth with one or more family members
  - Caregiver is generally knowledgeable of child's needs/strengths, but may require information or support in parenting skills
  - Caregiver has minimal difficulty in organizing household to support needs of child/youth
  - Caregiver is recovering from medical/physical, mental health and/or substance use problems

**Stage 2: Presence of obesity-related chronic diseases and associated health issues**

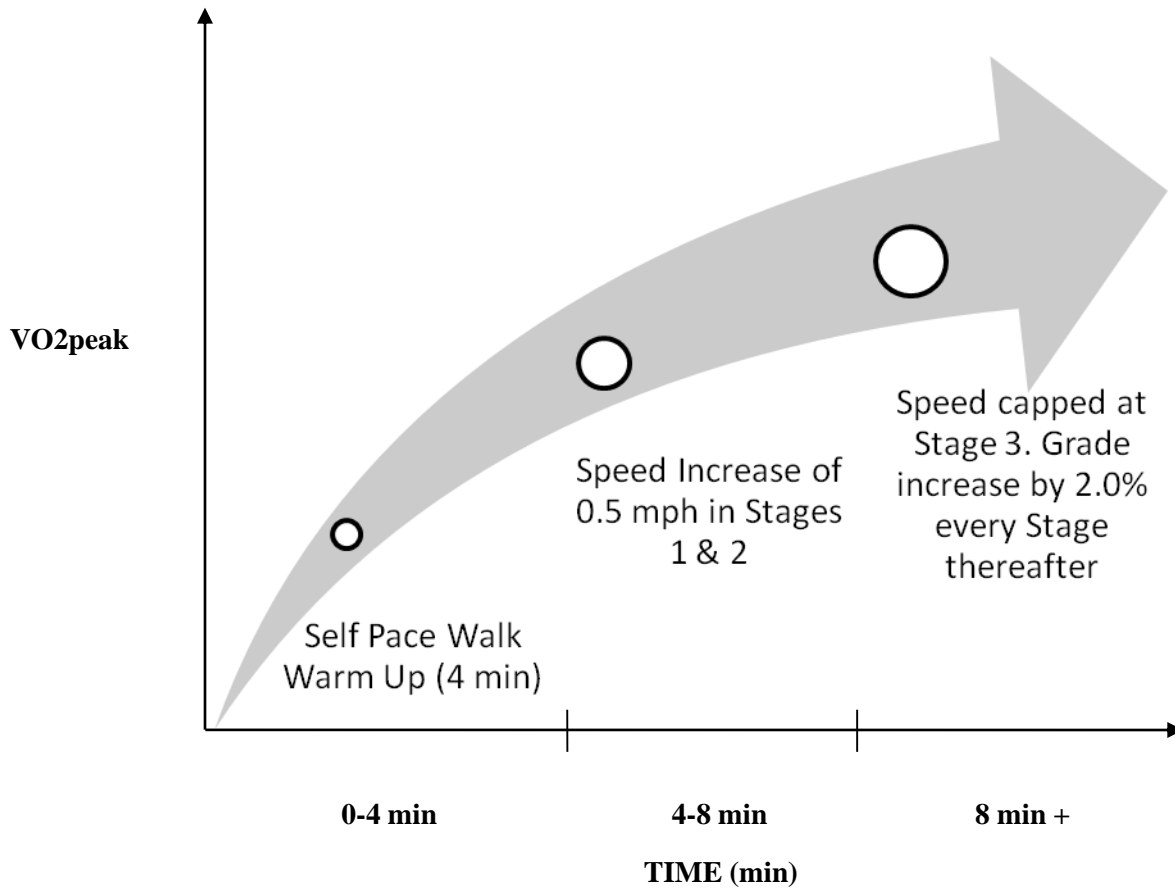
- Metabolic:
  - Type 2 diabetes without diabetes-related complications
  - Hypertension: Systolic or diastolic BP > 95<sup>th</sup>%
  - HDL-Cholesterol < 0.8 mmol/L
  - LDL-Cholesterol and/or non-HDL-Cholesterol > 4.9 mmol/L
  - Triglycerides > 3.5 mmol/L
  - ALT 2 – 3× normal and/or ultrasound evidence of severe fatty infiltration of the liver
  - Polycystic ovarian syndrome
- Mechanical:
  - OSA requiring BiPAP or CPAP
  - Gastroesophageal reflux disease
  - MSK pain / complications limiting physical activity
  - Moderate limitations in activities of daily living
- Mental:
  - Poor school attendance
  - Major depression or anxiety disorder
  - Moderate binge eating (frequent)
  - Significant bullying at school or at home
  - Significant body image disturbance
  - Moderate developmental delay
  - Moderately impaired quality of life
- Family:
  - Child/youth is having moderate problems with parents, siblings and/or other family members, frequent arguing, difficulty maintaining positive relationships
  - Need for information on parenting skills; current lack of information interfering with ability to parent effectively
  - Moderate difficulty organizing household to support needs of child/youth
  - Has medical/physical problems that interfere with parenting
  - Has some mental health, substance use and/or developmental challenges that interfere with parenting

### Stage 3: Presence of established chronic diseases and associated health issues

- Metabolic:
  - Focal Segmental Glomerulosclerosis
  - Type 2 diabetes with diabetes-related complications or HgA1C  $\geq 8$
  - Cardiomegaly
  - Liver enzymes  $>3\times$  normal limits and/or liver dysfunction
  - Gall bladder disease or stones
  - Hypertension on pharmacotherapy
  - Hyperlipidemia on pharmacotherapy
  - Gout
- Mechanical:
  - OSA requiring BiPAP or CPAP and supplementary oxygen overnight
  - Pulmonary hypertension
  - Limited mobility
  - Shortness of breath when sleeping or sitting
  - Peripheral edema
  - Blount's Disease
  - Slipped Capital Femoral Epiphysis
  - Osteoarthritis
  - Incontinence
  - Encoporesis
- Mental:
  - Uncontrolled psychopathology
  - School refusal / absenteeism
  - Severe binge eating (daily)
  - Self/physical loathing
  - Severe developmental delay
  - Severely impaired quality of life
- Family:
  - Child is having severe problems with parent, siblings and or other family members. May include constant arguing, family violence
  - Unable to monitor or discipline child/youth
  - Unable to organize household to support needs of child/youth
  - Experienced recent periods of homelessness
  - Medical/physical, mental health, substance use or developmental challenges that make it impossible for caregiver to parent effectively
  - Dangerous home environment

## Appendix B

### Visual Depiction of the Maximal Cardiorespiratory Fitness Test



\*\*\*Maximal cardiorespiratory fitness test developed by Gutin et al. (123).

## Appendix C

### Abstract for Presentation Performed at the 3<sup>rd</sup> Canadian Obesity Summit

**Title: Do obese children perceive submaximal and maximal exertion differently?**

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**Abstract:** We examined how obese children perceive a maximal cardiorespiratory fitness test compared with a submaximal cardiorespiratory fitness test. Twenty-one obese children (body mass index  $\geq 95$ th percentile, ages 10–17 years) completed maximal and submaximal cardiorespiratory fitness tests on 2 separate occasions. Oxygen consumption ( $\text{VO}_2$ ) and overall perceived exertion (Borg 15-category scale) were measured in both fitness tests. At comparable workloads, perceived exertion was rated significantly higher ( $P < 0.001$ ) in the submaximal cardiorespiratory fitness test compared with the maximal cardiorespiratory fitness test. The submaximal cardiorespiratory fitness test was significantly longer than the maximal test ( $14:21 \pm 04:04$  seconds vs.  $12:48 \pm 03:27$  seconds,  $P < 0.001$ ). Our data indicate that at the same relative intensity, obese children report comparable or even higher perceived exertion during submaximal fitness testing than during maximal fitness testing. Perceived exertion in a sample of children and youth with obesity may be influenced by test duration and protocol design.