Edmonton Obesity Staging System for Pediatrics, Quality of Life, Fitness, and Adherence to Exercise in Adolescents with Obesity

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A Thesis

in

The Department

of

Health, Kinesiology, and Applied Physiology

Presented in Partial Fulfillments of the Requirements

for the Degree of Master of Science (Health, Kinesiology, and Applied Physiology) at

Concordia University

Montreal, Quebec, Canada

August 2018

CONCORDIA UNIVERSITY

School of Graduate Studies

This is to certify that the thesis prepared

By: Gabriel Kakon

Entitled: Edmonton Obesity Staging System for Pediatrics, Quality of Life, Fitness, Adherence to Exercise in Adolescents with Obesity

and submitted in partial fulfillment of the requirements for the degree of

Master of Science (Health, Kinesiology and Applied Physiology)

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

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ABSTRACT

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Gabriel A. Kakon

Background: The Edmonton Obesity Staging System-pediatrics (EOSS-p) is based on the EOSS for adults, which has shown better predictive value for mortality than BMI. To our knowledge, no study has examined the EOSS-p in relation to health and wellbeing outcomes in a pediatric sample with obesity. The purpose of this study was to compare the associations of EOSS-p and BMI percentile with quality of life (QOL), cardiorespiratory fitness (CRF), muscular strength, and adherence to an exercise intervention in adolescents with obesity.

Methods: Participants were enrolled in the Healthy Eating Aerobics Resistance Training in Youth trial (N= 299). QOL, CRF (peak oxygen uptake, VO_{2peak}) and muscular strength were assessed by the Pediatric QOL Inventory (PedsQL), indirect calorimetry during a maximal treadmill test, and 8-RM bench and leg press tests respectively. QOL, CRF, and muscular strength were assessed at baseline and 6-months after the intervention. Adherence was determined as a percentage of attended exercise sessions. Participants were staged from 0 to 3 (absent to severe health risk) according to EOSS-p. The association of EOSS-p and BMI percentile with outcomes were assessed using general linear models adjusting for age and sex.

Results: Baseline QOL decreased with increasing EOSS-p stages ($p<0.001$). QOL was 75.7 ± 11.4 in stage 0/1, 69.1 ± 13.1 in stage 2, and 55.4 ± 13.0 in stage 3. Stage 3 showed smaller improvements with 6-month CRF than stage 0/1 and 2 ($p=0.001$, B=-3.882 mlO_2/kg/min). BMI percentile was associated with baseline VO_{2peak} ($p<0.001$, B=-1.044 mlO_2/kg/min), bench press ($p=0.029$, B=0.832 kg) and leg press ($p=0.003$, B=3.992 kg). Similar associations were observed between BMI percentile and 6-month outcomes.

Conclusion: As EOSS-p stages increase, QOL decreases. EOSS-p stage 3 had lower 6-month CRF, which suggests stage 3 may require a longer, more intensive or different intervention to achieve similar CRF improvements. BMI percentile showed contradicting health associations with cardiorespiratory fitness and muscular strength.

AKNOWLEDGEMENTS

My MSc thesis would not have been possible without the help and support of the following peoples:

Dr. Angela Alberga, you have exceeded my expectations as an MSc supervisor. None of this would have been possible without your guidance and support. I am grateful for all the critical and honest feedback, which has enabled me to grow as a scientist. Working under you has been a privilege and I've learnt a great deal. Thank you for always believing in me and remaining positive!

To my labmates, Erica, Iyoma, Lara, and Trisha, thank you for bearing with me. Regardless of my rants, and watching me practice my golf swing, you have always been supportive, and never short of offering help. Thank you for making my MSc experience a great one.

To my committee members, Dr. Stasia Hadjiyannakis and Dr. Bacon, I am grateful to have such a talented researcher, and passionate clinician on my committee. You have always taken the time to see me when needed. Your insight and suggestions were impactful and critical to the development of this project.

To the co-authors, Dr. Ron Sigal, Steve Doucette, Dr. Gary Goldfield, Dr. Glen Kenny, Dr. Denis Prud'homme, Dr. Annick Buchholz, Megan Lamb, you sure know how to critique a paper (I mean that in the most endearing way).

Dr. Jordan Levy, you made the cut for an honorary mention! Thanks for listening to me, and always challenging my ideas.

Last but not least, thank you to my girlfriend Michelle and my family, you guys are the foundation to my success.

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ABBREVIATIONS

4M's – Metabolic Health, Mental Health, Mechanical Health, Social Milieu

ADHD – Attention Deficit Hyperactivity Disorder

ALT – alanine transaminase

AST – aspartate transaminase

BMI – Body Mass Index

CDC – Center for disease control

CDI – Child Depression Inventory

EOSS – Edmonton Obesity Staging System

EOSS-p – Edmonton Obesity Staging System for pediatrics

GERD – Gastroesophageal reflux disease

HbA1c – Hemoglobin A1c

HDL-C High density lipoprotein cholesterol

HEARTY – Healthy Eating Aerobics Resistance Training in Youth

HR – Hazard Ratio

kg – Kilograms

LDL-C – Low density lipoprotein cholesterol

m – Meters

MBSRQ-AS – Multiple Body Self-Relation Questionnaire – Appearance Scale

NHANES – National Health and Human Nutrition Examination Surveys

OGTT – Oral Glucose Tolerance Test

PCOS – Polycystic ovarian syndrome

QOL – Quality of Life

SD – Standard deviation

VO_{2peak} – Peak oxygen uptake

CHAPTER 1: Introduction

1.0 General introduction

Obesity has been considered a chronic disease due to the potential weight-related comorbidities associated with obesity (1). Weight-related comorbidities occur when excess adiposity negatively affects an individual's metabolic, mental, and biomechanical health and wellbeing. Examples of weight-related comorbidities include but are not limited to cardiovascular disease, type 2 diabetes, anxiety, and obstructive sleep apnea (2) which can ultimately lead to decreased fitness and quality of life (QOL) (3). Adolescents with obesity tend to have obesity in adulthood (4), and if left untreated or uncontrolled with a healthy lifestyle, weight-related comorbidities can progressively worsen leading to premature mortality (5, 6). Exercise interventions are commonly used to manage adolescent obesity and improve health and wellbeing (7-9), however, adherence is essential for the effectiveness of an intervention (10, 11). Adherence is defined as the percentage of attended session from a prescribed intervention. In adolescents with obesity adherence to exercise interventions has ranged between 56% to greater than 99% (8, 12-14). Thus, early assessment tools that can help detect overall health, wellbeing, and adherence to an exercise intervention are necessary tools for managing adolescents living with obesity (15-17).

Body mass index (BMI) is currently the most commonly used assessment tool to diagnose obesity in adolescents. BMI is calculated by dividing weight by height squared (kg/m^2). In pediatrics, a child or adolescent aged 2 to 19 with a BMI $\geq 85^{th}$ percentile for their age and sex would be considered to have overweight, while $\geq 95^{th}$ percentile they would be classified as having obesity. Although BMI is practical and inexpensive, in recent years, it has been heavily criticized due to its overly simplistic approach to determining severity and biopsychosocial impacts of obesity (18, 19), its limitations in pediatric populations (20), and its potential to misdiagnose overweight or obesity (21-24). Two adolescents with the same BMI can have very different body compositions and health status. In fact, some adolescents with elevated BMI may be metabolically healthy (25, 26). The obesity classification by BMI does not provide information on how adiposity may negatively impair health and wellbeing of an adolescent. The World Health Organization defines health, as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" (27). Having access to a staging system of obesity that allows healthcare professionals to better determine the health and wellbeing of adolescents with obesity is necessary for guiding clinical care.

Created in 2016, the Edmonton Obesity Staging System for pediatrics (EOSS-p) is the first assessment tool created to classify pediatric obesity by weight-related comorbidities and weight-management barriers. The EOSS-p takes into account patient's metabolic health, mental health,

biomechanical health, and social milieu to understand the severity of obesity prognosis and help guide future clinical care. EOSS-p was not intended to replace BMI percentiles, but rather to complement it by improving risk stratification of pediatric obesity. The EOSS-p is based on the already existing EOSS for adults, and is carefully tailored for usage in pediatrics (18). EOSS for adults was developed and proposed in 2009 by a team of Canadian medical doctors and researchers specialising in obesity (19) and was the first tool to classify adulthood obesity by weight-related comorbidities and weight-management barriers. Analogous to the staging of cancer, the EOSS staging system is based on a 5-point scale, ranging from stage 0 (no risk), stage 1 (mild risk), stage 2 (moderate risk), stage 3 (severe risk), to stage 4 (end stage). Unlike the adult version of EOSS with a 5-point staging system, the EOSS-p defines weight-related health-risk on a 4-point staging with four categories. The EOSS-p stages range from stage 0 (no risk), to stage 3 (severe risk). The EOSS-p stages are assigned for each of the following categories: metabolic health, mechanical health, mental health, and social milieu (4M's). These categories represent and encompass weight-related comorbidities and weight-management barriers in children and adolescents with obesity. The adult EOSS version does not include the category social milieu, however, in children and adolescents, family functioning, and relationship with peers and plays an important role as enablers in pediatric weight-related health risk (28). Since EOSS-p was proposed in 2016, no research has been published on the EOSS-p. Our current understanding of EOSS-p stems from studies investigating EOSS for adults. Since the proposal of EOSS for adults, three studies have begun demonstrating its predictive validity and potential clinical utility.

EOSS study #1: Kuk et al (2011) conducted an analysis on data from the Aerobics Center Longitudinal Study to assess if EOSS can identify individuals at greater mortality risk. They used a community cohort from Dallas, Texas of 99% white/well educated, and mid to high socioeconomic status. The analysis was conducted on 5483 men and 771 women (n = 6254) living with obesity, a control of individuals (n = 23309) with normal weight. Individuals with obesity were stratified into EOSS stages 0 to 3, since not enough information was provided for stage 4. The researchers found that when comparing all-cause mortality of individuals with normal weight control to those with obesity, hazard ratio (HR) for stage 2 was 1.6 (95% CI 1.3-2.0), and for stage 3 was 1.7 (95% CI 1.4-2.0). When comparing mortality caused by cardiovascular disease, the HR for stage 2 was 2.1 (95% CI 1.6-2.8), and for stage 3 was 2.1 (95% CI 1.6-2.8). Here, the HR indicates the rate that mortality would occur compared to the control group. Stage 0 and stage 1 were not associated with elevated mortality risk, while stages 2 and 3 had significant elevated risks of mortality, especially from cardiovascular disease. Other clinical variables were associated with elevated EOSS stage, including: low cardiorespiratory fitness, weight and

health history, weight at age 21, preferred weight, and dietary intake of fruits and vegetables. Lower cardiorespiratory fitness, weight, health history, weight at 21 associated with increased risk within EOSS stages 2 and 3. The findings suggested that EOSS is a useful tool at predicting mortality, and potentially to identify patients in need of weight-management interventions. Furthermore, EOSS stage 0/1 showed no increased risk of mortality, demonstrating that weight loss interventions may not be necessary for all individuals across the obesity spectrum. A limitation of this study was that the majority of participants were Caucasian males (>99%), therefore the results cannot be generalizable to the entire population. Despite these rich findings, more research is needed to determine if this system can be generalized in a pediatric population and in females, as well as if it can predict other important outcomes of health and wellbeing, and adherence to an exercise intervention.

EOSS study #2: Padwal et al. (2011) assessed the ability of EOSS for predicting mortality compared to BMI from the largest US population representative cohort, the National Health and Human Nutrition Examination Surveys (NHANES) 1988-1994 and 1999-2004. Padwal et al.'s study included participants from NHANES III from 1988-1994 (n=4367) and NHANES 1999-2004 (n=3600). Participants were stratified into BMI categories and EOSS categories. The BMI categories were overweight, class 1 obesity, class 2 obesity, and class 3 obesity. EOSS categories were stage 0, 1, 2, and 3 obesity. They were unable to assign EOSS stage 4, because NHANES did not have end-stage participants to assign stage 4. They found that 75% of the participants from the population-based sample had scores of 1 or 2. They found EOSS was a stronger predictor of mortality than BMI in the control group with healthy weight and in the sample with obesity (independent of BMI, metabolic syndrome and/or hypertriglyceridemia waist). Data from NHANES III 1988-1994 showed that after adjusting for BMI and metabolic syndrome, the survival rates were for EOSS stage 2 HR 1.57 (95% CI 1.16 to 2.13) and 3 HR 2.69 (95% CI 1.98-3.67) using EOSS stages 0/1 as reference; and for BMI class 1 obesity had HR 1.22 (95% CI 1.01-1.48), class 2 obesity had HR 1.73 (95% CI 1.23-2.46), and class 3 obesity had HR 1.52 (95% CI 0.94-2.46). After adjusting for BMI and presence of hypertriglyceridemic waist (combination of a waist circumference >90 cm in men or >85 cm in women, and elevated plasma triglyceride concentrations), EOSS stages and BMI showed consistent trends. Survival curves were used to graphically illustrate the predictive ability of EOSS stages versus BMI classifications for survival rate. According to the survival curves, the EOSS obesity stages were visibly better predictors of mortality than BMI obesity classifications, and are able to predict mortality rate within BMI obesity classification (overweight, class 1, class 2, and class 3). These findings suggest the potential clinical utility in prioritizing patients for bariatric surgery (29). A limitation of this study was the lack of mental health

assessments. Therefore, more research needs to be conducted to include EOSS mental health assessments, and to determine if EOSS can be used in a pediatric population. Lastly, the authors suggested that other outcomes such as QOL are worth investigating (6).

EOSS study #3: Canning et al. (2015) sought to compare the effects of EOSS stage on weight loss of patients with obesity (n=5787) attending a referral-based weight-management clinic. They found a frequency distribution of 1.7% for stage 0, 10.4% for stage 1, 84% for stage 2, and 3.9% for stage 3. There were no EOSS stage 4 patients being treated at this weight-management clinic. The most common weight-related comorbidities were prehypertension, hypertension, and knee replacement surgery. They found that lower EOSS stages were associated with shorter treatment times. The treatment times (± SD) were 10.4 months (±11.7) for Stage 0, 9.4 months (± 11.5) for EOSS stage 1, 12.7 months (± 15.0) for EOSS stage 2, and 14.7 months (± 16.0) for EOSS stage 3. There was no significant difference between treatment times for stage 0 and stage 1, but there were significant differences between stage 1, 2 and 3. When adjusting for treatment time, lower EOSS stage was associated with greater weight loss in absolute kg ($p<0.01$) and in percentage of body weight ($p<0.01$). The authors suggest that weight loss programs should be tailored to EOSS staging, more specifically for EOSS stage 2, and 3. A limitation in this study was the disproportionate distribution of EOSS stages. EOSS stage 0 and 1 should be suggested weight-gain prevention program instead. Another limitation of the study is that each participant underwent a different medical assessment by their physicians, meaning that not all participants had the same assessments done when staging with EOSS. Future research evaluating EOSS should use a sample with more participants in lower stages, use participants who have undergone a standardized set of assessments, and should investigate adherence and attrition factors.

The three studies by Kuk et al. (2012), Padwal et al. (2012), and Canning et al (2015) shared some similar patterns in their findings. All four studies have found that EOSS stage 0/1 show a no risk to low health-related risk. Kuk et al. (2012) showed no difference in predicting all-cause mortality between EOSS stage 0/1 and normal weight individuals; Padwal et al. (2012) showed little to no differences between stage 0 and stage 1 for predicting mortality; and Canning et al. (2015) found no significant differences between treatment times of stage 0 and 1. Obesity in adults is traditionally defined by BMI ≥30 kg/m^2, which has been identified as a risk-factor for poor health. However, based on the findings of these EOSS studies, people with similar BMI seem to have a very different health risk status according to EOSS. These promising studies have created awareness in the international bariatric community, and the EOSS for adults is starting to be used as an assessment tool in bariatric surgery research in Canada, Germany and Brazil (30). However, for the EOSS-p to create similar awareness, it

too must be studied. The only outcomes studied regarding EOSS to date are mortality, and weight-loss. To date, no study has evaluated how EOSS-p is associated with health and wellbeing, and adherence to exercise in children or adolescents with obesity. In order for the EOSS-p to help guide clinical treatment, it must be studied in a pediatric sample with obesity.

1.1 QOL, cardiorespiratory fitness, and muscular strength

Previous studies evaluating the EOSS for adults used mortality risk as an adverse health outcome. While mortality risk is difficult to predict in children, QOL, cardiorespiratory fitness, and muscular strength are feasible measures known to be good representations of health and wellbeing in adolescents (31, 32). QOL is consistently lower in populations with chronic disease (33), and promotion of QOL has been identified as an over-arching public health goal from Healthy People 2000, 2010, and 2020 (34). Cardiorespiratory fitness is the capacity of an individual to deliver oxygen to working muscles and carry out long, strenuous exercise (35). Cardiorespiratory fitness has been proposed by the American Heart Association for routine assessment in clinical practice because of its strong association with cardiovascular disease and all-cause mortality (36). Higher levels of cardiorespiratory fitness and physical activity has been shown to significantly reduce the risk of mortality in individuals with obesity (5). Muscular strength, which is a component of muscular fitness, refers to "the ability to carry out maximal force" against a resistance (37). Cardiorespiratory and muscular fitness are consistently lower in populations with chronic diseases and are independently associated with metabolic risk factors in adolescents (31, 38). Muscular strength is associated with higher insulin sensitivity in adolescents (39), and is a strong predictor of mortality and life expectancy in adults (40). A single assessment tool that is associated with QOL, cardiorespiratory fitness, and muscular strength in a population of adolescents with obesity would be optimal for healthcare professionals to help guide clinical treatment for their patients.

1.2 Adherence

The most common obesity treatments for weight management are lifestyle behavioural programs, such as exercise interventions. Exercise interventions in adolescents with obesity have demonstrated significant physiological, biomechanical, and mental health benefits (7, 11, 41-45), including improvements in cardiorespiratory fitness and QOL (7, 44). A major obstacle facing the effectiveness of

exercise interventions is low adherence and attrition to the intervention (46, 47). Adherence can be defined as the extent to which a person's behaviour corresponds to agreed intervention (48). For this thesis project, adherence to an exercise intervention is defined as a percentage of sessions attended out of the total prescribed sessions. Identifying predictors of adherence to exercise interventions would inform ways to address these predictors and ultimately improve adherence to exercise interventions in the long term.

The body of literature assessing adherence factors in pediatric obesity weight management interventions is scarce, however it has been investigated in adults (46). A systematic review focusing on adulthood obesity, found lower baseline BMI, lower depression, stress, and anxiety to be predictors of adherence (46). While this systematic review identifies many potential predictors of adherence in adults with obesity, the number of contributing factors identified can be complex to interpret for evaluators, as it requires identifying each variable individually. It would be beneficial to investigate if a multidisciplinary pediatric obesity assessment tool like EOSS-p could predict adherence to an exercise intervention in adolescents with obesity.

1.3 Objective

The primary purpose of this thesis is to investigate EOSS-p and BMI percentile regarding their associations with QOL, cardiorespiratory fitness, and muscular strength. QOL, cardiorespiratory fitness, and muscular strength were assessed at baseline and at 6-month time points. The secondary objective is to determine how EOSS-p and BMI percentile are associated to adherence to an exercise intervention in a community sample of adolescents with overweight and obesity who participated in the Healthy Eating and Aerobics Resistance Training in Youth (HEARTY) randomized controlled trial (see Figure 1).

1.4 Hypothesis

1) Baseline EOSS-p stages will be negatively associated with baseline and 6 months QOL, cardiorespiratory fitness, and muscular strength.
2) Baseline BMI percentile will be negatively associated with baseline and 6 months QOL, cardiorespiratory fitness, and muscular strength.
3) Baseline EOSS-p stages will be negatively associated with adherence to exercise at 6 months.
4) Baseline BMI percentile will be negatively associated with adherence to exercise at 6 months.

1.5 Structure of thesis

To achieve the objectives, this thesis is structured in the following manner to:

1) Outline the overall HEARTY trial, design and methods, with specific methodology used for this thesis project (Methods);
2) Identify and discuss baseline associations of EOSS-p and BMI percentile with baseline QOL, cardiorespiratory and muscular fitness (Manuscript 1);
3) Identify associations of EOSS-p in comparison to BMI percentile with 6-month QOL, cardiorespiratory fitness, muscular fitness, and adherence to the HEARTY exercise intervention (Additional results);
4) Discuss the additional results reporting associations of EOSS-p in comparison to BMI percentile with 6-month outcomes and adherence to the HEARTY exercise intervention (Discussion) and;
5) Conclude with a brief summary of the thesis' purpose, results and discussion (Conclusion).

CHAPTER 2: Methods

2.0 General Methods

2.1 General research plan / HEARTY overview

This thesis project is a secondary data analysis from the Healthy Eating, Aerobic and Resistance Training in Youth (HEARTY) randomized controlled trial completed between 2005 and 2011 (49) where primary outcomes have been previously reported (50). At baseline, participants completed a series of metabolic, mechanical, mental health, and social milieu assessments over four visits (see Figure 2 and Table 1). Baseline assessments included a medical history (see section 2.3), physical exam (see section 2.4), laboratory blood tests (see section 2.5, and 2.6), mental health questionnaires (see section 2.6), QOL questionnaire (see section 2.7), cardiorespiratory fitness (see section 2.9), and muscular fitness (see section 2.10) assessments. After baseline assessments, participants entered a 4-week run-in period with combined aerobic and resistance exercise sessions four times per week (see section 2.11.1). Participants who adhered to at least 13 of the 16 prescribed exercise sessions were then randomly assigned into three different exercise interventions (aerobic, resistance or combined aerobic + resistance) or a non-exercise control group (see section 2.11.2 and 2.11.3). QOL, cardiorespiratory fitness, and muscular fitness were re-assessed at 6-months. Adherence was monitored throughout the intervention.

2.2 Participants

The participants (N=304) included in HEARTY were inactive post-pubertal adolescents (Tanner stage 4-5) with obesity aged 14-18 years old. Five participants were lacking mental health data so the final analysis included N=299. Participants were included in the study if their BMI was ≥95th percentile for their age and sex or ≥85th percentile (https://www.cdc.gov/growthcharts/) with an additional risk factor for diabetes or cardiovascular disease. Twenty-two (7%) participants had overweight, while n=282 (93%) had obesity. Our sample had a mean BMI percentile of 97.8, ranging from 87.2 to 99.8. The exclusion criteria were:

1) BMI larger than 45kg/m^2, pregnancy, performance enhancing medications, medical conditions, use of medication or herbal supplement likely to affect body composition, lipids or glucose metabolism (metformin use was permitted if participants were on metformin prior to enrollment);

2) Significant weight change (increase or decrease of ≥5% during the two months before enrolment); uncontrolled hypertension (blood pressure >150 mmhg systolic or >95 mmhg diastolic in sitting position);
3) Activity restriction due to disease, such as unstable cardiac or pulmonary disease, or significant arthritis;
4) Other illnesses such as eating disorders or depression;
5) Inability to communicate in English or French;
6) Unwillingness, inability, or unavailable to exercise;
7) Unwilling of subject or parent/guardian to sign the informed consent.

Recruitment was done via advertisements on city busses, referrals from the obesity clinic at the Children's Hospital of Eastern Ontario and physicians in the community, word of mouth, poster print advertisements, radio campaigns and in schools. Informed consent was obtained by participants and by a parent or legal guardian for participants under 16. The Research Ethics Boards at the Children's Hospital of Eastern Ontario and the Ottawa Hospital approved this study.

2.3 Medical history

The research coordinator asked HEARTY participants a series of questions to assess their medical history. The medical history questions included demographic information regarding age, race, description of family unit, parental depression, parent employment status and education level, subject employment status, subject academic status and academic performance. Open-ended questions were asked regarding previous injuries/surgeries, history of smoking, history of alcohol consumption/recreational drug use, medication use, and self-reported depression or other psychological disorders such as ADHD. If the participant was female, she was asked if she has had irregular menses. Parents were asked to leave the room during medical history examination while discussing drug, alcohol, smoking or depression.

2.4 Physical exam

A research coordinator conducted a physical examination as part of the medical history. BMI (see section 2.4.1), blood pressure (see section 2.4.2), and acanthosis nigricans (see section 2.4.3) and tanner stage were assessed (51-53).

2.4.1 BMI

The research coordinator measured height and weight to calculate BMI. Participants were instructed to remove shoes, jacket, and anything that could add weight (e.g. Keys, wallet, phone, etc.). Height was measured in meters (m), and weight was measured in kilograms (kg) using the Health-O-Meter manual scale (Health O Meter, Continental Scale Corp., Bridgeview, ILL). Percentile ranks were attributed using CDC age- and sex-specific growth charts (≥95 percentile is obesity and ≥85 percentile is overweight). CDC growth charts are developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion in 2000 (54).

2.4.2 Blood pressure

The participant was seated in a chair with back support for four minutes at rest. Blood pressure was then taken three consecutive times with one-minute breaks in between. The mean of the final two measurements was used as the final blood pressure value.

2.4.3 Acanthosis nigricans

A research coordinator evaluated acanthosis nigricans using the Burke Scale. The Burke Scale requires an observer to visually evaluate potentially affected areas, such as neck, axilla, knuckles, elbows, and knees. Neck severity, neck texture, and axilla are ranked on a 4-point scale. Knuckles, elbows and knees are reported as present or absent. The Burke Scale for assessing acanthosis nigricans has been validated in participants with type 2 diabetes (55).

2.5 Oral Glucose Tolerance Test

An oral glucose tolerance test (OGTT) was completed at the Ottawa Hospital, Riverside Campus. The OGTT test indicates the ability for the participants' body to metabolize blood glucose (blood sugars). This test compares glucose levels in the blood pre- and post- ingestion of a sugary drink.

For the OGTT, participants were instructed to follow an unrestricted diet consuming a minimum of 150g of carbohydrates daily, and perform usual physical activity for 3 days prior to testing. They were then instructed to fast overnight for 12 hours, drink a lot of water during the fast, and abstain from any strenuous physical activity for 24 hours prior to the appointment. If applicable, participants were told to continue any long-term drug treatments on day of testing (medications affecting glucose tolerance were noted).

Participants received the OGTT the morning. Trained staff collected venous blood samples from participants upon their arrival at the clinic. Participants were given a 75-gram 250-300 ml glucose solution to drink within 10 minutes. The glucose solution was kept at room temperature between 20-25^{o}c. Another venous blood sample was collected two hours after glucose ingestion. Participants were permitted to drink water during the test, however, smoking and exercise were not permitted. Insulin resistance was estimated from fasting plasma glucose and insulin concentration values using the Homeostatic Model Assessment (56).

2.6 Other laboratory blood tests

A research coordinator collected blood samples from participants to perform various blood tests. Participants fasted for 12 hours, and refrained from physical activity for 48 hours prior to blood draws. The blood tests included: Hemoglobin A1c (hba1c) was evaluated using tubidimetric immunoinhibition; total cholesterol, HDL-C, and triglyceride levels measured using a Beckman-Coulter LX20 analyzer (Beckman Instruments, Brea, California, USA); low-density lipoproteins cholesterol (LDL-C) levels calculated using the Friedewald equation (57); blood analysis for liver enzymes aspartate transaminase (AST) and alanine transaminase (ALT); and testosterone levels. The Ottawa hospital biochemistry/hematology department conducted these blood tests.

2.7 Mental health questionnaires

The Child Depression Inventory (CDI) (58) is a questionnaire intended to measure symptoms of depression in school aged children and adolescents. CDI measures five sub-factors including negative mood, ineffectiveness, negative self-esteem, interpersonal problems, and anhedonia. CDI is a 27-item questionnaire, which asks participants to pick one sentence out of three that best describes them in the past two weeks. Each item is scored from 0 to 3 (0=symptoms absent, 1=mild, 2=definite), with a total score of 52.

To assess body image, a validated questionnaire called the Multiple Body Self-Relations Questionnaire – Appearance Scales (MBSRQ-AS) was used (59). The appearance evaluation (AE) subscale of the MBSRQ was used (7-item) for this study. The items are on a 5-point Likert scale from "definitely disagree" to "definitely agree". AE is the degree of satisfaction with their overall appearance (60). The AE has a .88 Cronbach's alpha with a .81 1-month test-retest for males, and a .88 Cronbach's alpha and a .91 1-month test-retest for females (60).

The Dutch Eating Behaviour Questionnaire (DEBQ) was used to assess eating behaviour. The emotional eating subscale (13-items) was used for this study. The items are on a 5-point Likert scale from "never" to "very often".

2.8 QOL questionnaire

HEARTY participants completed the 23-item Pediatrics QOL Inventory 4.0 (PedsQL) (32). The PedsQL is divided into four categories including: physical functioning (eight items), emotional functioning (five items), social functioning (five items) and school functioning (five items). Each item is ranked using a 5-point Likert scale ranging from "Never" to "Almost Always". The PedsQL is a reliable and feasible questionnaire that has been validated to assess QOL in a sample of adolescents with obesity (3, 61). This study showed that PedsQL had an internal consistency alpha of 0.80 (61). PedsQL was administered at baseline and 6-months.

2.9 Cardiorespiratory fitness

A certified exercise physiologist assessed peak oxygen uptake (VO_{2peak}) with indirect calorimetry (MOXUS Modular Metabolic System, AEI Technologies Naperville, IL, USA) during a maximal treadmill test, the gold standard for measurement of cardiorespiratory fitness (62). During the VO_{2peak} test participants were instructed to walk on a treadmill at a progressively increasing incline following the modified Balke and Ware incremental treadmill protocol (63) until the participant was too tired to continue. Treadmill time (i.e. The duration of the cardiorespiratory fitness test from start to finish) was also measured. Cardiorespiratory fitness was assessed at baseline and 6-months.

2.10 Muscular strength

An exercise specialist assessed upper body (bench press) and lower body (leg press) muscular strength using 8-repetition maximum (8RM) tests. Muscular strength was assessed at baseline and 6-month.

2.11 Study protocol

2.11.1 Run-in phase (weeks 1-4)

After baseline assessments, participants entered a 4-week run-in period to qualify for randomization. The run-in program was a low intensity aerobic and resistance exercise program for four sessions per week. A personal trainer supervised then twice a week during, while the other two sessions were unsupervised. The requirement to qualify for randomization into intervention or control groups was a minimum of 80% adherence (13 out of 16 sessions). Once completed, the participants were randomized.

2.11.2 Randomization

The participants (N=304) were randomized into one of four groups: diet & aerobic (n=75), diet & resistance (n=78), diet & combined aerobic and resistance (n=75), or diet-only control group (n=76). Participants were stratified into groups by their degree of overweight (ie. $\leq 95^{th}$ percentile or $\geq 95^{th}$ percentile) and sex in random blocks of 4 to 8 participants. A statistician performed randomization via

the randomization program IVRS,vbvoice v5.3, Pronexus. The research coordinator remained blinded throughout the randomization process.

2.11.3 Intervention phase (weeks 5-26)

2.11.3.1 Diet

Participants assigned to all four groups received a diet plan. During run-in, participants attended a small group education seminar on the topics of barriers in achieving healthful eating and solutions to overcome them, taste panels of fruits and vegetables, label reading, healthful snacks, and healthier eating at fast food outlets. At baseline, 3- and 6-months a dietitian hosted visits for all individuals involved in preparing the meals for the participants to discuss weight history, diet history, current eating habits and fast food consumption. Participants received additional support by phone at 6 weeks and 4 months.

The dietitian and the participants collaborated on establishing dietary goals. Participants were recommended to reduce their energy consumption by 250kcal/day and balance their energy sources with 15–20% protein, 50– 55% carbohydrates and 30% fat, as per (64).

2.11.3.1 Exercise protocol

After run-in, participants were allocated into exercise groups or control group. All exercise groups shared similarities in their protocol. Exercise interventions happened across gyms in the Ottawa and Gatineau regions. A binder with prescribed exercises were given to each participant. Participants were required to attend 4 sessions per week, with a certified personal trainer. The personal trainers would ensure proper technique, introduce modifications to exercises if necessary, and would ensure safe progressions of exercises. An exercise specialist would meet with participants every second week during the exercise intervention. The exercise specialist monitored adherence by reviewing sign-in sheets, electronic sign-in software at host gym, and exercise logs. Details of the exercise protocols can be found the HEARTY methods paper (49).

2.12 Edmonton Obesity Staging System for pediatrics (EOSS-p)

EOSS-p categorizes obesity using a 4-point staging system ranging from stage 0 (no risk), stage 1 (mild risk), stage 2 (moderate risk), and stage 3 (severe risk). The EOSS-p stages 0-3 are assigned for each of the following categories: Metabolic, Mechanical, Mental health, and Social Milieu (4M's). First, I assigned an EOSS-p stage to each participant for each of the 4M's. Second, I assigned each participant an overall EOSS-p stage. The overall EOSS-p stage was determined as the highest EOSS-p stage from the 4m's. For example, if a participant had a metabolic stage 1, mechanical stage 1, mental health stage 2, and social milieu stage 1, then their overall EOSS-p would have been stage 2 (moderate risk).

Using EOSS-p guidelines from the original EOSS-p tool development (18), I consulted a team consisting of five experts (two clinical pediatric psychologists, one pediatric endocrinologist, and two obesity researchers) in May 2018 to create the EOSS-p algorithm applicable for assessment of HEARTY participants (see Table 2). S.H. and A.B. were two of the original creators of the published EOSS-p (18) and they have both contributed substantially to my Manuscript 1 as co-authors. During each consultation, each variable was discussed at length until a consensus was reached. In the event that there was disagreement between two experts, I would discuss it with the other members of the expert team to make a final decision. Individual one-hour weekly meetings were held with my supervisor to discuss the HEARTY EOSS-p algorithm prior to consulting with other experts. In addition, four 1-2 hour team consultation meetings by teleconference and in-person in Ottawa (including two EOSS-p experts) were held over a period of 1.5 months to get a final consensus for the HEARTY EOSS-p algorithm. I staged all participants, and a second evaluator (M.L.) evaluated a random sample (n=30, 10% of total sample) for interrater reliability, indicating near-perfect agreement. The interrater Cronbach's alpha was 0.959.

2.13 Statistical analysis

Descriptive statistics were conducted to describe baseline characteristics of the HEARTY sample. Baseline characteristics were compared between EOSS-p stages using ANOVA. I created general linear models to determine associations of EOSS-p and BMI percentile with QOL, cardiorespiratory fitness, and muscular strength. For baseline outcomes, I adjusted for age, and sex in my analysis. For 6-month outcomes, I adjusted for age, sex, group assignment, and the baseline assessment of outcome variable in question. Confounding variables (age, sex, group assignment, and baseline assessment of outcome variable) were determined a priori. Bonferroni's post hoc test was used to assess differences between

EOSS-p stages. All analyses were conducted using statistics software IBM SPSS Statistics for Windows, version 24 (IBM Corp., Armonk, N.Y., USA).

CHAPTER 3: Results

Manuscript 1: Edmonton Obesity Staging System for Pediatrics and Quality of Life in Adolescents with Obesity

Manuscript formatted for *Pediatric Obesity* in preparation for submission in September 2018.

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Statement of contributions of collaborators:

G.A. Kakon generated the idea for this secondary data analysis, carried out the bibliographic search, article screening, created the EOSS-p algorithm specific to HEARTY, coded all the HEARTY data for EOSS-p staging, conducted the statistical analysis, and drafted and edited the manuscript.

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Edmonton Obesity Staging System for Pediatrics and Quality of Life in Adolescents with Obesity

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ABSTRACT

Background: The Edmonton Obesity Staging System-Pediatrics (EOSS-P) is a clinical staging system that uses weight-related comorbidities to determine health risk in pediatric populations. The purpose of this study was to investigate the associations of EOSS-P and BMI percentile with quality of life (QOL), cardiorespiratory fitness (CRF) and muscular strength in adolescents with obesity.

Methods: Participants were enrolled at baseline in the Healthy Eating, Aerobic and Resistance Training in Youth trial (BMI=34.6 ± 4.5 kg/m^2, N=299). QOL, CRF (peak oxygen uptake, VO_{2peak}) and muscular strength were assessed by the Pediatric QOL Inventory (PedsQL), indirect calorimetry during a maximal treadmill test, and an 8-RM bench and leg press tests respectively. Participants were staged from 0 to 3 (absent to severe health risk) according to EOSS-P. Associations assessed using age- and sex-adjusted general linear models.

Results: QOL decreased with increasing EOSS-p stages ($p<0.001$). QOL was 75.7 ± 11.4 in stage 0/1, 69.1 ± 13.1 in stage 2, and 55.4 ± 13.0 in stage 3. BMI percentile was associated with VO_{2peak} (B= –0.044 mlO_2/kg/min, $p<0.001$), bench press (B=0.832 kg, p=0.029) and leg press (B=3.992 kg, p=0.003).

Conclusion: As EOSS-p stages increase, QOL decreases. BMI percentile showed opposite health associations with CRF and muscular strength.

INTRODUCTION

Obesity has been considered a chronic disease due to the potential comorbidities (1). Weight-related comorbidities occur when excess adiposity negatively affects an individual's metabolic, mental, and/or biomechanical health and wellbeing. Examples of comorbidities include but are not limited to cardiovascular disease, type 2 diabetes, obstructive sleep apnea, anxiety and depression (2) which can ultimately lead to decreased fitness and quality of life (QOL) (3). Adolescents with obesity tend to have obesity in adulthood (4), and if left unmanaged, weight-related comorbidities can progressively worsen leading to premature mortality (5, 6). Thus, early assessment tools that can help detect overall health and wellbeing are necessary in adolescents living with obesity (7-9).

Body mass index (BMI) is currently the most commonly used measure to diagnose obesity in adolescents. BMI is calculated by dividing weight by height squared (kg/m^2). In pediatrics, children or adolescents aged 2 to 19 with BMI in the 85^{th} to 94^{th} percentile for their age and sex would be classified as overweight, while with BMI $\geq 95^{th}$ percentile they would be classified as having obesity (https://www.cdc.gov/growthcharts/). Although BMI is practical and inexpensive, in recent years, it has been heavily criticized due to its overly simplistic approach to determining severity and biopsychosocial impacts of obesity (10, 11), its limitations in pediatric populations (12), and its potential to misdiagnose overweight or obesity (13-16). Two adolescents with the same BMI can have very different body compositions and health status. In fact, some adolescents with elevated BMI may be metabolically healthy (17, 18). The classification of obesity by BMI does not provide information on how excess adiposity may negatively impair health and wellbeing of an adolescent. The World Health Organization defines health, as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" (19). Having access to a clinical staging system of obesity that allows healthcare professionals to better determine the health and wellbeing of adolescents with obesity is necessary for guiding clinical care.

Created in 2016, the Edmonton Obesity Staging System for pediatrics (EOSS-P) is the first assessment tool created to classify pediatric obesity by weight-related comorbidities and weight-management barriers. EOSS-P takes into account the patient's metabolic health, mental health, biomechanical health, and social milieu (4Ms) to determine the severity of obesity and provide prognostic information and to help guide future clinical care. EOSS-P was not intended to replace BMI percentile, but rather to complement it by improving risk stratification of pediatric obesity. EOSS-P is based on the Edmonton Obesity Staging System (EOSS) for adults and is carefully tailored for usage in pediatrics (10). The obesity stages of EOSS for adults have been shown to be better predictors of mortality than BMI-based obesity classifications (6, 20). Adults with higher EOSS stages (e.g. stages 2 and 3) require longer weight-management treatment-time than adults with lower EOSS stages (e.g. stages 0 and 1) to achieve similar weight loss outcomes (21). EOSS for adults is being used as an assessment tool in bariatric clinics in Canada, Germany and Brazil (22). To date, no studies have evaluated how EOSS-P is associated with health and wellbeing in children or adolescents with obesity. In order for EOSS-P to help guide clinical care, it must be studied in a pediatric sample with obesity.

Previous studies evaluating EOSS for adults used mortality risk as an adverse health outcome. However, mortality due to chronic disease in adolescents is extremely low, we chose instead to focus on markers of future morbidity and mortality. QOL, cardiorespiratory fitness, and muscular strength are feasible measures known to be good representations of health and wellbeing in adolescents (23, 24). QOL is consistently lower in populations with chronic disease (25), and promotion of QOL has been identified as an over-arching public health goal from Healthy People (United States governmental public health organization) 2000, 2010, and 2020 (26). Cardiorespiratory fitness is the capacity of an individual to carry out long, strenuous exercise (27). Cardiorespiratory fitness has been proposed by the American Heart Association for routine assessment in clinical practice because of its strong association with cardiovascular disease and all-cause mortality (28). Higher levels of cardiorespiratory fitness and

physical activity are associated with significantly lower risk of mortality in individuals with obesity (5). Muscular strength, which is a component of muscular fitness, refers to "the ability to carry out maximal force" against a resistance (29). Cardiorespiratory and muscular fitness are consistently lower in populations with chronic diseases and are independently associated with metabolic risk factors in adolescents (23, 30). Muscular strength is associated with higher insulin sensitivity in adolescents (31), and higher strength is a strong predictor of lower mortality and longer life expectancy in adults (32). QOL, cardiorespiratory fitness, and muscular strength are, therefore, good measures of general health and wellbeing and a single assessment tool that demonstrates associations with these measures in a population of adolescents with obesity would be optimal to help healthcare professionals guide clinical care for their patients.

The purpose of this study was to investigate EOSS-P and BMI percentile regarding their associations with QOL, cardiorespiratory and muscular strength in a sample of adolescents with overweight and obesity. We hypothesized that both EOSS-P and BMI percentile would be negatively associated with QOL, cardiorespiratory fitness and muscular strength. To our knowledge, this is the first study investigating the relationship of EOSS-P with important pediatric health and wellbeing outcomes.

METHODS

Study design

This is a secondary data analysis from the Healthy Eating, Aerobic and Resistance Training in Youth (HEARTY) randomized controlled trial completed between 2005 and 2011 (33), for which primary results have been previously reported (34). At baseline, participants completed a series of assessments that were used to establish EOSS-P scores. QOL, cardiorespiratory fitness, and muscular strength were also assessed at baseline.

Participants

Baseline participants (N=304) included were physically inactive post-pubertal adolescents (Tanner stage 4-5 (35, 36)) with overweight or obesity aged 14-18 years old. Five participants were lacking mental health data so the final analysis included N=299. Participants were eligible for the study if their BMI was ≥95th percentile for their age and sex or ≥85th percentile (https://www.cdc.gov/growthcharts/) with an additional risk factor for diabetes or cardiovascular disease. Twenty-two (7%) participants had overweight, while n=282 (93%) had obesity. Our sample had a mean BMI percentile of 97.8, ranging from 87.2 to 99.8. Informed consent was obtained from participants and from a parent or legal guardian of participants under 16. The Research Ethics Boards at the Children's Hospital of Eastern Ontario and the Ottawa Hospital approved this study.

EOSS-P

EOSS-P categorizes obesity using a 4-point staging system ranging from stage 0 (no risk), stage 1 (mild risk), stage 2 (moderate risk), and stage 3 (severe risk). Using EOSS-P guidelines from the original EOSS-P tool development (10), a team consisting of five experts (two clinical pediatric psychologists, one pediatric endocrinologist, and two obesity researchers) was consulted to create the EOSS-P algorithm applicable for assessment of HEARTY participants (Table 1). A primary evaluator (GAK) staged all participants, and a secondary evaluator (ML) evaluated a random sample (n=30, 10% of total sample) for interrater reliability. The interrater Cronbach's alpha was 0.959, indicating near-perfect agreement. Information on mental health questionnaires used in HEARTY that were specific to the EOSS-P algorithm used in this study are provided in a supplementary appendix.

Cardiorespiratory fitness

A certified exercise physiologist assessed peak oxygen uptake (VO_{2peak}) with indirect calorimetry (MOXUS Modular Metabolic System, AEI Technologies Naperville, IL, USA) during a maximal treadmill test, the gold standard for measurement of cardiorespiratory fitness (37). During the VO_{2peak} test participants were instructed to walk on a treadmill at a progressively increasing incline

following the modified Balke and Ware incremental treadmill protocol (38) until volitional fatigue. Treadmill time (i.e. the duration of the cardiorespiratory fitness test from start to finish) was also measured.

Muscular strength

An exercise specialist assessed upper body (bench press) and lower body (leg press) muscular strength using 8-repetition maximum (8RM) tests (the maximum weight that could be lifted eight times for each exercise while maintaining proper form through the full range of motion).

Quality of life

HEARTY participants completed the 23-item Pediatrics QOL Inventory 4.0 (PedsQL) (24) as part of a larger battery of measures. The PedsQL is divided into four categories including: physical functioning (eight items), emotional functioning (five items), social functioning (five items) and school functioning (five items). Each item is ranked using a 5-point Likert scale ranging from "Never" to "Almost Always". The total score was used for the analyses. The PedsQL is a reliable and feasible questionnaire that has been validated to assess QOL in a sample of adolescents with obesity (3, 39). This validation study showed that PedsQL had an internal consistency alpha of 0.80 (39).

Statistical analysis

Baseline characteristics were compared between EOSS-P stages using ANOVA. We created general linear models to determine associations of EOSS-P and BMI percentile with QOL, cardiorespiratory fitness, and muscular strength. We adjusted for age, and sex in our analysis. Confounding variables were determined *a priori*. Bonferroni's post hoc test was used to assess differences between EOSS-P stages. Mean PedsQL scores were compared for each successive EOSS-P stage using the Student's T-test. All analyses were conducted SPSS Statistics for Windows, version 24 (IBM Corp., Armonk, N.Y., USA).

RESULTS

Table 2 displays the baseline characteristics of the 299 participants included in our study. The sample included a total of 88 (29%) males and 211 (71%) females. The EOSS-P distribution of our sample in stage 0 was n=7 (2%), stage 1 n=116 (39%), stage 2 n=146 (49%), and in stage 3 n=30 (10%). The mean BMI of the overall sample was 34.6 ± 0.5 kg/m^2, and mean BMI percentile was 97.8 ± 1.9. There were no significant baseline differences in age, BMI, BMI percentile, VO_{2peak}, treadmill time, leg press, and bench press between the four EOSS-P stages except for QOL ($p<0.001$).

Table 3 shows parameter estimates for EOSS-P, BMI percentile, sex, and age for each outcome, including QOL, cardiorespiratory fitness, muscular strength. Since only 2.5% of our sample was stage 0, we grouped stage 0 and 1 together for our analysis. In all general linear models, stage 0/1 was used as the reference variable for EOSS-P, and female sex was the reference variable for sex.

Quality of life

Three participants were missing QOL assessments. For QOL as the outcome, there were significant differences between stage 0/1 and stage 2 ($p<0.001$), and between stage 0/1 and stage 3 ($p<0.001$). BMI percentile showed no significant association with QOL. The greatest differences in QOL scores were found between stage 0/1 and stage 3. Post-hoc analysis revealed significant differences between stages 2 and 3 (see figure 1). Sex was associated with QOL, with males having higher QOL scores ($p=0.008$) (see Table 3).

Cardiorespiratory fitness

There were no significant differences in VO_{2peak} between EOSS-P stages ($p=0.32$). BMI percentile was negatively associated with VO_{2peak} ($p<0.001$), with a decrease of 1.05 mlO_2/kg/min for each unit increase in BMI percentile.

Cardiorespiratory fitness and BMI percentile are outcome variables measured relative to a person's body weight, thus we created similar models replacing VO_{2peak} with VO_{2peak} treadmill time

(time to reach VO_{2peak}) as the outcome, to account for body weight. We found no significant differences in treadmill time between EOSS-P stages ($p=0.31$). BMI percentile was negatively associated with treadmill time ($p<0.001$). There were sex differences in treadmill time ($p<0.001$), with males taking on average 97 seconds more time to reach VO_{2peak}. Age showed no significant association with treadmill time (see Table 3).

Muscular strength

Fifty-one participants were missing muscular strength assessments. There were no associations found between EOSS-P and upper body strength ($p=0.71$). BMI was positively associated with upper body strength ($p=0.029$), with an increase of 0.8 kg per unit of BMI percentile. Males had significantly greater upper body strength than females ($p<0.001$). Age was positively associated with upper body strength ($p=0.011$).

There were no associations found between EOSS-P and lower body strength ($p=0.94$). BMI percentile showed a positive association with lower body strength ($p=0.003$), with an increase of 4.0 kg per unit of BMI percentile. Males had significantly greater lower body strength than females ($p<0.001$). Age was positively associated with lower body strength ($p=0.001$) (see Table 3).

DISCUSSION

The purpose of this study was to contrast EOSS-P and BMI percentile regarding their associations with QOL, cardiorespiratory fitness and muscular strength. We hypothesized that both EOSS-P and BMI percentile would be negatively associated with QOL, cardiorespiratory fitness and muscular strength. Our results showed that EOSS-P was associated with QOL, but not associated with cardiorespiratory fitness or muscular strength. In contrast, BMI percentile was not associated with QOL, but was negatively associated with cardiorespiratory fitness and positively associated with muscular strength. The contrasting findings between EOSS-P and BMI percentile provide insight on how they can complement each other.

Previous EOSS studies have only been conducted in adults. Padwal et al. (2011), found no observable differences in mortality-risk between stages 0 and 1, but found elevated mortality-risk in stage 2, and more so in stage 3. Kuk et al (2011), observed individuals with normal weight as the reference group, and found stage 0/1 to have no difference in all-cause mortality, but stage 2 and stage 3 had elevated risks of all-cause of mortality. Consistent with these prior studies in adults, stage 2 had lower QOL than stage 0/1, and stage 3 had lower QOL than stage 0/1 and 2.

QOL, and all-cause mortality are associated with individual's psychological, social and physical health (6, 20, 25, 39). Conversely, cardiorespiratory and muscular fitness are predominantly reflective of physical health (23, 28, 40). Since EOSS-p is a tool that reflects 4Ms (metabolic health, mental health, biomechanical health, and social milieu), this may explain, this may explain why we did not find an association between EOSS-P and cardiorespiratory fitness or muscular strength. Considering the evidence surrounding cardiorespiratory fitness and muscular strength as important markers of health (23, 28, 40), and the lack of association between EOSS-P and fitness, it is plausible that EOSS-P is lacking physical activity and/or fitness components. Our study, however, treated cardiorespiratory fitness and muscular strength as baseline outcomes. It would be advantageous to conduct follow-up longitudinal studies utilizing EOSS-P with adolescents and measuring long-term outcomes such as cardiovascular disease incidence and all-cause mortality.

One review pooled data from 13 studies in pediatric populations, and found a negative association between BMI and QOL (via PedsQL) ($r= –0.7$, $p=0.008$) (41). The lack of association between BMI percentile and QOL in our study might be attributed to the narrow range of BMI percentiles in this sample of adolescents with high BMIs, as found in other studies with adolescents with severe obesity (42). Although we also had participants with overweight, they comprised only 7.4% of our sample and required an additional weight-related comorbidity to qualify for this study. We observed a negative association between BMI percentile and cardiorespiratory fitness. Conversely,

BMI percentile was positively associated with upper and lower muscular strength. BMI is strongly associated with percent body fat at the population level (13, 16), however it is a poor predictor of body fat at the individual level (13, 16). Although BMI is a crude measure of body composition (16) and has received criticism in being an over-simplistic approach of determining pediatric obesity (12), it gives an indication of relative body size. A greater BMI would correspond to more fat mass and/or fat free mass. Excess body fat has already been shown to be closely and negatively associated with cardiorespiratory fitness (30), while muscle mass (a major component of fat free mass) has been shown to be positively associated with muscular strength (43, 44). This can explain the positive association between BMI percentile and muscular strength, and its negative association with cardiorespiratory fitness.

Practical applications

Many healthcare professionals are ill-equipped to address the needs of children and youth with obesity (45). EOSS-P and its 4Ms (metabolic health, mental health, biomechanical health, and social milieu) are intended to provide a more comprehensive individualized health risk assessment of a patient with obesity than the currently used anthropometric measurements (i.e. BMI). EOSS-P provides healthcare professionals with a structured framework containing a checklist of assessments on weight-related comorbidities, and barriers to weight management that can help guide weight-management plans for their patients (10). A recent study investigated the perceived usefulness of the EOSS-P across various levels of care provided for pediatric patients with obesity (46). They found that EOSS-P was ranked as a very useful tool by 52.6% and somewhat useful by 31.6% from a sample of 57 referring healthcare professionals. Thus, the EOSS-P provides an improved and feasible methodology for stratifying health risk in pediatric obesity.

Obesity Canada refers to obesity as a “progressive chronic disease which is characterized by abnormal or excessive fat accumulation that may impair health”. Given this definition of obesity as a

"progressive chronic disease", EOSS-P would offer healthcare professionals a staging system to monitor the progression of obesity, analogous to staging of cancer. Our study showed that participants with similar BMI, or BMI percentile can present across the EOSS-P staging spectrum. Assessing BMI with EOSS-P would provide a more comprehensive health risk assessment, and help distinguish individuals with similar BMIs at different stages in their obesity.

Our findings indicate that as EOSS-P stages increase, QOL of a patient tends to decrease. Although it is reasonable to believe that improvements in EOSS-p stage would likely signify improvements in QOL, this issue warrants further investigation. Our results also showed a lack of cross-sectional associations between EOSS-P, cardiorespiratory fitness and muscular strength. Since muscular strength and cardiorespiratory fitness are important physical health outcomes, one might consider measuring physical activity or fitness to improve assessment of obesity-related health risk in addition to EOSS-P in adolescents. However, determining if a physical activity or fitness assessment will improve obesity-related health risk remains to be investigated.

The American Heart Association in 2016 issued a scientific statement attesting to cardiorespiratory fitness being a vital sign that should be assessed routinely in clinical practice (28). It stated that the addition of cardiorespiratory fitness to other risk factors improves the classification of risk for adverse outcomes (28). Considering the cost, time, and requirement for additional personnel to conduct a fitness test, accelerometers or a physical activity and sedentary behaviour questionnaire might be more easily implemented or added to EOSS-P instead. However, it is important to acknowledge limitations with questionnaires, in that they may not provide the same quality of information as a fitness test, or an objective measure of physical activity and sedentary time would (i.e. accelerometry). Physical activity plays a pivotal role in the development of weight-related comorbidities (47) and it has already been suggested to include questions on physical activity in routine healthcare assessments (48).

Limitations

We acknowledge several limitations of our study. Firstly, the sample was mainly Caucasian (72%) and female (71%), which would affect the generalizability of the results to Canadian adolescents. Secondly, mental health assessments were derived from self-report questionnaires. Our team of five experts came to a consensus on how to interpret a set of validated questionnaires for EOSS-P staging (see Table 1). It is recommended that a clinical interview be done by a health care professional for the EOSS-P mental health assessment as opposed to solely depending on self-report questionnaires to make a diagnosis. Thirdly, this is a secondary data analysis on variables that were not intended specifically for EOSS-P, thus we had limited data on mechanical and social milieu categories. The limited data may have caused underestimation of EOSS-p scores. Lastly, this study was a cross-sectional design, which limits the causal inferences regarding associations.

Future studies should assess EOSS-P through a clinical evaluation of the 4Ms (metabolic health, mental health, biomechanical health, and social milieu), as is intended for the EOSS-P. With this approach, researchers will have a better understanding of the EOSS-P because all EOSS-P variables would be measured. Future studies should also assess EOSS-P across various Tanner stages, as there are considerable physiological differences among people at different Tanner stages (35, 36). Longitudinal health outcomes, such as development of cardiovascular disease, all-cause mortality, EOSS stage in late adulthood, in larger samples are of interest to understand how EOSS-P can predict risk of obesity related comorbidities over time.

Conflict of interest statement:

The authors declare no conflicts of interest.

Acknowledgments

The HEARTY trial was supported by grant MCT-71979 from the Canadian Institutes of Health Research. We gratefully acknowledge all HEARTY participants who dedicated their time to participate in this study. We acknowledge Dr. Simon Bacon for his thoughtful contributions to the EOSS-P

algorithm, and study design. GAK was supported by the Faculty of Art & Science Fellowship at Concordia University and les Fonds de Recherche du Québec- Santé (Master's Training Scholarship). ASA was supported by les Fonds de Recherche du Québec- Santé (Chercheur Boursier Junior 1 at Concordia University).

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Table and figure legends

Table 1:

Note: ǂ, indicates our HEARTY diagnostic criteria for this specific EOSS-P variable
LDL-C: low density lipoprotein - cholesterol
HDL-C: high density lipoprotein - cholesterol
ALT: alanine transaminase
CDI: Children's Depression Inventory
MBSRQ: Multidimensional Body–Self Relations Questionnaire
DEBQ: Dutch Eating Behavior Questionnaire
ADHD: attention deficit hyperactivity disorder

Table 2:

Note: * $p<0.001$

Table 3:

Note: Parameter estimates (B) are the change in the dependent variable associated with each unit increase of the independent variable, while all other variables are constant.

Figure 1:

Note: ***$p<0.001$ when compared to previous stages

Table 1. EOSS-P staging criteria.

Stage 1: Presence of subclinical obesity-related risk factors
Acanthosis Nigricans
Pre-hypertension: Systolic or Diastolic
Impaired glucose tolerance (7.8-11.0 mmol/L) and/or Impaired fasting glucose (6.1-6.9 mmol/L)
LDL-C and/or Non-HDL-C 3.4-4.1 mmol/L
HDL-C 0.8-1.03 mmol/L
Triglycerides 1.5-4.0 mmol/L
ALT 1.5-2.0x normal values
Mild depression or anxiety that does not interfere with functioning
ǂ (Diagnosis of anxiety of depression greater than two years ago with no current treatment) or (CDI score in 84th-92th percentile (above average))
Mild body image preoccupation/concern
ǂ (MBSRQ Appearance Evaluation mean score 2-2.99 (neither agree of disagree to mostly disagree))
Mild emotional/binge eating (occasional)
ǂ (1x/month to <1x/week) or (DEBQ emotional eating subscale mean score 3-4 (sometimes to often))
ADHD and/or learning disability
Caregiver has or is recovering from medical/physical, mental health and/or substance-use problems
Stage 2: Presence of OB-related chronic diseases/health issues
Type 2 Diabetes without diabetes-related complications
Hypertension: Systolic or Diastolic
LDL-C or Non-HDL-cholesterol >4.2 mmol/L
HDL-Cholesterol <0.8 mmol/L
Triglycerides >4.0 mmol/L
ALT 2-3x normal values
Polycystic ovarian syndrome
Gastroesophageal reflux disease
Major depression or anxiety disorder
ǂ (Diagnosis of anxiety of depression within two years ago) or (on pharmacological treatment) or (CDI score in 93rd-97th percentile (much above average))
Moderate binge eating (frequent)
ǂ (1x/week to 6x/week) or (DEBQ Emotional Eating subscale 4.01 to 5 (often to always))
Significant body image disturbance
ǂ (MBSRQ Appearance Evaluation subscale mean score 1 to 1.99) or (mostly disagree to definitely disagree))
Stage 3: Presence of established chronic diseases/health issues
Type 2 Diabetes with diabetes-related complications or HbA1c ≥ 8
Elevated lipids requiring pharmacotherapy
ALT >3x normal limits and/or liver dysfunction
Hypertension on pharmacotherapy
Uncontrolled hypertension on pharmacotherapy
Uncontrolled psychopathology
ǂ (CDI score greater than 98th percentile (very much above average))
Sever binge eating (daily)
ǂ (Bing eating 7x/week)
Self/physical loathing

Note: ǂ, indicates our HEARTY diagnostic criteria for this specific EOSS-P variable
LDL-C: low densitry lipoprotein - cholesterol
HDL-C: high density lipoprotein - cholesterol
ALT: alanine transaminase
CDI: Children's Depression Inventory
MBSRQ: Multidimensional Body–Self Relations Questionnaire
DEBQ: Dutch Eating Behavior Questionnaire
ADHD: attention deficit hyperactivity disorder

Table 2. Baseline participant characteristics.

	Total Sample (N=299)	Stage 0 (n=7)	Stage 1 (n=116)	Stage 2 (n=146)	Stage 3 (n=30)
	N (%)	**N (%)**	**N (%)**	**N (%)**	**N (%)**
Male	88 (29.4)	1 (14.3)	33 (28.4)	46 (31.5)	8 (26.7)
Female	211 (70.6)	6 (85.7)	83 (71.5)	100 (68.5)	22 (73.3)
	Mean (SD)	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**
Age (years)	15.6 (1.4)	15.9 (1.3)	15.6 (1.4)	15.6 (1.3)	15.8 (1.5)
BMI (kg/m^2)	34.6 (4.5)	35.4 (6.2)	34.0 (3.9)	35.2 (4.8)	34.2 (4.1)
BMI percentile	97.8 (1.9)	97.5 (1.9)	97.8 (1.5)	97.9 (2.0)	97.6 (2.3)
PedsQL	70.4 (13.8)*	81.1 (10.1)	75.4 (11.4)	69.1 (13.1)	55.4 (13.0)
VO_{2peak} ($mlO_2/kg/min$)	30.4 (5.0)	31.6 (7.5)	30.7 (4.7)	30.1 (5.2)	29.8 (4.9)
VO_{2peak} treadmill time (s)	993.3 (177.5)	1045.7 (184.2)	1009.0 (178.1)	980.7 (180.3)	982.5 (161.0)
Bench press (kg)	22.0 (11.6)	32.7 (17.7)	28.1 (10.7)	28.1 (12.0)	26.3 (11.5)
Leg press (kg)	102.3 (37.7)	123.0 (52.9)	101.7 (34.4)	102.9 (39.1)	98.2 (41.3)

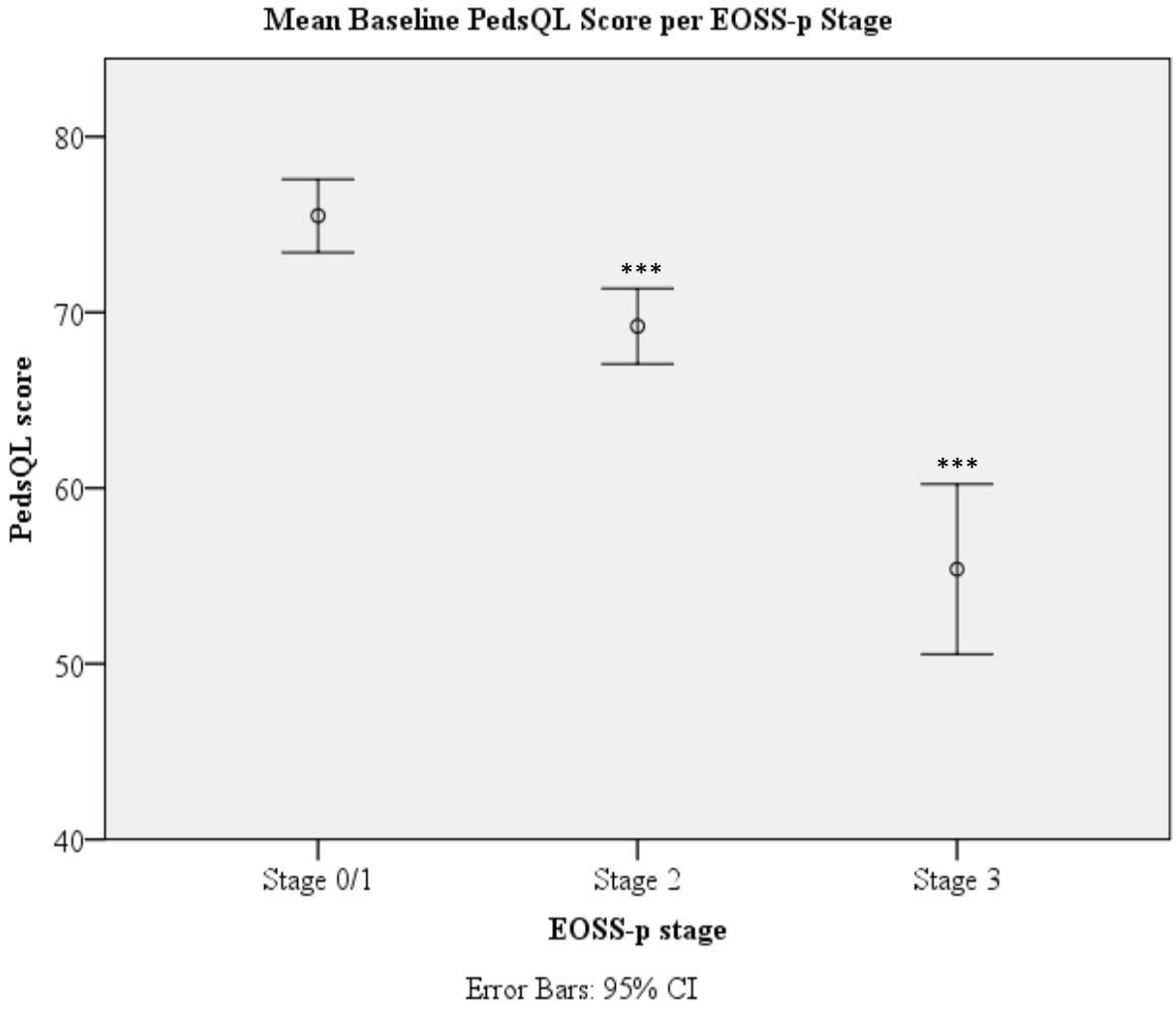
Note: * $p<0.001$

Table 3. Parameter estimates for each outcome.

	PedsQL (n=296)			**VO_{2peak} (mlO_2/kg/min)** (n=299)			**Treadmill time (s)** (n=299)			**Seated bench press (kg)** (n=248)			**Leg Press (kg)** (n=248)		
	B	Std. Error	Sig.	B	Std. Error	Sig.	B	Std. Error	Sig.	B	Std. Error	Sig.	B	Std. Error	Sig.
Stage 0/1	Reference			Reference			Reference			Reference			Reference		
Stage 2	-6.85	1.52	<0.001	-0.67	0.54	0.22	-30.90	34.92	0.39	-0.84	1.31	0.52	-0.66	4.56	0.89
Stage 3	-20.14	2.51	<0.001	-1.08	0.89	0.23	-30.84	20.99	0.14	-1.49	2.13	0.49	-2.54	7.43	0.73
BMI percentile	-0.10	0.42	0.82	-1.04	0.15	<0.001	-22.61	5.79	<0.001	0.83	0.38	0.029	3.99	1.32	0.003
Female	Reference			Reference			Reference			Reference			Reference		
Male	4.52	1.70	0.008	5.28	0.60	<0.001	96.94	23.59	<0.001	12.25	1.45	<0.001	26.68	5.03	<0.001
Age (per year)	-0.89	0.52	0.09	-0.33	0.19	0.08	-10.85	7.25	0.14	1.15	0.45	0.011	5.35	1.56	0.001

Note: Parameter estimates (B) are the change in the dependent variable associated with each unit increase of the independent variable, while all other variables are constant.

Figure 1. Graph demonstrating QOL at each EOSS-P stage.



Note: ***p<0.001 when compared to previous stages

3.1 Additional results

This 'additional results' section includes all analyses with outcomes assessed at 6-months. These outcomes include: 6-month QOL, 6-month cardiorespiratory fitness, 6-month muscular fitness, and adherence to exercise. Tables 3, 4, and 5 show results from the general linear models for EOSS-p, BMI percentile, sex, age, group assignment, and baseline assessment of the outcome variable.

From the overall N= 304, five participants were lacking EOSS-p mental health data so the final analysis included N= 299. Table 2 displays the baseline characteristics of the 299 participants included in our study. The sample included a total of 88 (29%) males and 211 (71%) females. The EOSS-p distribution of our sample in stage 0 was n= 7 (2.3%), stage 1 n= 116 (38.8%), stage 2 n= 146 (48.8%), and in stage 3 n= 30 (10%). Since only 2.5% of our sample was stage 0, we grouped stage 0/1 for our analysis. In all general linear models, stage 0/1 was used as the reference variable for EOSS-p, females was the reference variable for sex, and control group is the reference variable for group assignment.

3.1.1 6-month QOL

For 6-month QOL as the outcome, there were no significant associations with EOSS-p ($p=0.395$), nor with BMI percentile ($p=0.344$). Sex ($p=0.170$) and group assignment ($p=0.214$) showed no associations with 6-month QOL. There was a trend of association between age and 6-month QOL ($p=0.064$). Baseline QOL was associated with 6-month QOL ($p<0.001$, $F=156.62$, $Eta^2=0.44$).

3.1.2 6-month VO_{2peak}

EOSS-p ($p=0.001$, $F=7.43$, $Eta^2=0.01$), BMI percentile ($p<0.001$, $F=15.98$, $Eta^2=0.08$), sex ($p<0.001$, $F=18.55$, $Eta^2=0.09$), group assignment ($p=0.001$, $F=5.91$, $Eta^2=0.09$) and baseline VO_{2peak} ($p<0.001$, $F=98.45$, $Eta^2=0.35$) showed significant associations with 6-month VO_{2peak}. Age showed no significant associations with 6-month VO_{2peak} ($p=975$). Parameter estimates showed significant differences between EOSS-p stage 0/1 and stage 3 ($p<0.001$), but not between EOSS-p stage 0/1 and stage 2 ($p=0.921$). Bonferroni's post-hoc analysis showed significant differences between stage 2 and stage 3 ($p=0.001$).

Cardiorespiratory fitness and BMI percentile are outcome variables measured relative to a person's body weight, thus we created similar models replacing VO_{2peak} with VO_{2peak} treadmill time (time to reach VO_{2peak}) as the outcome, to account for body weight. 6-month treadmill time showed significant associations with EOSS-p ($p=0.044$), BMI percentile ($p=0.006$), group assignment ($p=0.001$) and baseline treadmill time. Parameter estimates showed significant differences between EOSS-p stage 0/1 and stage 3 in treadmill time ($p=0.013$).

3.1.3 6-month upper body strength

BMI percentile ($p=0.002$, $F=10.37$, $Eta^2=0.07$), sex ($p=0.007$, $F=7.49$, $Eta^2=0.49$), group assignment ($p<0.001$, $F=13.83$, $Eta^2=0.22$), and baseline upper body strength ($p<0.001$, $F=151.80$, $Eta^2=0.51$) were associated with 6-month upper body strength. EOSS-p and age were not associated with 6-month upper body strength ($p=0.693$, and $p=0.743$ respectively).

3.1.4 6-month lower body strength

BMI percentile ($p=0.005$, $F=8.04$, $Eta^2=0.05$), group assignment ($p<0.001$, $F=10.57$, $Eta^2=0.18$), and baseline lower body strength ($p<0.001$, $F=91.86$, $Eta^2=0.39$) show significant associations with 6-month lower body strength. EOSS-p, age, and sex showed no significant associations with lower body strength ($p>0.05$).

3.1.5 Adherence

Group assignment is the only variable showing significant associations with adherence ($p<0.001$, $F=80.38$, $Eta^2=0.45$). Age shows a trending association with adherence ($p=0.058$). EOSS-p, BMI percentile, and sex show no association with adherence ($p>0.05$).

CHAPTER 4: Discussion

4.0 Discussion

4.1 Summary of main findings

The purpose of this thesis was to contrast EOSS-p and BMI percentile regarding their associations with QOL, cardiorespiratory fitness, muscular strength, and adherence. Baseline outcomes have been discussed at length in Manuscript 1. This discussion will focus on 6-month outcomes (ie. 6-month QOL, 6-month cardiorespiratory fitness, 6-month muscular strength and adherence). Our results showed that EOSS-p was only associated with 6-month cardiorespiratory fitness, and showed no associations with 6-month QOL, 6-month upper and lower muscular strength, and adherence to exercise. BMI percentile showed negative associations with 6-month cardiorespiratory fitness, positive associations with 6-month upper and lower muscular strength, and no associations with QOL or adherence.

The majority of our sample was in stage 2 (49%), then stage 1 (39%), then stage 3 (10%), then stage 0 (2%). Studies examining EOSS in adults also found stage 2 to be the most common EOSS stage consisting of 53%, 70%, 82%, and 84% of their sample (6, 65-68). Another EOSS study had an equivalent number of adult participants in stage 2 and 3 (31.2% and 31.6% respectively) (69). This evidence suggests that the majority of adolescents and adults with obesity are classified as having stage 2. Our sample represents a community sample of inactive post-pubertal adolescents with obesity, with several exclusion criteria that may underestimate the distribution of EOSS-p stages in the general population of adolescents with obesity.

4.2 EOSS-p and BMI percentile with adherence

The results confirm the hypothesis that both EOSS-p and BMI percentile were not associated with adherence to the HEARTY exercise intervention. In addition, age, sex, and percent body fat were also not associated with adherence. Although studies investigating predictors of adherence to weight-management interventions in adolescents with obesity have not been identified, a review has explored *attrition* to paediatric weight-management programs in children and adolescents with obesity (47). Attrition is defined as dropping out of the agreed treatment or intervention. Skelton et al. 2011 identified that BMI has been shown to be a predictor of attrition in some pediatric obesity studies (74-76), but not in others (77, 78). A systematic review focusing on adulthood obesity, found lower baseline BMI, lower depression, stress, and anxiety to be predictors of adherence to weight management programs (46). Although EOSS-p contained many of the predictors of adherence for adulthood obesity listed above, it

is possible that predictors for adherence in adults may not reflect predictors of adherence in adolescents with obesity. Unlike adults, children and adolescents are dependent on their parents and/or guardians. Lower caregiver-related quality of care (79), and single parent households (76) have been identified as predictors of attrition in adolescents with obesity. The social milieu category of EOSS-p considers caregiver-related quality of care, and single-parent-households, however, we were limited in our evaluation of social milieu with the HEARTY participants. Previous reviews investigating adherence and attrition in adults (46) and pediatric (47) samples respectively, were investigating multidisciplinary weight management programs consisting of a combination of diet, exercise and other behaviour-focused strategies. The HEARTY trial was largely an exercise intervention, with a minor dietary component, thus it would be beneficial to investigate if EOSS-p can predict adherence to a *multidisciplinary* weight-management intervention in a clinical setting.

4.3 EOSS-p and 6-month QOL, cardiorespiratory fitness and muscular strength

It was hypothesized that EOSS-p would be negatively associated with 6-month QOL, cardiorespiratory fitness and muscular strength. EOSS-p was not associated with 6-month QOL, or muscular strength, but it was associated with 6-month cardiorespiratory fitness. We found that participants in stage 3 had significantly lower 6-month cardiorespiratory fitness than those in stage 0/1 and 2. A previous study showed that adults with higher EOSS stages (stage 2 and 3) required longer weight management intervention times to achieve similar weight loss outcomes (65). Canning et al.'s (2015) and our results suggest that perhaps participants in stage 3 do not benefit as efficiently from diet and exercise interventions than their counterparts in lower EOSS stages with lower health risks. I speculate that the weight lost from a diet and exercise intervention might be due to a decrease in percent body fat. A decrease in body fat is associated with increasing cardiorespiratory fitness (7, 50, 70). In my study, adolescents with obesity received the same duration of intervention, but stage 3 showed smaller improvements in cardiorespiratory fitness. To determine if the same trends in my results were due to the intervention and not just time, I conducted a supplementary analysis (see Table 6 – 11) within the control group only, and one for the exercise intervention group only. I found that only stage 3 participants in the exercise groups had lower 6-month cardiorespiratory fitness, while stage 3 participants in the control groups showed no differences in 6-month cardiorespiratory fitness compared to stages 0/1, and 2. Arguably, this evidence suggests longer, more intensive, or different interventions may be required for teens with obesity in stage 3 with more adverse co-morbidities and health risks. Improvements in

cardiorespiratory fitness are desired outcomes in adolescent obesity, therefore using EOSS-p can be practical for health-care professionals when determining treatment duration for patients with adolescent obesity. More research is needed to determine how the EOSS-p can be used to inform treatment time or other specific intervention designs/ components; especially for participants in more severe health risk stages (i.e. stage 3).

4.4 BMI with 6-month QOL, cardiorespiratory fitness and muscular strength

It was hypothesized that BMI percentile would be negatively associated with QOL, cardiorespiratory fitness and muscular strength. BMI percentile was not associated with 6-month QOL. Previous studies found that as BMI decreases over time, QOL increases proportionately in adolescents (71). In a review analyzing 13 studies, a negative association was found between BMI and quality of life (via PedsQL) ($r = -0.7$, $p=0.008$) (72). The lack of association between BMI percentile and QOL in our study is likely due to the truncated BMI range in this sample of adolescents with elevated BMI's. Although a portion of our sample had overweight, they only consisted of 7.4% of our total sample and possessed a weight-related comorbidity. Furthermore, as hypothesized, we found a negative association with BMI percentile and 6-month cardiorespiratory fitness; however, we found a positive association between BMI percentile and muscular strength. These results are contradictory with regards to health outcomes. It can be speculated that since BMI percentile does not distinguish between fat mass and muscle mass, a greater BMI percentile can reflect greater fat mass and/or muscle mass. It is well known that fat mass is closely linked with cardiorespiratory fitness (7, 50, 70), while muscle mass is closely linked with muscular strength (73). This could account for BMI percentile's contradicting associations with cardiorespiratory fitness and muscular strength. This contradicting finding reinforces the notion that BMI percentile should not be used as a sole measure of determining health risk.

CONCLUSION

Obesity affects a third of the Canadian pediatric population, and several adverse health risks can ensue. The optimal assessment tool to determine severity and risk stratification of pediatric obesity is warranted. The purpose of this thesis was to compare EOSS-p with BMI percentile, in their associations with QOL, cardiorespiratory fitness, muscular strength, and adherence to exercise. We found that as QOL decreases as EOSS-p stages increase. Although baseline EOSS-p was not associated with baseline cardiorespiratory of muscular fitness, EOSS-p stage 3 had significantly lower improvements in cardiorespiratory fitness after 6-months than other stages after the HEARTY exercise intervention. However, BMI percentile was not associated with QOL or adherence, but was negatively associated with cardiorespiratory fitness and positively associated with strength. Our findings suggest that EOSS-p can be beneficial in determining relative QOL according to stage, and that stage 3 may require a longer duration of intervention or a different type of intervention to see health improvements. BMI percentile, showed contradictory associations with our health outcomes, highlighting flaws when determining severity of obesity according to BMI percentile. EOSS-p can improve risk stratification of children and adolescents with obesity rather than the traditional BMI percentile method. This is the first study to investigate the relationship of EOSS-p with health outcomes in pediatric obesity. More research is warranted to determine the long-term relationships between EOSS-p and health outcomes, and its ability to predict adherence and attrition to other interventions with children and adolescents living with obesity.

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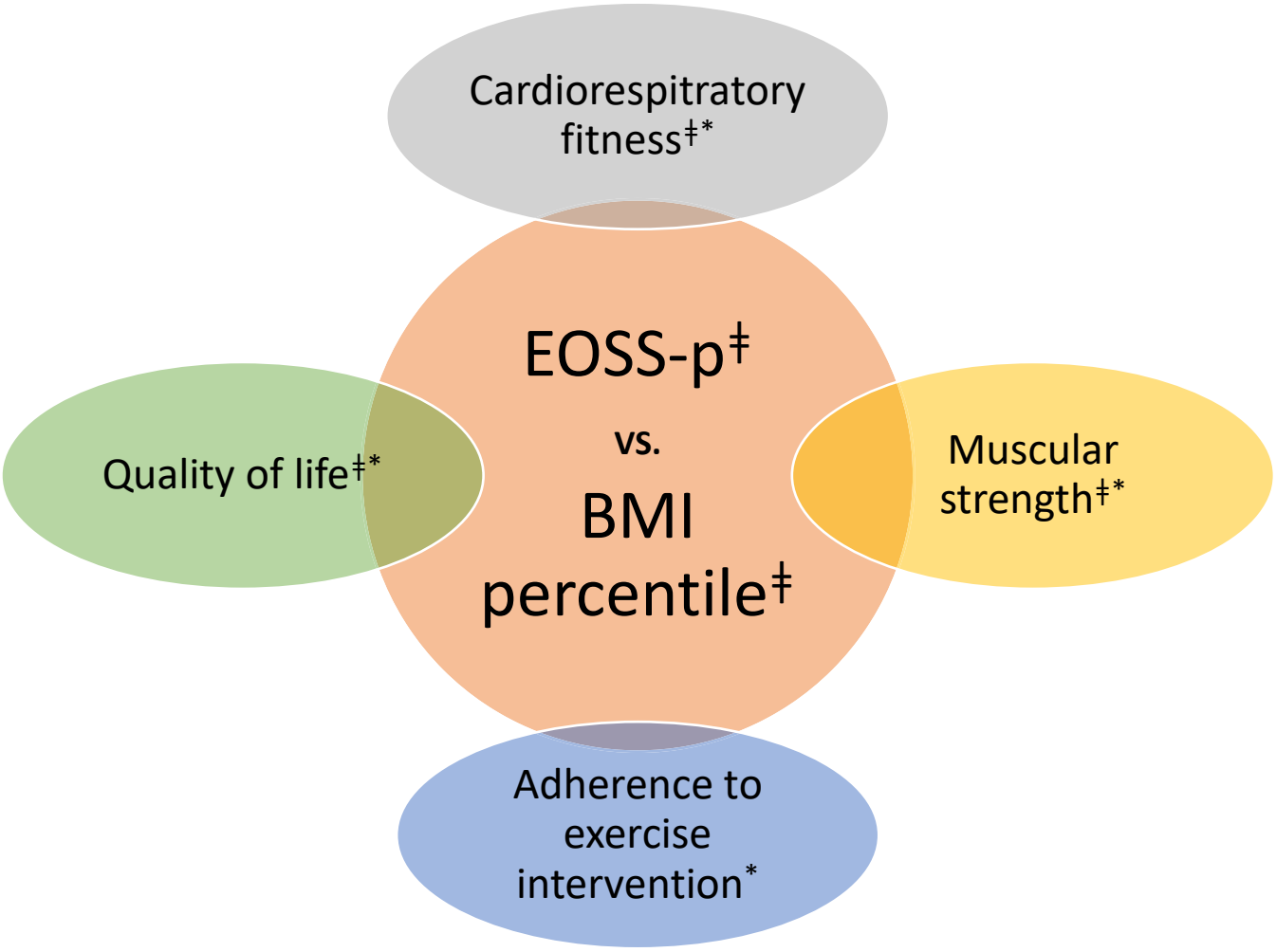
APPENDIX

Figures

Tables

Figure 1: Graphic illustration of thesis objective



‡ Variable assessed at baseline

* Variable assessed at 6-month

Figure 2: Flow diagram of HEARTY study overview

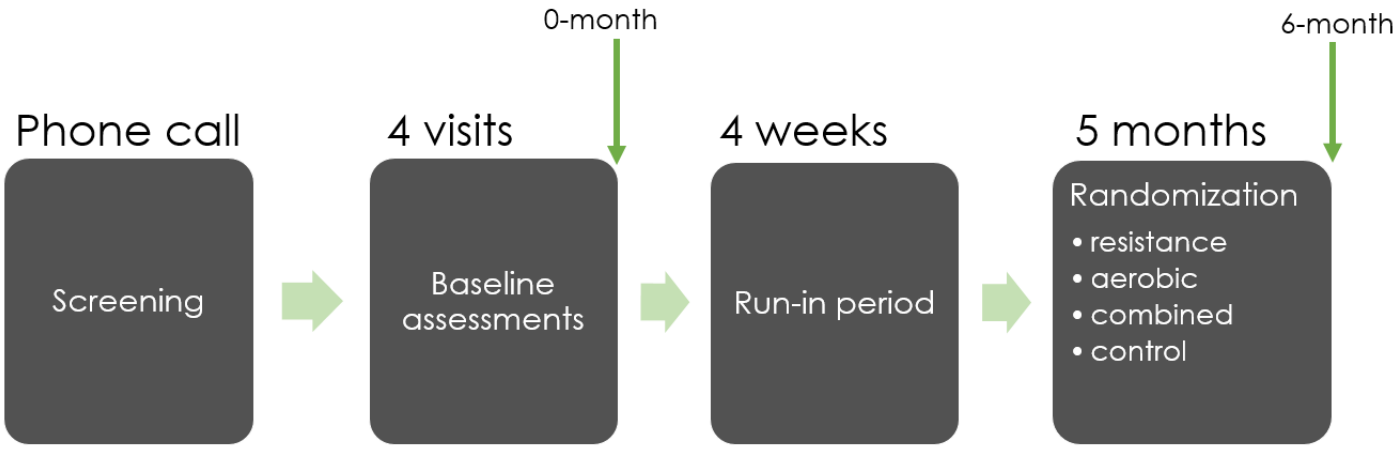
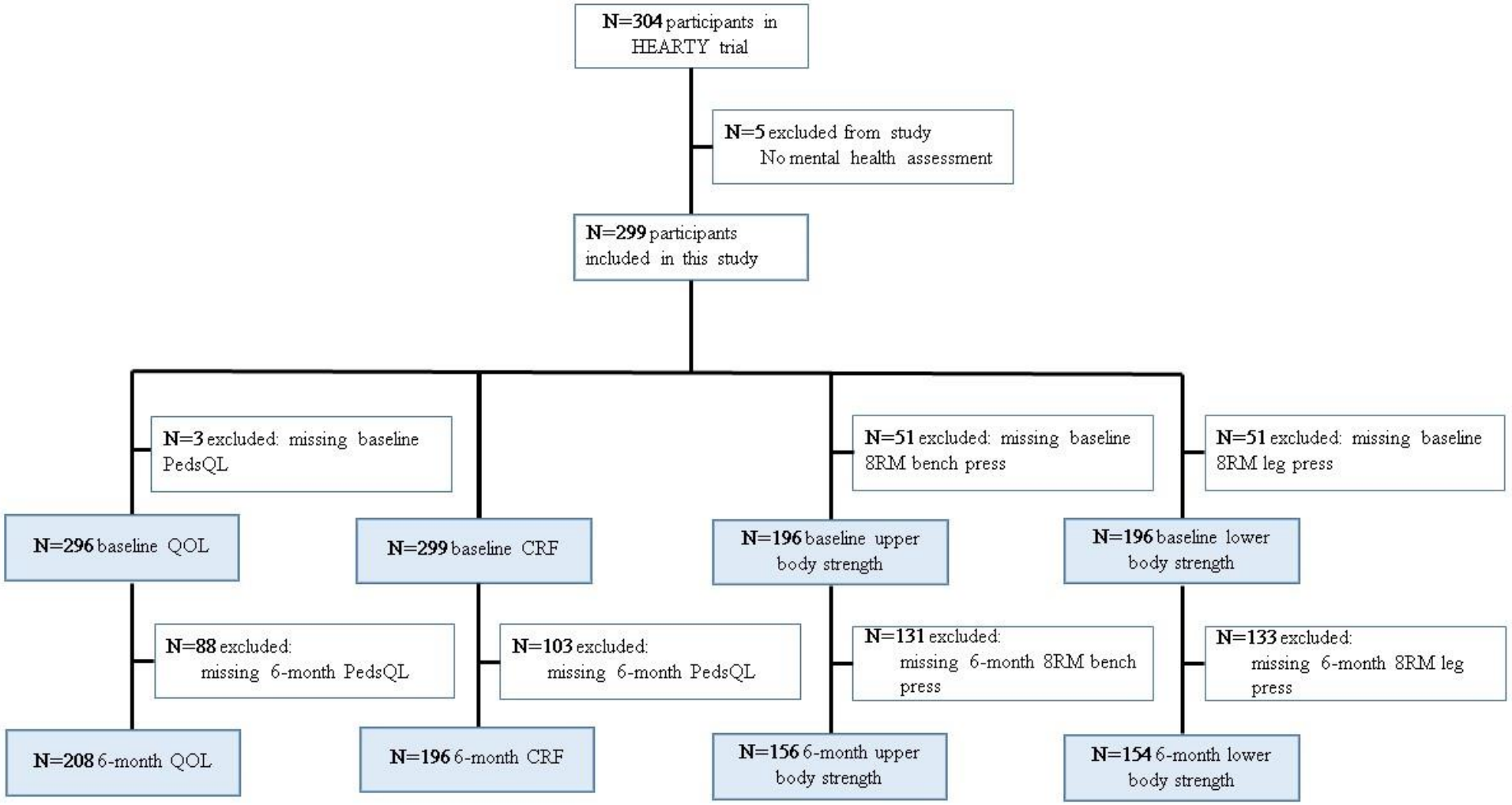


Figure 3: Number of participants analyzed for each outcome



Note: Boxes in light blue correspond to the N used in each analysis.

Table 1: Modified HEARTY testing timeline (49)

Variable	Baseline Assessments					Run-in period (4 weeks)	Intervention (6 months)
	screening	visit 1	visit 2	visit 3	visit 4		6-month
Inclusion/exclusion criteria	X						
Informed consent		X					
Medical history		X					
Complete physical exam		X					
Total cholesterol			X				
HDL-C			X				
Triglycerides			X				
LDL-C			X				
Liver enzymes (AST/ALT)			X				
Serum Testosterone			X				
Hemoglobin A1C			X				
OGTT			X				
Mental health questionnaires (CDI & MBSRQ-AS)			X				
QOL questionnaire (PedsQL4.0)			X				X
VO_{2peak}					X		X
Musculoskeletal fitness					X		X

Table 2: EOSS-p staging algorithm for HEARTY trial

CATEGORY	Variable	Variable code	Values	Stage
Metabolic	acanthosis nigricans	acannigr	0 (no)	stage 0
			1 (yes)	stage 1
	systolic blood pressure	systolic (use this for <18)	<90th percentile	stage 0
			90th to <95th percentile or ≥120/80 mm Hg	stage 1
			95th to 99th percentile plus 5 mm Hg / >99th percentile	stage 2
		(use this for 18+)	<120 mmHg	stage 0
			120 to 139 mmHg	stage 1
			≥140 mmHg	stage 2
	diastolic blood pressure	diastolic (use this for <18)	<90th percentile	stage 0
			90th to <95th percentile or ≥120/80 mm Hg	stage 1
			95th to 99th percentile plus 5 mm Hg / >99th percentile	stage 2
		(use this for 18+)	<80 mmHg	stage 0
			80 to 89 mmHg	stage 1
			≥90 mmHg	stage 2
	triglycerides	triglicer	>1.5	stage 0
			1.5-4	stage 1
			>4.0	stage 2
	fasting glucose	preglucose	<6.1	stage 0
			6.1 - 6.9	stage 1
			≥7 (T2D)	stage 2
	glucose tolerance	postglucose	<7.8	stage 0
			7.8 - 11	stage 1
			>11	stage 2
	Low density lipoprotein -	ldl	<3.4	stage 0
			3.4-4.1	stage 1
			≥ 4.2	stage 2

	cholesterol (LDL-c) or non-HDL-c			
		non-HDL-c = totchol - hdl	<3.35	stage 0
			3.35-4.14	stage 1
			≥ 4.15	stage 2
	high density lipoprotein - cholesterol	hdl	>1.03	stage 0
			0.80-1.03	stage 1
			<0.80	stage 2
	Alanine Aminotransferase (alt)	alt	normal	stage 0
			1.5-2.0x normal values	stage 1
			2.1-3.0x normal values	stage 2
			>3.0x normal values	stage 3
		(use this for <18)	< 46.5	stage 0
			46.5 to 62 (for male) / 37.5 to 50 (for female)	stage 1
			62.01 to 93 (for male) / 50.01 to 75 (for female)	stage 2
			> 93 (for male) / > 75 (for female)	stage 3
		(use this for 18+)	< 46.5	stage 0
			67.5 to 90 (for male) / 49.5 to 66 (for female)	stage 1
			90 to 135 (for male) / 66 to 99 (for female)	stage 2
			>135 (for male) / > 99 for female)	stage 3
	Type 2 diabetes with diabetes-related complication	HbA1c		
			≥0.08 (T2D)	stage 3
		medcode		
			5 to 14 (example for medname: lipitor, lipidil, monopril/fosinopril, norvasc, cozaar)	stage 3
	polycystic ovarian syndrome	previnjury		

			PCOS /polycystic ovarian syndrome	stage 2
Mental Health	Binge eating	bingfreq bing time	no binge eating	stage 0
			1x/month to < 1x/week = occasional	stage 1
			1x/week - 6 x/week = frequent	stage 2
			7x/week = daily	stage 3
		DEBQ emtn	<39	stage 0
			39 to 52	stage 1
			52.01 to 65	stage 2
	Body Image	apev	≥3	Stage 0
			2-2.99	Stage 1
			1-1.99	Stage 2
	Anxiety/Depression	depress / anxiety/ (**also look at**: *depress_age/ anxiety_age/ depress_treat/ anxiety_treat*)	0 (no) and 0 (no)	stage 0
			1 (yes) and/or 1 (yes)/ (diagnosis grater than 2 years ago)	stage 1
			1 (yes) and/or 1 (yes) / (diagnosis within last 2 years, any treatment within 2 years)	stage 2
		CDI_totalscore use criteria for all participants - regardless of age	<84th percentile	stage 0
			84th-92th percentile	stage 1
			93th-97th percentile	stage 2
			>98th percentile	stage 3
		medcode/ medname		
			20, 21, 22/ if 20 (cipralex, seraquil, valproid acid)	stage 2
	ADHD or learning disability	medcode/medname		
			20 / ritalin, stratera, dextroamphetamine, concerta, dexedrin	stage 1
		previnjury		

			ADHD / ADD / Learning difficulty	stage 1
Mechanical	GERD	Medcode medname		
			20 (pantoloc or ranitidine)	stage 2
Social Milieu	Parental education level	meduc / feduc (stage according to higher number between both variables)	3 or 4	stage 0
			2	stage 1
			1	stage 2
	parental health	m_depress/ f_depress / m_other / f_other (stage according to any mental physicalhealth issue)	0 (no)	stage 0
			1 (yes)	stage 1

Table 3: Tests of Between-Subjects Effects

	6-month PedsQL (n=209)			6-month VO2peak (mlO2/kg/min) (n=196)			6-month treadmill time (n=196)			6-month Seated bench press (kg) (n=156)			6-month Leg Press (kg) (n=154)			6-month adherence (n=299)		
	F	**Sig.**	**Eta²**	**F**	**Sig.**	**Eta²**	**F**	**Sig.**	**Eta²**	**F**	**Sig.**	**Eta²**	**F**	**Sig.**	**Eta²**	**F**	**Sig.**	**Eta²**
Corrected Model	23.45	<0.001	0.52	28.46	<0.001	0.58	12.29	<0.001	0.37	45.18	<0.001	0.74	21.21	<0.001	0.57	31.09	<0.001	0.46
EOSS-p	0.93	0.40	0.01	7.43	0.001	0.07	3.17	0.044	0.03	0.37	0.69	0.01	1.08	0.34	0.02	0.08	0.92	<0.01
BMI percentile	0.90	0.34	0.01	15.98	<0.001	0.08	7.83	0.006	0.04	10.37	0.002	0.07	8.04	0.005	0.05	0.04	0.84	<0.01
Sex	1.90	0.17	0.01	18.55	<0.001	0.09	1.62	0.21	0.01	7.49	0.007	0.05	<0.01	0.97	<0.01	1.61	0.21	0.01
Age	3.47	0.06	0.02	<0.01	0.98	<0.001	0.26	0.61	<0.01	0.11	0.74	<0.01	0.15	0.67	<0.01	3.62	0.06	0.01
Group assignment	1.51	0.21	0.02	5.91	0.001	0.09	5.48	0.001	0.08	13.83	<0.001	0.22	10.57	<0.001	0.18	80.38	<0.001	0.45
Baseline assessment of outcome variable	156.62	<0.001	0.44	98.45	<0.001	0.35	54.54	<0.001	0.23	151.80	<0.001	0.51	91.86	<0.001	0.39			

Table 4: Parameter estimates for total sample

	6-month PedsQL (n=209)			6-month VO2peak (n=196)			6-month treadmill time (n=196)		
	B	**Std. Error**	**Sig.**	**B**	**Std. Error**	**Sig.**	**B**	**Std. Error**	**Sig.**
Stage 0/1	Reference			Reference			Reference		
Stage 2	1.207	1.373	0.381	-0.059	0.594	0.921	-20.133	22.833	0.379
Stage 3	-1.542	2.408	0.523	-3.882	1.038	0.000	-99.621	39.725	0.013
BMI percentile	-0.385	0.406	0.344	-0.791	0.198	0.000	-20.181	7.213	0.006
Control	Reference			Reference			Reference		
Aerobic	3.561	1.766	0.045	2.776	0.793	0.001	96.967	30.408	0.002
Resistance	1.897	1.779	0.288	0.385	0.798	0.630	73.613	30.595	0.017
Combined	2.746	1.752	0.119	2.261	0.804	0.005	115.253	30.894	0.000
Female	Reference			Reference			Reference		
Male	2.054	1.491	0.170	3.072	0.713	0.000	32.465	25.550	0.205
Age	0.863	0.464	0.064	0.006	0.205	0.975	-4.010	7.859	0.611
Baseline assessment of outcome variable	0.651	0.052	0.000	0.646	0.065	0.000	0.471	0.064	0.000

Table 5: Parameter estimates for total sample (Table 4 continued)

	6-month Seated bench press weight in kg (n=156)			6-month Leg Press weight in kg (n=154)			6-month adherence (n=299)		
	B	**Std. Error**	**Sig.**	**B**	**Std. Error**	**Sig.**	**B**	**Std. Error**	**Sig.**
Stage 0/1		Reference			Reference			Reference	
Stage 2	-0.433	1.498	0.773	9.208	7.696	0.233	0.010	0.026	0.694
Stage 3	-2.178	2.546	0.394	15.606	13.515	0.250	0.002	0.043	0.963
BMI percentile	1.432	0.445	0.002	6.387	2.252	0.005	-0.001	0.007	0.836
Control		Reference			Reference			Reference	
Aerobic	0.313	2.032	0.878	22.162	10.373	0.034	0.457	0.034	0.000
Resistance	9.456	1.992	0.000	53.514	10.262	0.000	0.420	0.034	0.000
Combined	9.343	1.973	0.000	43.185	10.387	0.000	0.428	0.035	0.000
Female		Reference			Reference			Reference	
Male	5.009	1.830	0.007	-0.301	8.948	0.973	0.036	0.029	0.205
Age	-0.172	0.525	0.743	-1.073	2.737	0.696	-0.017	0.009	0.058
Baseline assessment of outcome variable	0.870	0.071	0.000	1.050	0.110	0.000			

Table 6: Associations table for control group only

	6-month PedsQL (n=54)	6-month VO2peak (mlO2/kg/min) (n=51)	6-month treadmill time (n=51)	6-month Seated bench press (kg) (n=41)	6-month Leg Press (kg) (n=41)	6-month adherence (n=75)
	Sig.	**Sig.**	**Sig.**	**Sig.**	**Sig.**	**Sig.**
EOSS-p	0.955	0.564	0.825	0.747	0.924	0.262
BMI percentile	0.115	0.411	0.305	0.085	0.021	0.504
Age	0.894	0.326	0.149	0.908	0.766	0.495
Sex	0.334	0.328	0.043	0.333	0.400	0.336
Outcome variable assessed at baseline	0.000	0.000	0.000	0.000	0.004	

Table 7: Parameter estimates for control group only

	6-month PedsQL (n=54)			6-month VO2peak (n=51)			6-month treadmill time (n=51)		
	B	**Std. Error**	**Sig.**	**B**	**Std. Error**	**Sig.**	**B**	**Std. Error**	**Sig.**
Stage 0/1		Reference			Reference			Reference	
Stage 2	0.618	2.812	0.827	0.029	0.994	0.977	-20.714	35.201	0.559
Stage 3	-0.908	6.911	0.896	-3.675	3.470	0.295	-36.684	123.637	0.768
BMI percentile	-1.455	0.905	0.115	-0.298	0.360	0.411	13.689	13.199	0.305
Age	0.138	1.033	0.894	-0.390	0.393	0.326	-20.693	14.105	0.149
Female		Reference			Reference			Reference	
Male	3.083	3.158	0.334	1.289	1.302	0.328	-95.111	45.621	0.043
Outcome variable assessed at baseline	0.726	0.099	0.000	0.730	0.112	0.000	0.610	0.095	0.000

Table 8: Parameter estimates for control group only (Table 7 continued)

	6-month Seated bench press weight in kg (n=41)			6-month Leg Press weight in kg (n=41)			6-month adherence (n=75)		
	B	**Std. Error**	**Sig.**	**B**	**Std. Error**	**Sig.**	**B**	**Std. Error**	**Sig.**
Stage 0/1		Reference			Reference			Reference	
Stage 2	-0.482	2.367	0.840	4.883	12.371	0.696	-0.026	0.016	0.108
Stage 3	5.083	7.426	0.498	1.050	40.162	0.979	-0.026	0.035	0.459
BMI percentile	1.502	0.847	0.085	11.078	4.573	0.021	0.003	0.005	0.504
Age	-0.117	0.999	0.908	-1.591	5.304	0.766	-0.004	0.006	0.495
Female		Reference			Reference			Reference	
Male	3.022	3.079	0.333	-13.352	15.660	0.400	0.018	0.019	0.336
Outcome variable assessed at baseline	0.861	0.137	0.000	0.629	0.200	0.004			

Table 9: Associations table for exercise groups only

	6-month PedsQL (n=155)	6-month VO2peak (mlO2/kg/min) (n=145)	6-month treadmill time (n=145)	6-month Seated bench press (kg) (n=115)	6-month Leg Press (kg) (n=113)	6-month adherence (n=224)
	Sig.	**Sig.**	**Sig.**	**Sig.**	**Sig.**	**Sig.**
EOSS-p	0.284	0.001	0.048	0.657	0.374	0.824
BMI percentile	0.923	0.000	0.002	0.011	0.073	0.745
Age	0.029	0.703	0.960	0.744	0.751	0.086
Sex	0.314	0.000	0.042	0.015	0.585	0.249
Group assignment	0.620	0.012	0.373	0.000	0.031	0.641
Outcome variable assessed at baseline	0.000	0.000	0.000	0.000	0.000	

Table 10: Parameter estimates for exercise groups only

	6-month PedsQL (n=155)			6-month VO2peak (n=145)			6-month treadmill time (n=145)		
	B	**Std. Error**	**Sig.**	**B**	**Std. Error**	**Sig.**	**B**	**Std. Error**	**Sig.**
Stage 0/1		Reference			Reference			Reference	
Stage 2	1.643	1.591	0.304	0.044	0.734	0.952	-15.288	28.092	0.587
Stage 3	-1.888	2.617	0.472	-4.021	1.142	0.001	-107.734	43.436	0.014
BMI percentile	0.045	0.463	0.923	-0.918	0.239	0.000	-27.053	8.527	0.002
Age	1.167	0.528	0.029	0.093	0.244	0.703	-0.466	9.327	0.960
Female		Reference			Reference			Reference	
Male	1.726	1.708	0.314	3.567	0.857	0.000	62.118	30.297	0.042
Combined		Reference			Reference			Reference	
Aerobic	0.721	1.776	0.686	0.446	0.860	0.605	-21.622	32.909	0.512
Resistance	-1.039	1.776	0.559	-1.960	0.843	0.022	-45.540	32.342	0.161
Outcome variable assessed at baseline	0.606	0.062	0.000	0.613	0.080	0.000	0.450	0.083	0.000

Table 11: Parameter estimates for exercise groups only (Table 10 continued)

	6-month Seated bench press weight in kg (n=115)			6-month Leg Press weight in kg (n=113)			6-month adherence (n=224)		
	B	**Std. Error**	**Sig.**	**B**	**Std. Error**	**Sig.**	**B**	**Std. Error**	**Sig.**
Stage 0/1		Reference			Reference			Reference	
Stage 2	-0.362	1.905	0.850	8.983	9.429	0.343	0.021	0.034	0.536
Stage 3	-2.636	2.890	0.364	18.845	14.662	0.202	0.007	0.053	0.892
BMI percentile	1.400	0.539	0.011	4.730	2.612	0.073	-0.003	0.009	0.745
Age	-0.211	0.645	0.744	-1.026	3.222	0.751	-0.020	0.012	0.086
Female		Reference			Reference			Reference	
Male	5.660	2.293	0.015	5.860	10.695	0.585	0.044	0.038	0.249
Combined		Reference			Reference			Reference	
Aerobic	-9.069	2.223	0.000	-16.961	11.367	0.139	0.027	0.040	0.493
Resistance	0.078	2.139	0.971	12.092	10.861	0.268	-0.008	0.039	0.840
Outcome variable assessed at baseline	0.864	0.085	0.000	1.192	0.129	0.000			

Table 12: Summary of associations

			Independent Variables	
			EOSS-p	BMI percentile
Outcome Variables	Baseline	QOL	✓ (-)	X
		Cardiorespiratory fitness	X	✓ (-)
		Upper body strength	X	✓ (+)
		Lower body strength	X	✓ (+)
	6-months	QOL	X	X
		Cardiorespiratory fitness	✓ (-)	✓ (-)
		Upper body strength	X	✓ (+)
		Lower body strength	X	✓ (+)
		Adherence	X	X

Table 13: Tests of Between-Subjects Effects for Baseline Outcomes

	PedsQL (n=296)			VO_{2peak} (mlO_2/kg/min) (n=299)			Seated bench press (kg) (n=248)			Leg Press (kg) (n=248)		
	F	**Sig.**	**Eta²**	**F**	**Sig.**	**Eta²**	**F**	**Sig.**	**Eta²**	**F**	**Sig.**	**Eta²**
Corrected Model	16.06	<0.001	0.22	19.35	<0.001	0.25	22.17	<0.001	0.31	13.13	<0.001	0.21
EOSS-p	34.21	<0.001	0.19	1.14	0.32	0.01	0.34	0.71	<0.01	0.06	0.94	<0.01
BMI percentile	0.05	0.82	<0.01	49.71	<0.001	0.15	4.80	0.029	0.02	9.16	0.003	0.04
Sex	7.07	0.008	0.02	76.54	<0.001	0.21	71.90	<0.001	0.23	28.11	<0.001	0.10
Age	2.92	0.09	0.01	3.12	0.08	0.01	6.57	0.011	0.03	11.82	0.001	0.05

Table 13 was created to provide additional baseline data that could not be included in the manuscript.