

Validation of Cardiorespiratory Fitness and Body Composition Assessment Methodologies in the Obese Pediatric Population



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by

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Abstract

Rates of obesity (OB) are escalating among Canadian children and youth and the obesogenic environment is likely to cause further increases. An important aspect in providing clinical care to OB children is to have accurate assessment measures, particularly of their body composition and cardiorespiratory fitness. This project entails three interrelated projects aiming to develop novel cardiorespiratory fitness and body composition measurement techniques for an OB pediatric population. The purpose of the first project was to validate a new submaximal fitness protocol specifically geared towards OB children and youth. The second objective of this thesis involved assessing cardiorespiratory efficiency utilizing the Oxygen Uptake efficiency slope. The purpose of the third project was to determine the validity of a half-body scan methodology for measuring body composition in obese children and youth. The goal of developing these novel measurement techniques is improved design and evaluation of interventions aimed at managing pediatric obesity.

Co-Authorship

This thesis presents the work of Peter Breithaupt in collaboration with his supervisors Drs Kristi Adamo and Rachel Colley.

Manuscript 1. *Validation of the HALO submaximal treadmill protocol to measure fitness in obese children and youth.* Dr. Adamo, Dr. Colley, and Mr. Breithaupt were responsible for initialization, conceptualization and design of the project. The subject recruitment, statistical analysis, interpretation of results, and writing of the manuscript was completed by Peter Breithaupt under the supervision and with editorial comments provided by Drs Adamo and Colley. This manuscript has been submitted to *Applied Physiology, Nutrition, and Metabolism* and is presented as requested by the journal. Dr. Colley is the corresponding author for this manuscript.

Manuscript 2. *Submaximal OUES is a useful alternative to maximal exercise testing in the obese pediatric population.* Again, the conceptualization and design of the manuscript was through collaboration of Dr. Adamo, Dr. Colley, and Mr. Breithaupt. Subject recruitment, fitness testing, statistical analysis, interpretation of results, and writing of the manuscript was completed by Peter Breithaupt under the supervision and with editorial comments provided by Drs Adamo and Colley. This manuscript has been submitted to *Pediatric Exercise Science* and is presented as requested by the journal. Dr. Adamo is the corresponding author for this manuscript.

Manuscript 3. *Body Composition Measured by Dual-Energy X-ray Absorptiometry (DXA) Half-body Scans in Obese Children.* Again, the conceptualization and design of the manuscript was through collaboration of Dr. Adamo, Dr. Colley, and Mr. Breithaupt.

Subject recruitment, fitness testing, statistical analysis, interpretation of results, and writing of the manuscript was completed by Peter Breithaupt under the supervision and with editorial comments provided by Drs Adamo and Colley. This manuscript has been published in *Acta Paediatrica* and is presented as requested by the journal. Dr. Adamo is the corresponding author for this manuscript.

The Introduction, Review of Literature, General Discussion, and Appendices were completed by Peter Breithaupt with suggestions and editorial comments from Drs Adamo and Colley.

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CHAPTER 1

Introduction

Objectives and Hypotheses

As the obesity epidemic persists amongst the pediatric population the need for more effective intervention strategies comes to the forefront. There are a number of important variables, including the measurement of physical activity and fitness, which are important to both tailor the intervention to the individual, and allow for more rigorous evaluation of the interventions. Similar to the interventions, the baseline measures must not only be robust, but also appropriate for the obese, pediatric population. When performing an assessment on obese children it is important that there be adapted measures which can produce more accurate measures, and ensure that the experience of being measured is not an uncomfortable or traumatic one for the child. The proposed studies hope to address some of these clinical gaps for assessment methodologies in the obese pediatric population by:

1) Determining if the new Healthy Active Living and Obesity Research Group (HALO) sub-maximal aerobic fitness testing protocol for obese children and youth provides a comparable estimate of VO_{2max} to that measured using validated i) maximal and ii) sub-maximal equation-based protocols in the obese pediatric population. It is hypothesized that the proposed HALO submaximal cardiorespiratory fitness measure will be found to be valid means of providing an understanding of the variability in VO_{2max} prediction.

2) Exploring the relationship between oxygen uptake efficiency slope (OUES) and other measures of cardiorespiratory fitness at maximal and submaximal intensities in the obese pediatric population. Once these values have been established they will be compared to published OUES values in a healthy weight population to better understand different movement efficiency between the groups. It is hypothesized that 1) The obese population of children will be more efficient at submaximal work rates than at maximal work rates, 2) the obese children will be less efficient when controlling for body weight, body surface area, and fat free mass, and 3) in absolute measure of efficiency, the obese population will be less efficient than the healthy population.

3) Determining the validity of a half-body scan methodology for measuring body composition in a sample of obese children and youth. It is hypothesized that the half-body DXA scan methodology for measuring body composition will provide valid estimates in the obese pediatric population. This hypothesis is largely based on the observation that this methodology provided valid body composition estimates in a sample of obese adults.

Overview

The rate of obesity has reached epidemic proportions among Canadian children and youth (1-5) and the current obesogenic environment is likely to result in further increases in overweight and obesity. Excess adiposity can lead to co-morbidities such as type 2 diabetes (6-8), cardiovascular disease (7;9), hypertension (10-12), osteoarthritis (13;14), sleep apnea (15;16), and a number of types of cancer (17). Without lifestyle changes, obesity is likely to be sustained into adulthood (18-20). Despite the urgent need for lifestyle changes in this population, interventions within this population continue to suffer from high attrition and modest success rates (21). To improve the effectiveness of interventions, it is crucial to individualize the approach based on accurate and thorough assessment of the children. Two such assessments which play a vital role in developing and evaluating interventions are cardiorespiratory fitness and body composition.

Cardiorespiratory fitness is a powerful indicator of health and therefore accurate measurement of physical fitness is essential to the evaluation of intervention programs and understanding relationships between fitness and health. When measuring fitness in overweight and obese children, it is important to consider that they will respond differently both physically and emotionally to exercise than children classified as healthy weight (22-24). Aerobic capacity, considered “the total chemical energy available to perform aerobic work”(25), is often used interchangeably with a similar, yet more clinical term in cardiorespiratory fitness. Cardiorespiratory fitness is defined as “the ability to transport and utilize oxygen during prolonged strenuous physical activity...” (26). Although these terms are inequivalent, to stay consistent with the body of literature reviewed for this project the

term cardiorespiratory fitness will be used throughout. The current gold standard method for measuring cardiorespiratory fitness requires a child to exercise until exhaustion; an experience which may be particularly negative for an obese child, especially when considering the psychological pitfalls associated with obesity at a young age (27). Submaximal testing can be used to predict maximal fitness but there is very little known about how well this works in obese children and youth. Given that submaximal intensities are better tolerated and more reflective of the intensity of movement obese children would undertake in the real world, it is appropriate to assume a validated submaximal protocol would likely be far more effective fitness measurement for this population.

Accurate measurement of body composition is also of utmost importance while planning an obesity-intervention program. Dual-energy X-ray absorptiometry (DXA) has become the gold standard for clinical assessment of human body composition (28). DXA is based on differing absorption rates of photons emitted at two energy levels by body tissue allowing for quantification of bone mineral, lean and fat soft tissue masses separately (29). DXA scans are short in duration (5-20 min) (30), relatively inexpensive, and have been found to be very precise while having very low radiation exposure ($<0.1 \mu\text{Gy}$) (31). Despite the tremendous upside of DXA scans, it is unfortunate that a large segment of the population may not be able to receive a scan due to either their width exceeding the scan area (~60 cm) or their mass exceeding weight limitations for the scanner (~136 kg) imaging capabilities. This remains true even in the pediatric obese populations making it timely that an alternative means of estimating body composition for those whom surpass the limits of standard DXA equipment be developed. A half-body scan methodology has been validated

to overcome these limitations in an obese, adult population but no such validation has been completed within the pediatric population.

In order to successfully mitigate the adverse effects and eventually reverse current trends in rates of overweight and obese, it is important to develop effective weight management intervention programs and encourage appropriate lifestyle changes in this population. To improve program design and provide an increased capacity to properly evaluate interventions it is imperative that there are accurate means of measuring body composition and fitness.

Ethical Considerations and Safety Issues

There is little risk to participants participating in either of these studies. Participants may benefit from the feedback they receive on the results of the aerobic fitness level, as it may identify where improvements could be made in lifestyle in order to attenuate obesity or better manage co-morbidities. They will benefit from the DXA scan by obtaining a detailed body composition analysis which can aid in clinical treatment of their obesity and related comorbidities while the radiation exposure experienced is extremely minimal (0.003mGy). In the unlikely event that participants experience an injury, medical or psychological crisis during the fitness test, a safety protocol is in place and the hospital emergency response team will be contacted immediately. All tests will be conducted at CHEO by certified exercise physiologists with CPR and first aid training and in close proximity to the CHEO emergency room should it be required. Informed consent (>16 years) or assent (<16 years) will be obtained before study initiation. Both protocols have been approved by the CHEO Research Ethics Board (Appendix E) and the University of Ottawa Research Ethics Board (Appendix D).

Thesis Organization

This MSc thesis conforms to the regulations outlined by the University of Ottawa and School of Human Kinetics. After an introduction and overview in chapter 1, chapter 2 provides the reader with a review of the current literature in areas related to the thesis topic including obesity, fitness testing and body composition assessment. Chapter 3 contains the first manuscript entitled “Validation of the HALO submaximal treadmill protocol to measure fitness in obese children and youth”. This manuscript, which has been submitted to and is under revision with *Applied Physiology, Nutrition, and Metabolism*, is formatted according to the requirements of the journal. Chapter 4 contains the second manuscript “Submaximal OUES is a useful alternative to maximal exercise testing in the obese pediatric population”. This manuscript has been submitted and is currently under review with *Pediatric Exercise Science* and is formatted according to the requirements of the journal. Chapter 5 contains the third manuscript “Body Composition Measured by Dual-Energy X-ray Absorptiometry (DXA) Half-body Scans in Obese Children”. This manuscript has been published in *Acta Paediatrica* (See Appendix F) and is formatted according to the requirements of the journal. Chapter 6 contains a general discussion that summarizes key findings, potential implications of the research, and overall conclusion of the thesis.

List of Abbreviations

BAI	Body Adiposity Index
BIA	Bioelectrical Impedance Analysis
BMC	Bone Mineral Content
BMI	Body Mass Index
BSA	Body Surface Area
CAFT/mCAFT	Canadian Aerobic Fitness Test/modifiedCAFT
CDC	Centres for Disease Control and Prevention
CHEO	Children's Hospital of Eastern Ontario
CSEP	Canadian Society for Exercise Physiology
CT	Computer Tomography
DXA	Dual-Energy X-ray Absorptiometry
FFM	Fat Free Mass
HALO	Healthy Active Living and Obesity Research Group
HR	Heart Rate
Ht	Height
Kgm	Kilogram-meters per minute
MRI	Magnetic Resonance Imaging
MRT	Medical Radiation Technologist
OB	Obese
OUES	Oxygen Uptake Efficiency Slope
OW	Overweight
POC	Pediatric Obesity Cohort
RER	Respiratory Exchange Ratio
SPW	Self-Paced Walk
T2D	Type 2 Diabetes
V_E	Minute Ventilation
VO₂max	Maximal Oxygen Consumption
VT	Ventilatory Threshold
WHO	World Health Organization
Wt	Weight

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CHAPTER 2

Review of Literature

Obesity

Obesity is often defined simply as a condition of abnormal or excessive fat accumulation in the fat tissues (adipose tissue) of the body leading to health hazards (32). The underlying cause is a positive energy balance, which occurs when the calories consumed exceed the calories expended (33). Obesity is a multi-factorial condition involving environmental, behavioural, and genetic factors that, in association with an ever-increasing obesogenic environment, contribute to an imbalance between energy intake and expenditure (34). Body mass index (BMI) is a simple means of estimating body by comparing the relationship between ones height (m) and weight (kg) (35). Specifically, an obese adult is defined as one whose BMI is great than 30 kg/m^2 and someone whom is overweight has a BMI between $25\text{-}29.9 \text{ kg/m}^2$.

In the past 50 years the prevalence of obesity and overweight has increased exponentially, and there does not seem to be an end to this escalation in the immediate future. Between 1981 and 1996 the prevalence of overweight in Canada increased from 48 to 57% among men and from 30 to 35% among women, while the prevalence of obesity increased from 9% to 14% in men and from 8 to 12% in women (36). Canadian Adults have seen a 70% increase in the prevalence of obesity from 1978-2004 (37). Among American adults aged at least 20 years in 1999-2002, 65.1% were overweight or obese, 30.4% were obese, and 4.9% were extremely obese (38). In 2004 the overall prevalence of obesity in Canadian adults was 22.9% for men and 23.2% for women (39). Similar trends have been

seen world-wide with measured obesity rates of 22.0% in England, 25.0% in Scotland and 28.5% in New Zealand. Even in countries with historically low obesity rates, like Japan and Norway, the prevalence is increasing. While these countries still have lower prevalence relative to other countries, they have experienced a nearly a 2-fold increase from 1995-2005 with increases from 2.6%-3.9% and 5.0%-9.0% respectively (40). More alarming yet is that the level of the most extreme classifications of obesity are also increasing showing this is the increase of class 3 obesity ($\text{BMI} \geq 40$) from 0.78% to 2.2% from 1990-2000 amongst American adults (41). This higher classification of obesity can be linked to an even greater risk of developing a multitude of obesity related co-morbidities than class 1 or 2 obesity (41). The co-morbidities associated with obesity can potentially be broken into two major classifications: physical and psychological.

Obese persons may suffer from a number of physiological co-morbidities which often correlate positively with increasing levels of obesity. These co-morbidities include increased risk for type 2 diabetes (6-8), cardiovascular disease (7;9), stroke (42) , hypertension (10-12), osteoarthritis (13;14), sleep apnea (15;16), and a number of types of cancer (17). It has been found that specific cancer sites with the greatest mortality risk in obese compared to healthy weight include colon, rectum, breast and prostate (43). Obesity is clearly a major factor for the current prevalence rates of many diseases. In Canada, for example, if the entire population were of healthy weight there would be ~30% reduction in the prevalence of hypertension, type-2 diabetes, and gallbladder disease (3) . Obesity has also been closely linked with dermatological diseases such as psoriasis (44;45), which can magnify some psychological obesity related co-morbidities. Obese individuals may suffer from an array of

psychological co-morbidities including disordered eating (46;47), reduced quality of life (48-50), diminished self-esteem (23;51), and depression/depressive symptoms (52-54). These psychological limitations combined with physiological impairments can lead to a fairly crippling lifestyle for some obese persons. There are arguably even greater implications from these negative contributors on the pediatric population, as will be covered in the next section.

In excess of the physiological and psychological issues directly associated with obesity and the obese, there are also substantial financial burdens that place great strain on health care systems. The total direct cost of obesity in Canada in 1997 was estimated to be over \$1.8 billion (55). At present hypertension (\$656.6 million), type 2 diabetes mellitus (\$423.2 million) and coronary artery disease (\$346.0 million) are the 3 largest contributors to total of the associated co-morbidities (55). In 2000, an “Economic Burden of Illness in Canada” (EBIC) study showed that the total cost of illness reached \$202 billion (56). By 2001, the economic burden of obesity reached 2.2% (or \$4.3 billion) of the total cost of illness. Of this, \$1.6 billion was related to direct costs and \$2.7 billion to indirect costs. The three most expensive co-morbidities associated with obesity are coronary artery disease (\$1.3 billion), hypertension (\$979 million), and osteoarthritis (\$881 million) (45). These numbers continue to grow and in 2006, the total costs attributable to overweight and obesity in Canada was \$6.0 billion. Even though the total cost of illness has decreased to \$148 billion, the percentage of total costs related to obesity and overweight has nearly doubled from 2001 (2.2 to 4.1% of total cost of illness in Canada) (57). The problem is not only in Canada,

the WHO reports that international studies on the economic costs of obesity show they account for between 2-7% of total health care costs in countries world-wide (58).

The annual economic burden of obesity in Ontario alone is \$2.35 billion, representing 5.3% of the total Provincial Health Care budget (4). These costs will continue to increase given compelling evidence showing that pediatric obesity is also on the rise in Canada (3;59).

Why Pediatric Obesity?

According to the World Health Organization, obesity is now the most common non-communicable pediatric disorder in the developed world (60). Similar to obesity in the adult population, pediatric obesity is a serious issue because it exposes children to a vast number of physical and psychological health risks (61). The elevated concern with this population is that they are exposed to these conditions at an earlier age, possibly resulting in further exaggeration of issues than we have seen develop in an adult population. The major mechanisms associated with the widespread increase in the pediatric population relate to unhealthy lifestyles, including an increase in energy intake, and decrease in energy expenditure through regular physical activity (62). In support of this, over 88% of children and youth in Canada are insufficiently active to accrue the health benefits (63;64). Technological advancement, societal influence, and the built environment are all contributing factors resulting in a considerable amount of time spent engaging in sedentary pursuits on a daily basis (65). Compounding those factors, excess weight leads to higher costs of locomotion combined with the discomfort associated with transporting that excess weight, which may deter obese children from participating in activities that are considered appropriate for normal-weight children (34).

In children, rather than general classifications based directly on BMI, there are reference growth curves which use age, height and weight to appropriately classify overweight and obese in children. Reference values for body mass index (BMI) are available from the US Centers for Disease Control and Prevention (CDC) (66) and the International Obesity Task Force (IOTF) (67). These reference curves are appropriate for children and

youth up until adulthood. Recently the World Health Organization (WHO) has released a new set of growth curves which are meant to be the optimum measure and means of classifying overweight and obese in children world-wide under the age of the 6 (68).

Mirroring the adult population, from 1981-1996 there was a nearly three-fold increase in over weight among the pediatric population from 11 to 33% in boys and 13 to 27% in girls and an even greater increase in the prevalence of obesity in children where rates have gone from 2 to 10% in boys and from 2 to 9% in girls over the same time frame (69). From 1999-2002, 31.0% of children aged 6 through 19 years old were at risk for overweight or obese, and 16.0% were obese (38). These trends are comparable to other Western countries (40). Even in countries where obesity was formerly uncommon there has been a slow upward progression in prevalence (70-72). For example, the prevalence in China among preschool-aged children living in urban areas has increased eightfold—from 1.5% in 1989 to 12.6% in 1997 (73). Similarly, in developing countries such as Kenya, the prevalence of overweight and obesity is as high as ~7% in boys, and ~17% in girls (74). Currently, it is estimated that 26% of Canadian children and youth aged 2-17 years are overweight or obese (59).

Obese children are at increased risk of several health conditions (75;76) including asthma (77), atherosclerosis (78), chronic back pain (42) hepatic steatosis (79), hypertension (80;81), non-alcoholic fatty liver disease (82), sleep apnea (83), and type 2 diabetes (84-88) Furthermore, these children are at greater risk for longer term chronic conditions such as cardiovascular disease (3;89-91), cancer (17;92), musculoskeletal disorders (13;42;93), and gall bladder disease (34;42). It has also been found that childhood

obesity, glucose intolerance and hypertension are all correlated to premature death (94). Not only should these medical issues related to pediatric obesity be alarming but there is also a further myriad of psychosocial consequences directly related to childhood obesity.

Due to differing age-related psychological and physical development amongst children various psychosocial problems may not only be far more abundant, but also more difficult to deal with than in an adult population. In children the most common psychosocial issues include depression (27;53;54;95), diminished self-esteem (23;51), body image disturbance (96;97), reduced well-being (98;99), and reduced quality of life (22;49;100). Being obese at a young age is also related to weight-related teasing; consequently, weight-related teasing was also found to have potentially harmful effects on emotional well-being (98;99), and could often lead to disordered eating in children (96). In addition to the direct physical and psychological effects on the obese child there is also the contribution that the young obese population is making towards the serious financial burden on Canada's health care system associated with the increasing rates of obesity (45;55). Moreover, since 6 in 10 obese children have at least 1 risk factor for cardiovascular disease, and an additional 25% have 2 or more risk factors (41), the long-term health care burden is even more significant if we include the obesity associated chronic co-morbid conditions. In addition to these values there is also \$10 million+ spent annually to provide a strategy meant to encourage children to eat healthy and be physically active (3) in hopes of combating the childhood obesity epidemic.

Not only are risks directly associated with the pediatric population of concern, but research had also identified that 50% of elementary school-age children and 80% of

adolescents who are obese remain so into adulthood (101). Carrying excessive weight during adolescence is a strong predictor of numerous obesity related health issues later in life (102). Once obesity has been established in adulthood, the probability of successfully achieving an ideal body weight through voluntary weight loss is exceptionally low (101). This places obese children at an even greater risk for longer term chronic conditions such as stroke, cancer, musculoskeletal disorders, and gall bladder disease if their obesity persists into adulthood (34).

It has even been proposed that 1- and 2-year-olds with an obese parent may garner the greatest benefits from intervention efforts to prevent obesity (102), while other studies take it a step further suggesting that interventions should be completed in mother prior to conception and during pregnancy (103). Regardless, the association between childhood obesity and adult morbidity and mortality strongly suggests that a more effective strategy for the prevention and treatment of childhood obesity should be pursued (104). Providing optimal intervention design and effective means of evaluating lifestyle change strategies demands improved clinical assessment methodologies for body composition and cardiorespiratory fitness in the obese pediatric population.

The importance of Assessment Methodologies and Intervening with an Obese, Pediatric Population

Changing the “obesogenic” environment is a critical step toward reducing obesity. However, reversing these factors will require major changes in urban planning, transportation, public safety, and food production and marketing (32). Due to the overwhelming amount of work which would likely be required to make these changes most political leaders are failing to adequately address the issues. The end result of this is an attempt towards more small scale interventions attempting, albeit unsuccessfully, to make the entire population healthier. The ultimate goal when intervening with an obese, pediatric population is to regulate body weight through decreasing fat mass and maintaining or increasing lean mass, while ensuring adequate nutrition for healthy development. Physical activity and physical fitness are both inversely associated with the clustering of metabolic abnormalities associated with obesity (105), further magnifying the importance of effective interventions which include both regular physical activity and a healthy diet.

Interventions should be associated not only with positive physiological changes but also psychological changes; they should aim for an ultimate goal of long-term weight maintenance which can be achieved by replacing poor eating and exercise habits with new, healthier behaviours (106). One study found that social physique anxiety rather than self-efficacy was inversely related to pleasure and energy, suggesting that low levels of pleasure and energy found in obese compared to non-obese may be related to their low levels of physical activity. They also recommend that psychosocial interventions should aim to

modify the cognitive antecedents of social physique anxiety as it may be an effective means of increasing physical activity rates within this population (107). The importance of this emerges especially in the pediatric population since patients who are active at an early age are likely to enjoy active lifestyles as adults and thus attenuate expected age-related losses in cardiorespiratory endurance, strength, and flexibility (108). Promoting physical activity early in life could help to help to reverse the current increases in the prevalence of obesity in the pediatric population and reduce associated co-morbidities. Physical activity and fitness are both inversely related to metabolic abnormalities (105), therefore measurement of physical activity and fitness is important to both tailor the intervention to the individual, and to evaluate the effectiveness of interventions.

Accurate and reliable assessments of health measures in obese children are crucial for effective intervention design and evaluation. Two particularly important avenues are cardiorespiratory fitness and body composition. Accurate quantification of physical fitness, through fitness testing, is essential in terms of both health outcome and the effectiveness of intervention programs (109). Establishing a clear understanding of an obese child's physical capacity through a proper assessment of their cardiorespiratory fitness, should enable far more effective and efficient intervention. Clinicians who understand how an individual responds to exercise, will be better able to make exercise recommendations that are appropriate for their needs, goals and functional capacity (108).

Numerous studies have shown that risk for insulin resistance, type 2 diabetes, high blood pressure, elevated blood cholesterol levels and stroke as well as risk for death are increased in persons with obesity (particularly abdominal obesity) (89;110-117). Thus

thorough quantification of body composition is also an important concept when considering the health implications of pediatric obesity and providing appropriate clinical care. An accurate, objective assessment of body composition is incredibly valuable given the evidence indicating that self-report systematically under represents the extent of the obesity problem (118-121). In addition to providing fundamental whole-body descriptive characteristics, accurate measures of body composition often are required as comparative factors to normalize physiologic variables (eg, metabolic rate, physical activity, and physical fitness).

Cardiorespiratory Fitness Testing

Aerobic capacity is considered “the total chemical energy available to perform aerobic work” (25) and there are many accepted means to estimate its value, such as endurance time, time to exhaustion, or biochemical indicators of capacity for prolonged work (25). Aerobic capacity is often mistaken with a similar, yet more clinical term in cardiorespiratory fitness. Cardiorespiratory fitness is defined as “the ability to transport and utilize oxygen during prolonged strenuous physical activity. It reflects the overall transporting efficiency of the lungs, heart, circulation, and active muscles, and the ability of the muscles to use the oxygen supplied” (26). Concurrent with the rise in childhood obesity is evidence that fitness has declined substantially between 1981 and 2009 in Canada (122). The best available data tell us that only 12% of Canadian children and youth are presently meeting Canada’s physical activity guidelines (63). When compared to healthy weight individuals, obesity has the strongest negative association with not only cardiorespiratory fitness but also muscle endurance, and explosive power tests (123). Since fitness is such a powerful indicator of health (124;125), it is almost always assessed before and after pediatric lifestyle interventions. Incremental exercise testing intended to achieve maximal oxygen consumption (VO_2max) is considered the gold standard in the assessment of cardiorespiratory fitness (109). Some popular tests utilized for maximal fitness testing include the Bruce and Balke treadmill protocols, and CSEP cycle protocol. Although many of these tests have been adapted for use in children, exercise testing is more challenging in this age group than in adolescents and adults (126), and this is further magnified when the children are overweight or obese (127).

Submaximal VO₂ Testing

The goal of fitness testing should be to produce a sufficient level of exercise stress to obtain an accurate measure of maximal oxygen consumption without physiologic, psychological or biomechanical strain (128). Successful maximal exercise testing is difficult for a fit population and within an obese, pediatric population fitness testing is even more problematic (126). A stressful fitness evaluation opens the door to increased overall risk of physiological co-morbidities, an array of related psychosocial factors, and decreased motivation to complete the test. Some researchers have explored alternative outcomes to VO₂max that can be obtained from incremental maximal protocols such as time to exhaustion (129) or oxygen consumption at a specific heart rate (HR) (127). These approaches provide some data when true maximum is not achieved; however, these protocols still require exertion to volitional fatigue.

Submaximal protocols have several practical benefits over maximal protocols including being potentially less expensive, easier and safer to administer, better tolerated by children (130), resulting in increased likelihood of obtaining complete data (i.e. more children finish the full protocol) (127), and provide the ability to adapt work rates across a wide variety of individual fitness levels (131). More effective submaximal protocols still allow for the prediction of VO₂max (132) while also providing the steady-state submaximal data required to better understand an individual's exercise efficiency and endurance across a range of intensities.

There are many submaximal tests in use today; one of the most commonly used submaximal field tests for the prediction of VO_2max is the Astrand-Ryhming test (133) which uses a linear extrapolation method with heart rate at different work rates to predict VO_2max . Another common field test used is the Canadian aerobic fitness test (CAFT) (134), or modified version the CAFT (mCAFT) (135) which estimates fitness based on a step test, heart rate levels and heart rate recovery. Some tests such as the CAFT, mCAFT, and the Rockport fitness test (or 1-mile track walk test) (136) use a predictor equation combined with data acquired through the test. Some other submaximal exercise protocols include the YMCA cycle protocol (137), Cooper 12 min walk-run test (138), and a multi-stage progressive shuttle run test (MST) (139). While there probably will never be an optimal protocol for all situations and populations, existing guidelines for pediatric exercise testing are recommended for use when selecting or developing a protocol (140).

Why Submaximal Cardiorespiratory Testing for this Population?

Pushing overweight and obese children to physical exhaustion has a high potential of being a physically and psychologically negative experience for the child and a futile method of obtaining a 'true' maximum effort because children may stop the test prematurely or be afraid to do future fitness testing (127). However, the current approach to measuring fitness requires that children exercise until exhaustion; an experience which can be particularly negative for overweight and obese children. While we know that it is possible to predict maximal fitness using a submaximal test (128;141;142), we currently know very little about how well this works in obese children and youth. Submaximal intensities of

exercise are better tolerated (143) and are more reflective of the intensity of movement overweight and obese children and youth would undertake in the real world.

It is believed that assessing a child's fitness in a less stressful manner (i.e. submaximal) would be less intimidating and decrease pre-test anxiety (23), while possibly increasing overall confidence as they are able to complete the test rather than facing the possibility of failing before reaching maximal effort during a maximal test. This may also minimize/alleviate any mental health issues such as depression and low-self esteem (61), often associated with obesity, that may be exacerbated by a poor performance on a very challenging test (144). If the concept of a maximal exercise test is discouraging to prospective subjects (27), being able to propose a submaximal test could be far more appealing and provide much needed ammunition for developing appropriate interventions for overweight children (130) and increase participation numbers. With a submaximal test there is also an increased likelihood of receiving complete data from a greater number of participants since they are less likely to quit as is often the case with a maximal test. To summarize, submaximal tests are quite simply easier to administer for the tester, easier to complete by the subject, and well tolerated by children in comparison to the maximal exercise test (130).

Being able to accurately measure the fitness of this population through easily obtained means, such as submaximal testing, is vital to their assessment and implementation of future weight management intervention efforts (145). Thus through the development and use of a valid and reliable submaximal exercise testing protocol for the obese, pediatric population it allows for an assessment of the movement efficiency and

fitness of this population. Additionally, given the unique psychosocial characteristics of this population, the ideal submaximal testing protocol should be relatively comfortable for the child and not be perceived as intimidating (126;140). The importance of regular physical activity for the health of all children is well documented (146-148), and a submaximal fitness testing protocol tailored for the obese pediatric population should make for a less intimidating, more positive experience for the subjects that will hopefully not discourage them from exercising or 'turn them off' physical activity. In addition to these benefits, the ideal protocol would still allow ample data collection in order to predict maximal physical capacity and offer the same intervention-related benefits which a maximal test may offer. A potential complementary means to assess the fitness of children at submaximal work rate may be to analyze their efficiency at differing work rates.

Efficiency

Mechanical efficiency of muscular work is defined as the ratio of work accomplished to the amount of energy expended (149). Often expressed as a percentage, mechanical efficiency is easily determined during cycle ergometry; however it is not as easily computed during horizontal walking or running because technically no external work is accomplished (150). Efficiency measurements are taken at steady work rates and completed under the assumption that energy needs are met by respiration (151). One's efficiency has been found to be closely tied to body mass (152), age (149;153), sex (154), and training/type and intensity of exercise (154;155).

Due to the difficulty in expressing mechanical efficiency during walking, most research is centered on cycle ergometers (152;156;157). The work measuring mechanical efficiency during running or walking is dependent upon having a number of biomechanical markers such as lower limb length, stride length, force displacement during movement, and the displacement of the centre of mass (158). Donovan and Brooks also suggest that much of the difference in efficiency may “be the result of the manner in which forces are distributed over the body during walking” (159). Unlike cycling efficiency, there little research in the area of running efficiency due to measurement difficulties for those researchers whom are not biomechanists. Rather than directly measuring mechanical efficiency during walking or running a supplemental measure is generally used, this is referred to as economy of movement, or walking/running economy.

Economy of movement refers to measure of efficiency but rather than having the denominator as mechanical work or power, the denominator is a quantitative value of the task performed, normally speed (25). It has been found that contrary to efficiency, exercise economy is inversely related to cardiorespiratory fitness (160), but like most other exercise measures is closely related to body size and hence age with progressive improvements during biological maturation (149). Due to the nature of the measure of economy of movement, it cannot be expressed as a ratio or percentage and also therefore is not recommended to compare among individuals, rather it is more useful for change over time in the same individual (25). It is also of limited value during growth and development (161).

A newer measure proposed by Baba et al. (165) which can be used to classify efficiency easily, and potentially more precisely than walking or running economy is the

oxygen uptake efficiency slope (OUES). OUES is derived from the relation between oxygen uptake (VO_2 [mL/min]) and minute ventilation (VE [L/min]). OUES is determined by:

$$\text{VO}_2 = a \log \text{VE} + b, \text{ where } a = \text{OUES} \text{ (162)}$$

OUES was found to be a clinically useful measure of evaluating exercise tolerance in the pediatric population (163) and, as it does not require maximal effort, it is a quite tolerable alternative to maximal testing in the pediatric population (161). Since OUES is a relatively new index it does require the generation of appropriate reference values (164), but has been proven to have strong correlations with VO_2 peak (164), peak minute ventilation (VE peak), and Ventilatory Threshold (VT) (165). OUES has also been found to be sensitive to the effects of physical training, making it a strong predictor of change in fitness over time (166). Since OUES is so strongly dependant on anthropometric variables, it has been recommended that OUES values be expressed relative to Body Surface Area (BSA) or Fat Free Mass (FFM) (165).

Have any protocols already been developed?

Frequently the submaximal tests being put into practice in the pediatric population are adult protocols which have been altered to accommodate the smaller muscle mass and lesser physiological capabilities of a child. For example Buono et al. modified the Astrand-Rhyming submaximal test to enable children and adolescents to successfully complete the test (130). Since children will have a greater physiological response, including increased heart rate, ventilatory exchange, and cardiac output (167-169) amongst others, to a lesser

absolute workload the original Astrand-Ryhming protocol had to be altered to provide work rates suitable for use with children. The original protocol had initial work rates of 300 kilogram-meters per minute (kgm) for women and 600 kgm for men, this was modified to consist of an initial work rate of 150 kgm, after which it increased to 150 kgm every 3 minutes until the subject reached 70% of his or her age-predicted ($220 - \text{age}$) maximal heart rate for the pediatric population (130).

Similarly, a submaximal treadmill test protocol was recently developed with the goal of predicting VO_2max in overweight children. Based on a protocol originally developed Ebbeling, et al. (170) and since validated in an adult population (142), Nemeth, et al. (132) validated an altered version in a sample of overweight children. The protocol is based on an equation that uses sex, weight, height, heart rate after 4 minutes of exercise, heart rate difference, and submaximal treadmill speed to predict VO_2max (132). The protocol they developed had the subjects select a comfortable walking speed and walk for 4 minutes on 0% grade. After 4 minutes warm-up the grade was increased to 4% and after another 4 minutes the heart rate was recorded before cool down began. They compared the results with their submaximal exercise test to directly measured results through a progressive maximal exercise test with measurements of maximum oxygen consumption (132).

The protocol Nemeth et al. use for their submaximal test is simply a single stage test lasting 4 minutes and then a prediction equation (132); even though the predicted fitness may be accurate, this may not be sufficient for improving the design and ability to properly evaluate intervention programs. It is important to have not only this estimated measure of maximal fitness but also an assessment of how differing work rates across a wide variety of

individual fitness levels found in this population change on a case-by-case basis. It is possible that a longer protocol with gradually increasing workloads that does not elicit maximal effort can offer greater opportunity to display the relationship between heart rate, ventilatory exchange, and exercise intensity; therefore possibly allowing for a more precise estimation of the subjects maximal VO_2 measurement. The importance of having not only a clear picture of a child's fitness but also physiological and psychological responses to a set of increasing workloads, and movement efficiency is fundamental for the implementation of an effective intervention program.

Also, since age is an important factor for developing a protocol, especially in a younger age range, due to developmental and maturation differences between participants it is important to know; 1) whether Nemeth's protocol is still valid with a greater range of ages within the population (age range of 8-18 vs. 11-14) and 2) If there is a more reliable protocol which can be used across a greater array of ages, obesity levels and stage in physical, emotional, and intellectual development.

Dual-Energy X-Ray Absorptiometry (DXA)

An important aspect in providing clinical care to an obese pediatric population is to have an accurate measure of their body composition. Although generally the most widely used measurement, BMI, can be unreliable at times since as it is calculated using only height and weight there is no acknowledgement of other possible contributing factors such as muscle mass or growth stage so a more accurate measure is required. Originally developed by Peppler and Mazess to measure bone mineral density (171), dual-energy X-ray absorptiometry (DXA) has since become the gold standard for clinical assessment of human body composition (28). Based on the three-compartment model that divides bone mineral content, fat-free (lean) mass and fat mass, DXA works on the assumption that body composition is directly proportional to the energy absorbed by each tissue. Quantification of body composition is made possible because the DXA scanner emits photons at two energy levels and absorption rates of this energy provide the accurate body composition measures (29). Typical measures of body composition provided through a DXA scan include %body fat, fat mass, lean tissue mass, total tissue mass, and bone mineral content (BMC). The main burden placed on a subject is that they must remain motionless for the extent of the scan, however a DXA scan will pass over an entire body very quickly (5-20 min) (30). DXA is also relatively inexpensive compared to MRI, and has been found to be very precise while having very low radiation exposure ($<0.1 \mu\text{Gy}$) compared to CT scan (31).

DXA vs. Other Measures of Body Composition

There are several methods for measuring or estimating human body composition, and dual-energy X-ray absorptiometry (DXA) is one of the most commonly used clinical benchmarks (28). Differentiation between scanners and software used during analysis has been responsible for small differences in measures (172-174), yet when compared to other means of assessing body composition in children, DXA has been found to be the most reliable in repeat-measure studies (175).

Body mass index (BMI) is the most widely used method for estimating body composition due to its low cost and simplicity. Based solely on a ratio of one's height and mass, it is often criticized for its inaccuracies which arise from the same factors that produce its ease of use. Since BMI is based only on one's height and weight, there is no accurate representation of true fat mass, or lean mass, rather just mass as a whole. This means an individual, whom may be incredibly fit and has large lean mass, may have a BMI that identifies them as at-risk or even obese. A recent paper found that over the past 30 years Canadians at a given BMI were found to have higher waist circumference and skinfold thickness (176), this further supports the possible differentiation between BMI and true body composition, placing emphasis on a need for a more precise body composition measure than BMI. Recently a new scale has been proposed as a more flexible alternative to BMI, the body adiposity index (BAI) (177). BAI is a complex ratio of hip circumference to height which has only been tested in Mexican-American adults but may be a more accurate, non-invasive means of estimating body composition than BMI once its validity has been

confirmed in further populations (177). Another issue with BMI is that even when accurately classifying an obese person as 'obese' it does not give us information about the total fat or how the fat is distributed in the body. This understanding of fat distribution is important as abdominal fat is implicated in greater health risk, even when BMI is classified as normal (178;179). In this light, a measure of waist circumference can be a simple and practical method of identifying overweight people who are at increased risk of obesity-related conditions. Waist circumference is an effective means of dividing obese individuals as either an 'apple' or a 'pear'. 'Apples', more often men, have android fat distribution where the bulk of their fat mass is on their stomach and chest. 'Pears', more often women, have gynoid distribution where more of their fat mass is located in their hips, thighs and bottom. Android obesity entails a greater risk of obesity related co-morbidities, while gynoid suggests greater risk of mechanical issues particularly at the hip and knee joints (180). A combination of waist circumference and BMI measures can be an economical, and a useful combination to more accurately suggest obesity and fat distribution than either on their own. However there are more 'accurate' or 'reliable' assessment techniques which have been developed and are used in an array of populations regularly.

DXA has been validated in many populations against several other body composition measures such as skinfold-thickness assessments (175;181;182), bioelectrical impedance analysis (181;183-186), air displacement plethysmography, (187;188), and hydrostatic weighing (189;190) where it was found to be more accurate as well as more reliable on a trial-by-trial basis. When compared to magnetic resonance imaging (MRI) which has been recommended "as a reference measure of adiposity for testing the efficacy of future

therapies for obesity” (28), there were very strong correlations between the two in measuring lean and fat mass (191-193). DXA was found to be equivalent for whole-body body composition measurements in comparison to computed tomography (CT), for a number of populations (194;195). DXA is seen as especially effective due to its ability to segregate body sections and provide direct measures of fat tissue, non-bone lean tissue, and bone compositions in given body sections, or over the body as a whole (31;196;197), something the majority of other body composition measures are incapable of.

DXA for use in Obese Populations

DXA is very advantageous in comparison to other measures of body composition with its pros outnumbering cons in most scenarios. It is unfortunate that one of the obstacles with DXA is the size of the scan area which results in a large segment of the population, including the pediatric population, being unable to receive a scan. As a DXA scanner has a limited scan area in which a subject must fit in order to get a full body scan as well as weight restrictions this becomes an issue when scanning an obese population. Due to either width exceeding the scan area (~60cm) or mass exceeding weight limitations for the scanner (~300lbs) imaging capabilities it becomes key to have alternative means of estimating body composition for those whom surpass the limits of standard DXA equipment. Aside from the construction of a large and strong scanner (iDXA) there has been little research into alternative means of accommodating the obese population for accurate body composition measures via DXA. Since the custom software accompanying DXA scanners allows for defined regional body fat distribution it is likely that a half-body scan

used to estimate full-body body composition may be a beneficial alternative method to do so.

When Tataranni and Ravussin first compared half- and whole-body scans (n=183) in the adult population, they found very similar results in that whole-body scans were similar to the half-body estimations (198). When a sub-group of 21 obese subjects did not fit within the scanning area and could not be given a whole-body scan, they were given two separate scans for each half of the body for comparison which were then compared to hydrodensitometry for validation. The separate scans were found to have slightly larger discrepancies between the two sides for fat mass and non-bone lean mass which could be attributed to inaccurate body placement during the subsequent scan. These discrepancies suggest that in a study where only one scan will be taken and a half-body method will be used to determine total body measures the placement of the sagittal line for analysis purposes is vital to the accuracy of these whole-body estimations.

More recently, Rothney et al. assessed a single DXA scan of 52 obese adults (BMI > 30 kg/m²) using the Lunar iDXA and GE Encore 11.10 software (199). Unlike Tataranni and Ravussin they used a whole-scan on their subjects and used the full-scans to simulate half-body scans. This was done through manual placement of an appropriate sagittal line, which allowed them to analyze each subject's scan as a whole-body scan, left-side scan, and right-side scan. Using this methodology on their population they presented promising results. At the conclusion of their study they found left-side scans to be slightly lower, although not significantly, in absolute terms for fat mass (-0.10 ± 0.51 kg) and percent body fat ($-0.06 \pm 0.28\%$). They also found that non-bone lean mass was slightly lower than the whole-body

analysis for both right side (-0.04 ± 0.54 kg) and left side (-0.04 ± 0.51 kg). Not all measures were comparable as Rothney et al. found that there was a significant difference in overestimating BMC in the half-body for the right side (23 ± 31 g) and underestimating in the left side (-27 ± 32 g). The authors attributed these differences to handedness, which has been found to produce higher BMC in the dominant limb compared to the off-limb (200). The results Tataranni and Ravussions (198), and Rothney et al. (199) found both suggest that half-body scans and whole-body scans may be used interchangeably within a single study when a whole-body scan may not be possible.

Although Rothney et al. (199) determined that a half-body analysis in an obese adult population is closely comparable to a whole-body analysis; such a validation has not been completed in a pediatric population thus it is important to determine whether the same adapted technique would be valid in this population.

CHAPTER 3

Manuscript #1: Validation of the HALO submaximal treadmill protocol to measure fitness in obese children and youth

Validation of the HALO submaximal treadmill protocol to measure fitness in obese children and youth

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Abstract

There are motivational and subjective factors associated with completing maximal exercise in the obese (OB) pediatric population. The aim of this study was to determine if the new Healthy Active Living and Obesity Research Group (HALO) sub-maximal aerobic fitness testing protocol for OB children and youth provides a comparable estimate of VO_{2max} to that measured using validated i) maximal and ii) sub-maximal equation-based protocols in the OB pediatric population. In comparing the three exercise testing protocols, we found significant correlations between estimates of VO_{2peak} from the HALO submaximal protocol and measures of VO_{2peak} during maximal aerobic testing. This supports the use of the HALO submaximal protocol as a valid measure to estimate maximal cardiorespiratory fitness within the OB pediatric population.

Keywords: Cardiorespiratory Fitness, Pediatric, Obesity, Exercise Testing,

Introduction

The rate of obesity has reached epidemic proportions among the world's children and youth (1), (2). Excess adiposity leads to obesity related co-morbidities such as type 2 diabetes(3), cardiovascular disease(4), hypertension(5), osteoarthritis(6), sleep apnea(7), and various types of cancer (8). Without lifestyle changes, obesity is likely to be sustained into adulthood (9). Given the serious consequences associated with obesity, there is an urgent need for lifestyle changes, yet interventions within the obese pediatric population continue to suffer from high attrition and modest success rates (10). Successful interventions to decrease obesity require a decrease in caloric intake, an increase in physical activity, or some combination of both dietary improvement and increases in physical activity (11). Both physical activity (12) and fitness (13;14), independent of weight loss, are powerful indicators of health. Cardiorespiratory fitness can be measured relatively quickly and easily in laboratories, therefore making it a useful measure to obtain on individuals undergoing any type of active living or obesity intervention.

Maximal aerobic fitness, or VO_{2max} , is considered the maximal ability of the body to use oxygen during physical exertion. This is most often measured with indirect calorimetry measurements during incremental exercise testing in a laboratory setting. When measuring fitness in obese children, it is important to consider that they may respond differently both physically and emotionally to exertion than their healthy weight peers (15;16). The current "gold standard" method for measuring fitness requires a child to exercise until exhaustion; an experience which may be particularly negative for an obese child, especially when considering the possible psychological difficulties associated with obesity at a young age

(17). While submaximal testing can be used to predict maximal fitness (18), there is very little known about how applicable this is for the obese children and youth.

A commonly used submaximal field test for the prediction of VO_2max is the Astrand-Rhyming test (19), which uses linear extrapolation of heart rates collected at different exercise intensities to predict VO_2max . Another common field test used is the Canadian Aerobic Fitness Test (CAFT) (20) or modified version of the CAFT (mCAFT), (21) which estimate fitness based on heart rate recovery during a step test. Other protocols use simple data (e.g., resting heart rate, age, weight, etc.) in a validated prediction equation to obtain an estimate of a VO_2max (22-24). All these protocols have the ability to estimate or predict fitness in a variety of populations, yet getting direct measures of fitness through indirect calorimetry in the laboratory is arguably a more accurate approach to obtaining distinct fitness estimates at the individual level. It is unlikely there will ever be an optimal protocol for all situations and populations, especially among children of various shapes and sizes. In view of this, a protocol which utilizes an individual's 'self-paced walk' (SPW) may be an option worth exploring further in order to tailor exercise testing individual needs, abilities, and preferences (25).

Given the importance of developing effective weight management intervention programs and encouraging appropriate lifestyle changes in the obese pediatric population, it is crucial to avoid experiences that may discourage future physical activity. In order to personalize intervention strategies or counseling it is important to have a practical or 'real-life' measure of fitness that will also allow for an estimation of maximal aerobic fitness. Thus, the objective of this study was to determine if the new HALO submaximal aerobic

fitness testing protocol for obese children and youth provides a comparable estimate of VO_2max to that measured using two protocols validated (24;26) in this specific pediatric population.

Methods and Procedures

Subjects

A sample of obese children ($\geq 95^{\text{th}}$ WHO BMI percentile) (www.who.int/growthref) were recruited from the Children's Hospital of Eastern Ontario (CHEO) pediatric endocrinology clinic to participate in the *Physiological and psychological predictors and determinants of metabolic complications of pediatric obesity* (POC) study (Canadian Diabetes Association Innovation Grant #IG-1-07-2307-KA). All new patients visiting the pediatric endocrinology clinic for obesity assessment were eligible to participate. POC participants were required to complete a maximal aerobic fitness test as part of their assessment, providing us with peak exercise measures. At completion of their POC assessment, subjects who were able to achieve maximal exertion (as was defined by meeting 2 of these 4 criteria: 1) achieving VO_2 plateau, 2) $\text{HR} > 200$, 3) $\text{RER} > 1.00$, or 4) reaching volitional fatigue) were asked to voluntarily participate in a second study which would require two additional submaximal aerobic fitness tests. The second visit was completed at the earliest possible date following completion of the POC study. The order in which the two additional tests were completed was randomized (*See Appendix A*). The protocol was approved by the CHEO Research Ethics Board and informed consent (>16 years) or assent (<16 years) was obtained before study initiation.

Instrumentation

Anthropometric Measures

Body mass (kg) was assessed by use of a medical-grade SECA 634 digital scale. Height (cm) was assessed using a SECA 222 stadiometer. Body Mass index (kg/m^2) was calculated and BMI percentiles were determined based on WHO growth curves (www.who.int/growthref). Resting heart rate was determined as the lowest heart rate achieved during a 3 minute rest period prior to the testing.

Aerobic Fitness Measures

Maximal aerobic fitness was measured as part of the initial POC study assessment. Submaximal aerobic fitness was assessed by two separate submaximal treadmill test protocols under the supervision of two certified exercise physiologists. Oxygen consumption (VO_2) was measured breath-by-breath using a MedGraphics Ultima (Medical Graphics Corporation, St. Paul, Minn.) metabolic cart and exercise HR was measured with a Polar HR monitor. To mimic conditions of the POC study, participants were asked to come to the laboratory at the same time of day as their POC test had been completed and were asked to consume a light snack 30 minutes prior to arriving. A warm-up and cool-down was included with each protocol. In the rest period between the two submaximal fitness tests, subjects were required to be within 25% of their measured resting heart rate before beginning the alternate test. The 20-point Borg scale of perceived exertion was used in all three protocols.

Protocol #1 (Direct Measure of VO₂max): A progressive maximal treadmill test, developed by Gutin et al. (26) was completed by all POC study participants. Following a 4-minute warm-up at a self-selected walking speed, participants started walking at a speed of 2.0, 2.5, 3.0, or 3.5 miles per hour (mph) and a grade of 0%. The speed was increased by 0.5 mph after 2 minutes and remained at this speed for the duration of the test. The grade increased by 2% every 2 minutes until the participant indicated they could no longer continue.

Protocol #2 (Equation-Based Estimation of VO₂max): A 2-stage treadmill-based protocol developed by Ebbeling et al. (23) and adapted for testing in children and youth by Nemeth et al. (24), was completed by participants on a separate testing day. Participants were asked to select a brisk but comfortable walking pace, identified as their self-paced walking pace. Participants walked at this speed at 0% grade for an initial 4-minute warm-up phase and then completed a 2nd stage where the speed did not change and grade was increased to 5%. At the end of the 2nd stage HR was recorded as the “4 min HR”. VO₂max was estimated using the following equation:

$$VO_{2max} = -1772.81 + 318.64 * Sex (F=0, M=1) + 18.34 * Weight(kg) + 24.45 * Height(cm) - 8.74 * 4minHR - 0.15 * Weight(kg) * HR difference + 4.41 * Speed(mph) * HR difference$$

Protocol #3 (HALO Protocol: Submaximal Protocol for the Estimation of VO₂peak): Similar to the previously described test, participants were asked to select a brisk but comfortable walking pace for which they walked for the entirety of the test. Each stage lasted 4 minutes to ensure steady-state VO₂ and HR data could be captured. Given the variable termination criteria for the protocol there was no set number of stages, but the maximum was 6. The

incline of the treadmill was increased by 3% over each subsequent stage. Participants continued through the stages until: (1) they reached 85% of maximal HR (HR_{max}); defined as $HR_{max} = 220 - \text{age}$, (2) they completed 24 minutes of exercise, or (3) they indicated that they could no longer continue. VO_{2peak} was predicted in the HALO protocol by extrapolating the HR - VO₂ linear relationship to age-predicted HR_{max} (*See Appendix B*). The corresponding VO₂ at that point was the predicted VO_{2peak}.

Statistical Analysis

Descriptive statistics were used to summarize the characteristics of the group with respect to BMI status, age, gender and fitness outcomes. Continuous variables were summarized using mean, standard deviation, and range. Pairwise scatterplots were used for graphical examination of the relationship between the estimates and predictions. Paired t-tests were used to test for significant differences between protocols. Bland-Altman analysis was used to examine agreement between the protocols, 95% limits of agreement were computed and displayed. Mean square error was computed in order to assess criterion validity of protocol 3 against the validated maximal protocol 1 (26) and equation-based protocol 2 (23).

Results

Twenty one participants consented to participate in this study (mean age = 14.5 years, 47% boys). Participant characteristics are depicted in Table 1. There were no significant differences between males and females for baseline anthropometric measures including age, weight, height, BMI and resting HR. Mean absolute and relative VO_{2peak} were similar amongst all three protocols (Table 2). Using absolute terms (mL/min),

significant correlations were found between observed VO_2peak and predicted VO_2peak for both protocol 3 ($r=0.000$, $p=0.750$) and protocol 2 ($r=0.001$, $p=0.656$) submaximal protocols. A similar correlation was found between observed and protocol 3-predicted relative (body mass adjusted) VO_2peak (ml/kg/min) ($r=0.012$, $p=0.537$), but not for protocol 2. Despite significant independent correlations for both protocols 2 and 3 predicted values and protocol 1 measured values; there was no such correlation found between the predicted values from protocols 2 and 3.

Predicted VO_2peak values were calculated and plotted against directly measured (protocol 1) VO_2peak (Figure 1) and found to be highly correlated ($r^2=0.996$, $p<0.001$). An identical relationship was found when plotting VO_2peak vs. predicted VO_2peak from the protocol 2 ($r^2=0.996$). Further examination of the predicted VO_2peak values for protocol 3 identified that only 1/21 (~5%) deviated >25% from the directly measured values, 17/21 (~81%) deviated <20%, and 14/21 (67%) were within 10% of the observed values. Comparing the values obtained using the protocol 2 prediction to that those obtained through the protocol 1 showed that 3/21 (~14%) deviating >25%, 15/21 (~71%) <20%, and only 8/21 (~38%) <10% from the direct measure. The Bland-Altman analysis, displayed in figure 2, illustrated the mean difference between protocols to be $-201.75 \text{ mL}\cdot\text{min}^{-1}$ (95% CI: $\pm 1293.87 \text{ mL}\cdot\text{min}^{-1}$); only a single value fell outside these 95% limits.

Discussion

We identified that the use of the HALO submaximal fitness test is an appropriate means of estimating maximal oxygen uptake when compared to values measured during maximal exertion testing. The HALO protocol was also found to be a less variable means of

predicting maximal VO_2 in obese children than the other submaximal protocol comparator which has also been validated in this population (24).

Considering the strong and well-known relationship between fitness and health (13;14), the ability to measure fitness is crucial. This is particularly important for an obese pediatric population where fitness is an important clinical measure to track progress within individualized weight management intervention programs. It is also imperative to encourage appropriate lifestyle changes in the population by providing positive, encouraging and knowledgeable physical activity experiences hopefully leading to future involvement in physical activity by avoiding a negative association with physical activity. One possible strategy to help mitigate the adverse effects, and potentially play a role in reversing current trends in rates, of obesity, is improving intervention program design. Being able to acquire baseline measures of cardiorespiratory fitness to explore relationships to health measures, as well as prospectively track changes in fitness throughout an intervention would enable improved program design with far more individualization.

The current “gold standard” method of measuring maximal aerobic fitness ($\text{VO}_{2\text{max}}$) requires indirect calorimetry measures during exhaustive exercise in a laboratory setting. The pediatric population is unique in many ways and interacting with the obese pediatric population often involves navigating added intricacy, especially while performing cardiorespiratory fitness testing (15;16). Our test may be longer than a maximal test, yet given the lower intensity, it provides greater real-world validity. A submaximal fitness testing protocol tailored to the obese pediatric population can be completed by most and should make for a less intimidating, more positive experience for the participants/patients.

Additionally, it is believed that such a test would be less discouraging and thus not 'turn them off' physical activity, but rather increase motivation to complete the test. Another issue often seen in the obese pediatric population during maximal testing is early termination (prior to attaining maximal effort). By providing a set end-point for the test, rather than a self-determined termination point based on self-perceived maximal exertion, we are hoping to increase the probability of the child completing the test to its necessary end-point.

Submaximal intensities of exercise are better tolerated (27) and are more reflective of the intensity of movement overweight and obese children and youth would undertake in the real world. Some tests utilize cycle-ergometers, such as that performed by Buono et al. (using a modified version of the Astrand-Rhyming submaximal test), to enable children and adolescents to successfully complete the test (28). Since children, in comparison to adults, will have a greater physiological response, (i.e. increased heart rate, ventilatory exchange, and cardiac output (29-31) etc.) in response to a lower absolute workload, the original Astrand-Ryhming protocol had to be altered to provide work rates suitable for use with children. The original protocol had initial work rates of 300 kilogram-meters per minute (kgm) for women and 600 kgm for men, and these start points were modified to utilize an initial work rate of 150 kgm, after which it increased by 150 kgm every 3 minutes until the subject reached 70% of his or her age-predicted maximal heart rate for the pediatric population (28). While others (24) have used a cycle ergometer when evaluating obese children because of its lower weight bearing requirements, a treadmill was selected for this study because a treadmill is more representative of typical activity for this population (e.g.

walking). Given the children were asked to select their own walking speed and it did not change throughout the test, it can be assumed the children were not pushed outside of their comfort zone.

Nemeth and colleagues based their protocol on one originally developed by Ebbeling, et al. (23) that has since been validated in an obese, adult population (32). After making slight alterations to the equation Nemeth et al., (24) were able to validate the protocol in a sample of overweight children. The protocol they developed had the subjects select a comfortable walking speed and walk for 4 minutes on 0% grade. After 4 minutes warm-up the grade was increased to 4% and after another 4 minutes the heart rate was recorded before cool down began. They compared the results of estimated VO_{2max} from their submaximal exercise test to directly measured oxygen consumption values acquired through a progressive maximal exercise test (24). The protocol is based on an equation that uses sex, weight, height, heart rate after 4 minutes of exercise, heart rate difference, and submaximal treadmill speed to predict VO_{2max} (24). Although the predicted fitness may be accurate, this may not be sufficient for improving the design of, and ability to properly evaluate, intervention programs. It is important to have not only an estimated measure of maximal fitness, but also an understanding of how differing work rates across a wide variety of individual fitness levels change on a case-by-case basis. The proposed HALO protocol takes this into account by allowing for multiple stages at a self-paced walk speed, or more comfortable work-rates. It is thought that a longer protocol, with gradually increasing workloads, that does not elicit maximal effort can offer greater opportunity to display the relationship between heart rate, ventilatory exchange, and exercise intensity; therefore

allowing for precise estimation of the subjects maximal VO_2 measurement. Being able to look at changes in submaximal levels of exercise is another benefit of the HALO protocol. For example, by being able to detect changes in the slope of the HR- VO_2 relationship can be a supplementary means of tracking changes in the submaximal fitness or efficiency of the children. The importance of having a clear picture of a child's fitness, as well as their physiological and psychological responses to a set of increasing workloads, is fundamental for the implementation of an effective intervention program or behavior change strategy.

Strengths of this study include equal distribution amongst males and females, and an absence of significant age related differences, for both anthropometrics and exercise measures, suggesting results can be generalized across the sample. In comparison to an already validated submaximal protocol (24), the HALO protocol displayed smaller deviation from measured $\text{VO}_{2\text{max}}$ values indicating that it may provide a greater ability to estimate oxygen consumption. The fact that the HALO protocol can do so with a submaximal effort is particularly beneficial given an accurate measure of fitness is an important contributor to the development and evaluation of individualized weight loss programs. However, given the relatively small, physician recruited clinical sample it is recommended further testing be completed within the obese population to ensure confirmation of results seen in this study. Another potential limitation of the current study is its inclusion as part of a larger study, making it impossible to randomize the order of which the participants completed all of the three study protocols; specifically, the maximal test was always completed at the initial visit. The two submaximal protocols were then completed on a second follow-up visit, which may have led to better performance during the submaximal protocols because of

learning that occurred during the maximal protocol of visit 1. In attempts to limit methodological bias, the two submaximal protocols were randomized on the additional test day.

Conclusion

Given that sub-maximal intensities are better tolerated and more reflective of the intensity of movement obese children would undertake in the real world, it is appropriate to assume a validated submaximal protocol would likely be a useful means of obtaining an estimate of fitness for this population. Furthermore, by ensuring a more tolerable and less physically exerting experience it is less likely to act as a deterrent for future physical activity. In comparing the three completed exercise testing protocols, we found significant correlations between estimates of VO_2peak from the HALO submaximal protocol and measures of VO_2peak during maximal aerobic testing. The strong relationship between measured and HALO estimated oxygen uptake supports the use of the HALO submaximal protocol as a valid means of estimating maximal cardiorespiratory fitness within the obese pediatric population.

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Tables

Table 1 Population Characteristics for Validation of HALO Submaximal Fitness Protocol

	Boys (n =10)		Girls (n=11)		Total (n =21)	
	Mean $\pm$ SD, Range		Mean $\pm$ SD, Range		Mean $\pm$ SD, Range	
Age (years)	14.31 $\pm$ 2.11	(10.4-17.5)	14.48 $\pm$ 1.82	(10.5-16.9)	14.41 $\pm$ 1.91	(10.4-17.5)
Height (cm)	170.15 $\pm$ 12.40	(148.5-190.5)	166.32 $\pm$ 6.91	(153.7-180.0)	168.15 $\pm$ 9.84	(148.5-190.5)
Body mass (kg)	102.56 $\pm$ 17.93	(74.1-141.5)	99.20 $\pm$ 17.64	(71.9-126.1)	100.80 $\pm$ 17.41	(71.9-141.5)
BMI (kg·m ⁻²)	35.00 $\pm$ 3.03	(30.7-40.6)	35.44 $\pm$ 4.25	(28.4-42.6)	35.23 $\pm$ 3.63	(28.4-42.6)
Resting HR	82.55 $\pm$ 8.58	(68-100)	85.60 $\pm$ 10.28	(56-112)	84 $\pm$ 13.58	(56-112)

Abbreviations: BMI = body mass index; HR= heart rate. No significant differences.

Table 2 Population Exercise Parameters for Validation of HALO Submaximal Fitness Protocol

	Protocol 1	Protocol 2	Protocol 3
	Mean $\pm$ SD, Range	Mean $\pm$ SD, Range	Mean $\pm$ SD, Range
Speed (mph)	3.43 $\pm$ 0.88 (2.5-4.0)	2.29 $\pm$ 0.47 (1.4-3.0)	2.33 $\pm$ 0.67 (1.4-3.0)
HRpeak (beats $\cdot$ min ⁻¹)	199.01 $\pm$ 6.09 (191-207)	143.95 $\pm$ 14.15 (126-174)	171.65 $\pm$ 6.51 (157-179)
RERpeak	1.15 $\pm$ 0.099 (0.95-1.26)	N/A	1.04 $\pm$ 0.171 (0.93-1.10)
VO ₂ peak (mL $\cdot$ min ⁻¹)	3060.89 $\pm$ 808.50 (1798.4-4260.7)	3132.21 $\pm$ 425.03 (1892.9-3743.2)	2835.51 $\pm$ 787.69 (1776.6-3721.4)
VO ₂ peak/kg (mLO ₂ $\cdot$ min ⁻¹ $\cdot$ kg ⁻¹)	28.90 $\pm$ 6.03 (16.5-37.4)	31.40 $\pm$ 3.69 (25.2-37.4)	28.14 $\pm$ 6.28 (18.3-45.9)

Abbreviations: HR=heart rate; RER=respiratory exchange ratio; VO₂ = oxygen uptake; SPW= Self Paced Walk Speed.

Figures

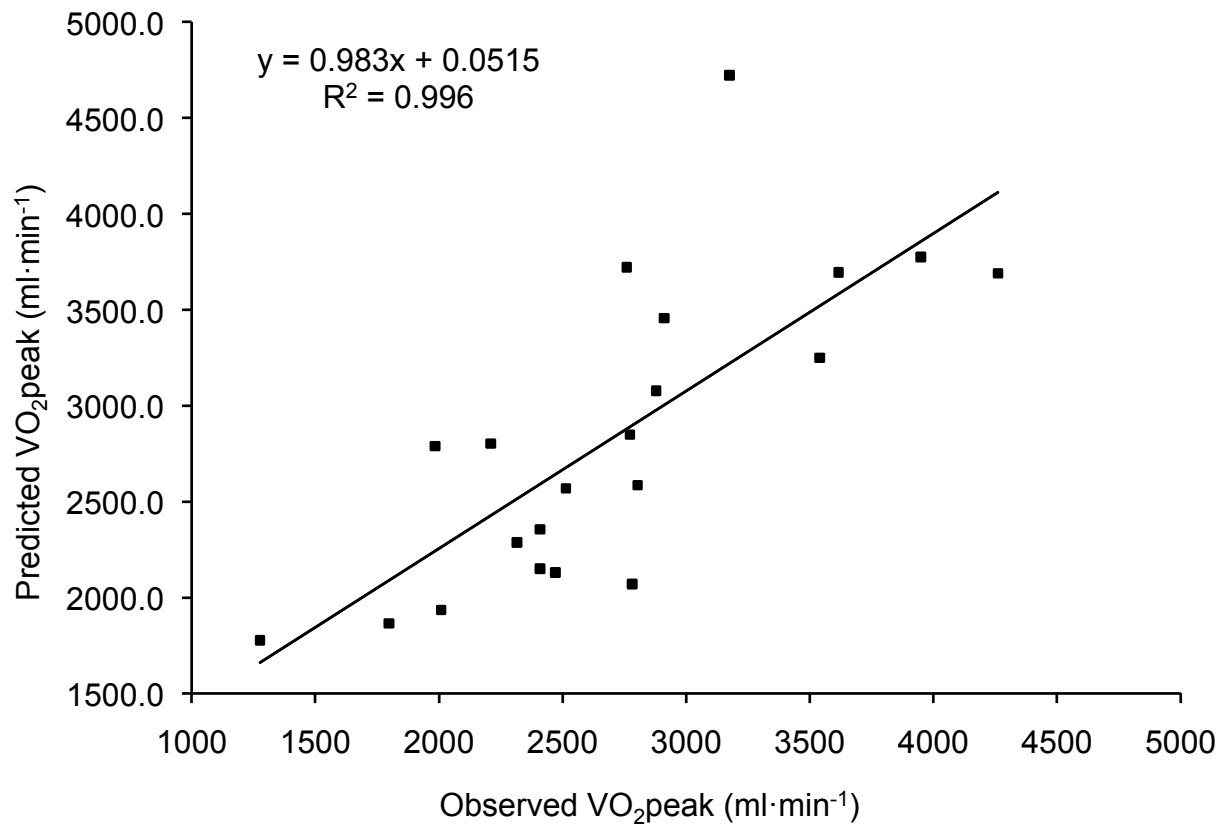


Figure 1 Observed versus predicted VO₂peak values for protocols 1 and 3(n=21).

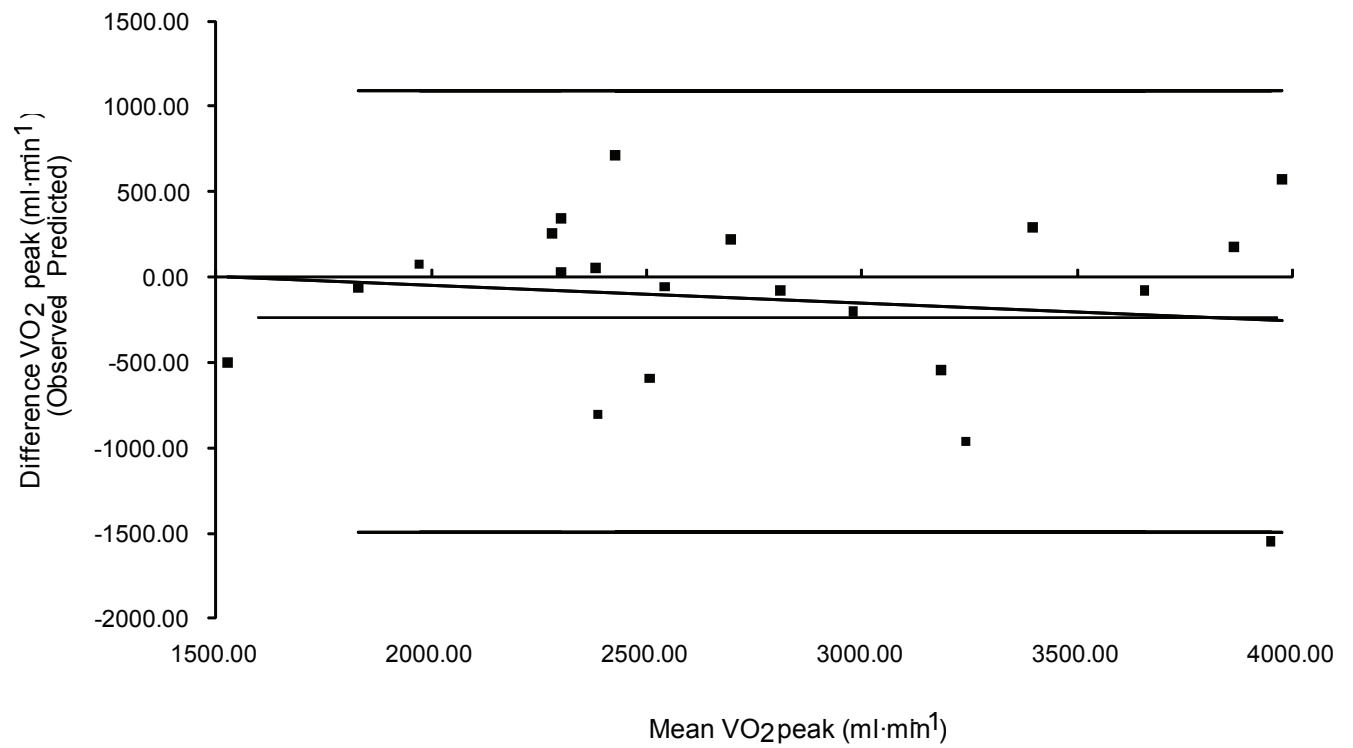


Figure 2 Bland-Altman plots comparing observed and predicted VO_2peak between protocols 1 and 3 (n=21).

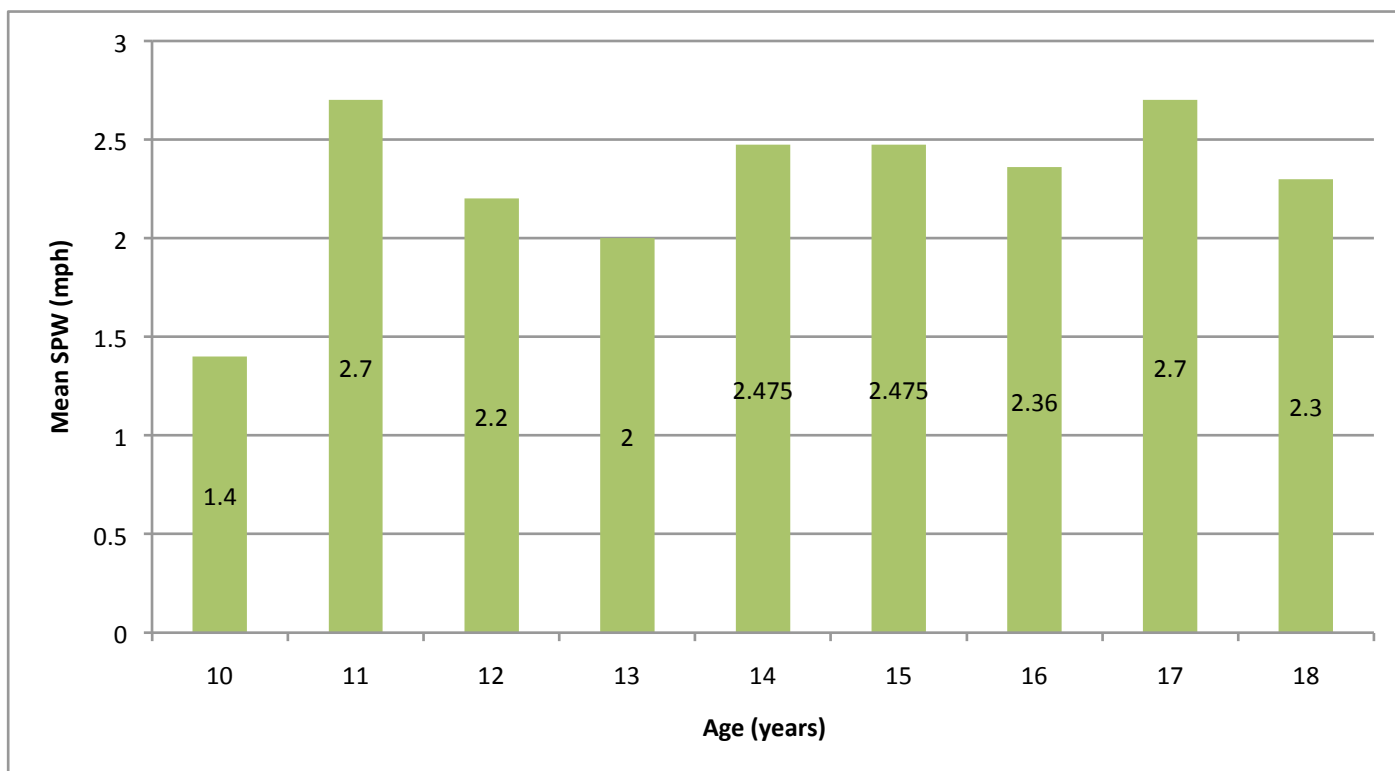


Figure 3 Mean SPW for age

CHAPTER 4

Manuscript #2: Submaximal OUES is a useful alternative to maximal exercise testing in the obese pediatric population

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Abstract

The aim of the current study was to investigate the relationship between the Oxygen Uptake Efficiency Slope (OUES) and traditional measures of cardiorespiratory function in an overweight/obese pediatric population. Treadmill exercise testing with indirect calorimetry was completed on 21 obese children aged 10-17 years. Maximal OUES, submaximal OUES, $\text{VO}_{2\text{peak}}$, V_{Epeak} , and ventilatory threshold (VT) were determined. In line with comparable research in healthy populations, maximal and submaximal OUES were both correlated with $\text{VO}_{2\text{peak}}$, V_{Epeak} , and VT ($r^2 = 0.289-0.734$). Strong correlations were also found with anthropometric variables, including height (cm), body surface area (m^2), body mass (kg), and fat free mass (kg). The results of this study suggest the use of OUES to be an appropriate measure of cardiorespiratory function in obese children. Future work focusing on the utility of OUES with this difficult population is encouraged.

Keywords: Aerobic Capacity, Oxygen Uptake Efficiency Slope, Fitness, Obese, Pediatric

Introduction

Rates of obesity and its associated co-morbidities are high amongst children and youth worldwide (1-4). As childhood obesity has increased, there has been a concurrent decline in fitness in this population (5-7). When compared to healthy weight individuals, obese individuals display the poorest cardiorespiratory fitness, muscle endurance, and performance on explosive power tests (8).

Cardiorespiratory fitness is a powerful indicator of health in children (9). Therefore, accurate measurements of physical fitness are essential for gaining a better understanding of the relationships between fitness and health as well as facilitating the rigorous evaluation of intervention programs and behavior change strategies (10;11). Maximal exercise testing is generally regarded as the gold standard for assessing fitness by means of measuring maximal oxygen uptake (VO_2max), or the highest rate at which an individual can consume oxygen during exercise without physiologic, psychological or biomechanical strain (12). Given that successful maximal exercise testing is difficult for a fit population, it is not surprising that this difficulty is magnified in an obese, pediatric population (13). Submaximal indicators of fitness hold merit in this population because these intensities are better tolerated and more reflective of the intensity of movement obese children would undertake in the real world (14).

Originally proposed by Baba et al. (15) as a submaximal index of cardiorespiratory functional reserve, the oxygen uptake efficiency slope (OUES) has been examined in multiple healthy populations (15-18). There has also been work examining the use of OUES

in those with heart disease (15;19). OUES is derived from the relationship between oxygen uptake (VO_2 [mL/min]) and minute ventilation (VE [L/min]). OUES is determined by:

$$\text{VO}_2 = a \log \text{VE} + b, \text{ where } a = \text{OUES} \text{ (15)}$$

To the best of our knowledge there has been limited research exploring OUES in overweight or obese children and adolescents (17;20). OUES is thought to be a clinically useful measure of evaluating exercise tolerance in the pediatric population (16) and, as it does not require maximal effort, it is a more tolerable alternative to maximal testing in the obese pediatric population (17). OUES has also been found to be sensitive to the effects of physical training, making it a strong predictor of change in fitness over time (21). Since OUES is highly dependent on anthropometric variables, it has been recommended that it be expressed relative to Body Surface Area (BSA) or Fat Free Mass (FFM) (22); a methodology often employed to examine differences in oxygen uptake between healthy weight and obese individuals.

In examining OUES differences between healthy weight and overweight adolescents, the National Institutes of Health found very wide inter-individual variation, leading them to suggest that OUES may not be appropriate for use in clinical practice as a predictor of $\text{VO}_{2\text{peak}}$ (17). Considering its strong correlations with VO_2 peak (18), peak minute ventilation (V_E peak), and Ventilatory Threshold (VT) (22) it is not unrealistic to suggest OUES has the ability to be a valid index for cardiorespiratory reserve. It is, however, necessary for the development of appropriate reference values, as suggested by many previous studies examining OUES (15;18;21;22). Taking into account these suggestions the aim of the current study was to investigate the characteristics of OUES in an obese pediatric

population and perform a comparison between our obese population and a similar, but healthy weight population (22).

Methods and Procedures

Subjects

A sample of obese children ($\geq 95^{\text{th}}$ WHO BMI percentile, 10-17 years) (www.who.int/growthref) were recruited from the Children's Hospital of Eastern Ontario (CHEO) pediatric endocrinology clinic to participate in the *Physiological and psychological predictors and determinants of metabolic complications of pediatric obesity* (POC) study (Canadian Diabetes Association Innovation Grant #IG-1-07-2307-KA). All new patients visiting the pediatric endocrinology clinic for obesity assessment were eligible to participate. POC Participants were required to complete a maximal aerobic fitness test as part of their study assessment. At completion of their POC assessment subjects were asked to voluntarily participate in a secondary study requiring them to return to the lab to complete a submaximal aerobic fitness test. The second visit was completed at the earliest possible date following completion of the POC study assessments. The study protocol was approved by the CHEO Research Ethics Board. Informed consent (≥ 16 years) or parental consent and assent (< 16 years) was obtained before study initiation as required by the institutional ethics board.

Instrumentation

Anthropometric Measures

Body mass (kg) was assessed by use of a medical-grade SECA 634 digital scale. Height (cm) was assessed using a SECA 222 stadiometer. Body Mass index (kg/m^2) was calculated

and BMI percentiles were determined based on WHO BMI percentiles (www.who.int/growthref). Based on the equation of Haycock et al. (23), which has been validated in infants, children, and adults, BSA was calculated using (where Ht is height in cm and Wt is body mass in kg):

$$BSA (m^2) = 0.024265 \cdot Ht^{0.03964} \cdot Wt^{0.5378}$$

Body Composition Measures

Percentage body fat and FFM (kg) were estimated using a DXA scan which was required as part of study participant's initial POC assessment. Measurements were made by a Medical Radiation Technologist using the GE Lunar Prodigy ADVANCE DEXA scanner (GE Healthcare, Madison, WI). Prior to any measurements, secondary calibration and quality assurance measurements of the DXA machine were completed. The Prodigy ADVANCE provides direct calculation of total fat, lean tissue mass, and bone mineral content, density and area for the pediatric population. Results are calculated automatically, via DXA software, for bone mineral density (BMD), fat tissue, and lean tissue for the total body & sub-regions. Scan analysis was performed using GE enCORE 11.40 software (GE Healthcare, Madison, WI).

Aerobic Fitness Measures

Maximal aerobic fitness was measured as part of the initial POC assessment using the protocol developed by Gutin et al. (24). Submaximal aerobic fitness was assessed by a submaximal treadmill test protocol under the supervision of two certified exercise physiologists. Oxygen consumption (VO₂) was measured using breath-by-breath analyses

via a MedGraphics Ultima (Medical Graphics Corporation, St. Paul, Minn.) metabolic cart for both exercise testing sessions. Before each exercise test, the gas analyzers and flow meter were calibrated using gas mixtures of known concentrations and a 3-L syringe. Exercise heart rate (HR) was measured with a Polar HR monitor (Polar FT7, Polar Electro Canada Inc., Lachine, Quebec). To mimic conditions of the POC study, participants were asked to come to the lab at the same time of day that their POC maximal test had been completed and were asked to consume a light snack 30 minutes prior to arriving. The 20-point Borg scale of perceived exertion was used in both protocols. The two protocols included in this current analysis were:

A progressive maximal treadmill test, developed by Gutin et al. (24), which was completed by all participants during their participation in the POC study. Following a 4-minute warm-up at a self-selected walking speed, participants were asked to walk at a speed of 2.0, 2.5, 3.0, or 3.5 miles per hour (mph) and a grade of 0%. The speed was then increased by 0.5 mph after 2 minutes and remained at this speed for the remainder of the test. The grade was increased by 2% every 2 minutes from then on until the participant indicated that they were unable to continue. Data from this protocol supplied maximal exercise indicators such as peak HR, peak resting energy expenditure (RER), and measured peak oxygen consumption values.

The submaximal exercise protocol, developed by our team (Breithaupt, et al., 2011, unpublished), is based on self-paced walk. Participants were instructed to choose a brisk but comfortable walking pace at which they were to walk at throughout the test. The test began at 0% grade and each subsequent 4 minute stage, the grade was increased by 3%

until the participant reached 85% of their age predicted HR ($HR = 220 - \text{age}$). Other termination criteria for the protocol included completion of 24 minutes of exercise, or the participant indicating that they could no longer continue. In this study, 76% (16/21) achieved 85% of age predicted maximal HR with the length of tests ranging between 13:06-23:55, 19% (4/21) finished 24 minutes of exercise without achieving 85% HR_{max} , and 5% (1/21) terminated their test due to physical discomfort (~18min.).

Statistical Analysis

All statistical analyses were completed using SPSS 19.0 (SPSS, Chicago, IL). All data are presented as mean values $\pm$ SD and range where appropriate. Descriptive statistics were used to summarize the characteristics of the group with respect to BMI status, age, gender and fitness outcomes. Continuous variables were summarized using mean, standard deviation, range, and interquartile range. Comparisons between obese and healthy weight children were completed by evaluating means, standard deviation and range for both maximal and submaximal OUES between the two groups was completed; both absolute and relative (body mass, BSA, and FFM) values were included for comparison. One-way ANOVA was used to examine the impact of age and gender differences on the outcomes. Significance was set at $p < 0.05$.

Results

Twenty one participants consented to participate in this study (mean age = 14.5, 47% boys). Participant characteristics are depicted in Table 1. No significant differences were found between boys and girls in age, height, body mass, BMI; however, FFM was

significantly higher in boys when compared to girls and conversely, %BF was significantly higher in girls when compared to boys.

All exercise testing was completed without adverse affects and results are presented in Table 2. A distinguishable ventilatory threshold (VT), identified using V-slope methodology (25), was found for all participants. Boys were found to have significantly higher $\text{VO}_{2\text{peak}}$ ($\text{mL}\cdot\text{min}^{-1}$), V_{Epeak} ($\text{L}\cdot\text{min}^{-1}$), and $\text{V}_{\text{Epeak}}/\text{BSA}$ ($\text{L}\cdot\text{min}^{-1}\cdot\text{m}^{-2}$) compared to girls. Unlike other studies of OUES in pediatric populations, there were no significant, age-related differences within the exercise results suggesting that age had little effect on exercise parameters in this sample. (18;21;22). High correlations were found between the submaximal OUES and basic anthropometric variables including height ($r=0.646$), BSA ($r=0.624$), body mass ($r=0.568$), and FFM ($r=0.641$) where $p\leq 0.01$ and age ($r=0.528$) where $p\leq 0.05$. A reduction in variation of both maximal and submaximal OUES values were found when absolute values were adjusted for body mass, BSA, or FFM (Figure 1).

Maximal and submaximal OUES were highly correlated ($r=0.774$, $p<0.001$). This remained the case when OUES values were adjusted for body mass ($r=0.593$, $p=0.005$), BSA($r=0.619$, $p=0.03$), or FFM ($r=0.569$, $p=0.007$). Maximal OUES showed a high correlation with $\text{VO}_{2\text{peak}}$, V_{Epeak} , and VT. When normalized for BSA the correlations with $\text{VO}_{2\text{peak}}$, V_{Epeak} , and VT all declined but remained significant, while the relationship disappeared after adjustment for body mass (kg) and FFM. Submaximal OUES was also shown to be highly correlated with $\text{VO}_{2\text{peak}}$, V_{Epeak} , and VT. When normalized for body mass, BSA, or FFM, correlations with $\text{VO}_{2\text{peak}}$ and V_{Epeak} significantly declined. The only correlations that

remained significant were between submaximal OUES and VT when accounting for body mass and body surface (Table 3).

In comparing our obese population to the healthy-weight population described by Akkerman et al. (22), it was found that the mean age (~14 years vs. ~12 years), and height (~170 cm vs. ~160 cm) had small differences. Larger discrepancies were found in body mass (45 kg vs. 100 kg), BMI (~18 kg·m² vs. ~35 kg·m²), and BF% (~18% vs. ~47%), while all values were higher in our population. Comparing exercise parameters in our study sample with those reported elsewhere (Table 4) showed that despite our population having higher mean absolute OUES values than the healthy population for both boys and girls, the healthy population had higher submaximal measures of OUES. Maximal and submaximal OUES were also lower in the obese pediatric population when adjusting for body mass (kg), body surface area (m²), and fat free mass (kg).

Discussion

This study describes the relationships between OUES and other measures of cardiorespiratory fitness in an obese pediatric population, aged 10-17 years. The relationship between submaximal and maximal OUES is not yet clearly established as some studies have shown slight, but significant differences between the two (15;17;20). Others have shown no significant difference between the two (18;22), which matches well with our data. We found a number of trends which have also been observed in healthy children (18;20-22), including OUES being strongly correlated with exercise parameters such as VO₂peak, V_Epeak, and VT. Strong correlations between maximal and submaximal OUES and baseline measures of height, BSA, body mass, FFM, and age were also present.

Akkerman et al. (2010) examined the characteristics of OUES in 46 (27 boys and 19 girls) healthy weight and similarly aged children (aged 7-17 years) (22) and reported similar results to those in the current study. Our mean absolute OUES values were higher than those measured in a healthy population (22) for both boys and girls (2883.40 ± 742.68 vs. 2185.2 ± 676.2 for boys, and 2500.91 ± 373.7 vs. 2237.0 ± 759.5 for girls, respectively). Our higher OUES values may be explained, in part, by the use of treadmill testing given there are strong correlations between OUES and $\text{VO}_{2\text{peak}}$ and that $\text{VO}_{2\text{peak}}$ is generally higher on a treadmill vs. cycle ergometer test (26). Another possible contributor might be our higher mean age (14 vs. 11 years) and the linear relationship found between increasing age and OUES in other populations (21). Our population had lower absolute submaximal measures of OUES, maximal and submaximal OUES were also lower when adjusting for body mass (kg), body surface area (m^2), and fat free mass (kg), when compared to the healthy population described by Akkerman et al. (22). Since we used treadmill testing our values may have been inherently higher, and given the strong relationship between OUES and $\text{VO}_{2\text{peak}}$, our lower values of relative OUES suggest both lower fitness and efficiency in our obese population compared to the healthy-weight population(22).

Only two other studies have looked at OUES in overweight (17) and obese (20) children. Drinkard et al., (2007) compared 107 overweight children to 43 non-overweight children and found there were stark differences between the two groups. This study required all children to perform a maximal cycle ergometer test and then examined OUES at three different exercise intensities. Most notably they found that when adjusted for lean body mass, both $\text{VO}_{2\text{peak}}$ and OUES were lower in overweight subjects ($P < 0.0001$) at all

exercise intensities (17). Marinov and Kostianev compared 30 obese children to 30 healthy weight children (15 boys and 15 girls, aged 6-17 years, in each group) using standardized exercise tests and found that despite having greater absolute values for oxygen uptake, after adjusting for body mass, fitness in the obese decreased significantly. They also found powerful relationships between OUES and both height and weight, as well as between maximal and submaximal OUES (20). These trends are present in our comparison of obese and healthy weight children, suggesting body mass plays a large role in OUES. In the examined populations, larger body mass led to increased absolute OUES and oxygen consumption values. Initially this suggested the obese population may be more efficient than the healthy weight group; this was not the case after adjusting for body mass. Similarly, in our sample we found the obese population less efficient after also correcting for both FFM and BSA. In comparing populations it is most appropriate to use values which have been adjusted for anthropometric values such as body mass, FFM, or BSA. Both studies found strong correlations between OUES and VO_{2peak} (17;20), another relationship found in our analysis, which aids in the solidifying OUES as a supplemental or alternative measure to track or assess fitness and efficiency in obese children.

OUES does appear to have some merit as a submaximal index of cardiorespiratory fitness in the obese pediatric population. As found in our study, maximal and submaximal OUES both have a consolidated relationship with VO_{2peak} in the obese, pediatric population; a consistency was also found across healthy pediatric (18;22) and adult (15;19;21) populations. In examining comparisons of OUES in obese to healthy weight, it appears appropriate to suggest OUES may be able to discriminate differences in fitness

between different groups, especially when adjusting for anthropometric variables such as BMI, BSA or FFM. Given its submaximal nature, and correlations to fitness measures, using OUES as a supplementary or alternative measure of fitness or efficiency may be of great benefit for assessing or tracking these outcomes in a clinically obese, pediatric population. Further research should be completed comparing the obese to healthy weight populations. It is also important, to increase the clinical usefulness of OUES measure, that continuing research is completed assessing OUES which could lead to the development of adequate reference values in all populations.

Limitations in this study include a small and heterogeneous population, as well as the use of V-slope method for determination of VT (used as cut-off for submaximal OUES measures). Despite having been found to show good inter-observer agreement and to be least affected by the use of different exercise protocols (25), this methodology still has the potential of wide variation and inaccuracy during VT determination. Ideally a healthy-weight control group would have been assessed concurrently with the obese group to ensure consistency of measures; instead an external group of similar age and having completed similar exercise testing was used for comparative purposes. Considered potentially both a limitation and a strength, the population studied is clinically obese (BMI > 95th percentile). A limitation because it restricts analysis to an extremely heterogeneous population, but also a strength given both the importance and difficulties associated with assessing fitness in this specific population. Considering the aim of the study, being able to include participants from the highest BMI percentiles can imply conclusions will be appropriate for this challenging population. Being able to utilize indirect calorimetry for

both the submaximal and maximal fitness testing provides robust oxygen uptake data, while having DXA scan data provides accurate representation of body composition allowing for OUES measures to be adjusted relative to these measures. Further strengths include equal distribution amongst males and females, and being one of the first studies to assess the use of OUES in a clinically obese pediatric population for comparisons to a healthy-weight population.

The usefulness of OUES as a comparative measure between differing populations has yet to be confirmed and given its responsiveness to physical training in adults (21), we can speculate that OUES may be a useful clinical measure for tracking the fitness of participants, especially for those unable or unwilling to complete maximal exercise testing. Given OUES can be measured during a submaximal exercise effort, this would be particularly useful in the obese pediatric population where there are many motivational and subjective factors that deter or prevent this population from completing maximal testing.

Conclusion

Similar to trends found in healthy children, OUES was found to correlate highly with exercise parameters (such as $\text{VO}_{2\text{peak}}$, V_{Epeak} , and VT), independent of exercise intensity. OUES is noticeably affected by anthropometrics in this population; a finding consistently reported in other populations. In comparing an obese population to published data from a similarly aged healthy weight population (22), we found that our population of obese children have higher absolute maximal OUES values but are less efficient than their healthy counterparts for both maximal and submaximal OUES when adjusting for body mass (kg), body surface area (m^2), and fat free mass (kg), as well as absolute values during submaximal

measures. For a population which is often unable or unwilling to perform maximal testing, this study suggests submaximal OUES has a strong clinical utility, either independently or as a complementary measure to oxygen uptake. Thus submaximal OUES may provide an additional measurement tool to help assess, track and compare fitness and efficiency in the obese, pediatric population.

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Tables

Table 3 Population Characteristics for Obese Population used to Assess OUES

	Boys (n =10)		Girls (n=11)	
	Mean $\pm$ SD, Range		Mean $\pm$ SD, Range	
Age (years)	14.31 $\pm$ 2.11	(10.4-17.5)	14.48 $\pm$ 1.82	(10.5-16.9)
Height (cm)	170.15 $\pm$ 12.40	(148.5-190.5)	166.32 $\pm$ 6.91	(153.7-180.0)
Body mass (kg)	102.56 $\pm$ 17.93	(74.1-141.5)	99.20 $\pm$ 17.64	(71.9-126.1)
BMI (kg·m ⁻²)	35.00 $\pm$ 3.03	(30.7-40.6)	35.44 $\pm$ 4.25	(28.4-42.6)
BSA (m ²)	2.24 $\pm$ 0.26	(1.8-2.7)	2.17 $\pm$ 0.24	(1.8-2.5)
BF (%)	*43.1 $\pm$ 7.29	(33.7-57.7)	50.56 $\pm$ 3.60	(45.8-55.4)
FFM (kg)	*56.58 $\pm$ 13.54	(30.7-74.8)	45.89 $\pm$ 6.84	(35.7-54.2)

Abbreviations: BMI = body mass index; BSA = body surface area; BF = percentage of body fat; FFM = fat free mass; * $p \leq .05$.

Table 4 Population Exercise Parameters for Obese Population used to Assess OUES

	Boys (n =10)		Girls (n=11)	
	Mean $\pm$ SD, Range		Mean $\pm$ SD, Range	
HR _{peak} (beats·min ⁻¹)	199 $\pm$ 6.09	(191-207)	192 $\pm$ 11.09	(176-208)
RER _{peak}	1.15 $\pm$ 0.099	(0.95-1.26)	1.14 $\pm$ 0.081	(0.99-1.30)
VT (mL·min ⁻¹)	1212.0 $\pm$ 338.06	(570.0-1715.0)	1062.18 $\pm$ 281.4	(563.0-1691.0)
VO ₂ peak (mL·min ⁻¹)	*3060.89 $\pm$ 808.50	(1798.4-4260.7)	2384.85 $\pm$ 454.41	(1276.7-2804.1)
VO ₂ peak/kg (mL·min ⁻¹ ·kg ⁻¹)	28.90 $\pm$ 6.03	(16.5-37.4)	24.74 $\pm$ 5.11	(18.2-37.5)
VO ₂ peak/BSA (mL·min ⁻¹ ·m ⁻²)	1349.55 $\pm$ 240.43	(972.6-1728.7)	1095.22 $\pm$ 195.51	(717.4-1479.3)
VO ₂ peak/FFM (mL·min ⁻¹ ·kg ⁻¹)	54.21 $\pm$ 6.36	(40.7-62.8)	52.42 $\pm$ 10.69	(35.7-71.8)
V _E peak (L·min ⁻¹)	*103.30 $\pm$ 34.91	(48.0-152.0)	77.81 $\pm$ 15.0	(57.0-102.0)
V _E peak/kg (L·min ⁻¹ ·kg ⁻¹)	0.989 $\pm$.235	(0.64-1.35)	0.798 $\pm$ 0.184	(0.6-1.2)
V _E peak/BSA (L·min ⁻¹ ·m ⁻²)	*45.23 $\pm$ 11.66	(26.68-62.24)	35.88 $\pm$ 6.54	(26.6-47.6)
V _E peak/FFM (L·min ⁻¹ ·kg ⁻¹)	1.79 $\pm$ 0.262	(1.41-2.26)	1.72 $\pm$ 0.35	(1.2-2.3)
Maximal OUES	2883.40 $\pm$ 742.68	(1536.0-3602.0)	2500.91 $\pm$ 373.7	(1774.0-3117.0)
Maximal OUES/kg	27.94 $\pm$ 5.20	(20.2-35.0)	25.51 $\pm$ 3.26	(19.6-29.5)
Maximal OUES/BSA	1274.88 $\pm$ 254.74	(860.9-1607.5)	1149.54 $\pm$ 130.42	(932.2-1368.8)
Maximal OUES/FFM	51.10 $\pm$ 7.15	(36.9-60.2)	54.78 $\pm$ 5.83	(42.9-61.6)
Submaximal OUES	2057.30 $\pm$ 516.91	(1022.0-2858.0)	1809.82 $\pm$ 365.59	(1351.0-2700.0)
Submaximal OUES/kg	20.0 $\pm$ 3.81	(13.79-26.41)	18.45 $\pm$ 3.24	(14.6-24.7)
Submaximal OUES/BSA	911.56 $\pm$ 183.61	(572.8-1247.1)	831.09 $\pm$ 137.06	(676.4-1155.2)
Submaximal OUES/FFM	35.63 $\pm$ 6.75	(26.62-48.65)	39.94 $\pm$ 8.60	(31.0-58.4)

Abbreviations: HR=heart rate; RER=respiratory exchange ratio; VT=ventilator threshold; FFM = fat free mass; VO₂ = oxygen uptake; BSA = body surface area; FFM = fat free mass; OUES = oxygen uptake efficiency slope. **p*≤.05.

Table 5 Correlation coefficients of relation between oxygen uptake efficiency slope and main exercise parameters.

	VO ₂ peak	V _E peak	VT
Maximal OUES	*0.793	*0.721	*0.750
Maximal OUES/kg	0.430	0.373	0.290
Maximal OUES/BSA	**0.613	**0.534	**0.520
Maximal OUES/FFM	-0.017	-0.193	0.058
Submaximal OUES	**0.592	***0.538	**0.857
Submaximal OUES/kg	0.170	0.163	***0.448
Submaximal OUES/BSA	0.350	0.313	***0.657
Submaximal OUES/FFM	0.255	0.255	0.187

Abbreviations: BSA = body surface area; kg= kg of body mass; FFM = fat free mass; VO₂peak = peak oxygen consumption; V_Epeak = peak minute ventilation; VT = ventilatory threshold; * p<0.001, **p=0.01 ***p≤0.05.

Table 6 Exercise parameters for comparison between obese and healthy-weight, pediatric population

	Obese Population		Healthy Weight Population	
	Boys (n=10)	Girls (n=11)	Boys (n=27)	Girls (n=19)
HR _{peak} (beats·min ⁻¹)	199 ± 6.09	192 ± 11.09	193 ± 7.9	194 ± 6.8
RER _{peak}	1.15 ± 0.099	1.14 ± 0.081	1.15 ± 0.06	1.16 ± 0.08
VT (mL·min ⁻¹)	1212.0 ± 338.06	1062.18 ± 281.4	1533.6 ± 468.3	1425.4 ± 498.5
VO ₂ peak (mL·min ⁻¹)	3060.89 ± 808.50	2384.85 ± 454.41	2188.0 ± 671.4	2176.8 ± 807.8
VO ₂ peak/kg (mL·min ⁻¹ ·kg ⁻¹)	28.90 ± 6.03	24.74 ± 5.11	52.9 ± 6.7	43.6 ± 5.5
VO ₂ peak/BSA (mL·min ⁻¹ ·m ⁻²)	1349.55 ± 240.43	1095.22 ± 195.51	1633.0 ± 248.3	1449.3 ± 276.1
VO ₂ peak/FFM (mL·min ⁻¹ ·kg ⁻¹)	54.21 ± 6.36	52.42 ± 10.69	62.85 ± 7.26	55.75 ± 6.78
V _E peak (L·min ⁻¹)	103.30 ± 34.91	77.81 ± 15.0	77.7 ± 25.1	76.1 ± 28.1
V _E peak/kg (L·min ⁻¹ ·kg ⁻¹)	0.989 ± .235	0.798 ± 0.184	1.88 ± 0.28	1.55 ± 0.32
V _E peak/BSA (L·min ⁻¹ ·m ⁻²)	45.23 ± 11.66	35.88 ± 6.54	58.1 ± 9.6	51.2 ± 11.8
V _E peak/FFM (L·min ⁻¹ ·kg ⁻¹)	1.79 ± 0.262	1.72 ± 0.35	2.25 ± 0.29	1.96 ± 0.40
Maximal OUES	2883.40 ± 742.68	2500.91 ± 373.7	2185.2 ± 676.2	2237.0 ± 759.5
Maximal OUES/kg	27.94 ± 5.20	25.51 ± 3.26	52.9 ± 8.6	45.2 ± 6.1
Maximal OUES/BSA	1274.88 ± 254.74	1149.54 ± 130.42	1632.2 ± 294.3	1496.3 ± 261.3
Maximal OUES/FFM	51.10 ± 7.15	54.78 ± 5.83	62.71 ± 9.67	57.51 ± 7.13
Submaximal OUES	2057.30 ± 516.91	1809.82 ± 365.59	2156.8 ± 668.6	2260.3 ± 740.6
Submaximal OUES/kg	20.0 ± 3.81	18.45 ± 3.24	51.8 ± 10.3	46.3 ± 8.5
Submaximal OUES/BSA	911.56 ± 183.61	831.09 ± 137.06	1602.9 ± 323.8	1524.6 ± 283.9
Submaximal OUES/FFM	35.63 ± 6.75	39.94 ± 8.60	61.70 ± 11.80	59.15 ± 9.14

Abbreviations: HR=heart rate; RER=respiratory exchange ratio; VT=ventilator threshold; FFM = fat free mass; VO₂ = oxygen uptake; BSA = body surface area; FFM = fat free mass; OUES = oxygen uptake efficiency slope. Presented as, Mean ± SD. Healthy weight population values adapted from Akkerman et al, 2011 (22).

Figures



Figure 4 Variation of Absolute and Relative OUES Values

Abbreviations: BSA = Body Surface Area, FFM= Fat Free Mass, kg= Kilograms Body Mass. Presented as Mean ± S.D. (range).

CHAPTER 5

Manuscript #3: Body Composition Measured by Dual-Energy X-ray Absorptiometry (DXA) Half-body Scans in Obese Children

Body composition measured by dual-energy x-ray absorptiometry half-body scans in obese children

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Abstract

Aim: To perform a methods comparison of a left or right half-body scan versus whole-body scan for measuring body composition in a sample of obese children. **Methods:** A group of obese children ($n = 58$; $\geq 95^{\text{th}}$ BMI percentile; 8-18 yrs) were required to undergo a DXA body composition measurement as part of an ongoing cohort study; 34 fit within the imaging field of the DXA scanner and were eligible for inclusion in the present analysis. Percent fat, total mass, fat mass, lean mass, and bone mineral content (BMC) were estimated from half-body scans and compared to the whole-body results. Assessment was completed using GE enCORE 11.40 software. **Results:** In comparing left- and right-side scans to whole body scans there was significant correlation for all body composition variables ($P \leq 0.005$, $R^2 = 0.996 - 1.0$). Bland Altman analyses also showed high levels of agreement between half-body estimates and whole-body measurements. **Conclusion:** This study supports using a half-body scan methodology for percent fat, total mass, fat mass, lean mass, and BMC as a valid alternative to full-body analysis in obese children and youth.

Keywords: adiposity, body fat distribution, paediatrics, fat mass, lean body mass

Keynotes

- Evaluation of body composition is an important step in characterizing the health risk profile of an obese child.
- The present study supports the use of a left or right half body scan methodology as a valid alternative to full body analysis or percent fat, total mass, fat mass, lean mass, and BMC in obese children and youth whose dimensions are outside of the scanning surface.

Introduction

Increasing evidence indicates that excess adiposity is associated with a range of co-morbidities including type 2 diabetes (1), cardiovascular disease (2), hypertension (3), osteoarthritis (4), sleep apnoea (5), and a number of types of cancer (6). Robust evaluation of body composition is an important step in characterizing the health risk profile of an obese child. An accurate, objective assessment of body composition is incredibly valuable given the evidence indicating that self-report systematically under represents the extent of the obesity problem (7). Numerous studies have shown that risk for insulin resistance, type two diabetes, high blood pressure, elevated blood cholesterol levels and stroke as well as risk for death are increased in persons with obesity (particularly abdominal obesity) (2;8;9), thus appropriate quantification of these variables is essential. Originally developed by Peppler and Mazess to measure bone mineral density (10), dual-energy X-ray absorptiometry (DXA) has since become one of the most commonly utilized methods for clinical assessment of human body composition (11).

Dual-energy X-ray absorptiometry has been validated in many populations against other body composition measures such as skinfold-thickness assessments (12), bioelectrical impedance analysis (BIA) (13), and hydrostatic weighing (14). When compared to magnetic resonance imaging (MRI), which has been recommended 'as a reference measure of adiposity for testing the efficacy of future therapies for obesity' (11), there were significant correlations between the DXA and MRI in measuring both lean and fat mass (15). DXA was found to be equivalent to computed tomography (CT), for whole-body body composition measurements in comparison for a number of populations (16;17). DXA is especially

attractive because of its ability to segregate body sections and provide direct measures of fat tissue, non-bone lean tissue, and bone compositions in given body sections, or over the body as a whole (18;19). DXA is based on differing absorption rates of photons emitted at two energy levels by body tissue allowing for quantification of bone mineral, lean and fat soft tissue masses separately (20). DXA scans are short in duration (5-20 min) (21), relatively inexpensive, and have been found to be very precise while having very low radiation exposure (approximately 0.3 μ Sv) (22).

Despite the advantages of the DXA technique to measure body composition, it is limited by the reality that a growing segment of the paediatric population is too large for the scanning apparatus. This occurs because either their width exceeds the scan area (approximately 60cm) or their mass exceeds weight limitations for the scanner (approximately 136kg) imaging capabilities. It is therefore timely to develop alternative means of estimating body composition for those whose dimensions surpass the limits of standard DXA equipment.

Tataranni and Ravussin (23) originally used half-body scans in an obese population that did not fit within the scanning area and compared these DXA scans to hydrodensitometry for a means of predicting body composition. More recently, Rothney et al. (24) determined that a half-body analysis in an obese adult population is closely comparable to a whole-body analysis; however such a validation has not been completed in a paediatric population. Therefore, the purpose of this current study was to determine the validity of a half-body scan methodology for measuring body composition in a sample of obese children and youth.

Methods and Procedures

Subjects

A sample of 58 obese children ($\geq 95^{\text{th}}$ WHO BMI percentile) (www.who.int/growthref) were recruited from the Children's Hospital of Eastern Ontario (CHEO) paediatric endocrinology clinic to participate in the *Physiological and psychological predictors and determinants of metabolic complications of paediatric obesity* (POC) study (Canadian Diabetes Association Innovation Grant #IG-1-07-2307-KA and CFI/ORF Leaders Opportunity Fund Grant). All new patients visiting the paediatric endocrinology clinic for obesity assessment were eligible to participate. Participants were required to complete a body composition measurement as part of the POC study assessment. From the initial sample, 34 fit within the imaging field of the DXA scanner and thus were eligible for inclusion in the final comparison analysis. Further details of the study subjects are displayed in Table 1. The protocol was approved by the CHEO Research Ethics Board. Informed consent (≥ 16 years) or parental consent and assent (< 16 years) was obtained before study initiation as required by the institutional ethics board.

Instrumentation

Measurements were made by a Medical Radiation Technologist using the GE Lunar Prodigy ADVANCE DEXA scanner (GE Healthcare, Madison, WI). Each morning prior to subject evaluation secondary calibration and quality assurance measurements were completed. A calibration block representing three fat chambers was used specifically for body composition, and an aluminum step phantom in a container of rice was used to evaluate the machine's operating precision for bone density. These values are tested in the five rules of the Shewhart chart (25).

This procedure was used for quality control by taking measurements in three bone chambers and three fat chambers. Precision was analyzed using coefficients of variation and these ranged from 0.20-0.32%. The body composition in young children and infants feature of the Prodigy ADVANCE provides direct calculation of total fat and lean tissue mass and percentages thereof, as well as BMC, density and area within the paediatric population. Results were calculated automatically for BMD, fat tissue, and lean tissue for the total body and sub-regions and compared with gender specific paediatric reference data from the World Health Organization (WHO) Body Mass Index (BMI) graphs. Average scan time requires 4.5min and had a radiation dose approximately 0.3 μ Sv.

Scan analysis was performed using GE enCORE 11.40 software (GE Healthcare, Madison, WI). EnCORE uses an advanced intuitive graphical interface GE AutoAnalysis™ for premium precision. AutoAnalysis is capable of detecting whether a subject is within the scanning region and if they are not within the region, an automatic half-scan analysis is performed by assuming symmetry of the body. The software also allowed for adjusting regions of the body for specific analysis, a process used by the certified Medical Radiation Technologist (MRT) to isolate left and right body scans from full body scans by placing an appropriate sagittal line (Fig. 1). By utilizing this method we were able to determine the validity of a half-scan methodology in comparison to full-body while subjects required only a single scan.

Statistical Analysis

Mean values for percent body fat, fat mass, lean body mass, total tissue mass, and BMC were compared independently between whole-body left-side scans and whole body-right-side scans. After finding the impact of both age and gender to be negligible all data was pooled. Wilcoxon signed rank tests with Bonferroni adjustment for ten multiple comparisons were used and significance was set as $P \leq 0.005$. Correlation plots for whole body and each side are presented in Figure 2. Bland-Altman plots were created to test the magnitude of bias in measuring percent body fat, fat mass, lean body mass, total tissue mass, and BMC through a half-body scan versus a full-body scan (26). Statistical analyses were completed using SPSS 18.0 (SPSS, Chicago, IL).

Results

There were no significant differences between half- and full-body DXA scans for percent fat, total mass, fat mass, lean mass, and BMC (Table 2). Although statistically insignificant, small differences in absolute values were present within the data between left- and right-side scans. One trend observed was that percent fat was slightly underestimated by right side scans (mean Δ -0.01%), while left-side half-body scans were found to overestimate whole-body total mass ($0.14 \pm 0.01\text{kg}$), fat mass ($0.06 \pm 0.02\text{kg}$), and lean mass ($0.08 \pm 0.02 \text{ kg}$). Also, right-side half-body scans were found to underestimate whole-body total mass ($-0.17 \pm 0.01 \text{ kg}$), fat mass ($-0.08 \pm 0.01\text{kg}$), and lean mass ($-0.08 \pm 0.01 \text{ kg}$). Differences in BMC values showed no variation between right and left side scans.

As there was only a single scan taken for each subject whole-body and half-body scan data for each subject were taken simultaneously, eliminating any possible disparity

between scans. Descriptive statistics between participants and half-body scan estimates were closely comparable between sexes. In comparing left- and right-side scans to whole body scans there was very strong correlation for percent fat, total mass, fat mass, lean mass, and BMC ($P < 0.01$, $R^2 = 0.996 - 1.0$). Bland Altman analysis also showed high levels of agreement between half-body estimates and whole-body measurements in prediction of all body composition variables with 95% confidence intervals being closely comparable between right- and left-side techniques (Figure 3).

Discussion

In this study, we found that there were no significant differences in percent fat, total mass, fat mass, lean mass, and BMC when comparing half-body DXA scan with whole-body DXA scan in a group of obese children and youth. As DXA is often used to track change in fat mass in various regions of the body, being unable to measure in a portion of the population is a major limitation to providing effective care and intervention. The current study provides a new and accurate means for physicians to track the adiposity of their obese paediatric patients who would otherwise be unable to receive a whole-body scan because of size restrictions. Whether the goal is to track changes in adiposity or obtain a precise cross-sectional measure of adiposity for comparative purposes, being able to perform these measures in the children too large to fit within the scanning area is a step forward for comprehensive assessment of overweight and obese children.

Dual-energy X-ray absorptiometry, although originally intended for measuring bone density (10), has progressed to become a standard method for body composition analysis (11;18). When Tataranni and Ravussin (23) first compared half- and whole-body scans

(n=183) in the adult population, they found very analogous results in that whole-body scans were similar to the half-body estimations. In this particular study a sub-group of 21 obese subjects whose size prevented them from receiving a whole-body scan, underwent two separate scans of each half of the body for comparison. These separate scans were found to have slightly larger discrepancies between the two sides for fat mass and non-bone lean mass which may be attributed to inaccurate body placement during the subsequent scan. Although scans used in this particular study may have been subject to methodological limitations, if proper care is taken to ensure accurate placement of a sagittal line during analysis, half-body scans have been found to be a precise means of estimating whole-body body composition. For example, using the same methodology as employed in the present paediatric study, Rothney et al. (24) assessed a single DXA scan of 52 obese adults (BMI > 30 kg/m²) using the Lunar iDXA and GE Encore 11.10 software. They used the whole-scans on these subjects and proceeded to simulate half-body scans, through manual placement of an appropriate sagittal line, allowing them to analyze each subject's scan as a whole-body scan, left-side scan, and right-side scan. Using this methodology on their population, they found left-side scans to be slightly lower, although not significantly, in absolute terms for fat mass (-0.10 ± 0.51 kg) and percent body fat ($-0.06 \pm 0.28\%$). They also found that non-bone lean mass was slightly lower than the whole-body analysis for both right side (-0.04 ± 0.54 kg) and left side (-0.04 ± 0.51 kg).

Unlike our sample population, Rothney et al. found that there was a significant overestimation of BMC in the half-body for the right side (23 ± 31 g) and underestimation in the left side (-27 ± 32 g). They attributed these differences to handedness, which has been

found to produce higher BMC in the dominant limb compared to the off-limb (27). It is possible that our BMC estimations between the left and right sides are more comparable given that the younger population has not yet developed as great an imbalance in the upper-extremities as may be found in an adult population. Our data support with the findings of both Tataranni and Ravussions (23), and Rothney et al.(24) that half-body scans and whole-body scans can be used interchangeably within a single study when a whole-body scan may not be possible.

Variation between scanners and software used during analysis contributes to differences between studies; making standardization of hardware and software a necessity (28;29). There are certainly limitations to the DXA scan capabilities including an inability to effectively differentiate between visceral and subcutaneous fat (30), exposure to radiation (albeit very small), as well as scan area limitations and scanner mass restrictions (23). Although the mass restrictions are less likely to be an issue in the obese paediatric population (0/58 exceeded mass restrictions for our specific obese population), the scan area restrictions (24/58, 41% of our cohort population were unable to be receive whole-body analysis) are a major hurdle in accurate assessment of paediatric body composition via DXA.

Given the magnitude of childhood obesity and the clinical importance of accurate body composition assessment (31) contributing to diagnosis and treatment of the epidemic, it is crucial to have a validated means of measuring body composition in a young, obese population. The findings of the present study support the use of a half-body scan methodology for percent fat, total mass, fat mass, lean mass, and BMC as a valid alternative

to whole-body analysis in obese children and youth. Future work attempting to achieve similar validation using variations in DXA scanners, software, and populations of larger-still BMI is strongly encouraged.

Acknowledgements

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Abbreviations

BIA, Bioelectrical Impedance Analysis; BMC, Bone Mineral Content; BMD, Bone Mineral Density; BMI, Body Mass Index; CHEO, Children's Hospital of Eastern Ontario; DXA, Dual-Energy X-ray Absorptiometry; MRI, Magnetic Resonance Imaging; MRT, Medical Radiation Technologist; POC, Pediatric Obesity Cohort; T2D, Type two diabetes; WHO, World Health Organization.

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Tables

Table 7 Characteristics of study participants presented as mean $\pm$ SD. and range.

	All Subjects (n=34)	Female (n= 18)	Male (n=16)
Age (years)	12.8 $\pm$ 3.4 (7.7-18.1)	12.8 $\pm$ 3.9 (8.5-18.1)	12.8 $\pm$ 4.1 (7.7-17.8)
Height (cm)	158.8 $\pm$ 30.1 (138.5-190.5)	157.1 $\pm$ 37.7 (139-179)	160.7 $\pm$ 42.1 (138.5-190.5)
Body mass (kg)	82.3 $\pm$ 22.9 (53.4-119.1)	81.2 $\pm$ 25.1 (56.4-112.2)	83.6 $\pm$ 28.2 (53.4-119.1)
BMI (kg/m ²)	32.2 $\pm$ 6.3 (26.5-39.3)	32.5 $\pm$ 8.1 (26.5-39.3)	31.9 $\pm$ 8.4 (27.6-38.6)

Table 8 Comparison of mean values between the two simulated half scans, and total-body scan.

	Whole body	Prediction Using Left Side of Body	Prediction Using Right Side of Body
Percent fat (%)	46.4 $\pm$ 9.8 (32.2-56.7)	46.4 $\pm$ 9.7 (32.2-56.5)	46.4 $\pm$ 9.7 (32.1-56.9)
Fat (kg)	36.3 $\pm$ 9.9 (21.8-50.5)	36.37 $\pm$ 9.9 (22.0-50.2)	36.23 $\pm$ 9.9 (21.6-51.2)
Nonbone lean (kg)	42.7 $\pm$ 14.2 (25.9-69.0)	42.8 $\pm$ 14.2 (25.6-69.2)	42.6 $\pm$ 14.1 (25.6-68.9)
BMC (kg)	2.43 $\pm$ 0.80 (1.37-3.88)	2.42 $\pm$ 0.81 (1.30-3.89)	2.44 $\pm$ 0.80 (1.35-3.87)
Total tissue mass (kg)	79.0 $\pm$ 22.0 (51.3-108.4)	79.1 $\pm$ 22.0 (51.9-113.9)	78.8 $\pm$ 22.0 (50.7 - 113.5)

BMC, bone mineral content

Mean $\pm$ SD (range) (n=34)

P <0.005 vs. whole body

Figures

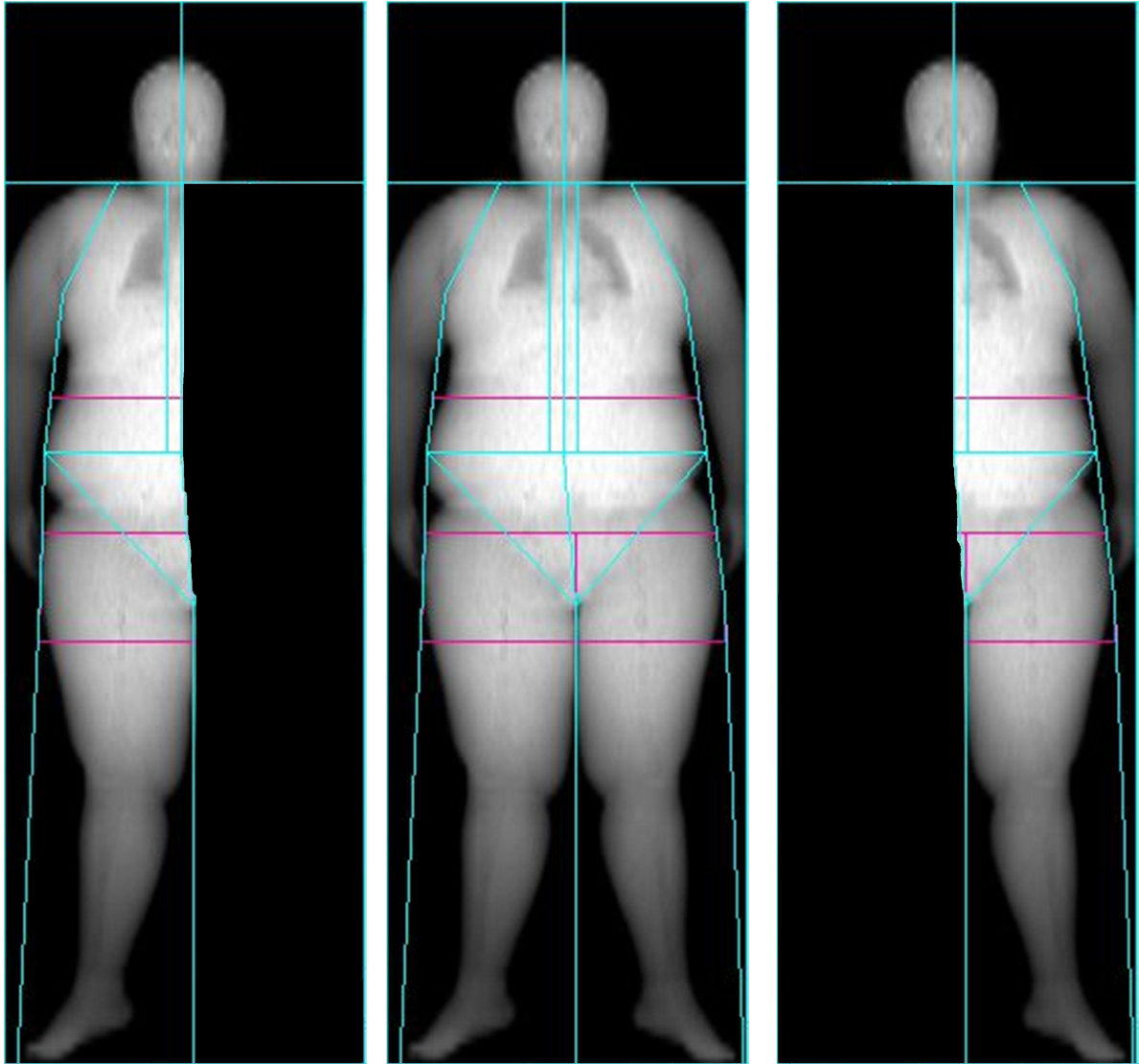


Figure 5 Example of full-body, left and right half-body scans used for analysis.

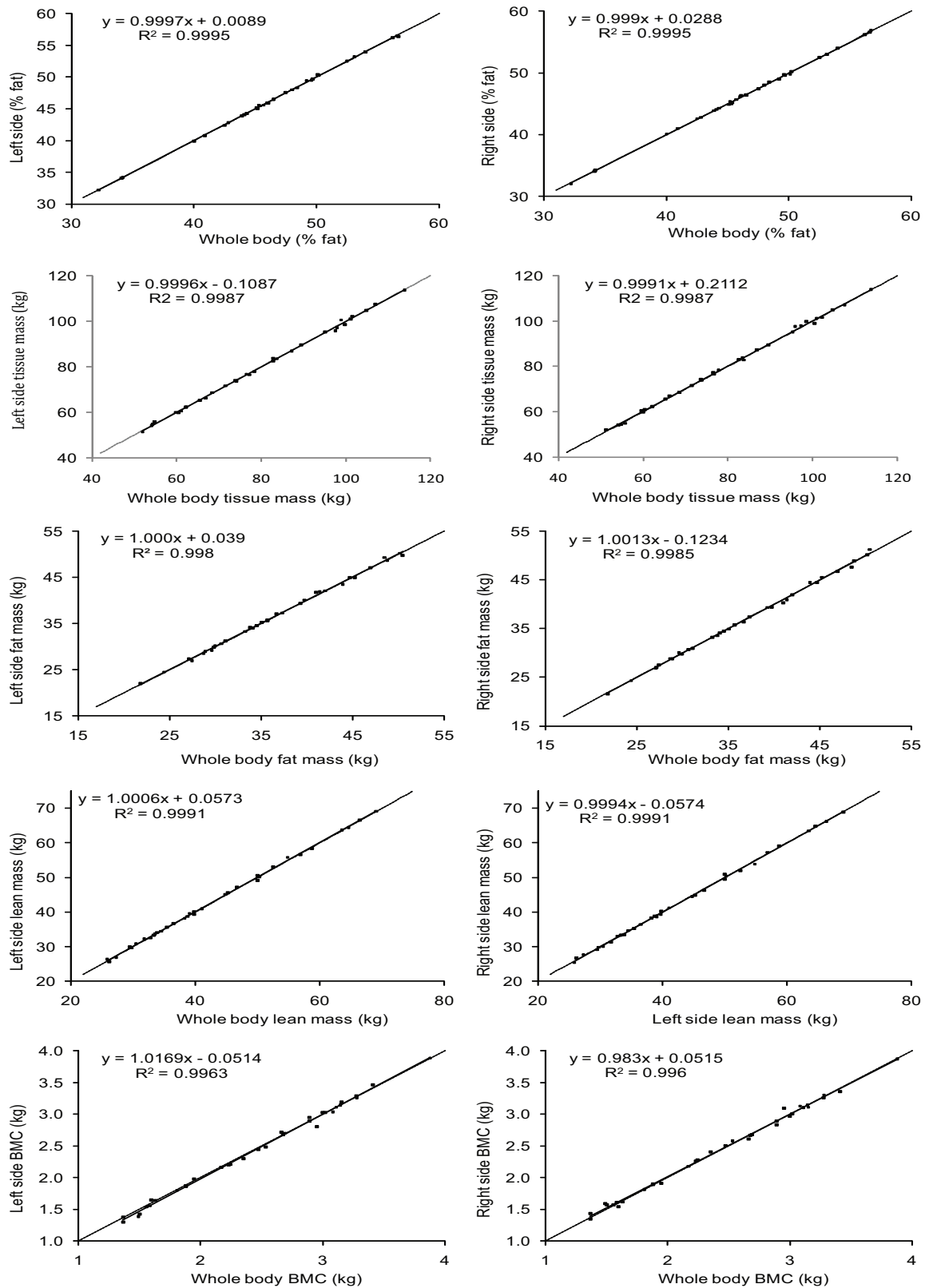


Figure 6 Correlation plots between left side, right side, and whole-body scans for total mass, percent body fat, fat mass, lean mass, and bone mineral content (n = 34). Dashed lines represent line of identity.

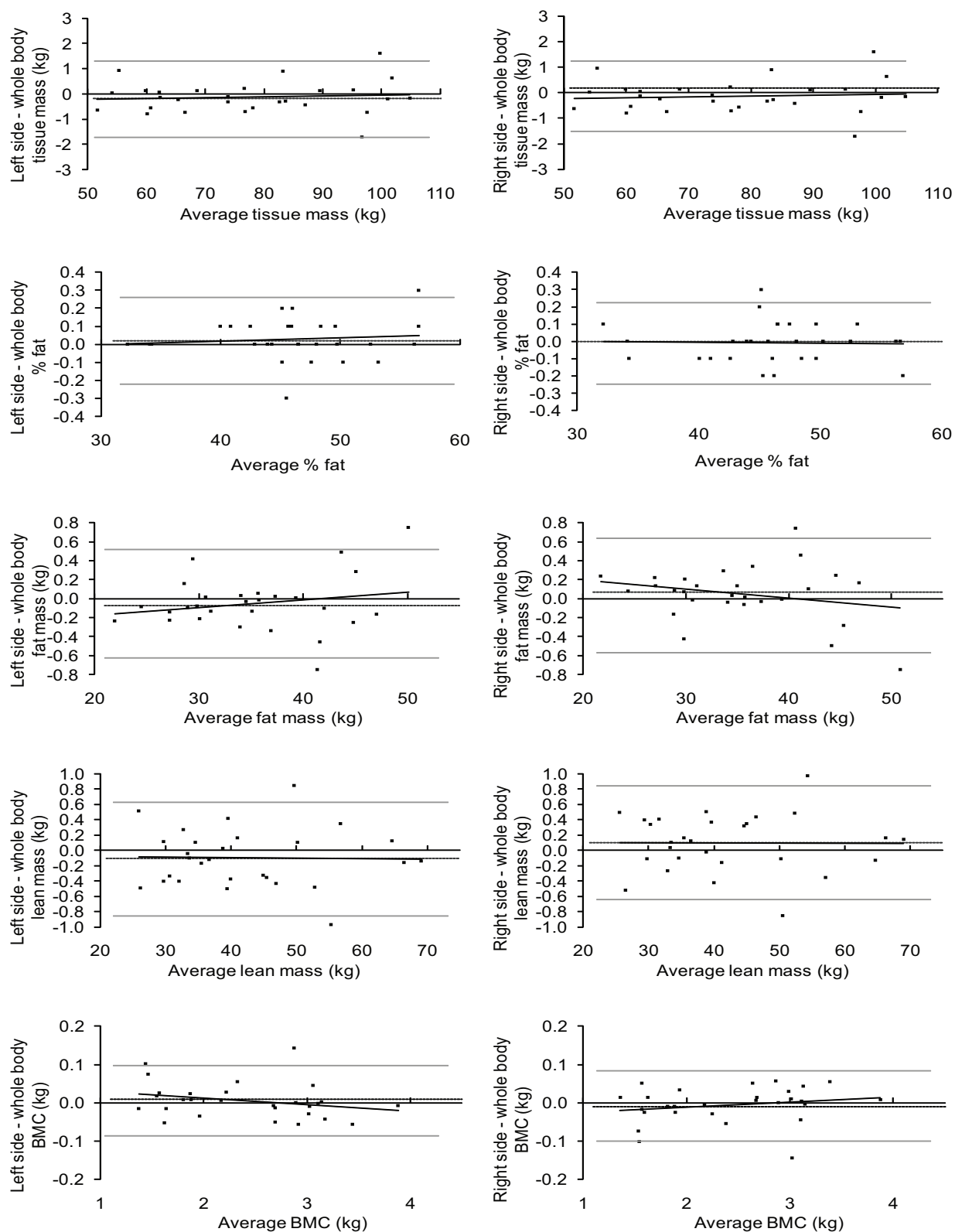


Figure 7 Bland-Altman plots comparing right side, left side, and whole-body scans for percent body fat, total mass, fat mass, lean mass, and bone mineral content. All $r^2 < 0.0405$, $n = 34$.

CHAPTER 6

General discussion, summary of results and conclusions

Summary of key findings

The overall purpose of this thesis was to improve upon methodologies for assessing body composition and cardiorespiratory fitness in obese children and youth. Specifically, this thesis work examined a cohort of OB children and youth to validate a newly developed sub-maximal cardiorespiratory fitness test for this specific population; to assess mechanical efficiency through evaluation of oxygen uptake efficiency slope (OUES); and finally to validate a new measurement protocol for body composition using half-body DXA scans.

The first manuscript within this thesis aimed to validate the newly developed Healthy Active Living and Obesity Research Group (HALO) submaximal aerobic fitness testing protocol for OB children and youth and to determine if it provided a comparable estimate of VO_2max to that measured using validated i) maximal and ii) submaximal equation-based protocols in the OB pediatric population developed by Nemeth et al (132). Twenty one OB participants (aged 10-17 years) completed all fitness test protocols. When comparing the three protocols, significant correlations were found between observed absolute VO_2peak and predicted VO_2peak using both the HALO extrapolation method and Nemeth equations, as well as between observed body mass relative VO_2peak and HALO body mass relative VO_2peak . There were no significant relationships between observed body mass relative VO_2peak and Nemeth body mass relative VO_2peak , nor amongst either absolute or relative HALO and Nemeth estimates. Strong linear regression was seen with plotted observed and

HALO estimated $\text{VO}_{2\text{peak}}$. Few participants estimated values deviated from observed values, and only a single value falling outside 95% limits on a Bland-Altman analysis. This led to this study supporting the use of the HALO submaximal protocol as a valid means of estimating maximal cardiorespiratory fitness within the OB pediatric population.

The second manuscript, a sub-analysis of the data collected during validation of the HALO submaximal exercise testing protocol, aimed to not only assess the efficiency of the subjects through the use of the oxygen-uptake efficiency slope (OUES) at both submaximal and maximal levels, but to compare their efficiency measured through OUES to that published for a population of healthy weight. Given that the OUES is expressed as a 'submaximal index of cardiorespiratory functional reserve'(162) the submaximal HALO protocol provided data which was more appropriate, steady-state submaximal measures with its longer, less demanding stages of incremental exercise. Again, twenty one participants were included in analysis. Results were contradictory to the first hypothesis and found that obese children were less efficient at submaximal work rates compared to maximal work rates. Similarly, the third hypothesis was disproved as our obese population was more efficient than a comparable healthy-weight population in absolute measures of oxygen uptake efficiency slope. However, the second hypothesis was confirmed as the obese children, in comparison to a healthy population, was less efficient after controlling for body weight, body surface area, and fat free mass. The analysis of OUES in obese children and comparison to healthy weight children found similar correlations to exercise parameters, as well as its dependence on anthropometrics amongst all populations. Comparing our population to a similarly aged healthy weight population(165), our obese

children appeared to have higher absolute maximal OUES values than their healthy counterparts yet were less efficient for absolute values during submaximal measures, as well as for both maximal and submaximal OUES after adjusting for body mass (kg), body surface area (m^2), and fat free mass (kg). OUES appears to have merit as a submaximal index to quantify and track changes in fitness/efficiency for an obese, pediatric population.

The objective of the final manuscript was to validate the use of partial (or half-body) dual energy x-ray absorptiometry (DXA) scans to measure body composition in OB youth. DXA measurement is considered the “gold standard” when measuring body composition, yet as obesity rates have increased, so has the number of those within the pediatric population that are too large for the scanning apparatus of a DXA scanner. This presents an important dilemma when trying to characterize the health risk profile of an obese child. Therefore, the aim of the project was to perform a methods comparison of a left or right half-body scan versus whole-body scan for measuring body composition in a sample of obese children, in hopes of validating the use of a partial (i.e. left or right half-body) scan as a means to estimate whole-body body composition in this population. In comparing left- and right-side scans to whole body scans there was significant correlation for all body composition variables. Bland-Altman analyses also showed high levels of agreement between half-body estimates and whole-body measurements. Based on these strong correlations this study resulted in a conclusion which supports using a half-body scan methodology for percent fat, total mass, fat mass, lean mass, and BMC as a valid alternative to full-body analysis in obese children and youth.

Clinical research implications

The goal of clinical research is, generally, to improve care provided to a particular population. Accurate and reliable assessments of health measures in obese children are crucial for effective weight management intervention design and evaluation. The ultimate goal while intervening with an obese, pediatric population is to regulate body weight through decreasing fat mass and maintaining or increasing lean mass, while ensuring adequate nutrition for healthy development. Physical activity and physical fitness are both inversely associated with the clustering of metabolic abnormalities associated with obesity (105), further magnifying the importance of effective interventions.

This thesis provides clinical improvements to two tremendously important avenues to providing high quality care to the obese, pediatric population: cardiorespiratory fitness and body composition. Our validation of a new submaximal exercise protocol for the obese, pediatric population provides a way to obtain accurate measures of cardiorespiratory fitness, without having this sensitive population complete exercise to uncomfortable levels of maximal exertion. Clinicians who understand how an individual responds to exercise, will be better able to make exercise recommendations that are appropriate for their needs (108), thus enabling far more effective and efficient intervention programs.

Oxygen uptake efficiency slope has been found to provide strong a relationship between both maximal and submaximal OUES with $\text{VO}_{2\text{peak}}$ across healthy pediatric (164;165) and adult (162;166;201) populations. Similar results were found in this study, and given OUES' potential as a submaximal index of cardiorespiratory fitness in the obese pediatric population, it could be used clinically as a complementary measure during fitness

testing to track efficiency of participants. The submaximal nature of the measure is of particular benefit for this population which is often unable or unwilling to complete maximal exercise testing. Between-population comparisons will be improved as appropriate reference values are developed across populations, thus further improving the clinical utility of the OUES.

By validating a half-body DXA scan approach, we have provided a means to obtain accurate whole-body body composition estimations for a population within which many would be otherwise unable to receive such measures due to exceeding the scan area on the DXA scanner. The relation between obesity and increased risk for insulin resistance, T2D, high blood pressure, elevated blood cholesterol levels, stroke, and mortality (89;110-117) confirms the importance of the quantification of body composition as an important concept when considering the health implications of pediatric obesity and providing appropriate clinical care.

Future research directions

Despite a vast increase in pediatric obesity research and intervention, rates continue to climb. Obesity at a young age is associated not only with an abundance of physiological comorbidities (42;82) but also with many possible psychological difficulties (27), and is likely to progress into adulthood (18;102). Given all the interrelated issues associated with pediatric obesity, the importance of accurately assessing this population to implement effective weight management interventions is very relevant and important. It is recommended that future research continue making strides towards ultimately improving risk-factor prevention and treatment strategies for this population.

Specifically, regarding measures of cardiorespiratory fitness, it is important that further testing be completed to strengthen the validation of the HALO protocol as an appropriate submaximal methodology with other valid means of estimating $\text{VO}_{2\text{max}}$. Given OUES can be measured during a submaximal exercise effort, this also could be particularly useful in the overweight and obese pediatric population where there are many motivational and subjective factors that deter or prevent this population from completing maximal testing. The usefulness of OUES as a comparative measure between differing populations has yet to be confirmed and given its responsiveness to physical training in adults(166), it could be suggested that OUES be a useful clinical measure in tracking the fitness of participants, especially for those unlikely to complete maximal exercise testing. A combination of estimating $\text{VO}_{2\text{max}}$ as well as measuring OUES may be clinically beneficial given the importance of tracking fitness and efficiency as a means of improving clinical weight management intervention. OUES appears to have some merit as a submaximal index of cardiorespiratory fitness in the obese pediatric population, however as suggested by many previous studies examining OUES in other populations (162;164-166), future research necessitates the development of appropriate reference values for OUES in the obese pediatric population.

Conclusions

The research in this thesis has provided three unique measures and perspectives on assessments, which are critical both pre- and post- intervention or treatment paradigm in order to aid in providing the most individualized and effective strategy for obese children. More specifically, the thesis supplies new means of measuring both cardiorespiratory fitness and body composition in an OB pediatric population through the validation of the HALO submaximal exercise testing protocol and a half-body DXA measurement respectively. Furthermore, the research has provided one of the first analyses for the submaximal and maximal cardiorespiratory efficiency of a clinically obese, pediatric population. This was performed through utilization of the oxygen uptake efficiency slope and subsequently compared to previously published values for a healthy-weight population.

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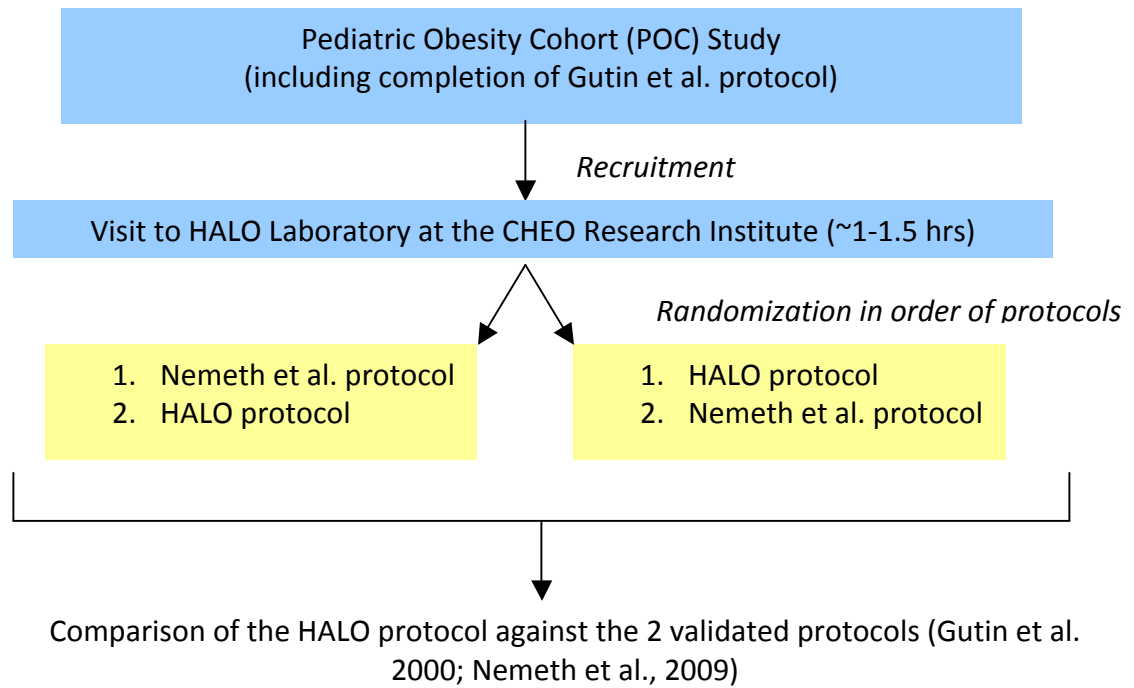
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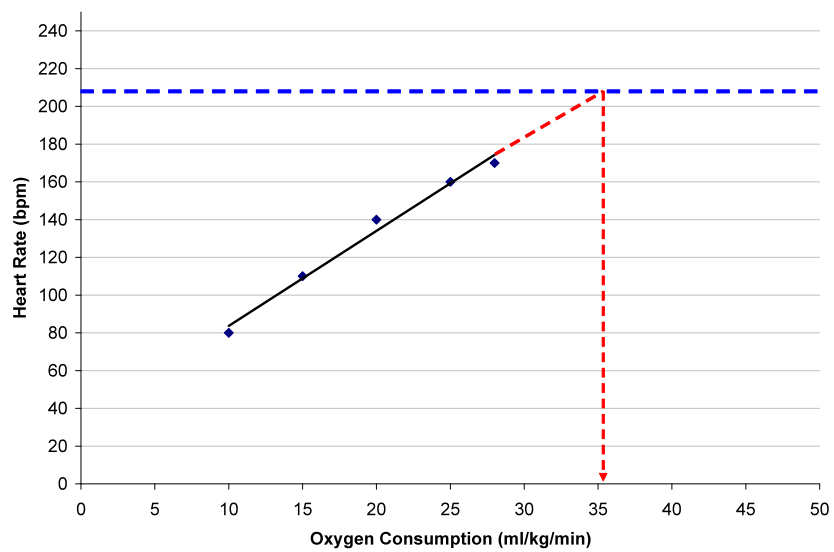
Appendix A

Manuscript 1 collection methodology



Appendix B

Theoretical model of how HALO protocol will predict $\dot{V}O_{2\max}$



Theoretical model of how the HALO submaximal fitness protocol will be used to predict VO2max.

Appendix C

University of Ottawa Report on Thesis Proposal



uOttawa

Université d'Ottawa
Faculté des sciences
de la santé

École des sciences de
l'activité physique

University of Ottawa
Faculty of Health
Sciences

School of Human
Kinetics

RAPPORT SUR LA PROPOSITION DE THÈSE REPORT ON THESIS PROPOSAL

DATE: Dec. 3rd, 2010

Nom/Name **P. Breithaupt** 4230978

Titre de la thèse/ Thesis Topic :

- ☐ La proposition de thèse est acceptée sans modification.
The thesis proposal is accepted without modification.
- ☒ La proposition de thèse est acceptée avec les modifications :
The thesis proposal is accepted with the following modifications:
- ☐ Des modifications sont nécessaires, le document doit être
revues par le comité examinateur.
Revisions are required which must be reviewed by the Examining
Committee.
- ☐ Document refusé, la proposition doit être inscrite à nouveau.
Document refused, and the proposal must be rescheduled.

- rework - clarify purpose & objectives upfront
- hypothesis clarification - consider mechanical
efficiency.
- clearer on 1/2 body scan methodology
- clarify CV fitness vs aerobic capacity

Ajouter des feuilles à ce rapport / If needed, attach additional sheets to this report

Kristi Adamo (Superviseur(e) / Supervisor)
Rachel Colley (Co-Superviseur(e) / Co-Supervisor)
F. Haman (Examineur(trice) / Examiner)
G. Kenny (Examineur(trice) / Examiner)
P. Breithaupt (Étudiant(e) diplômé(e) / Grad Student)
G. Karlis (Dir. du 2^e cycle / Director Grad Studies)

Appendix D

University of Ottawa Research Ethics Approval

File Number: H12-10-08

Date (mm/dd/yyyy): 01/24/2011



Université d'Ottawa
Bureau d'éthique et d'intégrité de la recherche

University of Ottawa
Office of Research Ethics and Integrity

Ethics Approval Notice
Health Sciences and Science REB

Principal Investigator / Supervisor / Co-investigator(s) / Student(s)

<u>First Name</u>	<u>Last Name</u>	<u>Affiliation</u>	<u>Role</u>
Kristi	Adamo	Others / Others	Supervisor
Rachel	Colley	Others / Others	Co-investigator
Peter	Breithaupt	Health Sciences / Human Kinetics	Student Researcher

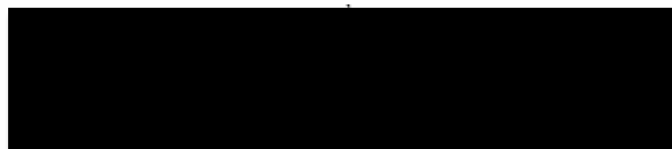
File Number: H12-10-08

Type of Project: Master's Thesis

Title: Validation of a Sub-maximal Treadmill Protocol to Measure Fitness in Overweight and Obese Children and Youth

Approval Date (mm/dd/yyyy)	Expiry Date (mm/dd/yyyy)	Approval Type
01/24/2011	01/23/2012	Ia
(Ia: Approval, Ib: Approval for initial stage only)		

Special Conditions / Comments:
CHEO REB File #06/36E Approval granted June 29, 2010.





Université d'Ottawa
Bureau d'éthique et d'intégrité de la recherche

University of Ottawa
Office of Research Ethics and Integrity

This is to confirm that the University of Ottawa Research Ethics Board identified above, which operates in accordance with the Tri-Council Policy Statement and other applicable laws and regulations in Ontario, has examined and approved the application for ethical approval for the above named research project as of the Ethics Approval Date indicated for the period above and subject to the conditions listed the section above entitled "Special Conditions / Comments".

During the course of the study the protocol may not be modified without prior written approval from the REB except when necessary to remove subjects from immediate endangerment or when the modification(s) pertain to only administrative or logistical components of the study (e.g. change of telephone number). Investigators must also promptly alert the REB of any changes which increase the risk to participant(s), any changes which considerably affect the conduct of the project, all unanticipated and harmful events that occur, and new information that may negatively affect the conduct of the project and safety of the participant(s). Modifications to the project, information/consent documentation, and/or recruitment documentation, should be submitted to this office for approval using the "Modification to research project" form available at:
http://www.rges.uottawa.ca/ethics/application_dwn.asp

Please submit an annual status report to the Protocol Officer 4 weeks before the above-referenced expiry date to either close the file or request a renewal of ethics approval. This document can be found at:
http://www.rges.uottawa.ca/ethics/application_dwn.asp

If you have any questions, please do not hesitate to contact the Ethics Office at extension 5841 or by e-mail at: ethics@uOttawa.ca.

Signature:

Catherine Paquet
Director, Office of Research Ethics and Integrity
For Daniel Lagarec
Chair of the Health Sciences and Science REB

Appendix E

Children's Hospital of Eastern Ontario Research Ethics Approval



CHEO Research Ethics Board - Approval of Minor Modification

Principal Investigator	Dr. Kristi Adamo
REB Protocol Number	06/36E
Protocol Title	Physiological and Psychological predictors and determinants of metabolic complications of pediatric obesity Adjunct Study: Validation of a sub-maximal treadmill protocol to measure fitness in overweight and obese children and youth
Department or PSU	Health Active Living and Obesity Research
Date Modifications Approved	June 29, 2010
Contingencies	☒ Not Applicable ☐ Applicable ~ Date contingencies were met:
Documents Reviewed & Approved	▪ Protocol (Version #1, Dated 01/06/2010); ▪ Consent Form for Participants ≤16 years (Version #1, Dated 01/06/2010); ▪ Consent Form for Participants ≥16 years (Version #1, Dated 01/06/2010); ▪ Assent Form (Version #1, Dated 01/06/2010);

This is to notify you that the Children's Hospital of Eastern Ontario Research Ethics Board has granted approval for the modifications to the above named research study. The minor modification was reviewed and approved by the Chair, and would be ratified by the full Board at its subsequent meeting.

In fulfilling its mandate, the CHEO REB is guided by: Tri-Council Policy Statement (TCPS); ICH Good Clinical Practice Practices: Consolidated Guideline; Applicable laws and regulations of Ontario and Canada (e.g., Health Canada Division 5 of the Food and Drug Regulations & the Food and Drugs Act-Medical Devices Regulations).

The investigator must meet the following requirements in conducting this research study:

- The investigator must submit to the Board in writing any changes to the study documentation (e.g., change in site investigator, protocol, informed consent letter, investigator's brochure, recruitment materials, etc. prior to implementation.
- Investigators must promptly report to the REB all adverse events or untoward occurrences that are both serious and unexpected (SAEs).
- Local medical Serious Adverse Events (SAEs) reports must also follow the hospital-wide Policy regarding, Procedures For Considering Medical Error In The Differential Diagnosis of Severe Adverse Events (SAE) Associated with the Drugs Administered in a Clinical Trial (see http://cheonet/data/1/rec_docs/3792_Medical%20Error%20Policy%20revised%20january%2020061.doc)
- Investigators must promptly report to the REB any new information regarding the safety of research subjects. Where applicable, reports produced by Data Safety Monitoring Board will be submitted to the REB.
- Investigators must notify the REB of any study closures (temporary, premature or permanent), with documentation regarding the rationale.
- Investigators must submit an annual renewal report to the REB 30 days prior to the expiration date.
- Investigators must submit a final report at the conclusion of the study.
- Investigators will provide the Board with French version of the consent form, unless a waiver has granted.

Regards,


for Dr. Carole Gentile, C.Psych.
Chair, Research Ethics Board

Letter issued on June 29, 2010

c.c. Jane Rutherford, Research Coordinator

<i>This is an official document. Please retain the original for your file</i> Minor Modification Approval Letter for REB #06/36E	<i>2010 Version</i>
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Page 2 of 2

Appendix F

Published Version of Manuscript 3: Body Composition Measured by Dual-Energy X-ray Absorptiometry (DXA) Half-body Scans in Obese Children

REGULAR ARTICLE

Body composition measured by dual-energy X-ray absorptiometry half-body scans in obese children

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Keywords

Adiposity, Body fat distribution, Fat mass, Lean body mass, Paediatrics

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ABSTRACT

Aim: To perform a methods comparison of a left or right half-body scan versus whole-body scan for measuring body composition in a sample of obese children.

Methods: A group of obese children ($n = 58$; ≥ 95 th BMI percentile; 8–18 years) were required to undergo a dual-energy X-ray absorptiometry (DXA) body composition measurement as part of an ongoing cohort study; 34 fit within the imaging field of the DXA scanner and were eligible for inclusion in the present analysis. Percent fat, total mass, fat mass, lean mass and bone mineral content (BMC) were estimated from half-body scans and compared with the whole-body results. Assessment was completed using GE enCORE 11.40 software.

Results: In comparing left- and right-side scans to whole-body scans, there was significant correlation for all body composition variables ($p \leq 0.005$, $R^2 = 0.996$ – 1.0). Bland Altman analyses also showed high levels of agreement between half-body estimates and whole-body measurements.

Conclusion: This study supports using a half-body scan methodology for percent fat, total mass, fat mass, lean mass, and BMC as a valid alternative to full-body analysis in obese children and youth.

INTRODUCTION

Increasing evidence indicates that excess adiposity is associated with a range of co-morbidities including type 2 diabetes (1), cardiovascular disease (2), hypertension (3), osteoarthritis (4), sleep apnoea (5), and a number of types of cancer (6). Robust evaluation of body composition is an important step in characterizing the health-risk profile of an obese child. An accurate, objective assessment of body composition is incredibly valuable, given the evidence indicating that self-report systematically under-represents the extent of the obesity problem (7). Numerous studies have shown that risk for insulin resistance, type two diabetes, high blood pressure, elevated blood cholesterol levels and stroke as well as risk for death are increased in persons with obesity (particularly abdominal obesity) (2,8,9); thus, appropriate quantification of these variables is essential. Originally

developed by Peppler and Mazess (10) to measure bone mineral density (BMD), dual-energy X-ray absorptiometry (DXA) has since become one of the most commonly utilized methods for clinical assessment of human body composition (11).

Dual-energy X-ray absorptiometry has been validated in many populations against other body composition measures such as skinfold-thickness assessments (12), bioelectrical impedance analysis (13) and hydrostatic weighing (14). When compared with magnetic resonance imaging (MRI), which has been recommended 'as a reference measure of adiposity for testing the efficacy of future therapies for obesity' (11), there were significant correlations between

Abbreviations

BIA, Bioelectrical impedance analysis; BMC, Bone mineral content; BMD, Bone mineral density; BMI, Body mass index; CHEO, Children's Hospital of Eastern Ontario; DXA, Dual-energy X-ray absorptiometry; MRI, Magnetic resonance imaging; MRT, Medical radiation technologist; POC, Paediatric obesity cohort; T2D, Type two diabetes; WHO, World Health Organization.

Keynotes

- Evaluation of body composition is an important step in characterizing the health-risk profile of an obese child.
- The present study supports the use of a left or right half body scan methodology as a valid alternative to full body analysis or percent fat, total mass, fat mass, lean mass, and bone mineral content (BMC) in obese children and youth whose dimensions are outside of the scanning surface.

the DXA and MRI in measuring both lean and fat mass (15). DXA was found to be equivalent to computed tomography (CT), for whole-body body composition measurements for a number of populations (16,17). DXA is especially attractive because of its ability to segregate body sections and provide direct measures of fat tissue, non-bone lean tissue, and bone compositions in given body sections, or over the body as a whole (18,19). DXA is based on differing absorption rates of photons emitted at two energy levels by body tissue allowing for quantification of bone mineral, lean and fat soft-tissue masses separately (20). DXA scans are short in duration (5–20 min) (21), relatively inexpensive, and have been found to be very precise while having very low radiation exposure (approximately 0.3 μ Sv) (22).

Despite the advantages of the DXA technique to measure body composition, it is limited by the reality that a growing segment of the paediatric population is too large for the scanning apparatus. This occurs because either their width exceeds the scan area (approximately 60 cm) or their mass exceeds weight limitations for the scanner imaging capabilities (approximately 136 kg). It is therefore timely to develop alternative means of estimating body composition for those whose dimensions surpass the limits of standard DXA equipment.

Tataranni and Ravussin (23) originally used half-body scans in an obese population that did not fit within the scanning area and compared these DXA scans to hydrodensitometry for a means of predicting body composition. More recently, Rothney et al. (24) determined that a half-body analysis in an obese adult population is closely comparable to a whole-body analysis; however, such a validation has not been completed in a paediatric population. Therefore, the purpose of this current study was to determine the validity of a half-body scan methodology for measuring body composition in a sample of obese children and youth.

METHODS

Subjects

A sample of 58 obese children (≥ 95 th WHO BMI percentile) (<http://www.who.int/growthref>) were recruited from the Children's Hospital of Eastern Ontario (CHEO) paediatric endocrinology clinic to participate in the *Physiological and psychological predictors and determinants of metabolic complications of paediatric obesity* (POC) study (Canadian Diabetes Association Innovation Grant #IG-1-07-2307-KA). All new patients visiting the paediatric endocrinology clinic for obesity assessment were eligible to participate.

Participants were required to complete a body composition measurement as part of the POC study assessment. From the initial sample, 34 fit within the imaging field of the DXA scanner and thus were eligible for inclusion in the final comparison analysis. Further details of the study subjects are displayed in Table 1. The protocol was approved by the CHEO Research Ethics Board. Informed consent (≥ 16 years) or parental consent and assent (< 16 years) was obtained before study initiation as required by the institutional ethics board.

Instrumentation

Measurements were made by a Medical Radiation Technologist (MRT) using the GE Lunar Prodigy ADVANCE DEXA scanner (GE Healthcare, Madison, WI, USA). Each morning prior to subject evaluation, secondary calibration and quality assurance measurements were completed. A calibration block representing three fat chambers was used specifically for body composition, and an aluminium step phantom in a container of rice was used to evaluate the machine's operating precision for bone density. These values are tested in the five rules of the Shewhart chart (25).

This procedure was used for quality control by taking measurements in three bone chambers and three fat chambers. Precision was analysed using coefficients of variation and these ranged from 0.20% to 0.52%. The body composition in young children and infants feature of the Prodigy ADVANCE provides direct calculation of total fat and lean tissue mass and percentages thereof, as well as BMC, density and area within the paediatric population. Results were calculated automatically for BMD, fat tissue, and lean tissue for the total body and sub-regions and compared with gender-specific paediatric reference data from the World Health Organization (WHO) Body Mass Index (BMI) graphs. Average scan time was 4.5 min with a radiation dose approximately 0.3 μ Sv.

Scan analysis was performed using GE enCORE 11.40 software (GE Healthcare). EnCORE uses an advanced intuitive graphical interface GE AutoAnalysis™ for premium precision. AutoAnalysis is capable of detecting whether a subject is within the scanning region, and if they are not within the region, an automatic half-scan analysis is performed by assuming symmetry of the body. The software also allowed for adjusting regions of the body for specific analysis, a process used by the certified MRT to isolate left and right body scans from full body scans by placing an appropriate sagittal line (Fig. 1). By utilizing this method, we were able to determine the validity of a half-scan

Table 1 Characteristics of study participants presented as mean $\pm$ SD and range

	All subjects (n = 34)	Female (n = 18)	Male (n = 16)
Age (years)	12.8 $\pm$ 3.4 (7.7–18.1)	12.8 $\pm$ 3.9 (8.5–18.1)	12.8 $\pm$ 4.1 (7.7–17.8)
Height (cm)	158.8 $\pm$ 30.1 (138.5–190.5)	157.1 $\pm$ 37.7 (139–179)	160.7 $\pm$ 42.1 (138.5–190.5)
Body mass (kg)	82.3 $\pm$ 22.9 (53.4–119.1)	81.2 $\pm$ 25.1 (56.4–112.2)	83.6 $\pm$ 28.2 (53.4–119.1)
BMI (kg/m ²)	32.2 $\pm$ 6.3 (26.5–39.3)	32.5 $\pm$ 8.1 (26.5–39.3)	31.9 $\pm$ 8.4 (27.6–38.6)

methodology in comparison with full-body while subjects required only a single scan.

Statistical analysis

Mean values for percent body fat, fat mass, lean body mass, total tissue mass and BMC were compared independently between whole-body left-side scans and whole-body right-side scans. After finding the impact of both age and gender to be negligible, all data were pooled. Wilcoxon signed-rank tests with Bonferroni adjustment for ten multiple comparisons were used, and significance was set as $p \leq 0.005$. Correlation plots for whole body and each side are presented in Figure 2. Bland-Altman plots were created to test the magnitude of bias in measuring percent body fat, fat mass, lean body mass, total tissue mass, and BMC through a half-body scan versus a full-body scan (26). Statistical analyses were completed using SPSS 18.0 (SPSS, Chicago, IL USA).

RESULTS

There were no significant differences between half- and full-body DXA scans for percent fat, total mass, fat mass, lean mass and BMC (Table 2). Although statistically insignificant, small differences in absolute values were present within the data between left- and right-side scans. One trend observed was that percent fat was slightly underestimated by right-side scans (mean $\Delta -0.01\%$), while left-side half-body scans were found to overestimate whole-body total mass (0.14 ± 0.01 kg), fat mass (0.06 ± 0.02 kg), and lean mass (0.08 ± 0.02 kg). Also, right-side half-body scans were found to underestimate whole-body total mass (-0.17 ± 0.01 kg), fat mass (-0.08 ± 0.01 kg), and lean

mass (-0.08 ± 0.01 kg). Differences in BMC values showed no variation between right- and left-side scans.

As there was only a single scan taken for each subject whole-body and half-body scan data for each subject were taken simultaneously, eliminating any possible disparity between scans. Descriptive statistics between participants and half-body scan estimates were highly comparable between sexes. In comparing left- and right-side scans to whole-body scans, there was very strong correlation for percent fat, total mass, fat mass, lean mass and BMC ($p < 0.01$, $R^2 = 0.996-1.0$). Bland-Altman analysis also showed high levels of agreement between half-body estimates and whole-body measurements in prediction of all body composition variables with 95% confidence intervals being closely comparable between right- and left-side techniques (Fig. 3).

DISCUSSION

In this study, we found that there were no significant differences in percent fat, total mass, fat mass, lean mass and BMC when comparing half-body DXA scan with whole-body DXA scan in a group of obese children and youth. As DXA is often used to track change in fat mass in various regions of the body, being unable to use this measure in a portion of the population is a major limitation to providing effective care and intervention. The current study provides a new and accurate means for physicians to track the adiposity of their obese paediatric patients who would otherwise be unable to receive a whole-body scan because of size restrictions. Whether the goal is to track changes in adiposity or obtain a precise cross-sectional measure of adiposity for comparative purposes, the ability to perform these measures in the children too large to fit within the scanning area is a step forward for comprehensive assessment of overweight and obese children.

Dual-energy X-ray absorptiometry, although originally intended for measuring bone density (10), has progressed to become a standard method for body composition analysis (11,18). When Tataranni and Ravussin (23) first compared half- and whole-body scans ($n = 183$) in the adult population, they found very analogous results in that whole-body scans were similar to the half-body estimations. In this particular study, a sub-group of 21 obese subjects whose size prevented them from receiving a whole-body scan, underwent two separate scans of each half of the body for comparison. These separate scans were found to have slightly larger discrepancies between the two sides for fat mass and non-bone lean mass which may be attributed to inaccurate body placement during the subsequent scan. Although scans used in this particular study may have been subject to methodological limitations, if proper care is taken to ensure accurate placement of a sagittal line during analysis, half-body scans have been found to be a precise means of estimating whole-body body composition. For example, using the same methodology as employed in the present paediatric study, Rothney et al. (24) assessed a single DXA scan of 52 obese adults ($BMI > 30$ kg/m²) using the Lunar iDXA

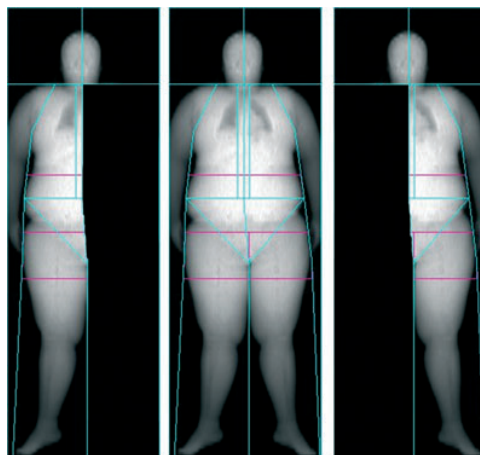


Figure 1 Example of full-body, left and right half-body scans used for analysis.

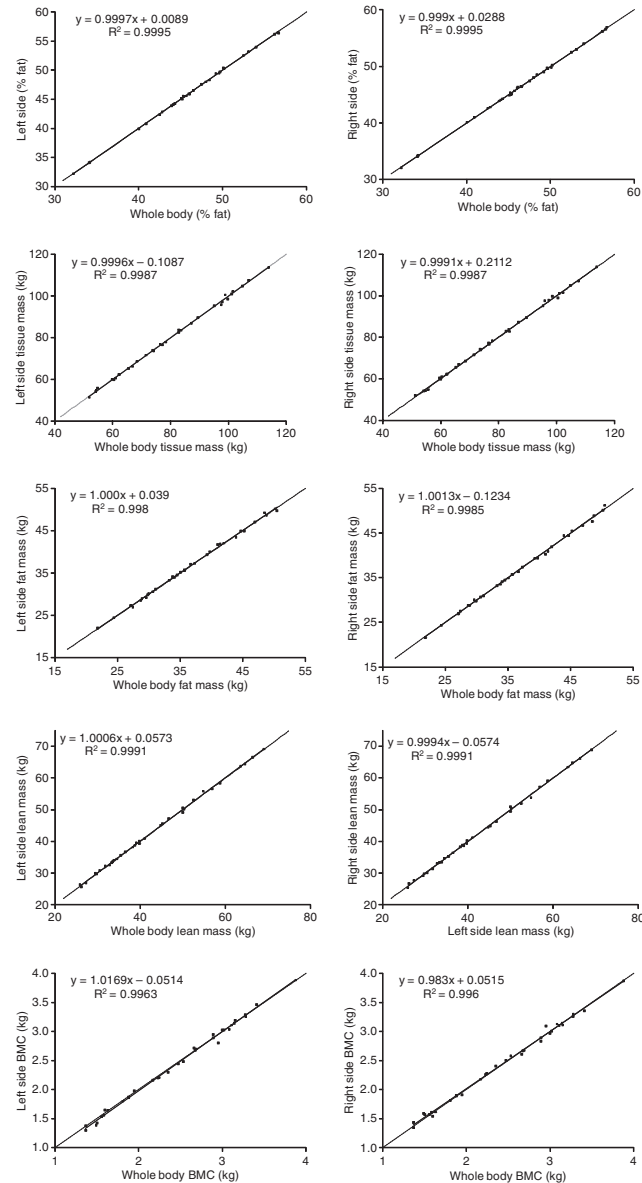


Figure 2 Correlation plots between left side, right side, and whole-body scans for total mass, percent body fat, fat mass, lean mass, and bone mineral content ($n = 34$). Dashed lines represent line of identity.

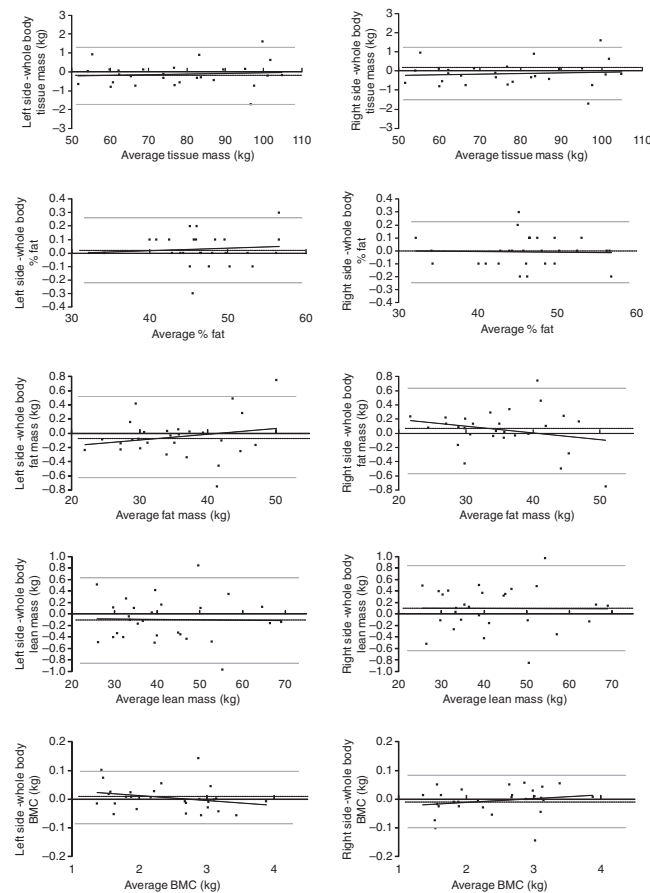
and GE enCORE 11.10 software. They used the whole scans on these subjects and proceeded to simulate half-body scans, through manual placement of an appropriate sagittal

line, allowing them to analyse each subject's scan as a whole-body scan, left-side scan and right-side scan. Using this methodology on their population, they found left-side

Table 2 Comparison of mean values between the two simulated half scans and total-body scan

	Whole body	Prediction using left side of body	Prediction using right side of body
Percent fat (%)	46.4 ± 9.8 (32.2–56.7)	46.4 ± 9.7 (32.2–56.5)	46.4 ± 9.7 (32.1–56.9)
Fat (kg)	36.3 ± 9.9 (21.8–50.5)	36.4 ± 9.9 (22.0–50.2)	36.2 ± 9.9 (21.6–51.2)
Non-bone lean (kg)	42.7 ± 14.2 (25.9–69.0)	42.8 ± 14.2 (25.6–69.2)	42.6 ± 14.1 (25.6–68.9)
BMC (kg)	2.43 ± 0.80 (1.37–3.88)	2.42 ± 0.81 (1.30–3.89)	2.44 ± 0.80 (1.35–3.87)
Total tissue mass (kg)	79.0 ± 22.0 (51.3–108.4)	79.1 ± 22.0 (51.9–113.9)	78.8 ± 22.0 (50.7–113.5)

BMC, bone mineral content.
Mean ± SD (range) (n = 34).
p < 0.005 vs. whole body.

**Figure 3** Bland-Altman plots comparing right side, left side, and whole-body scans for percent body fat, total mass, fat mass, lean mass, and bone mineral content. All $r^2 < 0.0405$, $n = 34$.

scans to be slightly lower, although not significantly, in absolute terms for fat mass (-0.10 ± 0.51 kg) and percent body fat ($-0.06\% \pm 0.28\%$). They also found that non-bone

lean mass was slightly lower than the whole-body analysis for both right side (-0.04 ± 0.54 kg) and left side (-0.04 ± 0.51 kg).

Unlike our sample population, Rothney et al. found that there was a significant overestimation of BMC in the half-body for the right side (23 ± 31 g) and underestimation in the left side (-27 ± 32 g). They attributed these differences to handedness, which has been found to produce higher BMC in the dominant limb compared with the off-limb (27). It is possible that our BMC estimations between the left and right sides are more comparable, given that the younger population has not yet developed as great an imbalance in the upper extremities as may be found in an adult population. Our data support the findings of both Tataranni and Ravussin (23), and Rothney et al. (24) that half-body scans and whole-body scans can be used interchangeably within a single study when a whole-body scan may not be possible.

Variation between scanners and software used during analysis contributes to differences between studies; making standardization of hardware and software a necessity (28,29). There are certainly limitations to the DXA scan capabilities including an inability to effectively differentiate between visceral and subcutaneous fat (30), exposure to radiation (albeit very small), as well as scan area limitations and scanner mass restrictions (23). Although the mass restrictions are less likely to be an issue in the obese paediatric population (0/58 exceeded mass restrictions for our specific obese population), the scan area restrictions (24/58, 41% of our cohort population were unable to be receive whole-body analysis) are a major hurdle in accurate assessment of paediatric body composition via DXA.

Given the magnitude of childhood obesity and the clinical importance of accurate body composition assessment (31) contributing to diagnosis and treatment of the epidemic, it is crucial to have a validated means of measuring body composition in a young, obese population. The findings of the present study support the use of a half-body scan methodology for percent fat, total mass, fat mass, lean mass, and BMC as a valid alternative to whole-body analysis in obese children and youth. Future work attempting to achieve similar validation using variations in DXA scanners, software, and populations of larger-still BMI is strongly encouraged.

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