Obesity-Associated Morbidities in Children and Adolescents: The Correlates Between Knee Biomechanics, Musculoskeletal Impairments, Limitations in Health Related Quality of Life, and Cardiovascular Risk

DISSERTATION

Presented in Partial Fulfillment of the Requirements for the Degree Doctor of Philosophy in the Graduate School of The Ohio State University

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Abstract

Alarmingly, pediatric obesity rates have tripled in the past 30 years and with over 30% of youth in the United States consider either overweight or obese. Children and adolescents who are obese face many of the same health concerns as adults including musculoskeletal, psychological, and cardiovascular morbidities. Furthermore, obese youth are more likely to be obese as adults. It could be hypothesized that in obese youth lower extremity musculoskeletal impairments and limitations may adversely impact functional ability and associated activity levels with subsequent limitations on health related quality of life and cardiovascular health. These negative attributes related to obesity in youth create a compelling the need to better understand their mechanisms and relationships. The overall purpose of this dissertation is to better understand the relationships between musculoskeletal impairments and limitations to components of health in obese youth.

The results outlined in this dissertation from two cross-sectional studies in 20 obese and 20 matched healthy weight youth indicate that obese youth stand in greater knee abduction alignment demonstrate decreased external frontal plane knee moments during walking. In addition measures of frontal plane knee alignment in obese youth do not correlate with frontal plane knee loading during walking or jogging. Further, hip and knee strength may adversely affect functional ability while performance on hopping and
balance related tasks may predict health related quality of life in obese youth. Finally, in a retrospective study of 183 obese youth enrolled in a medical weight management program it was determined that obese youth with high levels of C-reactive protein are at almost 5 times the odds of developing metabolic syndrome compared to obese youth with normal levels of C-reactive protein. However, measures of cardiorespiratory fitness, health related quality of life, and reports of musculoskeletal pain do not predict cardiovascular risk in obese youth.

Overall, results from these studies demonstrate frontal plane knee alignment and frontal plane knee joint loading patterns do not correlate while contributions of lower extremity strength to lower extremity function and lower extremity function to health related quality of life differ between obese and healthy weight youth. In addition, high levels of C-reactive protein increase the risk of metabolic syndrome in obese youth whereas poorer cardiorespiratory fitness, poorer health related quality of life, and reports of musculoskeletal pain do not increase the risk of metabolic syndrome in obese children and adolescents. These results have potentially significant clinical implications on how musculoskeletal morbidities in obese youth are addressed and evaluated. Future research should focus on determining how the factors related to musculoskeletal impairments and limitations may influence levels of physical activity participation and in turn overall health. Ultimately, the results from these current and future studies may be used to optimize and personalize treatment strategies to reduce cardiovascular risk and improve health related quality of life in obese youth and limit the consequences of obesity into adulthood.
Dedication

For Gena and the kids.
Acknowledgments

I am very grateful for the support of numerous individuals and organizations who have supported me along this journey and guided my development.

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**Fields of Study**

Major Field: Health and Rehabilitation Sciences
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List of Abbreviations

3-D: 3-dimensional
ASIS: anterior superior iliac spine
BMI: body mass index
BP: blood pressure
CRP: C-Reactive Protein
GLU: glucose
HA: hip abduction
HbA1C: hemoglobin A1C
HDL: high density lipoprotein
HE: hip extension
HKA: hip, knee, and ankle
HRQoL: health related quality of life
HW: healthy weight
IDF: International Diabetes Federation
iDXA: Lunar dual-energy x-ray absorptiometry
KE: knee extension
KF: knee flexion
LBA: load-bearing mechanical axis
LE: lower extremity
MetS: metabolic syndrome
MSK: musculoskeletal
OA: osteoarthritis
OB: obese
OW: overweight
PACER: Progressive Aerobic Cardiovascular Endurance Run
PAQ: Physical Activity Questionnaire
PAQ-A: Physical Activity Questionnaire for adolescents
PAQ-C: Physical Activity Questionnaire for older children
PedsQL: Pediatric Quality of Life Inventory
PedsQL-physical: Pediatric Quality of Life Inventory- physical health summary score
PedsQL-psychosocial: Pediatric Quality of Life Inventory- psychosocial health summary score
SLBAR: single leg balance anterior reach
SLHop: single leg hop
TG: triglycerides
UE: upper extremity
UMB: umbilicus measurement
UW: underweight
WC: waist circumference
Chapter 1 : General Introduction

1.1 Obesity in Children and Adolescents

Childhood obesity is growing at epidemic proportions as are the associated health concerns.\(^1-^3\) Over the past 30 years, the prevalence childhood obesity has tripled with 20% of children (6-11 years-old) and 18% of adolescents (12-19 years-old) classified as being obese in 2008.\(^4\) In 2008, greater than 30% of youth in the United States were considered overweight or obese.\(^4\) The prevalence of obesity in youth (2-19 years-old) (15.4-17.1%) has remained consistent according to data from the National Health and Nutrition Survey years 2003-2004 thru 2011-2012.\(^5\) In adults, obesity is the second leading cause of preventable death and has been associated with a variety of health concerns including cancer, cardiovascular disease, musculoskeletal (MSK) pain, osteoarthritis, decreased function, and poorer health related quality of life (HRQoL).\(^6-^8\)

The pediatric obesity trend is concerning as obese youth are less physically active than healthy weight children,\(^9-^11\) demonstrate similar health side-effects as obese adults\(^2,12,13\) and are more likely to be obese as adults.\(^14-17\)
1.2 Definition and Measures of Obesity in Children and Adolescents

Obesity is defined as having “excess body fat.” Body mass index (BMI) [kg/m²] is the most common measure of obesity status in adults and children and is highly correlated with other measures evaluating body fat composition. Weight status in children and adolescents is defined as the percentile ranking of BMI from the sex-specific Centers for Disease Control and Prevention 2000 BMI-for-age growth charts. Using percentile ranking allows for comparison of children and adolescents amongst each other while accounting for changes in growth and development. Initial BMI is determined from mass (kilograms) and height (meters) and then compared to a national growth chart to determine percentile ranking. Obese (OB) is defined as above the 95th percentile of BMI with morbid obesity being greater than the 99th percentile. Overweight (OW) is between the 85th and 94th percentiles, healthy weight (HW) is between the 5th and 84th percentiles, and underweight (UW) is less than the 5th percentile. BMI-Z scores are also another common format relating mass and height in children and adolescents. BMI-Z scores (standard deviation scores) offer an alternative interpretation of BMI0 and lend themselves better to statistical analysis versus BMI percentiles.

1.3 Health Effects of Obesity in Children and Adolescents

OB youth demonstrate many of the same health morbidities as OB adults. It is well accepted and there is substantial evidence relating cardiovascular risk and morbidity in OB youth including diabetes, metabolic syndrome, and elevated systemic inflammation. In addition, psychosocial and physical health related quality of life
Finally, when compared to their HW counterparts, OB youth demonstrate more MSK impairments and limitations including increased complaints of joint pain\textsuperscript{31-33}, altered lower extremity (LE) alignment\textsuperscript{32}, increased risk of poor joint health\textsuperscript{34,35}, and decreased physical function\textsuperscript{11,36,37}. The consequences of these aforementioned morbidities are thought to limit overall health in OB youth and may carry-over into adulthood\textsuperscript{12,13}. It could be hypothesized that in OB youth MSK impairments and limitations may adversely impact functional ability and associated activity levels with subsequent limitations on HRQoL and cardiovascular health (Figure 1.1). The components of MSK impairments, functional abilities, HRQoL, and cardiovascular health pertaining to OB youth will be the basis for subsequent studies in Chapters 2–4.
1.3.1 Musculoskeletal Pain in Obese Youth

In comparison to the evidence of cardiovascular risk in OB youth, there is much less research relating MSK impairments and limitations to obesity in children and adolescents. The available evidence demonstrates that OB youth report more MSK pain when compared to HW youth. More specifically, the LE and especially the knee are
the most prevalent regions of MSK pain in OB youth.\textsuperscript{31-33,39,40} Further, a recent retrospective study conducted by our lab demonstrated that OB youth who reported LE pain had worse physical function and psychosocial health compared to OB youth without reports of LE pain.\textsuperscript{41} It could also be speculated that the higher prevalence of MSK pain in OB youth may subsequently alter movement patterns, limit function, and decrease physical activity in this population.\textsuperscript{33,39}

1.3.2 Joint Health and Lower Extremity Biomechanics in Obese Youth

The function and health of the knee is important for mobility and movement. The presence of knee pain and damage may limit activity participation and theoretically increase disability in OB youth. OB youth demonstrate increased potential risk of poor knee joint health including pain and articular cartilage damage.\textsuperscript{34} This damage is speculated to increase the risk of developing knee OA as an adult.\textsuperscript{35,42,43} Further, altered LE alignment and mechanics\textsuperscript{24,25,44,45} have also been shown in OB children versus non-obese children and may contribute to the increased risk of poor knee joint health in this population.

1.3.2.1 Frontal Plane Static Standing Knee Alignment

Relative positions of the hip, knee, and ankle (HKA) will alter the compartmental load distribution of the knee. In the “neutrally” (0°) aligned knee [not adducted (varus), <0° or abducted (valgus), >0°] (Figure 1.2), the medial compartment bears approximately 60-70% of the load in weight bearing.\textsuperscript{46-48} In an adducted (varus) aligned knee the load-
bearing mechanical axis (LBA) passes farther medial to the knee and increases comressive forces across the medial compartment\textsuperscript{48-50} whereas in an abducted (valgus) aligned knee the LBA passes more lateral to the knee and increases comressive forces in the lateral compartment (Figure 1.2).\textsuperscript{48,50} The understanding of objectively measuring static standing frontal plane knee alignment in OB youth is limited, however available evidence indicates that OB youth stand in greater knee abduction (valgus) compared to HW youth.\textsuperscript{32,51} Understanding objective measures of static standing frontal plane knee alignment are important as they are often used in the attempt to infer frontal plane loading patterns and extrapolate them to dynamic movement.\textsuperscript{47,49} However, the relationship between knee alignment and knee joint loading patterns is not known in OB youth.
Figure 1.2 Frontal plane knee alignments of the left leg. Load-bearing axis (LBA); hip-knee-ankle (HKA) angle; femoral mechanical axis (FM); tibial mechanical axis (TM). A) Adducted (Varus) alignment-knee center is lateral to the LBA, <0º; B) Neutral alignment-knee center is located on the LBA, 0º; and C) Abducted (Valgus) alignment-knee center is medial to the LBA, >0º. (Cook et al49)

1.3.2.2. Frontal Plane Knee Joint Loading

Previous work is conflicting regarding frontal plane knee loading patterns in OB youth compared to HW youth during walking.23,25,52,53 Recent literature demonstrates decreased normalized external peak knee adduction moments in OB youth.23,25 Whereas, other evidence52,53 shows increased non-normalized external peak knee adduction
moments or no difference when normalized.\textsuperscript{52} Normalizing knee joint moments may reduce variability and allow for comparison between subjects but may limit the understanding of the true forces affecting the knee joint related to increased body mass. Better understanding frontal plane knee joint loading patterns is important in understanding how obesity may impact knee joint health in OB youth.

The study described in Chapter 2 includes 20 OB and 20 HW youth and evaluates static standing frontal plane knee joint alignment and frontal plane knee moments during walking and jogging. The \textbf{aims} of the study are to 1) compare static standing frontal plane knee alignment and frontal plane knee joint moments in OB youth and HW youth and 2) determine the relationship between static standing frontal plane knee alignment and frontal plane knee joint loading patterns during walking and jogging in OB youth.

\subsection*{1.3.3 Function and Health Related Quality of Life in Obese Youth}

Being OW or OB in early adulthood has been associated with decreased physical performance and mobility impairment throughout adulthood and into elderly age.\textsuperscript{54,55} Functionally, OB youth demonstrate poorer scores on measures of overall mobility,\textsuperscript{33} LE muscle performance,\textsuperscript{11,56,57} LE gross motor skills,\textsuperscript{11,58} jumping tasks,\textsuperscript{37} as well as static and dynamic balance skills.\textsuperscript{59} Further, OB youth are less physically active compared to HW youth.\textsuperscript{9-11} It is theorized that MSK impairments and limitations secondary to high adipose and body mass may limit physical activity participation in OB youth.\textsuperscript{11} The deficiencies in function and physical activity may contribute to decreased health related quality of life in OB youth.\textsuperscript{28,29,41,60-62} Ultimately, poor physical function in OB youth
may perpetuate a vicious cycle of persistent decreased physical activity and obesity in youth and increased disability in adults.63-66

1.3.3.1 Lower Extremity Strength in Obese Youth

Decreased LE strength has been shown to be associated with impaired LE function in OB adult populations.54,65,67 It has been suggested in OB adults that decreased LE muscle strength is potentially independent of physical activity level,68,69 yet decreased LE muscle strength in OB individuals may subsequently limit physical activity participation. However, current evidence regarding LE strength in OB youth is conflicting. Specific to knee extension strength in OB youth, results demonstrate both decreased strength as well as no differences in strength when compared to HW youth.56,57,70,71

1.3.3.2 Lower Extremity Functional Performance in Obese Youth

When evaluating LE function with hopping, jumping, sit-to-stand, and timed walking tests results consistently demonstrate poorer performance in OB youth compared to HW youth.11,33,37,57 Further, when using test batteries which evaluate LE motor control, coordination, and function such as the Bruininks-Oseretsky Test of Motor Proficiency11 and the Body Coordination Test for Children58 OB youth consistently demonstrate worse scores compared to HW youth. Further significant negative correlations have been demonstrated on measures of LE functional performance and measures of obesity in youth.11,58 Understanding the mechanism and contributors to
poorer LE functional performance are important in promoting an active, healthy lifestyle in OB youth.

1.3.3.3 Health Related Quality of Life in Obese Youth

Health related quality of life (HRQoL) is a measure of overall function and well-being. HRQoL is often used to characterize disease burden as it relates to an individual’s global health.\textsuperscript{28,60,72} The World Health Organization defines HRQoL as a multidimensional self-perception and awareness of an individual’s well-being comprised of physical, psychological, and social dimensions.\textsuperscript{29,61,73,74} OB youth consistently exhibit worse HRQoL compared to HW youth.\textsuperscript{28,29,60,62,75} More specifically, higher BMI and higher BMI combined with a greater number of co-morbidities in OB youth have been shown to associated with decreased HRQoL.\textsuperscript{60,76} However, identifying specific interventions aimed at improving HRQoL in OB youth has been hampered by a limited understanding of factors which may interact with obesity and also contribute to poor HRQoL.\textsuperscript{60} Improved LE physical function has been shown to positively correlate with improved HRQoL in OB adult females following gastric bypass surgery.\textsuperscript{77} However, the relationship between LE functional performance and HRQoL in OB youth is unknown.

Exploration of the associations between LE muscle strength, LE function, and HRQoL in OB youth forms the analysis in the study described in Chapter 3. The aims of the study are to 1) compare measures of LE muscle strength, LE functional performances, and HRQoL between OB and HW youth and 2) evaluate the contributions of LE muscle
strength to LE functional performance and LE functional performance to HRQoL in OB youth.

1.3.4 Cardiovascular Health in Obese Adults and Youth

Cardiovascular disease is the leading cause of death in adults.\textsuperscript{78} Obesity and other related cardiovascular risk factors including metabolic syndrome (MetS),\textsuperscript{79} systemic inflammation\textsuperscript{79-81}, and insulin resistance\textsuperscript{82-85} are often diagnosed in OB youth. Many of these factors are interrelated and their combination suggests a cycle of increasing cardiovascular risk.\textsuperscript{83} Further their presence increases the risk of cardiovascular disease in adulthood.\textsuperscript{2,12,13,86,87}

MetS specifically is a concerning condition in both adults and youth. MetS is a cluster of specific cardiovascular risk factors including obesity, high cholesterol, high blood pressure, insulin resistance, and elevated fasting plasma glucose.\textsuperscript{88,89} In adults, the presence of MetS increases the likelihood of myocardial infarctions and cerebral vascular accidents 2-3 fold\textsuperscript{89} and diabetes 5 fold.\textsuperscript{89} Further, in adults other components of health including MSK pain,\textsuperscript{90} cardiorespiratory function,\textsuperscript{91} and HRQoL\textsuperscript{92,93} have been shown to be associated with MetS.

The prevalence of MetS in OB youth ranges from 10-66%.\textsuperscript{94} The presence of MetS in youth increases the threat of adult onset cardiovascular disease 15 fold.\textsuperscript{86,87} However, the relationships between MetS and measures of MSK pain, cardiorespiratory function, HRQoL in OB youth are unknown. Understanding these relationships in OB youth is important as earlier identification of cardiovascular risk and potentially
concomitant aggravating factors may lead to earlier and more aggressive medical management in OB youth to halt or delay progression of cardiovascular disease.

Chapter 4 is a retrospective review of 183 OB youth enrolled in a hospital based medical weight management program and compares cardiovascular risk factors, including MetS, in OB youth based on measures of cardiorespiratory function, HRQoL, and reports of MSK pain. The aims of the study are to 1) compare the prevalence of cardiovascular risk factors and MeS as categorized by common clinical measures of cardiorespiratory function, HRQoL, and reports of MSK pain and 2) evaluate the odds of MetS based on common clinical and laboratory measures of health in OB youth enrolled in a hospital based medical weight management program.

1.4 Summary

Obesity in youth and associated health concerns have grown at epidemic proportions over the past 30 years.\(^1\)\(^-\)\(^3\) The consequences of obesity in children and adolescents are enormous with both immediate and long term side effects. These include a greater prevalence of MSK ailments,\(^31\)\(^-\)\(^33\) poorer physical function,\(^1\)\(^1\)\(^,\)\(^37\)\(^,\)\(^58\) poorer HRQoL,\(^2\)\(^8\)\(^-\)\(^30\) and increased cardiovascular risk.\(^1\)\(^2\)\(^,\)\(^13\)\(^,\)\(^26\)\(^,\)\(^27\) The consequences of these aforementioned morbidities in OB children and adolescents are thought to limit overall health in OB youth and carry-over into adulthood.\(^1\)\(^2\)\(^,\)\(^13\) The studies in this project provide insight into the inter-relationships of the MSK-related co-morbidities in OB youth. The results from the subsequent chapters may assist in the development of future studies focused on determining optimal strategies for improving the levels of function, physical
activity, and HRQoL while moderating the potential for joint damage and cardiovascular risk in OB youth.
1.5 References


Chapter 2: Static Standing Frontal Plane Knee Alignment Does Not Correlate with Peak Knee Frontal Plane Moments During Walking and Jogging in Youth Who are Obese.

2.1 Background

Risk factors for the development and progression of knee osteoarthritis (OA) and joint degeneration are multifactorial. Obesity is a primary risk factor for the development of knee OA\textsuperscript{1-3} An additional risk factor that has been suggested is knee malalignment.\textsuperscript{4-6} In adults, increased knee adduction (varus) alignment has been shown to increase the risk of medial knee OA\textsuperscript{7,8} whereas increased knee abduction alignment has been shown to increase the risk of lateral knee OA and meniscal damage.\textsuperscript{9} The combination of obesity and knee malalignment may substantially exacerbate the risk of joint damage and degeneration.\textsuperscript{4} The presence of these factors in children and adolescents may significantly increase the risk of poor knee health during development youth and into adulthood. As such Gelber et al\textsuperscript{2} showed that obesity in young adulthood triples the risk of knee OA by age 60. Further, in morbidly obese (OB) youth, articular cartilage lesions were observed in 100\% of the knees evaluated with magnetic resonance imaging while early onset OA was also detected in several subjects.\textsuperscript{10} Evaluating factors that may be related to knee health in OB youth, such as alignment, is critical for both immediate and long-term well-being.
Clinicians often utilize measures of static standing knee alignment in attempt to understand movement and loading patterns of the knee during dynamic activity.\textsuperscript{11} Static standing frontal plane knee alignment has been shown to strongly correlate with frontal plane knee moments, specifically the external knee adduction moment, during walking in adults with knee OA\textsuperscript{11} and in healthy adults without knee OA.\textsuperscript{12,13} Unfortunately, clinical assessment of static standing frontal plane knee alignment using other common techniques (e.g. inclinometer, calipers, etc.) in those who are obese can be limited secondary to increased soft tissue mass.\textsuperscript{14} The gold standard for measuring frontal plane knee alignment is with a standing long-legged radiograph.\textsuperscript{15} However, this method requires expensive equipment, personnel, and exposure to radiation.\textsuperscript{14,15} Thus, a reliable and accurate clinical measure of frontal plane knee alignment in OB youth would be valuable.

Recently, Gibson et al.\textsuperscript{14} developed a measurement technique to evaluate static standing frontal plane knee alignment specifically in obese adults. This technique, known as the umbilicus measurement (UMB), measures the frontal plane angle between the umbilicus, center of the knee, and center of the ankle. The UMB measurement has been validated against long cassette radiographs in OB adults with medial knee OA.\textsuperscript{14} Only 1 study has reported static standing frontal plane knee alignment in OB youth finding increased knee abduction (valgus) alignment compared to HW youth.\textsuperscript{16} However, the methods used to determine limb alignment were not described. The UBM measurement may offer the ability to objectively and reliably measure static standing knee alignment in OB youth.
An additional method for measuring standing frontal plane knee alignment that has been reported in both OB and HW adults uses 3-dimensional motion analysis techniques (3D). During 3-dimensional motion analysis a static standing calibration trial is recorded. This static recording serves to create the joint coordinate system and determine the joint positions during dynamic activity. From this static trial alignment of the hip-knee-ankle can be determined. This 3D alignment measurement technique has been shown to strongly correlate and predict frontal plane knee alignment in standing long-legged radiographs and thus may be less susceptible to the limitations of other clinical measures of static standing frontal plane knee alignment in OB individuals. However, this measurement technique for standing frontal plane knee alignment has not been reported in OB youth.

The data on frontal plane knee loading patterns in OB youth during walking is conflicting. Several studies demonstrate decreased normalized external peak adduction moments during walking in OB youth while and others have shown no difference in normalized peak external adduction or abduction moments compared to healthy weight (HW) youth during walking. Based on the observations of de Sa Pinto et al. of knee abduction (valgus) alignment in OB youth it could be hypothesized that OB youth would demonstrate decreased external knee joint adduction moments as observed by McMillan et al. during gait. However, the relationship between static standing frontal plane knee alignment and frontal plane knee moments in OB youth has not been explored.

The purposes of this study were to: 1) compare static standing frontal plane knee
alignment and frontal plane knee joint moments in OB youth and HW youth and 2) determine the relationship between static standing frontal plane knee alignment and frontal plane knee joint loading patterns during walking and jogging in OB youth. We hypothesized that: 1) OB youth would demonstrate increased standing knee abduction alignment using two different measurements compared to HW youth, 2) The UMB measure will positively correlate with a 3D measure of static standing frontal plane knee alignment in OB youth, 3) OB youth will demonstrate less peak knee adduction and greater peak abduction moments compared to HW youth during walking and jogging, 4) Measures of static standing knee alignment will positively correlate with peak frontal plane knee joint moments during walking and jogging in OB youth.

2.2 Materials/Subjects and Methods:

Two groups of participants (total n=40), ages 11-18 were recruited: 20 OB and 20 HW. OB participants were recruited from potential patients referred to a pediatric medical weight management program at a tertiary pediatric hospital, pediatric ambulatory clinics, and other local community pediatric clinics. Potential HW participants were recruited from local community pediatric clinics and via flyer postings. HW participants were matched to OB participants based on age and sex. OB was defined as BMI being greater than or equal to the 95th percentile and less than the 99th percentile. HW was defined as BMI greater than the 5th percentile but less than the 85th percentile for BMI.23,24
2.2.1 Exclusion Criteria

Potential participants with a history of or currently having any developmental (delayed walking, developmental coordination disorder, developmental delay, Down syndrome, muscular dystrophy, autism), neurological (e.g. cerebral palsy, nerve injury), or orthopedic (e.g. slipped capital femoral epiphysis, fracture, etc.) condition that would impact their gait or ability to run were excluded from the study. Potential participants with a genetic predisposition to obesity (e.g. Prader-Willi syndrome) or who were taking any medications that might impact muscle function or for pain/inflammation were also excluded. Children with a BMI > 99th percentile (morbidly/severely obese) were excluded due to the potential to increase the measurement error of the 3-dimensional motion capture secondary to greater amounts of soft tissue compared to OB youth. Further, potential interventions for those who are obese (e.g. dietary counseling, behavioral counseling, increasing physical activity, specific exercise interventions, etc.) versus morbidly/severely obese (e.g pharmacological intervention, bariatric surgery, etc.) may differ depending on obesity severity and presence of co-morbidities.\textsuperscript{25,26} Overweight children (BMI 85-94\textsuperscript{th} percentile) and underweight children (BMI <5\textsuperscript{th} percentile) were also excluded, as the focus of the current study was to compare children and adolescents of healthy weight (BMI <85\textsuperscript{th} percentile) and those who were obese (BMI >95\textsuperscript{th} percentile).\textsuperscript{19,20,27}
2.2.2 Data Collection and Procedures

Informed assent and consent were obtained from participating subjects and their parents/legal-guardians, respectively. Participant’s height and weight were measured on a standard physician’s combined stadiometer and weight beam scale (Detecto-Medic; Webb City, MO, USA) and recorded based on the National Health and Nutrition Examination Survey protocol.\textsuperscript{28} BMI was calculated from subject’s height and weight and sex and age adjusted BMI-Z scores were generated from an online calculator utilizing the Centers for Disease Control and Prevention 2000 data (Table 2.1).\textsuperscript{29-31} To assess maturation, participants completed a self-report Tanner Stage questionnaire.\textsuperscript{32} Seventeen of the 20 OB subjects and 20 of the HW subjects agreed to fill out the self-reported Tanner Stage questionnaire and were included in the pair-wise data analysis. Knee alignment and knee joint moments were measured on the tested limb determined by the participant’s report of which limb they would use to kick a soccer ball as far as they could.\textsuperscript{33,34}

2.2.3 The Umbilicus Measurement of Static Frontal Plane Knee Alignment

The umbilicus (UMB) measurement was performed as described by Gibson et al.\textsuperscript{14} Participants were instructed to march in place 3 times and then stand quietly with their feet in a “natural position.” Foot position was not explicitly controlled or constrained other than with the aforementioned instructions.\textsuperscript{14} Participants were then instructed to slowly adduct their legs until they felt either their mid-lower thighs, knees, calves, or ankles touch based on soft-tissue approximation. Participants were explicitly
instructed not to force their legs together. The axis of a standard 12 inch goniometer was aligned at the center of the tested knee at the joint line. The distal arm of the goniometer was aligned with the center of the ankle joint (equidistance between the medial and lateral malleolus) while the proximal arm was aligned with the umbilicus (Figure 2.1). The resulting angle was recorded as either adduction alignment (<0º) or abduction alignment (>0º). All measurements were taken by a single rater (MB) with 8 years of clinical outpatient, orthopedic experience. Intra-rater reliability was determined to be good (ICC3,1 = 0.788) and consistent with that previously reported.
Figure 2.1 Measurement of static standing frontal plane knee alignment using the umbilicus method. The femoral axis is formed by a line between the umbilicus (A) and the center of the knee (B). The tibial axis is formed by a line between the center of the ankle (C) and the center of the knee (B). The umbilicus measurement is the angle of intersection between the femoral and tibial axis denoted by the dashed line.
2.2.4 Motion Analysis

Retro-reflective spherical markers were attached directly to the skin on each subject’s bilateral lower extremities and pelvis. Anatomical markers were placed over the medial and lateral femoral condyles and malleoli to define the joint centers of the knee and ankle while tracking markers were placed on the thigh and shank (Figure 2.2).\textsuperscript{36,37} The medial anatomical/joint markers were only left on during the static calibration trial and were removed during the walking and jogging trials. Markers were placed over the bilateral anterior superior iliac spines (ASIS), posterior superior iliac spines, and iliac crests to define the pelvis. To account for the increased central soft tissue in the OB youth the ASIS markers were placed laterally versus directly over the ASIS. To correct for the lateralized placement of the ASIS markers, the distance between the left and right ASIS was measured (cm) with calipers and later entered into the computer software during processing to define the pelvis segment. Functional hip joint centers were created using the star-arc approach.\textsuperscript{38} This method identifies the hip joint center as the center of rotation of the femur relative to the pelvis during specific movements versus estimating the joint center based upon pelvic landmarks which may be confounded by excessive soft tissue present in OB individuals. The knee joint center was determined at the midpoint between the medial and lateral femoral condyle knee markers while the ankle joint center was determined to be between the medial and lateral malleolus markers.
Figure 2.2 Anterior and posterior views of the placement of the retro-reflective markers used for 3-dimensional motion analysis.
Kinematic data were collected using ten Vicon motion analysis cameras (Vicon Motion Systems, Denver, CO, USA) and kinetic data were collected using six synchronized triaxial force plates (Bertec Corporation, Columbus, OH, USA). Kinetic data was sampled at 1500Hz for all participants. Kinematic data of 32 subjects were captured at a sample rate of 300 Hz while 8 subjects (OB: n=1 HW: n=7) were sampled at 150Hz due to a technical problem. To evaluate for potential differences secondary to the sampling rates, data from the walking and jogging trials of 1 subject who was captured at 300Hz were down-sampled to 150Hz. Both the 300Hz and 150Hz trials were then compared to each other for potential differences. Visual inspection and comparison between the 300Hz and 150Hz frontal plane knee kinematic and kinetic time series curves was conducted by overlaying the time series curves. Consistency between the means and standard deviations between the curves was visually evident with no discernible deviations. Further the means of the specific variables of interest were subtracted from each other to determine the differences between the 300Hz and 150Hz trials. The differences between the means were not outside the ranges of standard measurement error. Thus, data from all subjects were included in the final analysis. The motion analysis data were exported for subsequent analysis in Visual 3D software (C-Motion, Inc. Germantown, MD, USA). Marker trajectories and analog force data were filtered using a 4th order Butterworth filter with cutoff frequencies of 12Hz and 40Hz, respectively. Three-dimensional Cardan joint angles for the knee were determined between the thigh and shank segments during a static standing trial as well as walking.
and jogging. Knee joint moments were calculated using standard inverse dynamics equations normalized to mass $\times$ height.

2.2.5 3-Dimensional Measurement of Static Frontal Plane Knee Alignment

Another measure of static standing frontal plane knee alignment was obtained from the 3-dimensional static standing calibration trial during motion analysis testing (3D). For the static calibration trial, participants stood in the anatomical position with their feet approximately shoulder width apart and their feet pointing straight ahead. A trial was collected for 3 seconds in this position. The 3D measurement was determined as the angle in the frontal plane between the relative positions of the thigh and shank segments on the tested limb. Consistent with the UMB measure the 3D measure of frontal plane knee position was classified as being in either adduction ($<0^\circ$) or abduction ($>0^\circ$).

2.2.6 Walking and Jogging Trials

With the retro-reflective markers on, participants were instructed to walk and jog down a 10 meter walkway at self-selected speeds while looking straight ahead. Each participant performed practice trials prior to data collection for both tasks to ensure consistency of speed and movement patterns during the captured trials. Participants first performed the walking trials. Depending upon their level of comfort and fatigue they were then 1-2 minutes of rest and next performed the jogging trials. A walking or jogging trial was considered successful if the foot of the test limb contacted a force platform with
no apparent change in gait pattern (e.g. shortening or lengthening their stride to deliberately attempt to contact the force platform), had no overlapping of foot contact with adjacent force plates, and had no apparent scuffing/dragging of the feet on the floor. During data processing, all data and trials were quality checked to ensure accurate labeling of the markers, appropriate contact with the force plates was made, and no obvious signs of data artifacts present. Three to 5 representative trials of both the walking and the jogging tasks were averaged for statistical analysis. During the walking and jogging trials if the participants reported pain the location was recorded.

The variables of interest during the walking and jogging tasks included the initial peak external knee adduction and initial peak external knee abduction moments during the stance phases of both walking and jogging. These were extracted during the first 60% of the stance phases of the tasks. Sixty percent of the stance phase was chosen to ensure the initial peaks were selected and this time frame represents the weight acceptance and midstance phases of gait as used in previous studies.\textsuperscript{19-21} The walking and jogging trials were analyzed separately. Averages of the peak knee adduction moment and peak knee abduction moments from the trials of both walking and jogging were used in the analysis. Negative values represented external knee adduction moments and positive values represented external knee abduction moments.

**2.2.7 Data Analysis**

Based on early study in healthy adults evaluating the relationship between static standing frontal plane knee alignment and peak knee adduction moments it was estimated
that at least 11 participants would be required in each group to achieve 80% power. Variables of interest were checked for normal distribution using the Shapiro-Wilk test and histograms. Parametric or non-parametric tests were utilized depending upon the tests of normality. Paired t-tests and Wilcoxon Signed Rank tests were used to compare participant characteristics between groups depending upon whether the data was normally distributed or not. McNemar tests were utilized to evaluate differences in frequency for the Tanner stage, sex variables, and classification of either static knee adduction or abduction alignment between groups.

To test the first hypothesis that OB youth would demonstrate increased standing knee abduction alignment (UMB and 3D measurements) compared to HW youth, paired t-tests were used. To test the second hypothesis that the measures of static standing frontal plane knee alignment would correlate with each other, Spearman’s rank correlation coefficients were used. To test the third hypothesis that OB youth would have less peak knee adduction moments and greater peak knee abduction moments during walking and jogging compared to HW youth, Multiple Analysis of Covariance (MANCOVA) was performed. The variables of walking and jogging velocities, age, and gender were used as covariates. Finally to test the fourth hypothesis that the UMB and 3D measures of alignment would correlate with peak frontal plane knee moments during walking and jogging, Spearman’s rank correlation coefficients were used. Significance was set at p<0.05 for participant characteristics. To correct for multiple comparisons regarding the variables of interest Bonferroni corrections were performed. Besides the
power analysis, all other statistical analysis was performed with IBM SPSS Statistics Version 21 (SPSS Inc, Chicago, IL, USA).

2.3 Results

Characteristics of age, pubertal status, and sex distribution were not different between groups. (Table 2.1) Results partially supported our first hypothesis that the OB youth demonstrated increased knee abduction position in standing when utilizing the 3D measure compared to the HW youth (p=0.023) (Table 2.2). However, the UMB measurement did not differ between groups (p=0.125). There was no difference in the frequency of participants classified as being in static knee adduction or abduction alignment. Nineteen OB and 20 HW weight participants were classified in knee adduction alignment using the UMB measurement (p=1.00) and 4 OB and 9 HW participants classified in knee adduction using the 3D measure (p=0.267). Results supported the second hypothesis demonstrating a moderate positive correlation between the UMB measurement and the 3D measurement in the OB group (\(\rho=0.539; p=0.014\)). No correlation was present in the HW group (\(\rho=0.196; p=0.407\)). Results partially supported the third hypothesis as results from the MANCOVA demonstrated less peak external knee adduction moments in the OB group compared to the HW group during walking (p=0.003) (Table 2.3) (Figure 2.3). There was no significant difference external knee adduction moments during jogging in the OB group (p=0.072) (Table 2.3) (Figure 2.4). Results did not support the fourth hypothesis as there was no correlation between frontal plane knee alignment and peak knee adduction or abduction moments during
walking (Table 2.4) or jogging (Table 2.5) in the OB group. However, there was a moderate positive correlation in the HW group between the 3D measure and peak knee adduction moments during walking (\(\rho=0.583; p=0.007\)) (Table 2.4).
Table 2.1 Subject Characteristics for the Obese and Healthy Weight Groups

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Obese</th>
<th>Healthy Weight</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>14.05(2.09)</td>
<td>14.10(2.02)</td>
<td>.33</td>
</tr>
<tr>
<td>Gender (female/male)</td>
<td>7/13</td>
<td>7/13</td>
<td>1.00</td>
</tr>
<tr>
<td>Tanner Stage (I/II/III/IV/V)</td>
<td>2/2/3/4/6†</td>
<td>2/4/1/10/3</td>
<td>.24</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.65(.10)</td>
<td>1.67(.11)</td>
<td>.56</td>
</tr>
<tr>
<td>Weight (kg)*</td>
<td>79.69(12.87)</td>
<td>58.00(12.59)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>BMI percentile*</td>
<td>96.75(.91)</td>
<td>56.45(22.24)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>BMI-Z score*</td>
<td>1.92(.15)</td>
<td>.19(.64)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

*mean(SD)
*significance p<0.05
†Data for 17 subjects available for the OB group. These 17 subjects were evaluated with their respective match in the HW group.

Table 2.2 Comparison of Static Knee Frontal Plane Angle Measurements Between Obese and Healthy Weight Youth

<table>
<thead>
<tr>
<th></th>
<th>Obese</th>
<th>Healthy Weight</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>UMB†</td>
<td>-7.85(5.08)</td>
<td>-10.05(2.54)</td>
<td>0.125</td>
</tr>
<tr>
<td>3D‡</td>
<td>3.72(3.44)</td>
<td>0.82(2.67)</td>
<td>0.023*</td>
</tr>
</tbody>
</table>

Mean(SD)
†Wilcoxon Signed Rank test
‡Paired t-tests
*Significance: p<0.025 (Bonferonni correction)
Table 2.3 Comparison of Peak External Frontal Plane Knee Moments During Walking and Jogging Between Obese and Healthy Weight Youth using Multiple Analysis of Covariance

<table>
<thead>
<tr>
<th>Task</th>
<th>Obese</th>
<th>Healthy Weight</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adduction Moment</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Walking</td>
<td>-0.202[-0.230 to -0.174]</td>
<td>-0.264[-0.292 to -0.236]</td>
<td>0.003*</td>
</tr>
<tr>
<td>Abduction Moment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Walking</td>
<td>0.079[0.065 to 0.093]</td>
<td>0.062[0.048 to 0.076]</td>
<td>0.098</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Task</th>
<th>Obese</th>
<th>Healthy Weight</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adduction Moment</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jogging</td>
<td>-0.281[-0.337 to -0.225]</td>
<td>-0.345[-0.401 to -0.288]</td>
<td>0.072</td>
</tr>
<tr>
<td>Abduction Moment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jogging</td>
<td>0.099[0.070 to 0.128]</td>
<td>0.06[0.031 to 0.089]</td>
<td>0.121</td>
</tr>
</tbody>
</table>

Adjusted Mean [95% CI]
Covariates: walking/jogging speed, age, gender
*Significance: p < 0.025 (Bonferonni correction)
No homogeneity of regression
Positive values are external knee abduction moments and negative values are external knee adduction moments

Table 2.4 Correlation between Static Standing Frontal Plane Knee Measurements and Peak Frontal Plane Knee Moments During Walking in Obese and Healthy Weight Youth

<table>
<thead>
<tr>
<th>Umbilicus Measurement</th>
<th>Moments</th>
<th>Obese</th>
<th>Healthy Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adduction</td>
<td>$\rho$=0.138; p=0.562</td>
<td>$\rho$=0.334; p=0.151</td>
<td></td>
</tr>
<tr>
<td>Abduction</td>
<td>$\rho$=0.184; p=0.436</td>
<td>$\rho$=-0.012 ; p=0.961</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>3D Measurement</th>
<th>Moments</th>
<th>Obese</th>
<th>Healthy Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adduction</td>
<td>$\rho$=0.337; p=0.146</td>
<td>$\rho$=0.583; p=0.007*</td>
<td></td>
</tr>
<tr>
<td>Abduction</td>
<td>$\rho$=0.195; p=0.409</td>
<td>$\rho$=0.430; p=0.058</td>
<td></td>
</tr>
</tbody>
</table>

*Significance: p < 0.013 (Bonferonni correction)
Table 2.5 Correlation between Static Standing Frontal Plane Knee Measurements and Peak Frontal Plane Knee Moments During Jogging in Obese and Healthy Weight Youth

<table>
<thead>
<tr>
<th>Umbilicus Measurement</th>
<th>Moments</th>
<th>Obese</th>
<th>Healthy Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adduction</td>
<td>$\rho = 0.077$; $p = 0.747$</td>
<td>$\rho = 0.086$; $p = 0.718$</td>
</tr>
<tr>
<td></td>
<td>Abduction</td>
<td>$\rho = 0.008$; $p = 0.972$</td>
<td>$\rho = 0.203$; $p = 0.392$</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>3D Measurement</th>
<th>Moments</th>
<th>Obese</th>
<th>Healthy Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adduction</td>
<td>$\rho = 0.132$; $p = 0.578$</td>
<td>$\rho = 0.078$; $p = 0.743$</td>
</tr>
<tr>
<td></td>
<td>Abduction</td>
<td>$\rho = 0.039$; $p = 0.870$</td>
<td>$\rho = -0.039$; $p = 0.870$</td>
</tr>
</tbody>
</table>

*Significance: $p < 0.013$ (Bonferroni correction)
Figure 2.3 Frontal Plane Joint Knee Joint Moments During the Stance Phase of Walking for Obese and Healthy Weight Youth. Negative values are external adduction moments and positive values are external abduction moments. The solid line is the unadjusted mean and shaded areas the standard deviation. The tick marks depict the peak adduction and peak abduction moments.
Figure 2.4 Frontal Plane Joint Knee Joint Moments During the Stance Phase of Jogging for Obese and Healthy Weight Youth. Negative values are external adduction moments and positive values are external abduction moments. The solid line is the unadjusted mean and shaded areas the standard deviation. The tick marks depict the peak adduction and peak abduction moments.
2.4 Discussion

The purpose of this study was to evaluate static standing frontal plane knee alignment and determine its correlation to frontal plane knee joint loading in OB youth. Overall, results from the study demonstrate that the UMB measurement correlates with 3D measures of static standing frontal plane knee alignment in OB youth but not HW youth. However, neither the UMB nor 3D measure correlate with peak frontal plane knee moments during walking and jogging in OB participants. Whereas, in the HW group, there is a moderate positive correlation between the 3D measure and peak knee adduction moments during walking. The hypothesis that OB youth would demonstrate less peak knee adduction moments compared to HW youth during walking was supported however the OB youth did not exhibit greater peak knee abduction moments than the HW youth as anticipated during walking or jogging.

2.4.1 Static Frontal Plane Knee Alignment

Relative positions of the hip, knee, and ankle will alter the compartmental load distribution of the knee. In the “neutrally” (0º) aligned knee [not adducted (varus), <0º or abducted (valgus), >0º], the medial compartment bears approximately 60-70% of the load in weight bearing. In an adducted (varus) aligned knee the mechanical axis passes farther medial to the knee and increases compressive forces across the medial compartment whereas in an abducted (valgus) aligned knee the mechanical load bearing axis passes more lateral to the knee and increases compressive forces in the lateral compartment. Measures of static standing frontal plane knee alignment attempt
to infer frontal plane loading patterns and extrapolate them to dynamic movement.\textsuperscript{11,42}

In OB youth we have demonstrated that the UMB measure moderately correlates to the 3D measure of static standing frontal plane knee alignment. However, this relationship is not present in the HW youth. The increased soft tissue of the legs in the OB group may account for some of this difference. The lack of excessive soft tissue in the HW group may limit the value of the UMB measurement technique in non-obese youth. Ultimately, the UMB measurement may not be an appropriate measurement technique of static frontal plane knee angles in non-obese youth.

In addition, the results from the UMB measure may not represent the true angle of the weight bearing mechanical axis of the knee. As noted by Gibson et al,\textsuperscript{14} a medial shift will result in the proximal landmark when utilizing the umbilicus compared to the center of the hip joint. Therefore, the femoral axis created when using the umbilicus will be more medially aligned than when using the center of the hip joint as the proximal landmark. This medial shift is inherent when using the UMB measurement and will cause a subsequent varus overestimation of the frontal plane alignment compared to when using the center of the hip joint. Therefore using the raw UMB measures will not represent the “true” weight bearing mechanical axis of the knee, but a relative one. Gibson et al\textsuperscript{14} generated a preliminary regression equation which may be used to predict the radiographic value of the frontal plane knee alignment $[0.746 \times \text{UMB measurement} + 5.22]$. This equation was modified to reflect the negative value denoting adduction in this study. Thus, a negative result using the aforementioned equation would indicate adduction alignment of the knee. If the mean values from this study are corrected based
on the above equation mean knee alignment of both the OB and HW youth would
demonstrate a more “neutral” alignment [-.64° (adduction) and -2.27° (adduction) respectively]. Our results still however, demonstrate a moderate correlation in OB youth between the UMB measure and the 3D measure which uses the hip joint center as the proximal landmark. Further, correction with above equation would not change the correlation results between the UMB measure and frontal plane knee joint loading patterns.

2.4.2 Static Frontal Plane Knee Alignment and Peak Frontal Plane Knee Moments

One of the goals of using static joint and body region alignment is to infer movement and joint loading patterns during dynamic activity. In healthy adults, measures of frontal plane knee alignment, using full-length radiographs or an inclinometer, have been shown to predict frontal plane external knee adduction moments ($r^2=0.48-0.53$) during walking. However, the relationship between static frontal plane knee alignment and frontal plane knee joint loading patterns in OB youth has not been reported. Our results do not demonstrate a relationship between measures of static frontal plane knee alignment and frontal plane loading patterns in OB youth.

However, compensatory movement patterns during activity may confounding the utility of static measures and limit their interpretation related to joint loading patterns during dynamic activity. More specifically, movement patterns such as increased toe-out, trunk lean, and pelvic drop may alter knee joint loading patterns that static standing alignment measures cannot identify. Muscle weakness that has previously been
reported in OB youth,\textsuperscript{48-50} may also be a factor related to movement and joint loading patterns. For example, decreased hip abductor strength is speculated to influence external knee adduction moments secondary to decreased pelvic control.\textsuperscript{51,52} Hip strength would not necessarily be a part of the assessment of static standing alignment. However, measuring these different factors was not part of the scope or purpose of this study, but should be evaluated in future studies.

2.4.3 External Knee Adduction Moments

Understanding, altered frontal plane knee loading patterns is important in potentially identifying and mitigating detrimental mechanical stress on cartilage and other soft-tissue of the knee which may increase the risk of pain and joint damage. Our results support the results of McMillan et al.\textsuperscript{19,20} who also demonstrated decreased peak external knee adduction moments during walking in OB youth compared to HW youth. However, other reports by Gushue et al.\textsuperscript{21} and Shultz et al.\textsuperscript{22} showed increased non-normalized external peak knee adduction moments in obese children but no difference when normalized.\textsuperscript{21} Although no participants (OB or HW) in our study reported knee pain, OB youth are at a potentially greater risk of knee pain and poor knee joint health and damage secondary to increased BMI.\textsuperscript{1,2,10,16,53} Notably, Widhalm et al.\textsuperscript{10} evaluated the knees of 20 morbidly OB youth (mean age 14.2 years) with complaints of knee pain and demonstrated articular cartilage lesions in 100% of the knees examined [medial (n=23), lateral (n=14), and patellofemoral (n=19)]. Locations of the cartilage lesions were not correlated to complaints of knee pain, joint alignment, or loading patterns. This study did
not have a control group to compare results thus comparisons to either non-morbidly OB or HW youth cannot be made. Further research is necessary to further elucidate this alternate loading pattern noted in OB youth compared to HW youth and its potential consequences.

2.4.4 Limitations

There are several limitations to this study. Our results are limited to a relatively small and homogenous group which may limit the generalizability of the results. Thus, our results may not be generalizable to morbidly OB youth who may have different alignment and loading patterns secondary to increased mass. A limitation relative to the UMB measurement identified by Gibson et al.\textsuperscript{14} is the utility of using the umbilicus as the proximal landmark for the static measurement. A larger abdominal region in OB youth may cause the umbilicus to drop inferiorly and potentially alter the measurement and contribute to the varus angle overestimation. However, no significant correlation has been shown between the error of the UMB measurement and BMI whereas other methods of static frontal plane knee measurement angle (e.g. ASIS) have shown significant correlations between error and BMI.\textsuperscript{14}

Additionally, during the 3-dimensional motion analysis the trials of walking and jogging of several participants were captured at a different sampling rate from the rest of the participants. However, we assessed for variances in regards to the different sampling frequencies of the kinematic data and determined it to be minimal and within the standard error of the measurement. Finally, with any 3-dimensional motion capture measurement
system there is the potential of error introduced by the increased soft tissue of the OB participants and marker placement error. Similar to other studies using 3-dimensional motion capture in OB youth and adhering to recommended methods\textsuperscript{19-22,27,54} we attempted to limit potential effects of excessive soft tissue movement and error by using a redundant marker set, placing additional markers over the iliac crests of the pelvis, utilizing a functional hip joint center, and having the same individual place the reflective markers on each participant.

2.4.5 Implications for Future Research and Clinical Practice

Characterizing the influence of altered knee joint loading patterns on physical function in OB youth is important in the promotion of physical activity. Future research should evaluate other factors that may impact frontal plane knee joint movement and loading patterns (e.g. lower extremity muscle strength, trunk lean, or pelvic drop, etc.). Evaluating movement patterns at proximal and distal joints to the knee may identify other compensatory strategies during walking and running which may place the knee and/or other joints at risk. Further, in order to protect the long-term health and function of the knee joint, characterizing the influence of knee joint loading patterns and mechanisms for the potential development of articular cartilage defects in OB is necessary.

2.4.6 Conclusion

OB youth demonstrated decreased peak knee adduction moments during walking but not jogging compared to HW youth. The UMB measurement of frontal plane knee
alignment moderately correlated with the 3D measure of standing knee position in OB youth. However, neither measure correlated with frontal plane knee joint loading patterns. Thus, neither the UMB measure nor 3D measure should be used to infer frontal plane knee joint loading patterns in OB. A better understanding of other mechanisms related to frontal plane knee joint loading in OB youth is necessary.

2.5 Acknowledgements:

We would like to thank the following individuals and organizations for their assistance with this project:

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2) Mike McNally MS and Louise Thoma DPT for assistance with data collection.

3) Katie Winters and Sarah Harwell for assistance with data processing.

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2.6 References


51. Bennell KL, Hunt MA, Wrigley TV, Hunter DJ, Hinman RS. The effects of hip muscle strengthening on knee load, pain, and function in people with knee


3.1 Introduction

Health related quality of life (HRQoL) in obese (OB) children and adolescents is consistently lower than that of their healthy weight counterparts. HRQoL is a measure of overall function and well-being and is often used to characterize disease burden as it relates to an individual’s global health. The World Health Organization defines HRQoL as a multidimensional self-perception and awareness of an individual’s well-being comprised of physical, psychological, and social dimensions. However, identifying specific interventions aimed at improving HRQoL in obese youth is hampered by a limited understanding of factors which may interact with obesity and also contribute to poor HRQoL.

Lower extremity (LE) function has also been shown to correlate with HRQoL in obese adults. In turn, LE function and performance may influence HRQoL in obese youth. Obese youth demonstrate poorer performance on measures of LE gross motor skills, jumping tasks, and dynamic balance skills. Performance of these functional skills is fundamental during participation in higher level physical activities, play, and sport in youth. Poorer LE functional performance may lead to decreased levels of...
physical activity. Obese youth with lower levels of physical activity have been shown to have decreased HRQoL compared to obese youth with higher levels of physical activity.\textsuperscript{14} As such deficiencies in functional performance may significantly contribute to the decreased self-efficacy and HRQoL that is well documented in obese youth.\textsuperscript{1-4} However, the relationship between LE functional performance and HRQoL in obese youth is unknown. Understanding this relationship is important as poor LE function and HRQoL in obese children may perpetuate a vicious cycle of persistent obesity and increased disability in obese adults.\textsuperscript{15-17}

Decreased muscle strength in obese adults has been suggested to be potentially independent of decreased physical activity\textsuperscript{18} however deficits in LE muscle strength in obese youth may directly impact their ability to perform and participate in higher-level physical activities. Substantial evidence demonstrates altered metabolism in skeletal muscle in severely obese adults.\textsuperscript{19-23} Increased intramuscular fat has also been shown to exist in obese adults versus non-obese adults and has been associated with decreased muscle strength and function.\textsuperscript{24} Further, decreased LE strength has been shown to be associated with impaired LE function in obese adult populations.\textsuperscript{25-27} However, the understanding of LE muscle strength in obese youth compared to health weight youth is conflicting and limited.\textsuperscript{28-31} The relationship between LE muscle strength and LE functional performance has not been explored in obese youth. Identifying factors influencing LE functional performance in obese youth could provide valuable information regarding intervention options promoting physical function and activity.
The goals of this study were to: 1) compare LE muscle strength, LE functional performance scores, and HRQoL between obese and healthy weight youth, 2) evaluate the contribution of LE muscle strength to LE functional performance in obese youth, and 3) evaluate the contribution of LE functional performance to HRQoL in obese youth. Our a-priori hypotheses were 1) obese youth will generate less LE muscle strength, have poorer scores on measures of LE functional performance, and reduced HRQoL than healthy weight youth, 2) LE muscle strength will predict LE functional performance in obese youth, and 3) LE functional performance scores will predict physical and psychosocial HRQoL in obese youth.

3.2 Materials/Subjects and Methods

Two groups of participants (total n = 40), ages 11-18 were recruited: 20 Obese (OB) and 20 Healthy Weight (HW). OB participants were recruited from potential patients referred to a pediatric medical weight management program at a tertiary pediatric hospital, pediatric ambulatory clinics, and other local community pediatric clinics. Potential HW participants were recruited from local community pediatric clinics and via flyer postings. HW participants were matched to OB participants based on age and sex. OB was defined as BMI being greater than or equal to the 95th percentile and less than the 99th percentile. HW was defined BMI greater than the 5th percentile but less than the 85th percentile for BMI.\textsuperscript{32-34}
3.2.1 Exclusion Criteria

Potential participants with a history of or currently having any developmental (delayed walking, developmental coordination disorder, developmental delay, Down syndrome, muscular dystrophy, autism), neurological (e.g. cerebral palsy, nerve injury), or orthopedic (e.g. slipped capital femoral epiphysis, fracture, etc.) conditions that would impact their gait or ability to jump were excluded from the study. Potential participants with a genetic predisposition to obesity (e.g. Prader-Willi syndrome) or who were taking any medications that might impact muscle function or for pain/inflammation were also excluded due to the potential to confound study findings. Children with a BMI > 99th percentile (morbidly/severely obese) were excluded as potential interventions for those who are obese (e.g. dietary counseling, behavioral counseling, increasing physical activity, specific exercise interventions, etc.) versus morbidly/severely obese (e.g. pharmacological intervention, bariatric surgery, etc.) may differ depending on obesity severity and presence of co-morbidities. Further morbid/severe obesity, compared to obese, is associated with a greater prevalence and severity of co-morbidities (e.g. metabolic syndrome, insulin resistance, etc.) which have also been shown to affect the variables of interest (e.g. physical function and HRQoL). Excluding those who were morbidly/severely obese would limit the potential interaction of these co-morbidities with the variables of interest in this study. Overweight children (BMI 85-94th percentile) and underweight children (BMI <5th percentile) were also excluded, as the focus of the current study was to compare children and adolescents of healthy weight (BMI <85th percentile) and those who were obese (BMI >95th percentile).
3.2.2 Data Collection and Procedures

Informed assent and consent were obtained from participating subjects and their parents/legal-guardians, respectively. Participant’s height and weight were measured on a standard physician’s combined stadiometer and weight beam scale (Detecto-Medic; Webb City, MO, USA) and recorded based on the National Health and Nutrition Examination Survey protocol.\(^{41}\) BMI was calculated from subject’s height and weight and sex and age adjusted BMI-Z scores were generated from an online calculator utilizing the Center for Disease Control and Prevention 2000 data.\(^{33,42}\) The tested limb for all activities was determined to be the limb the participants reported they would use to kick a soccer ball as far as possible.\(^{43,44}\)

3.2.3 Body Composition Measurements

Total body, regional lean, fat, and bone mass were all assessed using a Lunar dual-energy x-ray absorptiometry (iDXA) (GE Healthcare, Madison WI, USA). All scans, participant positioning and region of interest landmarks followed manufacturer's protocol. To maintain consistency, the same investigator performed all the scans and analyses on all subjects. Raw data from the region of interest software were exported from the iDXA database and body composition variables of body fat (kg) and lean mass (kg) were calculated for statistical analysis. Eighteen subject pairs (n = 36) received the iDXA scans as the iDXA was not available for the first two subject pairs.
3.2.1 Lower Extremity Strength

Knee extension (KE), knee flexion (KF), hip abduction (HA), and hip extension (HE) muscle strength were evaluated using a Biodex System III dynamometer (Biodex Medical Systems, Inc. Shirley, New York, USA) on each subject’s tested limb. KE and KF muscle strength were evaluated during an isokinetic protocol (2 sets of 10 maximal contractions at an angular velocity of 150 °/s) (Figure 3.1A). Thirty seconds rest time was allotted in between each set. HA and HE muscle strength were evaluated with an isometric protocol (5 seconds for 5 repetitions) (Figures 3.1B and 3.1C). Verbal and visual feedback were provided during all strength testing to encourage maximum effort.
Muscle strength was defined as the peak torque generated during each of the above tasks. Peak torque data were recorded as absolute values (Nm) then normalized to leg lean mass (Nm/kg) based on results from the iDXA scan. Normalizing to leg lean mass allowed for comparison of torque output per unit of functional generating lean mass rather than per unit of total body mass. Normalizing by total body mass would include non-torque generating tissue such as body fat and potentially inflate any potential difference between the OB and HW groups. Rolland et al. performed similar normalization procedures when evaluating KE strength in elderly OB females. The normalized average peak torque for each muscle tested was used in the data analysis.
3.2.5 Lower Extremity Functional Performance Tasks

Participants performed two tasks to evaluate their LE functional performance: 1) single leg hop (SLHop) for distance (figure 1) and 2) single leg balance anterior reach (SLBAR) for distance (figure 2). The SLHop and SLBAR were specifically chosen as they 1) require skills previously shown to be deficient in OB youth compared to HW youth (e.g. LE gross motor ability\textsuperscript{10}, jumping\textsuperscript{11}, and dynamic balance\textsuperscript{12,13}), 2) have good reliability\textsuperscript{49} and are easily performed in a clinical setting, and 3) require fundamental movement skills that are also required during physical education, sport, and play.

Adequate LE strength and power are thought to be needed to appropriately perform the SLHop\textsuperscript{50-53} whereas adequate LE strength, dynamic balance and neuromuscular control are thought to be needed to appropriately perform the SLBAR.\textsuperscript{54-56}

For the SLHop (figure 3.2), participants were instructed to stand on their test limb and hop as far forward as they could and land on their test limb. For a trial to be considered successful, the participants were required to maintain balance after landing for 3 seconds without touching the ground with the contralateral foot. The distance (cm) from the heel at the start of the hop to the ipsilateral heel after landing was measured and recorded.
Figure 3.2 Single Leg Hop for distance: A) Starting Position and B) Landing Position. The distance hopped was measured (cm) from heel to heel of the stance foot.

For the SLBAR (figure 3), participants were instructed to stand on their test limb, cross their arms across their chest and maintain their balance. With the distal most aspect of their contralateral foot, participants then made an effort to reach as far as possible along a tape measure by bending their stance limb hip, knee, and ankle while maintaining their stance limb heel on the ground. They then lightly touched their contralateral foot to the floor and returned to the start position. For a trial to be considered successful, participants were required to keep their stance limb heel on the ground, keep their arms across their chest, and not use their contralateral LE for balance or support during the entirety of the task. The distance (cm) reached with the contralateral foot was measured and recorded.
Figure 3.3 Single Leg Balance Anterior Reach: Starting position; B) Reaching position; and C) Finish position. The reach distance was measured (cm) from the toe of the stance foot to the toe of the reaching foot.

For both tasks, participants were given the opportunity to practice each task up to 6 times until: 1) they felt comfortable with the task, 2) performed the task appropriately based on instructions, and 3) demonstrated consistent performance. Following practice, participants performed each task 3 times for measurement beginning with the SLHop and then the SLBAR. Subjects were given the opportunity to rest between each trial and task to minimize the potential of fatigue. Participants were instructed to report if they experienced any pain or discomfort during performance of the tasks. If pain or discomfort was reported the location was recorded. For each task, measures were normalized to each participant’s leg length for comparison. The average of the 3 trials for each task was used in the analysis.
3.2.6 Health Related Quality of Life

The Pediatric Quality of Life Inventory 4.0 Generic Scales (PedsQL) assessed self-reported HRQoL. The PedsQL is a valid measure of physical health and psychosocial health in many groups of children [ages 2-18] including those with chronic disease and who are obese. The 23-item questionnaire assesses physical, emotional, social, and school functioning from which physical health and psychosocial health summary scores are derived. The PedsQL physical health summary score (PedsQL-physical), PedsQL psychosocial health summary score (PedsQL-psychosocial) from each participant were recorded. The items for each subscale are reversed scored and transformed to a 0-100 point scale with higher scores indicating better HRQoL. The minimal clinically important differences of the PedsQL physical and psychosocial scores are 6.67 and 5.30 respectively. The mean of the transformed scores for both of the subscales for each group were used in the analysis.

3.2.7 Physical Maturity

Sexual maturity affects the developing musculoskeletal system and OB children and adolescents have advanced maturity compared to HW children and adolescents. To assess maturation, participants completed a self-report Tanner Stage questionnaire. Females rated their breast and pubic hair development and males rated their pubic hair and genital development using schematics of the 5 Tanner stages. Seventeen of the 20 OB subjects and 20 of the 20 HW subjects agreed to fill out the self-reported Tanner Stage questionnaire and were included in the pair-wise data analysis.
3.2.8 Physical Activity

The Physical Activity Questionnaire (PAQ) was used to evaluate physical activity level as physical activity level has been shown to be lower in OB youth compared to HW youth and thus may impact results related to the variables of interest.\textsuperscript{68,69} The PAQ is a valid and reliable measure of physical activity for older children (PAQ-C) [ages 8-14]\textsuperscript{70} and adolescents (PAQ-A) [ages 14-20]\textsuperscript{70} who are currently enrolled in school. Both PAQ-C/A are self-reports based on the last 7 days to assess general physical activity.\textsuperscript{70} There are 8 items on the questionnaire that are rated 1 to 5 with a higher score indicating greater physical activity. Responses on the PAQ-C/A are tabulated in a single physical activity score by taking the mean score of the 8 items.\textsuperscript{70} This score was used in the data analysis.\textsuperscript{70}

3.2.9 Data Analysis

Based on previous HRQoL data, an a-priori power analysis determined that at least 17 subjects in each group would be needed in order to achieve 80\% power.\textsuperscript{4,71} Power analysis and effect sizes were calculated with the statistical calculator G*Power.\textsuperscript{72} Tests for normality were performed on all variables and model residuals. Paired t-tests were used to compare participant characteristics between groups. Because the OB and HW groups were matched pairs, McNemar tests were utilized to evaluate differences in frequency for the Tanner stage and sex variables. To test the hypothesis that OB youth would demonstrate poorer LE muscle strength, LE functional performance, and HRQoL
than HW youth paired t-tests and Wilcoxon Signed Rank tests were used and effect sizes were calculated to evaluate the magnitude of difference between the OB and HW groups [small (.20), medium (.50), and large (.80)].

To test the second and third hypotheses that LE strength would predict LE functional performance and that LE functional performance would predict HRQoL in OB youth, respectively, separate multiple regressions were performed for the OB and then HW groups. Initially, the independent variables of age, sex, and physical activity score were entered into the regression models to evaluate for a relationships with dependent variables. If a relationship was present, then these variables would be included in the final regression models. If no relationship was present, then these variables would be excluded from the final regression analysis. Tests for multicollinearity among the variables were also performed. For the regression analysis associated with the second hypothesis the dependent variables included SLHop and SLBAR. For each dependent variable (SLHop and SLBAR), the independent variables (KE, KF, HA, HE) were entered in the model together. For the regression analysis associated with the third hypothesis the dependent variables included the PedsQL-psychosocial and PedsQL-physical. For each dependent variable (PedsQL-physical and psychosocial) the independent variables (SLHop and SLBAR) were entered into the model together.

Significance was set at $p \leq .05$ for participant characteristics and regression results. Bonferroni corrections were performed to correct for multiple comparisons on the PedsQL subscales, measures of LE muscle strength, and measures of LE functional
performance. Statistical analysis was performed with IBM SPSS Statistics Version 21 (SPSS Inc, Chicago, IL, USA).

3.3 Results

As expected based on the matching process, subject characteristics of age, pubertal status, and sex distribution were not different between groups (Table 3.1). There were no differences in physical activity scores (p = .28) between the OB and HW groups (Table 3.1). For body composition the OB group had higher BMI, body fat percentage, total lean mass, and leg lean mass compared to the HW group (p < .001) (Table 3.1). There were no differences in absolute LE muscle strength values, but when these were normalized to LE lean mass the OB group demonstrated lower muscle strength compared to the HW group [significance: p<.013 (KE: p = .032; KF: p = .005; HA: p = .010; HE: p = .031)] (Table 3.2). The OB group demonstrated poorer performance on both the SLHop (p < .001) and SLBAR tasks (p = .007) [significance: p<.025 (Table 3.3). Neither the OB nor HW participants reported pain during the SLHop or SLBAR tasks. The OB group reported worse PedsQL-physical scores (p = .02) when compared to the HW group but no difference was noted with PedsQL- psychosocial health scores between groups (p = .07) [significance: p<.025] (Table 3.4).
Table 3.1 Subject Characteristics for the Obese and Healthy Weight Groups

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Obese</th>
<th>Healthy Weight</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>14.05(2.09)</td>
<td>14.10(2.02)</td>
<td>.33</td>
</tr>
<tr>
<td>Gender (female/male)</td>
<td>7/13</td>
<td>7/13</td>
<td>1.00</td>
</tr>
<tr>
<td>Tanner Stage (I/II/III/IV/V)</td>
<td>2/2/3/4/6†</td>
<td>2/4/1/10/3</td>
<td>.24</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.65(1.0)</td>
<td>1.67(1.1)</td>
<td>.56</td>
</tr>
<tr>
<td>Weight (kg)*</td>
<td>79.69(12.87)</td>
<td>58.00(12.59)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Physical Activity Questionnaire score</td>
<td>2.38(.64)</td>
<td>2.57(.84)</td>
<td>.28</td>
</tr>
<tr>
<td>BMI percentile*</td>
<td>96.75(91)</td>
<td>56.45(22.24)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>BMI-Z score*</td>
<td>1.92(.15)</td>
<td>.19(.64)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Body Fat %*‡</td>
<td>36.5(7.3)</td>
<td>21.9(6.7)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Total Lean Mass (kg)* ‡</td>
<td>108.57(24.06)</td>
<td>94.73(26.85)</td>
<td>.007</td>
</tr>
<tr>
<td>Leg Lean Mass (kg)* ‡</td>
<td>20.83(8.01)</td>
<td>17.40(5.67)</td>
<td>.003</td>
</tr>
</tbody>
</table>

*significance p < .05
†Data for 17 subjects available for the OB group. These 17 subjects were evaluated with their respective match in the HW group.
‡18 pairs (n = 36) analyzed secondary to body composition from the iDXA not available for the first two pairs of subjects for the normalization procedure.

Table 3.2 Absolute and Normalized Peak Torque of the Tested Lower Extremity for the Obese and Healthy Weight Groups

<table>
<thead>
<tr>
<th>Strength Measure</th>
<th>Obese</th>
<th>Healthy Weight</th>
<th>Mean Difference</th>
<th>Effect Size‡</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>KE strength</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absolute Torque</td>
<td>119.53(34.51)</td>
<td>112.71(44.25)</td>
<td>6.82</td>
<td>.17</td>
<td>.432</td>
</tr>
<tr>
<td>Torque/LE lean mass (Nm/kg)†</td>
<td>5.76(65)</td>
<td>6.41(87)</td>
<td>.65</td>
<td>.55</td>
<td>.003</td>
</tr>
<tr>
<td>KF strength</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absolute Torque</td>
<td>65.03(26.31)</td>
<td>64.61(23.47)</td>
<td>.42</td>
<td>.017</td>
<td>.935</td>
</tr>
<tr>
<td>Torque/LE lean mass (Nm/kg)*†</td>
<td>3.15(35)</td>
<td>3.75(61)</td>
<td>.6</td>
<td>.75</td>
<td>.005</td>
</tr>
<tr>
<td>HA strength</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absolute Torque</td>
<td>58.74(32.82)</td>
<td>57.63(22.80)</td>
<td>1.11</td>
<td>.038</td>
<td>.826</td>
</tr>
<tr>
<td>Torque/LE lean mass (Nm/kg)*†</td>
<td>2.67(94)</td>
<td>3.33(62)</td>
<td>.66</td>
<td>.69</td>
<td>.010</td>
</tr>
<tr>
<td>HE strength</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absolute Torque</td>
<td>80.75(40.62)</td>
<td>85.09(30.30)</td>
<td>4.34</td>
<td>.12</td>
<td>.626</td>
</tr>
<tr>
<td>Torque/LE lean mass (Nm/kg)†</td>
<td>3.90(1.38)</td>
<td>4.80(93)</td>
<td>.9</td>
<td>.56</td>
<td>.031</td>
</tr>
</tbody>
</table>

mean(SD); KE = Knee Extensor; KF = Knee Flexor; HA = Hip Abduction; HE = Hip Extension
*significance p < .013 (Bonferroni correction)
†18 pairs (n = 36) analyzed secondary to body composition from the iDXA not available for the first two pairs of subjects for the normalization procedure.
‡ (d) Defined as small (.20), medium (.50), and large (.80).
Table 3.3 Comparison of Tested Lower Extremity Functional Performance Between the Obese and Healthy Weight Groups

<table>
<thead>
<tr>
<th>Functional Task</th>
<th>Obese</th>
<th>Healthy Weight</th>
<th>Mean Difference</th>
<th>Effect Size (d) ‡</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLHop for Distance^*</td>
<td>1.17(.33)</td>
<td>1.54(.20)</td>
<td>.37</td>
<td>1.36</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>SLBAR for Distance^*</td>
<td>.57(.05)</td>
<td>.63(.06)</td>
<td>.06</td>
<td>1.16</td>
<td>.007</td>
</tr>
</tbody>
</table>

mean(SD)
*Significance p ≤ .025 (Bonferroni Correction)
^normalized to leg length
‡Defined as small (.20), medium (.50), and large (.80).

Table 3.4 Comparison of Health Related Quality of Life Measures Between the Obese and Healthy Weight Groups

<table>
<thead>
<tr>
<th>PedsQL Subscale</th>
<th>Obese</th>
<th>Health Weight</th>
<th>Mean Difference</th>
<th>Met MCID†</th>
<th>Effect Size (d)‡</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PedsQL-Physical</td>
<td>87.19(10.53)</td>
<td>92.97(9.17)</td>
<td>5.78</td>
<td>No</td>
<td>.59</td>
<td>.020*</td>
</tr>
<tr>
<td>mean(SD) median (range)</td>
<td>90.62[28.12]</td>
<td>95.31[31.25]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PedsQL-Psychosocial</td>
<td>80.74(13.90)</td>
<td>85.67(13.21)</td>
<td>4.93</td>
<td>No</td>
<td>.36</td>
<td>.067</td>
</tr>
<tr>
<td>mean(SD) median (range)</td>
<td>83.33[50.00]</td>
<td>93.33[36.66]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

mean(SD)
Median[range]
*Significance p < .025 (Bonferroni Correction)
†Minimal Clinical Important Difference: PedsQL-Physical (6.67 pts.); PedsQL-Psychosocial (5.30pts.)
‡Defined as small (.20), medium (.50), and large (.80).
For the regression analysis no evidence of multicollinearity was present between the independent variables based on tolerance values and variance inflation factor statistics. No evidence of non-normal residuals was noted for the regression analyses indicating that a linear model was appropriate for the analysis for evaluating the dependent variables in the OB groups. The HW group regression models did not yield a significant relationship between outcome variables and were found to not have approximately normal residuals for the PedsQL scores. The variables of age, sex, and physical activity score were not predictive of SLHop performance, SLBAR performance, PedsQL-psychosocial score, or PedsQL-physical score in either the OB or HW groups and were subsequently excluded from the final regression models (tables 3.5-3.8).

Table 3.5 Regression Analysis for Lower Extremity Peak Torque and Lower Extremity Functional Performance in the Obese Group

<table>
<thead>
<tr>
<th>Dependent Variables</th>
<th>Independent Variables</th>
<th>Unstandardized Coefficients</th>
<th>Standardized Coefficients</th>
<th>t</th>
<th>Var. Sig.</th>
<th>R²</th>
<th>F</th>
<th>Model Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLHop</td>
<td>(Constant)</td>
<td>.526</td>
<td>.628</td>
<td>.837</td>
<td>.42</td>
<td>.556</td>
<td>4.072</td>
<td>.02</td>
</tr>
<tr>
<td>KE</td>
<td>-.086</td>
<td>.115</td>
<td>-.161</td>
<td>-.749</td>
<td>.47</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>KF</td>
<td>.191</td>
<td>.178</td>
<td>.304</td>
<td>1.077</td>
<td>.30</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HA</td>
<td>.214</td>
<td>.099</td>
<td>.581</td>
<td>2.159</td>
<td>.05</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HE</td>
<td>-.003</td>
<td>.061</td>
<td>-.011</td>
<td>-.046</td>
<td>.96</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dependent Variables</th>
<th>Independent Variables</th>
<th>Unstandardized Coefficients</th>
<th>Standardized Coefficients</th>
<th>t</th>
<th>Var. Sig.</th>
<th>R²</th>
<th>F</th>
<th>Model Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLBAR</td>
<td>(Constant)</td>
<td>.450</td>
<td>.144</td>
<td>3.117</td>
<td>.008</td>
<td>.093</td>
<td>.332</td>
<td>.85</td>
</tr>
<tr>
<td>KE</td>
<td>.028</td>
<td>.026</td>
<td>.328</td>
<td>1.067</td>
<td>.30</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>KF</td>
<td>-.011</td>
<td>.041</td>
<td>-.108</td>
<td>-.268</td>
<td>.793</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HA</td>
<td>-.011</td>
<td>.023</td>
<td>-.189</td>
<td>-.492</td>
<td>.631</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HE</td>
<td>.004</td>
<td>.014</td>
<td>.110</td>
<td>.316</td>
<td>.757</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The variables of age, sex, and physical activity score were not predictive of SLHop ($r^2 = .331; F(3,16) = 2.633; p = .09$) or SLBAR ($r^2 = .127; F(3,16) = 779; p = .52$) in the OB group and subsequently excluded from the final regression model.
Table 3.6 Regression Analysis for Lower Extremity Peak Torque and Lower Extremity Functional Performance in the Healthy Weight Group

<table>
<thead>
<tr>
<th>Dependent Variables</th>
<th>Independent Variables</th>
<th>Unstandardized Coefficients</th>
<th>Standardized Coefficients</th>
<th>t</th>
<th>Var. Sig.</th>
<th>R²</th>
<th>F</th>
<th>Model Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(Constant)</td>
<td>-.076</td>
<td>-.279</td>
<td>-2.73</td>
<td>.007</td>
<td>.705</td>
<td>8.966</td>
<td>.001</td>
</tr>
<tr>
<td></td>
<td>KE</td>
<td>.114</td>
<td>.036</td>
<td>.485</td>
<td>3.201</td>
<td>.006</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>KF</td>
<td>.121</td>
<td>.056</td>
<td>.356</td>
<td>2.151</td>
<td>.05</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>HA</td>
<td>.157</td>
<td>.046</td>
<td>.502</td>
<td>3.422</td>
<td>.004</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>HE</td>
<td>-.021</td>
<td>.028</td>
<td>-.118</td>
<td>-.742</td>
<td>.37</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The variables of age, sex, and physical activity score were not predictive of SLHop ($r^2 = .129; F(3,16) = 7.93; p = .01$) or SLBAR ($r^2 = .031; F(3,16) = .169; p = .92$) in the HW group and subsequently excluded from the final regression model.

Table 3.7 Regression Analysis for Lower Extremity Functional Performance and PedsQL Summary Scores in the Obese Group

<table>
<thead>
<tr>
<th>Dependent Variables</th>
<th>Independent Variables</th>
<th>Unstandardized Coefficients</th>
<th>Standardized Coefficients</th>
<th>t</th>
<th>Var. Sig.</th>
<th>R²</th>
<th>F</th>
<th>Model Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(Constant)</td>
<td>.921</td>
<td>.140</td>
<td>6.572</td>
<td>.000</td>
<td>.253</td>
<td>1.273</td>
<td>.32</td>
</tr>
<tr>
<td></td>
<td>KE</td>
<td>-.032</td>
<td>.018</td>
<td>-.428</td>
<td>-1.777</td>
<td>.10</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>KF</td>
<td>-.010</td>
<td>.028</td>
<td>-.092</td>
<td>-.349</td>
<td>.73</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>HA</td>
<td>-.023</td>
<td>.023</td>
<td>-.235</td>
<td>-1.004</td>
<td>.33</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>HE</td>
<td>.005</td>
<td>.014</td>
<td>.097</td>
<td>.383</td>
<td>.71</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The variables of age, sex, and physical activity score were not predictive of PedsQL-Psychosocial ($r^2 = .081; F(3,16) = .467; p = .71$) or PedsQL-Physical ($r^2 = .144; F(3,16) = .899; p = .46$) in the OB group and subsequently excluded from the final regression model.
Table 3.8 Regression Analysis for Lower Extremity Functional Performance and PedsQL Summary Scores in the Healthy Weight Group

<table>
<thead>
<tr>
<th>Dependent Variables</th>
<th>Independent Variables</th>
<th>Unstandardized Coefficients</th>
<th>Standardized Coefficients</th>
<th>t</th>
<th>Var. Sig.</th>
<th>R²</th>
<th>F</th>
<th>Model Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>PedsQL-Psychosocial (Constant)</td>
<td>71.611</td>
<td>50.387</td>
<td>1.421</td>
<td>.17</td>
<td>.007</td>
<td>.062</td>
<td>.94</td>
<td></td>
</tr>
<tr>
<td>SLHop</td>
<td>1.398</td>
<td>17.205</td>
<td>.021</td>
<td>.081</td>
<td>.94</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SLBAR</td>
<td>18.973</td>
<td>54.437</td>
<td>.091</td>
<td>.349</td>
<td>.73</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dependent Variables</th>
<th>Independent Variables</th>
<th>Unstandardized Coefficients</th>
<th>Standardized Coefficients</th>
<th>t</th>
<th>Var. Sig.</th>
<th>R²</th>
<th>F</th>
<th>Model Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>PedsQL-Physical (Constant)</td>
<td>78.955</td>
<td>34.935</td>
<td>2.260</td>
<td>.04</td>
<td>.011</td>
<td>.096</td>
<td>.91</td>
<td></td>
</tr>
<tr>
<td>SLHop</td>
<td>2.398</td>
<td>11.929</td>
<td>.052</td>
<td>.201</td>
<td>.84</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SLBAR</td>
<td>16.458</td>
<td>37.744</td>
<td>.113</td>
<td>.436</td>
<td>.67</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The variables of age, sex, and physical activity score were not predictive PedsQL-Psychosocial: (r² = .065; F(3,16) = .370; p = .78) or PedsQL-Physical: (r² = .179; F(3,16) = 1.160; p = .36) in the HW group and subsequently excluded from the final regression model.

Results partially support the hypothesis that LE muscle strength would predict LE functional performance in OB youth. In the OB group, HA was the only significant predictive variable (p = .05) of SLHop performance when evaluated together with KE, KF, and KE (Table 3.5). This model accounted for approximately 56% of the variance in SLHop performance (Table 3.5). In the HW group, the variables of KE, KF, and HA were all significant (p = .006, .05, and .004 respectively) and accounted for approximately 70% of the variance in SLHop performance (Table 3.6). LE muscle strength was not predictive of SLBAR performance in either group (Tables 3.5 and 3.6).

Finally, results also partially support the hypothesis that LE function would predict HRQoL in OB youth. In OB youth, both SLHop (p< .001) and SLBAR (p=.002) predicted PedsQL-physical health scores explaining approximately 48% of the variance to this subscale (Table 3.7). However, these tests were not predictive of PedsQL-
psychosocial health in the OB group (SLHop: p = .12 and SLBAR: p= .13) (Table 3.8).

Further, in the HW group, neither SLHop nor SLBAR were predictive of PedsQL-physical (SLHop: p=.84 and SLBAR: p= .67) or psychosocial scores (SLHop: p=.94 and SLBAR: p=.73) (Table 3.8).

3.4 Discussion

This study adds to the limited evidence regarding LE strength in OB youth and supports the hypothesis that OB youth have impaired muscle force generating capabilities compared to HW youth when normalized to lean mass. Our study supports previous findings that OB youth have worse LE function (in particular hopping performance),\textsuperscript{10,11} and lower HRQoL compared to HW youth.\textsuperscript{1-4,12,76,77} HA strength seems to provide the most significant contribution to performance on the SLHop task in the OB group whereas the HW group seems to adopt a more global strategy of muscle strength contribution to SLHop performance. Performance on both SLHop and SLBAR tasks contribute to the PedsQL-physical health score in the OB group however neither were significant in the HW group. To our knowledge, this is the first study demonstrating how LE strength may contribute to LE functional performance and how LE functional performance outcomes influence HRQoL in OB children.
3.4.1 Lower Extremity Strength

There is conflicting evidence regarding objectively measured LE strength in OB youth.\textsuperscript{28-31} Related to the LE, only KE strength has been previously reported in OB youth.\textsuperscript{18,28-31} Different methods of normalization make comparison and conclusions difficult between our results and previous studies.\textsuperscript{28-31} OB and adolescents have demonstrated less KE strength when normalized to body weight compared to HW counterparts.\textsuperscript{28-30} Conversely, Maffiuletti et al.\textsuperscript{31} and Blimkie et al.\textsuperscript{29,30} demonstrated no difference in KE strength in OB adolescent males when normalizing strength to fat-free mass,\textsuperscript{31} muscle cross sectional area,\textsuperscript{29,30} or cross sectional area and height.\textsuperscript{29,30} In the current study, we examined hip and knee muscle strength and the absolute values did not differ between the OB and HW groups. However, when normalizing strength values to leg lean mass, effectively evaluating strength of only force generating tissue, the OB group demonstrated decreased strength production for KF and HA compared to the HW group (table 3.2). Further a moderate effect size was present for all muscles tested.

Normalizing strength or force production is important in order to compare both between and within groups. It is suggested that utilizing absolute and ratio values of body size (e.g. muscle force / body mass) may potentially bias individuals with greater BMI and lower BMI respectively.\textsuperscript{45-48,78} Thus, normalizing muscle force to measures of body composition has been suggested as an alternative approach to control for differences in body composition.\textsuperscript{46} Muscle strength results in our study were normalized to the respective LE extremities’ lean mass to evaluate the ability of the OB youth to produce force in comparison to the HW youth, since excess fat mass does not generate force. This
allowed the ability to determine if the muscles in the OB group actually produced less force than those in the HW group versus being “appearing” weaker because of overall increased body mass.

Finally, changes in muscle metabolism that have been shown to occur in OB adults may account for the strength deficits noted in OB youth from our study. These changes include insulin resistance, reduction in fatty acid oxidation, smaller mitochondria, reduced mitochondrial content, and reduced electron transport chain activity. However, to the authors’ knowledge, the effects of these metabolic changes in skeletal muscle on muscle mechanics and force generating capacity in OB individuals have not been reported. Further research is necessary to determine the potential mechanisms of decreased strength in OB youth.

3.4.2 Lower Extremity Functional Performance

This study supports previous evidence that OB youth perform poorer than their HW counterparts on measures of physical function (table 3). Specific to LE function, Graf et al. evaluated 554 children with a “body coordination test” comprised of a battery of balance and hopping tasks. These tasks were scored individually and then combined into a final motor quotient score. Although individual task scores were not reported, results demonstrated significantly lower motor quotient scores in the OB group versus the HW group indicative of poorer LE function and categorized the OB group as having a “moderate motor disorder.” Secondly, Riddiford-Harland et al. compared “lower limb functionality” in 43 OB and 43 matched HW children with vertical jump and standing
long jump tasks. Results from the Riddiford-Harland study\textsuperscript{11} demonstrated that the OB children did not jump as high or as far as the HW children. However, these results were not normalized by subject height or leg length, making comparison difficult.\textsuperscript{11} Our results provide outcomes of specific, individual functional tasks that were normalized, comparable, and easily conducted in both OB and HW populations.

3.4.3 Health Related Quality of Life

The current study partially supports previous literature reporting poorer HRQoL in OB compared to HW youth.\textsuperscript{1-4} However, these differences were limited to the physical health summary scores (Table 3.4). These outcomes are consistent with the literature suggesting that physical domains of HRQoL are more affected by obesity than perhaps psychosocial domains.\textsuperscript{5,79}

In general, the PedsQL scores for both the OB and HW groups in the current study were higher when compared to previous studies.\textsuperscript{2-4} The older age of the subjects in our study [(mean years±SD) 14.05±2.09; table 1], compared to previous studies [(mean years±SD) HW: 8.7±1.9\textsuperscript{3}–11.4±4.2\textsuperscript{4}; OB: 8.6±1.9\textsuperscript{3}–11.3±3.4\textsuperscript{4}], may have contributed to the higher PedsQL scores in our study. This theory is supported by results from Riazi et al.\textsuperscript{2} who demonstrated lower PedsQL scores in both HW and OB pre-pubescents compared to older post-pubertal children and adolescents. Further, the BMI-Z scores in previous studies [(mean ±SD)HW: 0.2±.8\textsuperscript{4}–0.3±.1.4\textsuperscript{2}; OB: 3.0±0.1\textsuperscript{4}–3.5±0.1\textsuperscript{2}] are higher than those in the current study [(mean years±SD) 1.9±.15; table 1]. There is consistent evidence demonstrating an inverse relationship between HRQoL and BMI in children and
adolescents. As such, the lower BMI-Z scores in our study may also account for higher PedsQL scores and offer additional explanation to the variance in PedsQL values when compared to previous reports in the literature. These factors may offer some explanation regarding the differences observed by the current study and those results reported in the literature.

### 3.4.4 Lower Extremity Strength Associations with Lower Extremity Functional Performance

Our data partially support the hypothesis that LE strength predicts LE functional performance in OB youth, specifically for the SLHop task. Several studies evaluating LE strength in HW young male and female adults have demonstrated significant positive relationships between KE and KF strength and hop performance (r = .33 to .78). However, hip adduction and adduction strength in young HW adult male hockey players (mean 20 years ±3) did not correlate (p > .05; r values: -.26 to .26) with performance on a side hop. Finally, related to balance, hip strength in healthy adolescent female lacrosse players has been shown to be positively correlated (r = .30 to .36) with a balance task similar to the SLBAR. Conversely, our finding in OB youth demonstrate significant contributions of HA strength to SLHop performance but not KE or KR strength and no significant contributions of LE strength to SLBAR performance.

When interpreting the regression results, a notable difference is apparent related to the profile of LE muscle strength contributions to SLHop performance between the OB and HW groups. Specifically, HA is the singular significant contributor (t-score: 2.159; p = .05) to SLHop performance in the OB group. Whereas, the regression results in the
HW group indicate a more global strategy of LE muscle strength contribution to SLHop performance with KE (p = .006), KF (p = .05), and HA (p = .004) significantly contributing to SLHop performance with relatively similar t-scores (KE: 3.201; KF: 2.151; and HA: 3.422). Focusing strengthening interventions on KE, KF, and HA in OB youth may promote a similar global muscle contribution profile to that of the HW group. Further research is necessary to determine if strengthening interventions improve functional performance in OB youth.

3.4.5 Lower Extremity Functional Performance Associations with Health Related Quality of Life

Our results partially support our hypothesis that LE functional performance would predict HRQoL in OB youth. Although our study utilizes different measures of functional performance and HRQoL, our results are consistent with those of Tompkins et al.\textsuperscript{9} who demonstrated a positive correlation between improvement in functional performance (as measured by a 6 minute walk test) and physical component summary score on the SF-36 (r= .41, p<.05) in OB adult females following gastric bypass surgery. Interestingly our findings that functional performance did not correlate with the PedsQL-psychosocial summary score in OB youth also correspond with Tompkins et al.\textsuperscript{9} who did not show a correlation between functional performance and the mental health component of the SF-36 which encompasses social functioning, emotional limitations, mental health, and vitality. The lack of relationship between the functional measures and the PedsQL-psychosocial summary score in our study support Tompkins’ et al.\textsuperscript{9} assertion that perceived physical limitations may impede physical performance to a greater extent than
perceived psychosocial limitations. Based on our results and those of Tompkins et al.\textsuperscript{9}, it could be hypothesized that improvements in SLHop and SLBAR performance may correspond to improvements in the physical components of HRQoL in OB youth; however, this requires further research.

3.4.6 Limitations

Our study was cross sectional with a homogeneous sample which limits the predictive value and generalizability of the LE strength and LE functional performance variables and may not be applicable to youth who are overweight or morbidly obese. Secondly, data were not available for several subjects related to Tanner self-report and iDXA values. However, based on the low numbers of those without these variables, the matching strategy, and consistent LE strength results we do not expect these to have affected the outcomes of the study. Thirdly, although we measured the strength of the major muscle groups of the LE associated with movement patterns and control of the knee and hip during hopping and balance tasks\textsuperscript{86-90} the strength of the lower leg and calf was not measured and the contribution of these muscles cannot be discounted in the performance of the SLHop and SLBAR. Further, there are other factors that contribute to the LE functional performance measures and HRQoL scores that we did not measure in this study.

Finally, we expected the HW participants to report higher levels of activity compared to OB participants, but there were no differences between the groups. Potentially, recall bias of the PAQ may limit the accuracy of the participants’ responses.
related to physical activity. In addition the PAQ does not measure physical activity intensity which have been shown to be higher in HW youth compared to OB youth. Other methods evaluating physical activity, such as using an accelerometer and other approaches measuring energy expenditure, may better describe physical activity status. However, these methods are not without their own limitations and were not within the scope of this study.

3.4.7 Implications for Future Research and Clinical Practice

Future research is warranted in examining whether the singular profile of LE strength contribution to SLHop performance in OB youth can be altered to better represent the global profile of HW youth. In addition, assessing muscle activation patterns and strategies in OB youth during LE performance tasks may offer valuable information in terms of choice of exercise prescription and intervention. The relationship of SLHop and SLBAR performance to other functional and performance based activities should be evaluated while examining their relationship with physical activity participation in OB youth. Evaluating additional factors which may contribute to LE functional performance in OB youth may offer clinicians insight into interventions which may enhance LE functional performance and potentially HRQoL. Finally, examining measures of LE function with obesity specific measures of HRQoL may better focus strategies in addressing HRQoL in OB youth.
3.4.8 Conclusion

We demonstrated consistently poorer LE strength in OB youth compared to age- and sex-matched HW youth. Our results support previous evidence that OB youth also have poorer LE function and HRQoL compared to HW youth. Our findings indicate that in OB youth HA strength is the main contributor to SLHop performance and both SLHop and SLBAR performance contribute to the physical functioning component of HRQoL. Further study is required to identify factors in OB youth that may contribute and potentially improve LE strength, LE function, physical activity, and HRQoL of this population.

3.5 Acknowledgments:

We would like to thank the following individuals and organizations for their assistance with this project:

5) Judith Groner MD, Patricia Rosenstein and Sasigarn Bowden MD for assistance with subject recruitment.

6) Mike McNally MS and Louise Thoma DPT for assistance with data collection; Katie Winters and Sarah Harwell for assistance with data processing.

7) The Ohio State University Graduate School Alumni Grant (Briggs), The Ohio Physical Therapy Association Research Grant (Briggs), and the Arthritis Foundation (Bout-Tabaku) for their financial support to be able to conduct this research.
3.6 References


77. Williams GN, Snyder-Mackler L, Barrance PJ, Axe MJ, Buchanan TS. Neuromuscular function after anterior cruciate ligament reconstruction with


Chapter 4: Cardiovascular Risk and Metabolic Syndrome in a Sample of Obese Youth Enrolled in a Multidisciplinary Medical Weight Management Program: Implications of Cardiorespiratory Fitness, Health Related Quality of Life, and Musculoskeletal Pain.

4.1 Background

The epidemic of obesity in children and adolescents is leading to the recognition of obesity-associated conditions only previously identified in adults.\(^1,2\) Obesity related comorbidities now commonly diagnosed and evident in obese (OB) youth include: cardiovascular conditions (e.g. diabetes, metabolic syndrome, elevated systemic inflammation, and poor cardiovascular fitness), musculoskeletal (MSK) impairments (e.g. complaints of musculoskeletal pain, poor physical function, etc.) and psychological concerns (e.g. poor perceived health related quality of life, depression, etc.).\(^1-9\) Further, the consequences of these morbidities in OB children and adolescents are thought to carry-over into adulthood and limit overall health.\(^1,2,10,11\) This prompts the need to understand the impact of obesity-associated morbidities in youth to better inform the medical management of this population with the goal of improving health and quality of life in youth and preventing obesity-associated morbidities in adulthood.
Cardiovascular risk is multifactorial with interactions among many components. Adults who are OB and have additional risk factors (e.g. high cholesterol, hypertension, diabetes, etc.) demonstrate increased relative risk for both cardiovascular related death as well as all-cause death when compared to adults who are only OB.\textsuperscript{12} Moreover, measures of obesity in adults are associated with additional and exacerbating risk factors including: Metabolic Syndrome (MetS),\textsuperscript{13,14} elevated C-Reactive Protein (CRP),\textsuperscript{13,15} and elevated hemoglobin A1C (HbA1C).\textsuperscript{16} The combination of elevated CRP and HbA1C in overweight adults has been associated with advanced early carotid atherosclerosis progression and the development of MetS.\textsuperscript{17-19} The presence and combination of these factors compounded with obesity may lead to poorer cardiovascular prognosis specifically earlier and more severe cardiovascular disease and morbidity. Moreover, in both non-OB and OB adults MetS, elevated CRP, and elevated HbA1C have been linked to clinical measures of decreased cardiorespiratory fitness,\textsuperscript{20,21} poor health related quality of life (HRQoL),\textsuperscript{22-25} and complaints of MSK pain.\textsuperscript{26-33} These clinical measures may be useful in identifying those who are at greater cardiovascular risk.

First, in adults decreased cardiorespiratory fitness has been shown to be inversely related to MetS and levels of CRP and HbA1C.\textsuperscript{20,21} Poor cardiorespiratory fitness has also been shown to be an independent risk factor of cardiovascular disease beyond measures of obesity.\textsuperscript{12} Second, HRQoL is also associated with MetS and diabetes in adults.\textsuperscript{22-25} Although poor HRQoL may not directly mediate cardiovascular risk in those who are OB\textsuperscript{22-25,34} the secondary effects of poor HRQoL may influence risk. For example, in other populations such as adult cancer survivors, poorer HRQoL is associate with
The same relationship could be hypothesized in those who are OB, thus potentially propagating an unhealthy lifestyle and greater cardiovascular risk. Finally, MSK conditions in adults including fibromyalgia pain, chronic overuse MSK pain, low back pain, and osteoarthritis are associated with obesity and elevated levels of CRP. However, the presence of these relationships and potential consequences in OB youth are largely unknown.

The prevalence of MetS in OB youth ranges from 10-66%. Moreover, OB youth demonstrate the same obesity-associated morbidities observed in OB adults including poorer cardiopulmonary fitness, worse HRQoL, and more reports of MSK pain compared to healthy weight (HW) youth. As in OB adults, it could be hypothesized that cardiovascular risk in OB youth may have comparable relationships with poor cardiopulmonary fitness, decreased HRQoL, and MSK pain. In fact, youth with higher BMI and low fitness have been shown to have greater cardiovascular risk and measures of cardiovascular fitness have been shown to be confounded by increase waist circumference in non-obese youth. Measures of cardiovascular fitness, HRQoL, and MSK pain may function as additional clinical indicators of increased cardiovascular risk in OB youth. Accordingly, earlier recognition of cardiovascular risk (e.g. CRP, HbA1C and MetS) and identification of potentially concomitant aggravating factors, such as poor cardiopulmonary fitness, worse HRQoL, and MSK pain may lead to prompter and more aggressive medical management of these deficiencies to improve the health of OB youth and prevent or delay cardiovascular disease and associated co-morbidities in adults.
The purposes of this retrospective study in OB youth enrolled in a hospital based medical weight management program were to: 1) compare the prevalence of cardiovascular risk factors and MetS as categorized by common clinical measures of cardiorespiratory fitness, HRQoL, and reports of MSK pain and 2) evaluate the odds of MetS based on common clinical and laboratory measures of health. We hypothesized that: 1) Cardiovascular risk factors and MetS would be more prevalent in OB youth with low cardiorespiratory fitness scores, low HRQoL scores, and reports of MSK pain compared to OB youth with high cardiorespiratory fitness scores, high HRQoL scores, and no reports of MSK pain, and 2) The odds of MetS would increase in OB youth with low cardiorespiratory fitness, low HRQoL, reports of MSK pain, CRP above 3.0mg/dL, and HbA1C above 5.7% compared to OB youth with high cardiorespiratory fitness scores, high HRQoL scores, no reports of MSK pain, CRP levels less than 3.0mg/dL, and HbA1C levels less than 5.7%.

4.2 Methods

For the current study we utilized a database comprised of 183 OB youth (ages 9-19 years) who were enrolled in a hospital based multidisciplinary medical weight management program from 2009-2011. At the time of enrollment into the weight management program, a comprehensive medical (including blood serum evaluation) and physical fitness evaluation was conducted. A body mass index (BMI) of equal to or greater than the 95th percentile for age and gender was required to be enrolled in the program. Data of interest were extracted from both electronic and paper medical charts.
specific to the patient’s initial visit to the program (table 4.1). In a previous report utilizing the same database, Bout-Tabaku et al\textsuperscript{49} retrospectively compared HRQoL and cardiorespiratory fitness in OB youth with and without reports of lower extremity pain and reported on demographic characteristics, anthropometric variables, cardiorespiratory fitness scores, reports of MSK pain, and HRQoL scores for the entire sample (table 4.1).\textsuperscript{49} Analysis for the current study we use these data to study our objectives but also include markers of cardiovascular risk from laboratory data extracted from the medical chart.

Medical charts were excluded from further analysis if there was a documented history of factors which may not be related to typical growth and development including orthopaedic surgery, neuromuscular disease, inflammatory disease, or chronic arthritis. These factors may contribute to reports of pain and systemic inflammation due to the primary disease state rather than obesity which was beyond the scope and purpose of this study. In addition, the above conditions may require alternative interventions beyond obesity management and subsequently further limit the health of participants. This study was approved by the institutional review boards.

Based on the exclusion criteria, 8 charts were excluded from further review leaving 175 medical charts to be included in the final analysis. Two investigators (MT and SBT) were responsible for the extraction. As previously reported\textsuperscript{48} height, weight, age, sex and Tanner stage were recorded to describe the sample (table 4.1). Height and weight from the medical chart were used to calculate BMI. From these data, BMI-Z scores were generated in STATA 12.0 (STATA Corp, College Station, TX, USA) using
the Centers for Disease Control and Prevention 2002 data.\textsuperscript{48,50} Tanner stages were recorded to assess maturation. 2011.\textsuperscript{48,51} Because of the low numbers of Tanner stage I in the sample (n=7), Tanner stages I-II and III-V were pooled into prepubescent and pubescent/postpubescent groups, respectively, for data analysis.\textsuperscript{48,52} Previously reported demographic, anthropometric, cardiorespiratory fitness, and HRQoL results for the entire sample are presented in table 4.2.\textsuperscript{49}
Table 4.1 Data collected from medical record review of children and adolescents referred to weight management program, all data were collected from the initial assessment.¹

<table>
<thead>
<tr>
<th>Category</th>
<th>Specific Variables Recorded</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic Information¹</td>
<td>Age</td>
</tr>
<tr>
<td></td>
<td>Sex</td>
</tr>
<tr>
<td></td>
<td>Race</td>
</tr>
<tr>
<td>Anthropometric Information¹</td>
<td>Tanner Stage</td>
</tr>
<tr>
<td></td>
<td>Height</td>
</tr>
<tr>
<td></td>
<td>Weight</td>
</tr>
<tr>
<td></td>
<td>BMI</td>
</tr>
<tr>
<td></td>
<td>BMI Z-score</td>
</tr>
<tr>
<td>Cardiorespiratory Fitness¹</td>
<td>Progressive Aerobic Cardiovascular Endurance Run test (PACER score)</td>
</tr>
<tr>
<td>Musculoskeletal Pain Reports¹</td>
<td>Location</td>
</tr>
<tr>
<td></td>
<td>Frequency</td>
</tr>
<tr>
<td>Health Related Quality of Life¹</td>
<td>Pediatric Quality of Life Inventory 4.0</td>
</tr>
<tr>
<td></td>
<td>Generic Core (Peds QL)</td>
</tr>
<tr>
<td></td>
<td>Physical component</td>
</tr>
<tr>
<td></td>
<td>Psychosocial components</td>
</tr>
<tr>
<td>Markers of Cardiovascular Risk</td>
<td>High-sensitivity C-reactive protein (CRP)</td>
</tr>
<tr>
<td></td>
<td>Hemoglobin A1C (HbA1C)</td>
</tr>
<tr>
<td></td>
<td>Triglycerides (TG)</td>
</tr>
<tr>
<td></td>
<td>High-density lipoprotein (HDL)</td>
</tr>
<tr>
<td></td>
<td>Glucose (GLU)</td>
</tr>
<tr>
<td></td>
<td>Systolic/diastolic blood pressures (BP)</td>
</tr>
</tbody>
</table>

¹Previously reported by Bout-Tabaku et al.
¹All data collected at initial assessment into the weight management program.
Table 4.2 Characteristics of Entire Study Sample (*n=175*)

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of female/male</td>
<td>121/54</td>
</tr>
<tr>
<td>Age (years)</td>
<td>13.07±2.23</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.62±.09</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>96.24±25.19</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>36.18±7.04</td>
</tr>
<tr>
<td>BMI Z-score</td>
<td>2.41±.32</td>
</tr>
<tr>
<td>PedsQL Psychosocial</td>
<td>74.2±16.4</td>
</tr>
<tr>
<td>Health (n=145)</td>
<td></td>
</tr>
<tr>
<td>PedsQL Physical Function</td>
<td>77.6±15.9</td>
</tr>
<tr>
<td>(n=145)</td>
<td></td>
</tr>
<tr>
<td>PACER Score</td>
<td>13.4±6.3</td>
</tr>
<tr>
<td>(n=146)</td>
<td></td>
</tr>
</tbody>
</table>

mean±SD; NR = not reported; PACER = Progressive Aerobic Cardiovascular Endurance Run test PedsQL = Pediatric Quality of Life Inventory 4.0 Generic Core

4.2.1 Musculoskeletal Pain

As in our previous work, reports of current or recent MSK pain were obtained from a detailed medical problem list and self-report history questionnaire completed by both the participants and parents. Reports of non-musculoskeletal discomfort or pain were not recorded (e.g. stomach pain, head ache, etc.). From the medical history questionnaire MSK pain location (e.g. back, hip, knee, ankle, upper extremity, etc.) and frequency were recorded. MSK pain data were available from all 175 medical charts. Our previous work describes the frequency of MSK pain by location. For the current analysis, the sample was categorized into two groups, those who reported MSK pain in any location and those with no reports of MSK pain.
4.2.2 Cardiovascular Risk Factors and Metabolic Syndrome

As part of clinical evaluation for the medical weight management program, serum blood samples following an overnight fast were obtained. As this was lab data collected in the clinical context, obtaining lab tests was not always consistent for the 2 years we reviewed thus laboratory data was not available for all participants reviewed in this study. Reasons for lack of some of the data included no referral for blood work, patients did not fast overnight, or patients did not receive the blood work for some non-disclosed reason. For this analysis, recorded laboratory data included markers of potential cardiovascular risk: high-sensitivity CRP \( [n = 60] \), HbA1C \( [n = 116] \), triglycerides (TG) \( [n = 124] \), high-density lipoprotein (HDL) \( [n = 124] \), and glucose (GLU) \( [n = 114] \). Systolic and diastolic blood pressures (BP) were also recorded \( [n = 172] \). Cardiovascular risk related to high CRP and HbA1C was defined as levels being above 3.0mg/dL\(^{53}\) and 5.7%\(^{54,55}\) respectively. The presence of MetS was determined based on the clustering of cardiovascular risk factors determined by the International Diabetes Federation (IDF) Consensus definition (table 4.3).\(^{56,57}\) Measures of waist circumference (WC), one of the factors considered in the diagnosis of MetS, were limited in our sample \( (n=62) \). Instead, a BMI-Z score of 2 was used as a surrogate for central obesity, which has been done in previous work in obese children.\(^{10,58}\)
Table 4.3 The International Diabetes Federation Consensus Criteria for Metabolic Syndrome in Youth: At least 3 of the following factors must be present. 2,3

<table>
<thead>
<tr>
<th>Marker</th>
<th>Threshold Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Pressure</td>
<td>systolic $&gt;130$/diastolic $&gt;85$mmHg</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>$\geq1.7$mmol/L ($&gt;150$mg/dL)</td>
</tr>
<tr>
<td>High-density lipoprotein</td>
<td>male: $&lt;1.03$mmol/L (40mg/dL), female: $&lt;1.29$mmol/L (50mg/dL)</td>
</tr>
<tr>
<td>Glucose</td>
<td>$\geq5.6$mmol/L (100mg/dL)</td>
</tr>
<tr>
<td>Waist Circumference</td>
<td>$\geq90^{th}$ percentile or adult cut-off</td>
</tr>
</tbody>
</table>

4.2.3 Cardiorespiratory Fitness

The Progressive Aerobic Cardiovascular Endurance Run (PACER) score was recorded from the medical chart as a measure of cardiorespiratory fitness (n=146). The PACER is a common valid and reliable tool used to assess aerobic fitness in children and involves running between two lines (20 meters apart) in pace with audible cues. 59-61 The PACER is multistaged as the time between the audible cues becomes progressively shorter each minute, thus requiring a progressive increase in running pace as time progresses. The test is discontinued if the participant experiences extreme fatigue or cannot maintain the required speed to keep up with the audible cues. The PACER score was recorded from the medical chart as the number of laps completed. 49,62 These data were previously reported on for the entire sample. 48 Poorer aerobic or cardiovascular fitness align with lower PACER score. 59,63 For the current study, the PACER results were dichotomized by median score to designate a relative low group and high group within the sample.
4.2.4 Health Related Quality of Life

HRQoL was recorded from the medical charts using the Pediatric Qualify of Life Inventory 4.0 Generic Scales (PedsQL). The PedsQL is valid a 23-item questionnaire used to assess physical, emotional, social, and school functioning in children aged 2 to 18 years from which physical function and psychosocial health are determined. The questionnaire uses a 5-point Likert response scale for each question and scores are transformed into a 0 to 100 scale with higher scores indicating better well-being. The child report of the PedsQL physical function summary score (PedsQL-physical) and the PedsQL psychosocial health summary score (PedsQL-psychosocial) were recorded for analysis from the medical record. PedsQL data were available from 145 medical charts which were previously reported. For the current study, the PedsQL-physical and psychosocial summary results were dichotomized by median score to designate a relative low group and high group for each subscale within the sample.

4.2.5 Data Analysis

Tests for normality were performed on all data and residuals. Based on the tests of normality, Independent t-tests and Mann Whitney U tests were used to evaluate differences in mean levels of potential cardiovascular risk factors between groups as defined by 1) those with higher or lower PACER scores, 2) those with higher or lower PedsQL scores, and 3) those with and without reported MSK pain. Only subjects for which all data on the risk factors for MetS were included in the analysis of prevalence of MetS in the sample (n=112). Frequency and chi-square statistics were used to identify the
proportion of participants with 1) cardiovascular risk factors in the total sample, 2) cardiovascular risk factors per group, 3) presence of MetS risk factors for the total sample and per group, and 4) presence of MetS for the total sample and per group. Finally, logistic regression was used to evaluate the odds of the presence of MetS based on the clinical measures of PACER scores, HRQoL scores, and reports of MSK pain. Logistic regression was also used to evaluate the odds of MetS based on levels of CRP and HbA1C. Age and sex were controlled for in all logistic regression. Significance was set to p <0.05. Statistical analysis was performed with IBM SPSS Statistics Version 21 (SPSS Inc, Chicago, IL, USA).

4.3 Results

Overall demographic characteristics, anthropometric measurements, PedsQL summary scores, and mean PACER scores of the participants have been reported in our previous work and are presented in Table 4.2. The prevalence of specific cardiovascular risk factors are presented in Table 4.4. Low HDL was the most prevalent (75%) cardiovascular risk factor in the total sample whereas high levels of GLU were the least prevalent (2.6%) (Table 4.4). Thirty-three percent of the entire sample had high CRP values indicative of increased systemic inflammation and cardiovascular risk. Approximately 30% of those with MetS risk factor data (n = 112) were categorized as having MetS (Table 4.5) with a mean of 2.04±.86 MetS risk factors per subject (e.g. BP, TG, HDL, GLU, BMI-Z score). Approximately 65%, 56%, and 46% of those with MetS
had high BP, CRP, and TG, respectively, compared to 3%, 24%, and 0% in those without MetS (Table 4.4).

Subject characteristics and mean laboratory values categorized by grouping (e.g. low/high PACER score, low/high HRQoL scores, and yes/no MSK pain) are reported in Table 4.6. For the first purpose, those with lower PedsQL-psychosocial health scores demonstrated lower mean HDL values (mg/dL: 38.63±8.95 vs. 44.29±11.53; p = .02). There were no other differences in cardiovascular risk factors in any of the groups (Table 4.6). However, a greater percentage of those with lower PACER scores demonstrated CRP values above the threshold for increased cardiovascular risk (p = .01) when compared to the percentage of those with higher PACER scores (Table 4.7). Finally, when comparing groups, there were no differences in the prevalence of cardiovascular risk factors or MetS classification (Table 4.8).

For the second purpose, after controlling for age and sex, the logistic regression results indicated that those with high CRP demonstrated an increased odds of MeS [Odds( 95%CI): 4.93(1.24-19.61); p = .02] (Table 4.9). However, PACER scores, PedsQL scores, and reports of MSK pain were not significant predictors of MetS (Table 4.10).
Table 4.4 Prevalence of Cardiometabolic Risk Factors in the Total Sample

<table>
<thead>
<tr>
<th>Specific Risk Factor</th>
<th>Total Sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>High BP</td>
<td>31(18.0)</td>
</tr>
<tr>
<td>High TG</td>
<td>27(21.8)</td>
</tr>
<tr>
<td>Low HDL</td>
<td>93(75.0)</td>
</tr>
<tr>
<td>High GLU</td>
<td>3(2.6)</td>
</tr>
<tr>
<td>High CRP</td>
<td>20(33.3)</td>
</tr>
<tr>
<td>High HbA1C</td>
<td>56(48.3)</td>
</tr>
</tbody>
</table>

n(%)  
Threshold values for increased cardiovascular risk:  
- BP: systolic ≥ 130/diastolic ≥85mmHg  
- TG: ≥1.7mmol/L (≥150mg/dL)  
- HDL: male: <1.03mmol/L (40mg/dL); female: < 1.29mmol/L (50mg/dL)  
- GLU: ≥5.6mmol/L(100mg/dL)  
- CRP: >3.0mg/dL  
- HbA1C: ≥ 5.7%

Table 4.5 Prevalence of Metabolic Syndrome Risk Factors and Presence of Metabolic Syndrome in the Total Sample

<table>
<thead>
<tr>
<th>Potential Number of MetS Risk Factors^ Per Participant</th>
<th>Prevalence in Total Sample*</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>2(1.8)</td>
</tr>
<tr>
<td>1</td>
<td>29(25.9)</td>
</tr>
<tr>
<td>2</td>
<td>47(42.0)</td>
</tr>
<tr>
<td>3</td>
<td>30(26.8)</td>
</tr>
<tr>
<td>4</td>
<td>4(3.6)</td>
</tr>
<tr>
<td>5</td>
<td>0(0)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Presence of MetS</th>
<th>Total Sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>78(69.6)</td>
</tr>
<tr>
<td>Yes</td>
<td>34(30.4)</td>
</tr>
</tbody>
</table>

n(%)  
^MetS Risk Factors include: BP, TG, HDL, GLU, and BMI Z score.  
*Only participants with complete data for all risk factors of MetS were included in the final analysis of MetS (n = 112).
Table 4.6 Subject Characteristics and Mean Laboratory Values Categorized by PACER Score, PedsQL Summary Scores, and Reports of MSK pain.

<table>
<thead>
<tr>
<th>PACER</th>
<th>Psychosocial Health</th>
<th>Physical Function</th>
<th>MSK Pain</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex (M/F)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>21/52</td>
<td>22/51</td>
<td>1.00</td>
<td>23/45</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12.93 ±2.10</td>
<td>12.89 ±2.15</td>
<td>.91</td>
<td>13.26 ±2.12</td>
</tr>
<tr>
<td><strong>Tanner Stage (I-II/III-V)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11/54</td>
<td>8/52</td>
<td>.38</td>
<td>8/48</td>
</tr>
<tr>
<td><strong>Weight (kg)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>103.62 ±30.98</td>
<td>86.96 ±19.88</td>
<td>.002*</td>
<td>101.58 ±31.29</td>
</tr>
<tr>
<td><strong>BMI (kg/m²)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>38.95 ±9.25</td>
<td>32.71 ±4.45</td>
<td>&lt;.001*</td>
<td>38.3 ±9.61</td>
</tr>
<tr>
<td><strong>BMI-Z score</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.55 ±0.29</td>
<td>2.3 ±0.3</td>
<td>&lt;.001*</td>
<td>2.5 ±0.36</td>
</tr>
<tr>
<td><strong>Systolic BP (mmHg)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>123.94 ±11.9</td>
<td>120.1 ±9.22</td>
<td>.07</td>
<td>119.89 ±11.12</td>
</tr>
<tr>
<td><strong>Diastolic BP (mmHg)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>68.56 ±7.69</td>
<td>68.06 ±6.26</td>
<td>.72</td>
<td>67.65 ±6.96</td>
</tr>
<tr>
<td><strong>TG (mg/dL)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>109.56 ±57.43</td>
<td>129.02 ±83.84</td>
<td>.20</td>
<td>129.99 ±82.98</td>
</tr>
<tr>
<td><strong>HDL (mg/dL)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40.98 ±9.11</td>
<td>43.54 ±12.29</td>
<td>.61</td>
<td>38.63 ±8.95</td>
</tr>
<tr>
<td><strong>GLU (mg/dL)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>86.74 ±7.33</td>
<td>87.47 ±7.6</td>
<td>.64</td>
<td>87.12 ±6.53</td>
</tr>
<tr>
<td><strong>CRP (mg/dL)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.78 ±5.37</td>
<td>1.85 ±1.59</td>
<td>.19</td>
<td>3.45 ±3.64</td>
</tr>
<tr>
<td><strong>HbA1C (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.67 ±0.36</td>
<td>5.74 ±1.06</td>
<td>.71</td>
<td>5.64 ±0.35</td>
</tr>
</tbody>
</table>

N=SD
†Mann-Whitney U test
*Significance: p < .05
Table 4.7 Prevalence of Cardiometabolic Risk Factors Above Threshold Categorized by Available PACER Score, PedsQL Summary Scores, and Reports of MSK pain

<table>
<thead>
<tr>
<th></th>
<th>PACER</th>
<th>Psychosocial Health</th>
<th>Physical Function</th>
<th>MSK Pain</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>“Low”</td>
<td>“High”</td>
<td>“Low”</td>
<td>“High”</td>
</tr>
<tr>
<td><strong>BP</strong></td>
<td>15 (21.1)</td>
<td>10 (13.9)</td>
<td>.26</td>
<td>15 (22.1)</td>
</tr>
<tr>
<td><strong>TG</strong></td>
<td>7 (14.6)</td>
<td>15 (30.0)</td>
<td>.07</td>
<td>13 (25.0)</td>
</tr>
<tr>
<td><strong>HDL</strong></td>
<td>37 (77.1)</td>
<td>36 (72.0)</td>
<td>.56</td>
<td>41 (78.8)</td>
</tr>
<tr>
<td><strong>GLU</strong></td>
<td>2 (4.7)</td>
<td>1 (2.1)</td>
<td>.60</td>
<td>1 (2.1)</td>
</tr>
<tr>
<td><strong>CRP</strong></td>
<td>10 (45.5)</td>
<td>3 (12.0)</td>
<td>.01*</td>
<td>10 (37.0)</td>
</tr>
<tr>
<td><strong>HbA1C</strong></td>
<td>24 (52.2)</td>
<td>23 (50.0)</td>
<td>.84</td>
<td>18 (39.1)</td>
</tr>
</tbody>
</table>

n(%)  
*Significance p < .05  
BP: systolic ≥ 130/diastolic ≥ 85 mmHg  
TG: ≥ 1.7 mmol/L (≥ 150 mg/dL)  
HDL: male ≤ 1.03 mmol/L (40 mg/dL); female: ≤ 1.29 mmol/L (50 mg/dL)  
GLU: ≥ 5.6 mmol/L (100 mg/dL)  
CRP: ≥ 3.0 mg/dL  
HbA1C: ≥ 5.7%
Table 4.8 Prevalence of Metabolic Syndrome Risk Factors Categorized by PACER Score, PedsQL Summary Scores, and Reports of MSK pain

<table>
<thead>
<tr>
<th># Risk Factors</th>
<th>PACER</th>
<th>Psychosocial Health</th>
<th>Physical Function</th>
<th>MSK Pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0 (0)</td>
<td>2 (4.2)</td>
<td>0 (0)</td>
<td>2 (4.1)</td>
</tr>
<tr>
<td>1</td>
<td>10 (24.4)</td>
<td>13 (27.1)</td>
<td>12 (26.1)</td>
<td>12 (24.5)</td>
</tr>
<tr>
<td>2</td>
<td>19 (46.3)</td>
<td>18 (37.5)</td>
<td>18 (39.1)</td>
<td>23 (46.9)</td>
</tr>
<tr>
<td>3</td>
<td>11 (26.8)</td>
<td>13 (27.1)</td>
<td>14 (30.4)</td>
<td>11 (22.4)</td>
</tr>
<tr>
<td>4</td>
<td>1 (2.4)</td>
<td>2 (4.2)</td>
<td>2 (4.3)</td>
<td>1 (2.0)</td>
</tr>
<tr>
<td>5</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>MetS</td>
<td>12 (29.3)</td>
<td>15 (31.3)</td>
<td>16 (38.4)</td>
<td>12 (24.5)</td>
</tr>
</tbody>
</table>

n(%) Only participants with complete data for all risk factors of MS were included in the final analysis of MS (n = 112).

Table 4.9 Odds of Metabolic Syndrome based Laboratory Measures of CRP and HbA1C

<table>
<thead>
<tr>
<th>CRP</th>
<th>OR (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated CRP (&gt;3.0mg/dL)</td>
<td>4.93 (1.24 to 19.61)</td>
<td>.02*</td>
</tr>
<tr>
<td>Elevated HbA1C (&gt;5.7%)</td>
<td>3.26 (0.78 to 13.69)</td>
<td>.11</td>
</tr>
</tbody>
</table>

Overall Model p = .05*
*Significance: p < .05
Results after controlling for age and sex.
Table 4.10 Odds of Metabolic Syndrome based on Clinical Measures of Cardiorespiratory Fitness, HRQoL Components, and Reports of MSK Pain

<table>
<thead>
<tr>
<th></th>
<th>OR (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>“Low” Cardiorespiratory Fitness</td>
<td>1.79 (0.55 to 5.88)</td>
<td>.34</td>
</tr>
<tr>
<td>“Low” Psychosocial Health</td>
<td>.39 (0.08 to 1.94)</td>
<td>.25</td>
</tr>
<tr>
<td>“Low” Physical Function</td>
<td>.65 (0.12 to 3.40)</td>
<td>.61</td>
</tr>
<tr>
<td>Reports of MSK Pain</td>
<td>0.24 (0.06 to 1.04)</td>
<td>.06</td>
</tr>
</tbody>
</table>

Overall Model p = .19
*Significance: p < .05
Results after controlling for age and sex.

4.4 Discussion

The purposes of this study were to: 1) compare the prevalence of cardiovascular risk factors and MetS categorized by PACER score, HRQoL components (psychosocial/physical) and reports of MSK pain, and 2) evaluate the odds of MetS based on common clinical and laboratory measures of health. Our results demonstrate minimal differences in cardiovascular risk factors between obese youth with lower PACER scores, lower PedsQL scores, and reports of MSK pain, when compared to those with higher PACER scores, higher PedsQL scores, and no reports of MSK pain, respectively. Controlling for age and sex these factors did not predict the presence of MetS in OB youth. However, OB youth with CRP levels > 3.0mg/dL demonstrated almost 5 times the odds of MetS.

4.4.1 Cardiovascular Risk Factors and Metabolic Syndrome

Wickham et al. performed a similar study evaluating the prevalence of cardiovascular risk factors and MetS in 165 OB adolescents in a multidisciplinary weight
management program at initial enrollment and 6 months post treatment. The prevalence of cardiovascular risk factors in our study were similar to Wickham et al.\textsuperscript{10} regarding TG (21.8\% vs 29.1\%) and GLU (2.6\% vs. 2.6\%). However the prevalence of BP and HDL risk factors appears substantially different (BP: 18\% vs. 54.5\%; HDL: 75\% vs. 26.7\%). Overall, the number of cardiovascular risk factors for MetS per subject (2.04±.86 vs. 2.05±.91) and percentages of subjects with 0-5 criteria of MetS were similar between studies. Further, the prevalence of MetS in our study (30.4\%) is consistent with that reported in Wickham et al.\textsuperscript{10} (30.3\%) and previous studies of OB youth (median: 29.2\%; range 10-66\%).\textsuperscript{43} It should be noted that the “at risk” values used by Wickham et al.\textsuperscript{10} for TG (≥110mg/dL) and BP (>90\textsuperscript{th} percentile for age, sex, and height) are slightly different than used in our study (TG: ≥150mg/dL; BP: systolic ≥130/diastolic ≥85mmHg) based on the IDF Consensus definition.\textsuperscript{57} Overall, our results support those found by Wickham et al.\textsuperscript{10} and extend their findings by evaluating the relationship of MetS with clinical measures (PACER, HRQoL, and MSK pain) and markers of inflammation (CRP) and glucose intolerance (HbA1C).

Interestingly when evaluating CRP levels, even though there were no statistically significant differences between groups regarding CRP values (mean±SD), those with lower PACER scores (4.78±5.37mg/dL), lower PedsQL-psychosocial score (3.45±3.64mg/dL), and lower PedsQL-physical score (3.61±3.88mg/dL) consistently demonstrated mean CRP values above threshold for increased cardiovascular risk (>3.0mg/dL) whereas those in the higher groups and no reports of MSK pain were consistently below the threshold. Further, when evaluating the percentage of those with
CRP above threshold, those with low PACER scores demonstrated a greater prevalence of elevated CRP compared to those with high PACER scores (Table 4.7). It could be hypothesized that the participants in the study are just beginning to show signs of chronic inflammation. Perhaps with continued exposure to an obese state from childhood into adulthood, a more definitive difference in mean CRP values would be evident. In our study, categorizing groups by median score may have an effect on the lack of significance between PACER, PedsQL, and MSK groups. Perhaps in a larger sample, categorizing by tertiles would permit a better delineation potential of differences in CRP levels. Finally, although not within the scope of this study, our results and others\textsuperscript{73-75} may suggest that measures of cardiorespiratory fitness (e.g. PACER score) may be useful in predicting at risk levels of CRP in OB youth. This should be evaluated in future studies.

### 4.4.2 Metabolic Syndrome Risk

Our results demonstrate almost 5 times the increased odds of MetS in an OB sample of youth with high CRP. The importance of the increased odds of MetS with elevated CRP is reinforced by the results of several large longitudinal studies in adults demonstrating an additive effect of MetS and elevated CRP on the increased risk of cardiovascular events (Hazard Ratios range: 5.3-5.9) versus having no MetS or normal CRP.\textsuperscript{76,77} Further, the 15 fold increased risk of cardiovascular disease in adulthood when the MetS is present as a child\textsuperscript{10,11} underscores the importance of screening for systemic inflammation via CRP in OB youth to mitigate potential cardiovascular sequelae.
The IDF consensus group has recommended that future research regarding MetS include evaluating measures of systemic inflammation including CRP and the risk of developing MetS and cardiovascular disease.\textsuperscript{57,78-80} Several large population based studies have evaluated the association of MetS and its components to levels of CRP in children and adolescents.\textsuperscript{71,72,81,82} In general, results from these studies demonstrate higher levels of CRP in OB youth and youth with MetS. However, none of the studies have examined the relationship between CRP and MetS in OB youth. Our results extend the findings from these studies by evaluating the relationship between CRP and MetS in OB youth and demonstrate for the first time that OB youth with high CRP levels have increased odds of MetS.

Although HbA1C has been suggested as a potential surrogate for MetS for its utility in assessing long-term glycemic control and association with complications of diabetes and cardiovascular risk factors\textsuperscript{83-85} our results do not support the hypothesis that higher levels of HbA1C increase the odds of the presence of MetS in OB youth. Further, in spite of the fact that poorer cardiorespiratory fitness\textsuperscript{8,44,86} and HRQoL\textsuperscript{22-25,87} have also been shown to be associated with the presence of MetS in adults and increased cardiovascular risk factors in children, our results do not support the hypothesis that poorer outcomes of these variables increase the odds of the presence of MetS in OB youth. Our results also do not show an increased odds of MetS based on reports of MSK. However, when evaluating the logistic regression results, the significance of the model and independent variables of the clinical measures, the p-values consistently trended closer towards significance. Increasing our sample of subjects within our dataset and
collecting pre/post assessments of participants in the medical weight management program may provide a clearer understanding of these results and better answer the question of how cardiorespiratory fitness, HRQoL components, and reports of MSK pain relate to MetS in OB youth.

4.4.3 Limitations

There are several limitations inherent to the retrospective study design we used. First, unfortunately not all data were available for all subjects. Incomplete or missing information in the medical charts did not allow for a complete data set for the PACER, PedsQL, and laboratory variables in our analysis. PACER and PEDsQL scores were available for 82% and 83% of our sample respectively. Further, only 64% of the participants had a complete data set of MetS risk factors, 34% had CRP data, and 66% had HbA1C data. However, the prevalence of MetS (30.4%) and elevated CRP (33%) is consistent with previous studies [MetS: 29.2%; range 10-66%], (CRP: 36%)\textsuperscript{43}. Second, recall bias is a consideration which may limit the accuracy of the responses on the PedsQL questionnaire and reports of MSK pain. However, scores on the PedsQL and reports of MSK pain (reported elsewhere)\textsuperscript{48} are consistent with those previously reported by obese youth.\textsuperscript{6,7} Thirdly, although PACER and PedsQL scores in obese youth are consistently lower compared to healthy weight youth,\textsuperscript{6,7,88,89} there are not specific scores indicative of poor PACER or PEDsQL scores in obese youth. We dichotomized groups based on median scores, however, alternative methods of defining and comparing groups may yield different results. Fourth, other factors related to HRQoL (e.g. socioeconomic
status, family dynamics) or measures of physical activity (e.g. participation, time, intensity, etc) were not specifically collected or analyzed as part of this study. Finally, the cross-sectional nature of the study limits the predictive interpretation of the findings. Cause and effect of whether CRP predicts MetS in obese children cannot be established by the current study. However, our findings do support previous studies indicating that elevated CRP is an important risk factor when considering MetS in obese children.\textsuperscript{82}

\subsection{4.4.4 Future Research}

Future research should consider comparing multiple medical weight management programs to ensure generalizability of results. Additionally, a larger sample may permit different stratification regarding measures of cardiorespiratory fitness and HRQoL. Other measures such of physical activity (e.g. intensity, time, participation, etc.) may also prove useful when evaluating cardiovascular risk. Finally, longitudinal studies should be performed to both evaluate the long term implications of elevated CRP in obese youth, predictors of elevated CRP in obese youth, as well as to assess the efficacy of medical weight management programs and their ability to make potential changes to cardiovascular risk in obese youth. Ideally, results would then be used to optimize and personalize treatment strategies for program participants based on their cardiovascular profile to ultimately reduce their risk for a future cardiovascular event.
### 4.4.5 Conclusion

Our results provide a descriptive representation and comparison of cardiovascular risk factors related to MetS in obese youth enrolled in a hospital based medical weight management program. Overall the prevalence of cardiovascular risk factors and MetS in our sample is consistent with previous reports in the literature. Our results do not show differences in cardiovascular risk in obese children enrolled in a medical weight management program when categorized by cardiorespiratory fitness, HRQoL measures, or reports of MSK pain. Elevated CRP may be a useful predictor of MetS in obese youth and warrants further investigation.

### 4.5 Acknowledgments:

We would like to thank the following individuals and organizations for their support in conducting this research:

1. Ihuoma Eneli, MD and the Center for Healthy Weight and Nutrition at Nationwide Children’s Hospital for access to the patient data.
2. Christopher Taylor PhD, RD for his assistance with data analysis.
3. The Arthritis Foundation (Bout-Tabaku) for their financial support to be able to conduct this research.
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Chapter 5 Summary

Obesity in children and adolescents is concerning as OB youth are less physically active than healthy weight children,\textsuperscript{1-3} demonstrate similar health side-effects as obese adults\textsuperscript{4-6} and are more likely to be obese as adults.\textsuperscript{7-10} Health in OB youth is limited by the many obesity-associated morbidities such as MSK impairments and limitations,\textsuperscript{11-15} decreased physical function,\textsuperscript{3,16,17} poorer HRQoL\textsuperscript{18-20} and increased cardiovascular risk.\textsuperscript{4,5,21,22} The consequences of these morbidities limit overall health and wellbeing in OB youth and carry-over into adulthood.\textsuperscript{4,5} The studies outlined in this dissertation evaluate potential relationships of static frontal plane knee alignment to knee joint loading patterns, LE muscle strength to LE functional performance, and LE functional performance to HRQoL in OB youth. In addition, secondary factors potentially related to cardiovascular risk in OB youth were explored. The results outlined in this dissertation indicate that OB youth stand in greater knee abduction alignment and demonstrate decreased external frontal plane knee adduction moments. However measures of frontal plane knee alignment do not correlate to frontal plane knee loading during walking and jogging. Further, deficits in LE muscle strength may adversely impact functional performance and HRQoL in OB youth. Thirdly, although cardiovascular risk is generally greater in OB youth compared to HW youth, cardiorespiratory fitness, HRQoL, and
reports of MSK pain do not predict cardiovascular risk as identified by MS syndrome or its components in OB youth enrolled in a medical weight management program. However, measures of systemic inflammation (e.g. CRP) may be useful in predicting the severity of cardiovascular risk in OB youth. Future work is necessary to clarify the effects of altered knee mechanics on joint health, LE function, subsequent physical activity levels, and concurrent cardiovascular health in OB youth.

The aims of the work were to:

5.1 Aim 1 (Chapter 2): Compare static standing frontal plane knee alignment and frontal plane knee joint loading patterns during walking and jogging in OB and HW youth.

**Hypothesis 1.1**: OB youth will demonstrate increased standing knee abduction alignment compared to the HW youth.

Previous literature demonstrates increased knee abduction in OB youth when evaluated clinically. Results from our study partially support the first hypothesis demonstrating increased knee abduction position in OB youth compared to HW youth in static standing when utilizing the 3D measure. However, there was no difference between groups in static standing frontal plane knee angle using a clinical measure developed for use in OB adults (UMB measurement) which demonstrated an overall knee adduction position. The methodological differences in measurement techniques likely account for the differences in frontal plane knee alignment between the 3D and UMB measures. As the UMB measure will overestimate into knee adduction. Further, there was not a difference in the frequency of participants classified as being in static knee abduction or
adduction alignment using either the 3D or UMB measurement respectively. Thus both the OB and HW group demonstrated relatively the same direction of frontal plane angle. However, the magnitude of knee abduction was greater in the OB youth compared to the HW youth when using the 3D measure.

**Hypothesis 1.2:** Frontal plane knee alignment measured with the UMB method will strongly correlate with a 3-dimensional measure of static standing frontal plane knee angles in OB youth.

Results in our study support the second hypothesis demonstrating a moderate, positive correlation between the UMB measurement and the 3D measurement of static standing frontal plane knee alignment in OB youth ($\rho=0.539; p=0.014$). No relationship was evident in the HW youth ($\rho=0.196; p=0.407$). The overestimation of abduction associated with the UMB measurement technique may impact HW youth to a greater extent than OB youth.

**Hypothesis 1.3:** Obese youth will demonstrate less peak knee adduction and greater peak abduction moments compared to healthy weight youth during walking and jogging tasks.

The evidence of frontal plane knee moments in OB youth during walking is conflicting. Results from our study partially support the above hypothesis and demonstrate less peak external knee adduction moments in the OB group compared to the HW group during walking ($p=0.003$). Further, there was a trending toward significance of decreased external knee adduction moments during jogging in the OB group.
These results support the results of McMillan et al.\textsuperscript{23,24} who also demonstrated decreased peak external knee adduction moments during walking in OB youth compared to HW youth. Further research is necessary to further elucidate how differences in frontal plane loading patterns in OB youth affect function and the long term health of the joint.

5.2 Aim 2 (Chapter 2): Evaluate the relationships between static standing frontal plane knee joint alignment and frontal plane knee joint loading patterns during walking and jogging in OB youth.

Hypothesis 2.1: Measures of static standing knee alignment will positively correlate with peak frontal plane knee joint moments during walking and running in OB and HW youth.

Clinicians often utilize measures of static standing knee alignment in attempt to understand movement and loading patterns of the knee during dynamic activity.\textsuperscript{27} However, results do not support the third hypothesis as no relationships existed between the 2 measures of static standing frontal plane knee alignment and frontal plane knee adduction or abduction moments during walking and jogging in OB youth. However, there was a moderate positive correlation in the HW group between the 3D measure and peak knee adduction moments during walking ($\rho=0.583; p=0.007$). Further, in the HW group a trend toward significance was observed between the 3D measurement and peak knee abduction moments during walking ($\rho=0.430; p=0.058$). However, no correlations existed between the UMB measurement during walking or jogging in the HW youth. Using static standing frontal plane knee alignment to infer knee joint loading patterns in OB youth may not be appropriate.
5.3 Aim 3 (Chapter 3): To compare measures of LE muscle strength, LE functional performances, and HRQoL between OB and HW youth while evaluating the contribution of LE muscle strength to LE functional performance and LE functional performance to HRQoL in OB youth.

**Hypothesis 3.1**: OB youth will generate less LE muscle strength, have poorer scores on measures of LE functional performance, and reduced HRQoL than HW youth.

Our results support the above hypothesis and that OB youth have lower hip and knee strength when normalizing strength values to leg lean mass. This normalization procedure effectively evaluates strength of only force generating tissue. Further, our study reports hip muscle weakness in OB youth compared to HW youth for the first time.

In addition, this study supports previous evidence that OB youth perform worse on measures of physical function compared to their HW counterparts.\textsuperscript{17,28-32} The OB group demonstrated poorer performance on both the SLHop (p < .001) and SLBAR tasks (p = .007) (table 3). Our results provide outcomes of specific, individual functional tasks that were normalized, comparable, and easily conducted in clinical settings for both OB and HW populations.

Finally, the current study partially supports previous literature reporting poorer HRQoL in OB compared to HW youth\textsuperscript{18,19,33-36} demonstrating decreased PedsQL-physical health summary scores (p = .02) but no difference in PedsQL- psychosocial health scores (p = .07) in the OB group compared to the HW group. These outcomes are
consistent with the literature suggesting that physical domains of HRQoL are more affected by obesity than perhaps psychosocial domains.\textsuperscript{37-39} However, the difference in PedsQL-physical score between the OB and HW youth (5.78 points) did not meet the minimal clinically important difference of 6.67 points.

**Hypothesis 3.2**: LE muscle strength will predict LE functional performance in obese youth.

Our results indicate that the contribution of LE strength to LE functional performance may be different between OB and HW youth. Results partially support the hypothesis that LE muscle strength would predict LE functional performance in OB youth. Results from multiple linear regression model demonstrate that HA strength was a main contributing variable predictive of SLHop performance in the OB group. This model included the variables of KE, KF, HA, and HE and accounted for approximately 56\% of the variance in SLHop performance. In the HW group, the main contributing variables included KE, KF, and HA. This regression model, including HE, accounted for approximately 70\% of the variance in SLHop performance. However, LE muscle strength was not predictive of SLBAR performance in either group. These results may have implications on strategies of improving LE muscle strength and SLHop performance in OB youth.
Hypothesis 3.3: LE functional performance scores will predict physical and psychosocial HRQoL in OB youth.

Our results partially support our hypothesis that LE functional performance would predict HRQoL in OB youth. When using separate multiple linear regression models, results of our study demonstrated significant predictive value of SLHop and SLBAR performance in OB youth. Together, SLHop and SLBAR accounted for approximately 48% of the variance in PedsQL-physical health summary score in OB youth. However, these tests were not predictive of PedsQL-psychosocial health in OB youth. Further, in HW youth, neither SLHop nor SLBAR were predictive of PedsQL-physical or psychosocial scores. It could be hypothesized that improvements in SLHop and SLBAR performance may correspond to improvements in the physical components of HRQoL in OB youth; however, this requires further research.

5.4 Aim 4 (Chapter 4): To compare the prevalence of cardiovascular risk factors and MetS as categorized by common clinical measures of cardiorespiratory fitness, HRQoL, and reports of MSK pain and evaluate the odds of MetS based on common clinical and laboratory measures of health in OB youth enrolled in a hospital based medical weight management program.

Hypothesis 4.1: Cardiovascular risk factors and MetS will be more prevalent in OB youth with low cardiorespiratory fitness, low HRQoL, and reports of MSK pain compared to OB youth with high cardiorespiratory fitness, high HRQoL, and reports no of MSK pain.
In adults, cardiovascular risk factors have been linked to other conditions affecting daily life including poorer cardiorespiratory fitness\(^40\), decreased HRQoL,\(^{41-44}\) and increased musculoskeletal (MSK) pain,\(^{45-47}\) These conditions are also linked to measures of obesity in adults.\(^{48,49}\) Results from our study partially support our hypothesis and demonstrate an increase in cardiovascular risk in OB youth based on PACER scores and HRQoL. More specifically, a greater percentage of OB youth with low PACER scores demonstrated CRP values above the threshold for increased cardiovascular risk when compared to the percentage of those with high PACER scores. Further, OB youth with low PedsQL-psychosocial scores also demonstrated lower mean HDL values that were also below the cut-off threshold for increased cardiovascular risk compared to OB youth categorized with high PedsQL-psychosocial scores. Otherwise, when comparing high vs. low PACER groups, high vs. low HRQoL groups, and yes vs. no MSK pain groups there were no differences in the prevalence of cardiovascular risk factors or MetS classification.

**Hypothesis 4.2:** The odds of MetS would increase in OB youth with low cardiorespiratory fitness, low HRQoL, reports of MSK pain, high CRP, and high HbA1C.

Previous work in OB youth demonstrates conflicting results regarding the association of systemic inflammation and MetS.\(^{50-53}\) Further, poorer cardiorespiratory fitness\(^54\) HRQoL,\(^{41-44,55}\) and MSK pain\(^56\) have been associated with the development of MetS in adults but not in youth, specifically OB youth. Results from our study partially support the above hypothesis. Using logistic regression and controlling for age and sex,
results indicate that OB youth with high CRP demonstrate almost 5 times the increased odds of MS. Also, we evaluate for the first time how cardiorespiratory fitness, HRQoL, and reports of MSK pain may related to the development of MetS in OB youth. However, our results demonstrate that PACER scores, HRQoL scores, and reports of MSK pain were not significant predictors of MetS.

5.5 Overall Limitations

There are several overall limitations relevant to the above studies and results. Our results are limited to a homogenous group which may limit the generalizability of the results. Findings related to Aims 1-3 may not be generalizable to overweight or morbidly OB youth. The results related to Aim 4 may not be generalizable to OB youth not enrolled in a hospital based medical weight management program. Further, the studies are cross sectional which limits the predictive value related to the regression analysis performed for Aims 3 and 4. Thus cause and effect cannot be definitively established. Finally, detailed data regarding actual physical activity, such as intensity, was limited for the studies. This lack of data limits the ability to demonstrate relationships between physical activity and measures of LE function and HRQoL (Aim 3) or cardiovascular risk (Aim 4).

5.6 Clinical Relevance and Summary

The implications and negative consequences of obesity in children and adolescents are tremendous. Physical activity is one of the primary interventions focused
on preventing and minimizing the side-effects of obesity in youth.\textsuperscript{57-59} However, the efficacy of these recommendations and interventions may be hindered by many of the complications associated with obesity such as increased MSK pain, decreased joint health, decreased muscle strength, altered movement patterns, and poorer physical function. Thus, a continued cycle of obesity, poorer HRQoL, and increased cardiovascular risk potentially persist. However, the understanding of the interrelationships among the aforementioned factors in OB youth is limited. Clarifying these relationships are essential in the development and refinement of exercise and physical activity interventions and recommendations focused on limiting the cycle of obesity and mitigating the associated adverse health risks.

Obesity in adults is a risk factor for decrease knee joint health (e.g. osteoarthritis) which leads to decreased function, decreased physical activity, and increased disability.\textsuperscript{60-64} Compellingly, the results from Widhalm et al\textsuperscript{14} which demonstrated knee articular cartilage lesions in all of the knees of OB youth evaluated with MRI. Widhalm et al\textsuperscript{14} also documented initial signs of knee OA in several of these subjects. However, the relationship of loading patterns to articular damage in the knees of OB youth is only speculation. No direct correlation or link has been made to movement and loading patterns and knee joint health in OB youth. Measures, such as static standing alignment are thought to provide information regarding the loading patterns during dynamic activity and potential knee joint health.\textsuperscript{65,66} Although results from our study and others demonstrate that OB youth have different static standing knee alignment\textsuperscript{12} and altered knee joint loading patterns\textsuperscript{23-26} compared to HW youth, measures of static standing knee
alignment do not relate to knee joint loading patterns in OB youth during walking and jogging activities. Thus, relying on current measures of static standing knee measures may not prove useful in anticipation of loading patterns during dynamic physical activities in OB youth. However, identifying other mechanisms of potential knee joint damage is important in protecting the health and function of the knee while promoting exercise and physical activity in OB youth.

Measures of LE strength and LE function performance have been shown to be associated with exercise, physical activity levels, and health status in HW, OW, and OB adults. In addition, LE strength is associated with LE functional performance in adults. However these relationships in OB youth are unknown. First, understanding the relationship between LE strength and LE functional performance in OB youth is important when considering factors and limitations related to exercise and physical activity participation. Results from our studies indicate that measures of LE strength can predict LE functional performance in OB youth. Further, our results indicate that specific LE muscles contribute differently to LE functional performance, specifically SLHop performance, than HW youth. These results will help inform future research and clinical interventions focused on improving LE functional performance in OB youth with the ultimate goal of enhancing exercise and physical activity participation.

Obesity is consistently associated with reduced HRQoL in youth. However, other factors, such as functional performance may also influence HRQoL in OB youth. Obese youth have lower scores on measures of LE functional performance. These deficits may further contribute to the decreased self-efficacy
and HRQoL in OB youth. Identifying the relationship between LE functional performance and HRQoL may offer alternative interventions aimed at improving HRQoL in OB youth. Results from our studies demonstrate for the first time that measures of LE functional performance (e.g. SLHop and SLBAR) contribute to HRQoL in OB youth. Focusing on improving LE functional performance may enhance HRQoL in OB youth. Additionally, subsequent improvement in functional performance in OB youth may enhance physical activity participation and further improve HRQoL. Future research should explore these hypotheses.

Finally, increased cardiovascular risk in OB youth necessitates earlier recognition and intervention focused on preventing and limiting immediate and long term health consequences. Although clinical measures of cardiorespiratory fitness, HRQoL, and reports of MSK pain in our study did not identify OB youth who had more or less cardiovascular risk, higher levels of CRP increased the risk of developing MetS almost 5 fold. This is significant as CRP represents increased systemic inflammation (e.g. CRP) which is associated with cardiovascular events in adults. Further, elevated CRP adds subsequent risk of a cardiovascular event in adults who have MetS. Fortunately, increased exercise and physical activity have been shown to reduce levels of CRP. Thus, enhancing exercise and physical activity in OB youth may assist in the reduction of elevated systemic inflammation and potential overall risk of cardiovascular disease. The characteristics and relationships among knee mechanics, LE strength, and LE function identified in this dissertation may provide important information informing both future research and clinical interventions focused on enhancing and optimizing exercise and
physical activity levels in OB youth with the ultimate goal of reducing cardiovascular risk and improving HRQoL.

5.7 Future Directions

These results warrant asking the question whether knee joint loading patterns and LE strength profiles can be made similar to those of HW youth with a focus on improving function and HRQoL. In addition, characterizing the influence of knee joint loading patterns and mechanisms for the potential development of articular cartilage defects in OB is necessary for long term knee health in OB youth. Although results from our study in Chapter 2 did not reveal differences in physical activity levels based on a recall questionnaire between OB and HW youth, previous literature consistently demonstrates that OB youth are less physically active compared to HW youth.\textsuperscript{1-3} Thus, our findings warrant further investigation into the effects of how altered knee mechanics, decreased LE strength, and poorer LE function in OB youth may impact physical activity participation. Further, these results combined with an understanding of the cardiovascular profile of OB youth could then be used to optimize and personalized treatment strategies to ultimately reduce cardiovascular risk and improve their HRQoL now and into adulthood.
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