Pediatric Obesity Consequences and Interventions: Characteristics Associated with Successful Weight Management in Children and Adolescents with Obesity

By
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Abstract

Over the past three decades, pediatric obesity rates have tripled in the United States and affected 18.5% of children and adolescents. Obesity can affect all aspects of children and adolescents' life, including their physical and psychological health. Lifestyle modification interventions that target behavior change for weight loss are effective treatments for obesity. Despite the effectiveness of these interventions, there is variability in weight loss among individuals, with some children being more successful with weight loss outcomes. There is a lack of consistent baseline factors to assist in identifying for whom these behavioral interventions may be most effective as a treatment for obesity. This dissertation is aimed to investigate the factors associated with better treatment outcomes and to create awareness among health care professionals regarding the need for individualized intervention for treating youth with severe obesity. The current series of studies were conducted to 1) investigate the impact of pediatric metabolic syndrome and obesity on the development of type 2 diabetes and cardiovascular diseases, 2) identify the factors that can influence weight management interventions for successful weight reduction among children and adolescents with obesity, and 3) examine the potential relation between executive function and obesity-related behaviors and the effect of executive function on the treatment outcomes among adolescent bariatric candidates. Results from Study 1 demonstrate that nearly 13% of children and adolescents with obesity and metabolic syndrome developed at least one of the associated diseases including hypertension, cardiovascular diseases, or type 2 diabetes later in their childhood or adolescence. The number of metabolic syndrome factors was significantly associated with the disease risk and the duration of being diagnosed with the diseases. The results from Study 2 showed that among all the potential factors, early weight loss response was the strongest predictor of treatment response for weight

reduction at 6 months. These findings suggest that children and adolescents who lose more weight initially during treatment will continue to lose significantly more weight post-intervention. Findings from Study 3 revealed that executive function is associated with multiple obesity-related behaviors in adolescents with severe obesity during bariatric preoperative intervention. Candidates with poorer executive function skills in daily life reported higher dysregulated eating behaviors, lower physical activity levels, and less confidence in resisting overeating. Overall, these findings highlight the importance of early evaluation of individual and treatment-level factors associated with weight loss, facilitating individualized intervention and improved long-term outcomes.

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Table of Contents

Chapter 1: Introduction

Background: Pediatric Obesity

The prevalence of pediatric obesity remains an ongoing serious health concern, affecting ~18.5% of children and adolescents in the United States.[1] Data from the National Health and Nutrition Examination Survey (NHANES) for years 2015–2016 show that nearly 1 in 5 youth aged 6 to 19 years in the United States have obesity.[2] Rates of obesity also tend to be higher among children of low socioeconomic status and racial/ethnic minority group status.[3] African American and Hispanic children have higher rates of obesity compared with other races.[4]

It is well accepted that there is no single factor or behavior cause of obesity in children and adolescents. While a complex of biological and genetic risk factors influence the development of obesity, changes in children's behaviors, environments, and family structures have all contributed to the increase in pediatric obesity.[5] Factors, such as eating habits, physical activity, parent-child interactions, media exposure, school and neigborhood environments, and sleep have been identified as potentionally impacting child weight status.[6]

Pediatric obesity is a multifactorial disease with potentially several adverse consequences that require the attention of health professionals. Obesity affects and complicates a child's life in several aspects. The increasing prevelance and severity of pediatric obesity is associated with the emergence of serious health complications, previously considered rare in children including type 2 diabetes mellitus, cardiovascular diseases, obstructive sleep apnea and orthopedic problems.[7,8] In addition to chronic diseases, obesity is markedly linked to psychological and social consequences including higher risk of depression, anxiety, impaired body image, low self-esteem, and bullying.[9] All these consequences have a huge impact on their overall health-related quality of life. Children with obesity report severe impairments in health-related quality of life and similar quality of life as those diagnosed with cancer.[10] Furthermore, children with obesity continue to carry this condition into adulthood, raising chances of developing severe and sometimes life-threatening complications.[6]

Given the high prevalence rates and the complexity of pediatric obesity, there is a need for effective treatment approaches. Lifestyle modifications are the first line of treatment to promote weight reduction in children with obesity.[11] Pediatric weight management programs that incorporate behavioral skills into structured dietary and physical activity treatment guidelines can produce significant and clinically meaningful weight reduction.[12] Such treatment is usually delivered by a multidisciplinary team in an outpatient setting. Despite that lifestyle modifications remain the cornerstone for treating and managing obesity in children, pharmacologic interventions are considered for children struggling with extreme excess weight and associated comorbidies. To date, the primary medications that have been approved by the Food and Drug Administration (FDA) for the treatment of pediatric obesity are orlistat and liraglutide.[13] However, other off-label medications including metformin, phentermine, topiramate and exenatide have been used and show promise in the treatment of children with obesity.[14,15] Although nonsurgical strategies provide a certain degree of effective weight reduction, many adolescents with severe obesity warrant more aggressive treatment approaches including surgical procedures. The most common surgery being performed in children are Roux-en-Y gastric bypass (RYGB), laparoscopic adjustable gastric banding (LAGB) and vertical sleeve gastrectomy. Bariatric surgery has become more broadly accepted as a therapeutic approach to treatment of adolescents who are suffering from the health and psychosocial complications of severe obesity.[14] Recent studies have shown promising long-term outcomes on weight loss and remission of related comorbidities following bariatric surgery.[11]

Predictors of Successful Weight Loss

Behavioral interventions can result in weight loss and postive health benefits in children, however, not not all the children respond equally to the same intervention. Evidence indicates a high variability in response to the intervention and a high rate of regained weight among children and adolescents with obesity.[11,16,17] Therefore, it is crucial to identify children's characteristics affecting the successful outcomes of weight management treatment. A better understanding of predictive factors would help health providers and researchers in developing more individualized treatment strategies that are sensitive to patients' needs and individual differences.[18] Thus, it would improve the efficiency of current interventions to meet these demands. Conversely, recognizing the children who are less likely to benefit from the intervention allows the healthcare providers to establish an alternative treatment and help in matching individuals to different programs. Pairing patients' pretreatment characteristics and program features may improve retention and intervention outcomes.[19] It also may prevent the negative impact of failure on patients' self-esteem and motivation.[20]

Identifying accurate predictors is also a strategy allowing better allocation of the limited resources to those more likely to respond. The limited financial resources of the U.S health care system increases the importance of determining the pretreatment factors possibly associated with successful weight loss. Complete financial support for children with obesity is an exception in most countries. Therefore, from a cost-benefit perspective, it is vital to focus the existing resources, targeting those children who may benefit the most from weight management treatment and thus optimizing the therapeutic results.[18] Enrollment of children who are less likely to succeed may decrease money allocation for children who may benefit more from such intervention programs and encourage the health providers to find alternative approaches for those less successful.[21]

Simultaneously with the predictive factors for successful weight loss, it is important to address the predictors for attrition, a common problem in weight loss intervention. Evaluating the factors associated with attrition provides a more comprehensive overview of individual responses to weight management interventions. Better knowledge of dropout reasons helps to identify the barriers to continued participation in the weight loss intervention. Thus, it is then possible to facilitate more effective modification of treatment based on a patient's characteristics to improve weight loss program attendence.[22] In addition, early identification of those who are at high risk of dropping out may improve targeted efforts. These efforts may include frequent contact with the family or patients via phone calls or emails between visits, introduction of an intensive approach to diet and exercise and/or supplemental materials.[22,23]

The significant variability in weight loss among individuals has encouraged researchers and health professionals to examine the potential factors related to successful treatment outcomes. Several studies have evaluated pretreatment factors as predictors of weight loss and have reported mixed findings. Evidence suggests that successful response to pediatric weight control programs has been linked to several factors such as initial weight status, age, gender, socioeconomic status, motivational level, participation in an exercise group, and parental weight.[20,24,25] However, there are no reliable predictors of successful weight reduction in children and adolescents. The evidence shows that the response to the intervention varies widely among children and adolescents and it is crucial to identify both positive and negative predictors of treatment outcomes.[20,26]

The definition of weight loss success in response to the weight management interventions varies through studies evaluating predictors of weight loss success. Most of the studies have used the change in Body Mass Index (BMI) z-scores (standard deviation) or change in weight to assess the response to the intervention. Successful weight reduction was primarily defined as ≥ 0.2 reductions in BMI-SDS (Body Mass Index Standard Deviation) or as ≥5% weight loss of baseline weight by the end of the follow-up period of 6 to 12 months.[20,27,28]

Several studies have been conducted using BMI-z scores as an outcome measure; however, tracking changes using this approach is not recommended. Growing evidence suggests using change in the BMI-z score has limitations, especially for children with severe obesity.[29,30] Thus, researchers proposed that the BMI expressed as a percentage of the 95th percentile (%BMIp95) is the recommended outcome metric. The %BMIp95 is more predictive of adiposity than BMI-z scores and a more accurate measure of body size over time.[29] %BMIp95 is used to indicate changes in weight status due to its flexibility in describing BMI beyond the 97th percentile compared with the BMI-z scores.[29] The Pediatric Obesity Weight Evaluation Registry (POWER) study of children with obesity suggests a 5-point reduction in BMI percent of the 95th percentile (%BMIp95) to be correlated with improved cardiometabolic risk.[31]

This review of the literature is aimed at identifying the predictors of successful weight reduction in response to lifestyle intervention. Several potential predictors of successful weight loss during weight management treatment among children aged 2-19 years were identified.

Age. Age emerges as a predictor of weight loss among children and adolescents, with both older and younger age being linked with successful weight reduction. Sabin et al. reported that age was the most important predictor of weight loss among 137 children with obesity aged from 3 to 18 years who had attended a pediatric obesity program.[25] Younger children achieved greater weight reduction measured by BMI-SDS following the intervention. Gow et al. evaluated the outcome predictors for 111 adolescents aged from 10 to 17 years participating in a 12-month randomized control trial with a 24-month follow up.[26] The study found that younger children are more likely to succeed than older children. Younger age was also associated with the best long-term outcome after participation in the lifestyle intervention. The youngest children (<8 years) at the onset of the intervention had the greatest decrease in BMI-SDS over 5 years compared with the oldest children (>13 years).[32] These findings support the need for early treatment at a younger age, as this may be important in achieving greater weight loss. These findings pointed to a shorter history of unhealthy behaviors and greater parental control over the children's behaviors compared to older children.

Conversely, Braet et al. found that older age is associated with more success in total weight loss, even after adjusting baseline weight in children aged from 7 to 17 years who attended a 10-month inpatient weight management program.[17] Walker et al. also reported that adolescent females aged from 12 to 17 years were more likely to lose weight compared with school-age children aged from 6 to 11 years.[21] Notably, weight control recommendations including adopting healthy diet habits and increasing physical activity level require self-control skills that older children are more able to master. Mixed findings about age as a predictor for successful weight loss may be influenced by design of the intervention and different factors such as family support, self-motivation, and body satisfaction, especially for adolescents. Overall, this evidence may indicate that each age group would benefit from specialized intervention targeted for their age and needs. For example, intervention programs need to focus more on parental involvement to secure significant weight loss for young children whereas to concentrate more on self-management skills for adolescents.

Baseline Weight. Weight status at treatment onset has a role in predicting later weight loss among children and adolescents. Baseline degrees of obesity may serve as positive or negative predictors of weight loss following a lifestyle modification program for pediatric obesity. Higher initial BMI-SDS has been associated with favorable outcomes of weight control interventions in children and adolescents.[17,27,33] In contrast, a few studies suggested that higher baseline BMI either predicted a poor response[16] or did not affect the outcome.[25] These findings highlight the significance of treating a child's weight gain as early in life as possible for the best outcomes. However, additional efforts and time that providers and families provide to support children with higher baseline weight may contribute to greater success in this high-risk group.

Sex. Evidence showed that weight changes in response to weight control treatment were not independent of gender. The success rate in weight loss programs may vary by gender with females experiencing lower weight loss than males. Wiegand et al. analyzed 157 specialized childhood obesity centers that treat children with overweight and obesity.[28] This study indicated that males were more likely to lose and maintain their weight, compared with females. This finding is consistent with a previous studies that showed boys are more likely to achieve the target reduction in weight after weight management intervention, compared with girls.[25,28]

Socioeconomic Status. Low socioeconomic status (SES) might be a barrier to success in weight management intervention. Parents' educational level, family income, and employment status can negatively influence the social and financial support for lifestyle modifications, which in turn may affect the long-term treatment outcomes. Low parent education and history of single-parent family background have been identifed as predictors of unsuccessful long-term weight loss among children aged from 7 to 15 years.[34] However, the specific mechanism of the influence of SES on childhood obesity remains unclear. Both higher parental education and higher income predicted greater weight loss at 12-months.[26] Two studies have reported that children with immigration backgrounds have lower treatment success when compared with native children.[28,35] In contrast, several studies have found that SES had no role in predicting successful obesity treatment outcomes.[17,24,25,28] On that basis, it is important to offer interventions that address the difficulties of these families to better meet their needs. Facilitating treatment health care accessibility and providing additional resources targeting this group may assist children to achieve their weight control goals.

Early Weight Loss. Weight loss early in treatment is linked with greater total weight loss and long-term weight loss maintenance. Gow et al. concluded that weight loss at 3 months is a strong predictor of weight loss later at 12-months.[26] Similarly, Goldschmidt et al. identified children's percentage weight change at 2 months as the best predictor of weight loss within 2-years follow up to the intervention.[36] A recent study using the Pediatric Obesity Weight Evaluation Registry (POWER) found that early BMI reduction of 3% or greater at one month was associated with BMI reduction of 5% or greater at 6 and 12 months.[37]

Children unable to acheive early weight loss in the program may have additional barriers such as low motivation, inability to implement treatment recommendations, or lack of family support. It is also possible that children who successfully lose weight at the beginning of the treatment are more motivated to continue weight control and adhere to the treatment plan. In such cases, children may need further treatment intensification, i.e., replacing the intervention rather than continuing in the same program, to increase initial weight loss, thus promoting greater total weight loss and more weight loss maintanence.

Treatment Duration. Duration of treatment is another predictor of treatment success. Previous studies in children and adolescents have found that longer treatment times are associated with greater weight loss and lower attrition rates.[23] Moreover, the number of follow-up visits was a positive predictors for successful weight loss.[38,39] Long-term treatment may allow for continued support and greater opportunity to change behaviors required for successful weight loss. Therefore, extending treatment length may be one way to enhance program effectivness and improve treatment oucomes. However, the relation between the length of treatment on weight loss could be selection bias, with a sample more motivated or able to sustain work on long-term goals.

Psychological Factors. Several pretreatment psychological factors were linked to weight loss outcomes. Moen et al. investigated predictors associated with an 8-year outcome of an outpatient program treating overweight children. Baseline child's self-esteem was one of the most positive predictors of long-term treatment outcome at 8 years.[20] Another study found that baseline eating disorder symptoms adversely affect long-term treatment outcomes.[17] Identifying children who have less motivation or confidence to change their behavior allows healthcare providers to improve the psychological aspects and thus prevent the negative impact of failure on patient's self-esteem. Additionally, screening for eating disorders and disregulated eating behaviors is critical, espeacially in primary care and weight management to identify and treat these symptoms early as well.

Behavioral Factors. Successful weight loss is associated with eating and physical activity related behaviors. Reinehr et al. evaluated a number of pretreatment demographic, behavioral and biological factors to predict successful weight loss for 75 children with obesity aged from 7 to 15 years.[24] The successful children had a median weight loss of about 0.4 SDS-BMI after a 1-year outpatient training program consisting of physical exercise, a nutrition course, and behavioral therapy.[24] The only significant difference between successful and unsuccessful children was that the successful children had been involved in exercise sessions before the beiginning of the training. Another study by Mockus et al. found that self-monitoring of dietary intake in children aged 7-12 years was associated with significantly greater decreases in weight following a 20-week weight loss program.[40] The findings demonstrated the importance of recording food intake frequently during first months of the weight loss program. Adherence to dietary and physical activity recommendations promote successful outcomes.

Biological Factors. Some studies explored the influence of certain biomarkers on the success of weight loss. Previous studies have investigated the role of insulin resistance in children and adolescents with obesity. Pinhas-Hamiel et al suggested that baseline degree of insulin resistance estimated by elevated fasting insulin predicts poorer weight loss in response to intervention in children aged from 10 to 18 years. Insulin resistance expressed by elevated fasting insulin and the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) was negatively associated with the ability to improve the BMI-z score.[33] The absence of acanthosis nigricans, which is a sign of presence of insulin resistance and prediabetes, may serve as a positive predictor of weight loss following a lifestyle modification program for pediatric obesity. Shailitin et al found that responder children with ≥0.2 reduction in BMI-SDS had a significantly lower prevalence of acanthosis nigricans than non-responders.[27] Uysal et al. reported that insulin resistance and components of metabolic syndrome (MetS) including hypertension, dyslipidemia, and waist circumference were negatively associated with successful weight loss among children who had attended a 1-year lifestyle intervention.[41] Measurement of insulin resistance may faciliate identification of the children more likley to respond poorly to the treatment so that clinicians can offer additional support and treatment. There is a lack of significant evidence on biological and physiological predictors of successful weight loss and maintenance including hormonal, metabolic and genetics biomarkers, especially for children and adolescents with obesity.

Medication. While behavioral therapy including diet and physical activity is the first-line treatment for weight management, it may have limited efficacy among young individuals most severely affected. Intervention programs have recently combined weight loss pharmacotherapy with the lifestyle approach. A number of medications have received attention for their potential to assist in weight control in children and adolescents. However, until recently orlistat is the only obesity pharmacotherapy approved by the U.S. Food and Drug Administration (FDA) in the pediatric population (age ≥12 years).[42] Liraglutide was just FDA approved in the United States (age≥12 years), significantly changing the potential for increased use of pharmacotherpy as an adjuct to lifetlye modification in pediatric weight management.[13]

Several off label medications have shown promising outcomes, including metformin and topiramate. Metformin is a well-established oral antidiabetic agent in the treatment of individuals with type 2 diabetes mellitus. A series of randomized control trials (RTC) have demonstrated the effectiveness of metformin on body weight and insulin resistance in children and adolescents with obesity.[43-45] One RCT involved 100 children with severe obesity aged 9-13 years receiving metformin twice a day for 6 months.[45] A significant decrease in BMI-z score and fasting glucose was observed, compared with the placebo group. Another RCT suggested that metformin significantly decreased energy intake and ratings of hunger and increased ratings of fullness in 100 children aged 6-12 years.[43] The major effect of metformin may be a powerful reduction in the appetite which may lead to the modest effect on BMI.

Topiramate is an antiepileptic drug for treating selected seizure disorders in adults and children. Though the mechanism is unclear, topiramate may reduce food intake and affect energy expenditure. A retrospective chart review revealed that children treated with topiramate and lifestyle change therapy demonstrated a 4-6% weight loss over 6 months.[46] A pilot RCT assessed the efficacy of short-term meal replacement therapy followed by topiramate on BMI reduction in adolescents aged 12 to 18 years with severe obesity. The intervention of 4 weeks of meal replacement therapy followed by 24 weeks of low dose topiramate resulted in limited efficacy of BMI reduction compared to meal replacement therapy alone.[42] Evidence is still insufficient to conclude that pharmacological approaches are superior in the management of pediatric obesity, as they only promote short-term weight loss. However, there are promising outcomes of combining medications and lifestyle interventions such as cognitive behavioral therapy, and strategies to improve diet and physical activity.[47]

The Role of Executive Functioning on Successful Weight Loss

Given that the successful treatment outcomes is still challenging, there has been a call for increased focus on cognitive factors underlying successful weight loss.[48] Executive function has been identified as a novel path in understanding mechanisms of successful weight loss. Executive function is a set of "high-level" cognitive processes that enable a person to control both regulatory skills and goal-directed actions.[49] Executive function is an umbrella term for a variety of cognitive domains including inhibitory control, attention, working memory and cognitive flexibility. These domains play important roles in self-regulation and goal-driven processes necessary to manage caloric intake and physical activity in an obesogenic environment.

Growing evidence has revealed that executive function is an important factor to consider in successful weight loss in children and adolescents with obesity.[50,51] Variation in executive functions associated with self-regulatory thoughts and behaviors can make a case for, at least partially, individual differences in children's response to obesity treatment.[50] As executive function facilitates goal-oriented and self-regulatory processes in everyday life, it is critical for controlling eating and activity behaviors, the core of any weight management intervention[50] (See **Figure 1**). In particular, inhibitory control (the capacity to inhibit a pre-potent response provoked by an external cue) and delay discounting (the ability to delay an immediate desired reward for achieving a long-term goal) are two domains of executive function that are crucial in the control of obesity-related behaviors and potentially, differential response to behavioral treatment.[50] In the context of eating behavior, inhibitory control of food intake is needed to adhere to a healthy diet and resist the desire to consume unhealthy palatable foods. Working memory and planning are also significant skills that facilitate the capacities to plan ahead to eat healthy food or engage in exercise in support of losing weight.[52] Once individuals continue to exhibit a certain level of executive control or skills over their eating or physical activity behaviors, they then may be able to maintain or achieve a desirable weight. Therefore, deficits in executive function may present challenges to engaging in healthy behaviors including physical and eating behaviors and thereby may impact the ability to adhere to treatment recommendations and interfere with the completion of weight-loss goals.

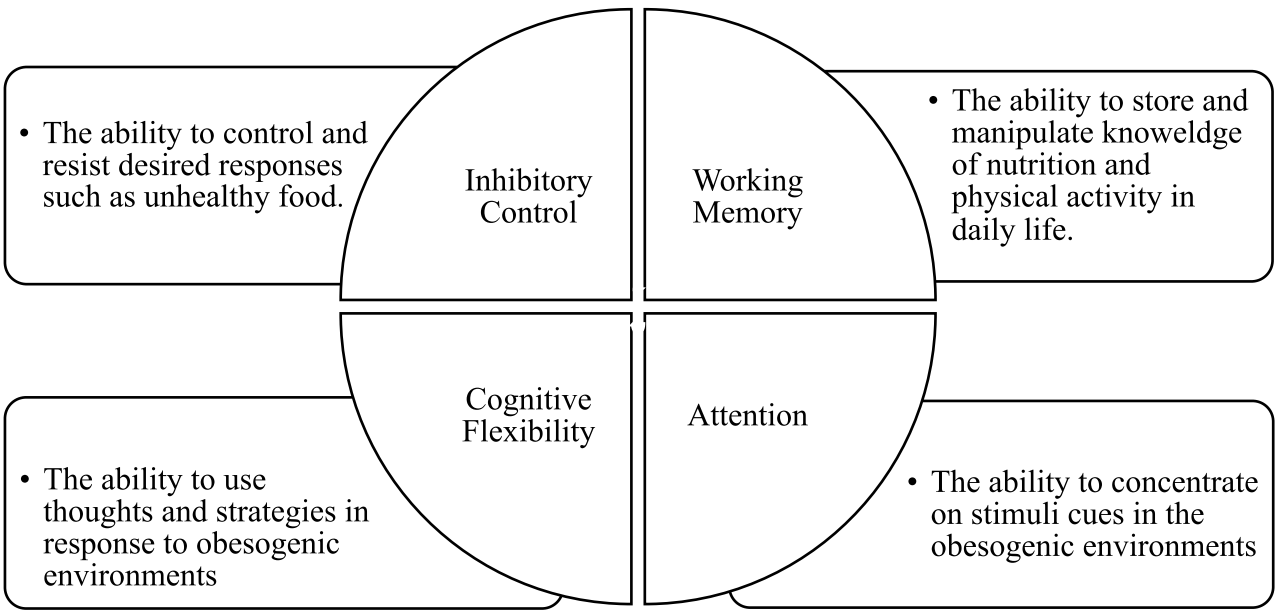

Figure 1. Executive function domains related to weight behaviors.[50]

Several studies have examined whether pretreatment assessment executive function domains predict success in weight managment programs for children and adolescents. Preliminary evidence suggests that inhibitory control predicts weight loss outcomes. One study found that adolescents aged 12 to15 years with poor inhibitory control performance lost less weight as a result of weight control intervention.[53] The same conclusion was also found in a study on 26 children with obesity aged 8 to12 years across the course of 12 months of a family-based intervention.[54] It suggests that low inhibitory control may contribute to a higher vulnerability to the temptations of tasty food, and consequently, this poor control presents challenges in adhering to the dietary plan.[53] However, contradictory results were found in a sample of 111 children and adolescents with obesity aged 8 to 15 years attending a one-year outpatient weight-reduction program.[55] Children who succeeded in the intervention (losing more than 5% of BMI-SDS; n=63) showed lower inhibitory control compared with those who failed, suggesting that high ''impulsivity'' may have some level of influence on success. The authors suggest that the children with lower inhibitory control may benefit more from the behavioral therapy strategies provided in the intervention. It is important to note that the type and the duration of the intervention program and/or neuropsychological assessments may contribute to these contradictory results regarding the role of inhibitory control in weight loss.

Delayed discounting also has been also assessed as a predictor of intervention outcomes. Children aged 7 to 12 years demonstrated that those who displayed greater discounting of future food rewards lost less weight as an outcome of a 16-week family-based obesity treatment.[56] In addition to inhibitory control and delayed discounting, investigators reported a correlation between executive function domains of attention and weight loss among children and adolescents. Previous studies have demonstrated that greater attention difficulty in children and adolescents predicted less weight loss following long-term weight loss treatment.[57,58] Overall, specific areas of executive functioning, particularly inhibition and delayed discounting, have a stronger evidence base supporting the relationship with weight loss outcomes. This implies that not all aspects of executive functioning are linked to weight loss by the same mechanisms.

Executive Functioning and Obesity-Related Behaviors

Poorer executive function is linked to obesity-related behaviors, such as high food intake, dysregulated eating, sedentary behaviors and sleep deprivation. Obesity-related behaviors may play a role in the relationship between exeuctive functioning and weight loss[51] (See **Figure 2**).

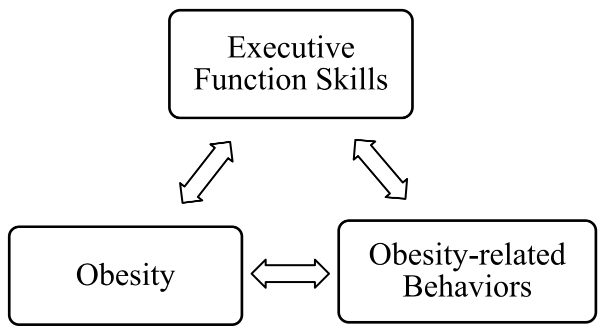

Figure 2. Executive function model of obesity and obesity-related behaviors[51]

Several studies reported a correlation between impaired executive functioning and dysregulated eating behaviors that lead to weight gain. High-sugar and high-fat food intake was adversely correlated with executive function in fourth-grade children.[59,60] Executive function was associated with food approach behaviors including responsiveness to food, desire to drink, and restrained eating in elementary-school girls (aged 6-11 years).[61] Poorer executive function, particularly planning and impulsivity, predicted weight gain from age 10 to 16 years that were mediated by binge eating behaviors.[62] Compared to lean adolescents, participants with obesity who had significantly higher ratings of disinhibition, hunger, and cognitive restraint had lower performance on the cognitive tests.[63] Poorer executive function was also associated with overating and binge eating across 195 youth with obesity aged 8 to17 years.[64] Closer examination of an associations between executive function and eating behaviors is needed to support intervention approaches, given that (1) disordered eating attitudes have an impact on excess weight gain and psychosocial health; and (2) executive function may be modifiable in childhood and adolescence through targeted intervention.[65]

Additionally, evidence supports the mediational role of low physical activity as well as sleep deprivation on executive function. Physical inactivity can adversely impact executive function through several mechanisms, thus interfering with goal-oriented actions required to facilitate changes related to healthy lifestyle behaviors.[66] Executive function skills were negatively associated with sedentary behaviors in fourth grade children.[59,67] Another study reported that better executive function, particularly working memory, was predicted by a higher level of physical activity in a sample of adolescents aged between 12 to16 years.

Poor sleep behavior has been proroposed as a mediator between executive function and weight gain. Sleep deprivation and obesity may be associated with neurocognitive impairments through an unknown mechanism. Evidence shows that both inadequate sleep duration and poor sleep quality may correlate with lower executive function. A longitudinal study suggested that executive function is strongly mediated by sedentary behaviors and sleep duration among 709 students aged 9 to 11 years.[68] A study by Pearce et al. demonstrated the contribution of sleep health to the association between obesity and executive function among children aged 7 to 18 years. Sleep quality was worse in children with obesity and contributed to executive dysfunction in their everyday behavior, compared to children without obesity.[69] However, working memory and decision-making were not associated with this factor.

In summary, these studies support the view that poor executive function would affect the individual's ability to engage in healthy choices and behaviors supportive of achieving weight control outcomes.

Mechanism for Executive Function and Obesity

Although the association between obesity and executive function is increasingly recognized, the direction of the relationship between executive functioning and obesity is still unclear. The evidence has revealed the bidirectional causality of this association. One theory suggests that deficits in executive function increase the risk of obesity-related behaviors including dysregulated eating, lack of physical activity, and poor sleep, as avoiding such behaviors require executive function skills.[70] This point of view suggests that executive dysfunction is considered as the predictor of unhealthy behaviors, and consequently, weight gain. Another theory supports that reduced blood circulation to certain areas of the brain, inflammation, and insulin and glucose dysregulation in the brain associated with obesity may exacerbate executive function decline.[50,71] This is further confirmed by the finding of improvement in the executive functioning performance following weight loss.[50,70] However, it is unlikely that there is a single neurobiological explanation in the link between obesity and executive function. This evidence suggests that the relationship between obesity and impaired executive functioning may be bidirectional. Future studies are needed to clarify the nature of the association and casual direction between executive function and obesity.

Identifying the directional pathways of the association between executive functioning may determine the nature of the treatment approach. For example, if poor executive functioning leads to obesity, the treatment approach should target executive function skills through integreating executive function training into weight loss programs. Whereas if the obesity leads to impaired executive function, the intervention should target obesity-related factors that negatively affect executive functioning skills through dietary, physical activity or surgical interventions.[52]

Intervention Implications

There is a significant need for novel intervention strategies to control the childhood obesity epidemic. Executive function deficits may contribute to the limited success of behavioral therapy to manage weight in children and adolescents.[52] Pretreatment evaluation of executive function may have implications for the intervention strategies for those with poor executive function, especially for children who have not been successful in losing weight after a traditional obesity intervention. Early identification of executive dysfunction has the potential to effect treatment plan design, improve effectiveness of interventions and treatment outcomes, and reduce attrition rate in weight management programs.[50-52]

Alternative treatment approaches may be designed for children and adolescents with executive function deficits, addressing the developmental and individual needs of each child. Interventions that targeted specific executive skills within pediatric obesity treatments show promise in positively affecting eating behaviors and weight loss outcomes.[50] Executive function training with game elements, which specifically targeted inhibition and working memory skills in children with obesity aged 8 to 14 years, resulted in lower weight regain at the 8-week intervention program.[65] An attention modification intervention and an executive function training intervention resulted in a reduced level of overeating in an ad libitum taste test in children with obesity aged 8 to 12 years, compared to control groups. The findings support integrating executive function training components to the structured behavioral treatment for children and adolescents with obesity. Nevertheless, studies with more rigorous methodological designs are needed to increase understanding of how executive functioning contributes to treatment outcomes.

Conclusion

Obesity rates in children and adolescents have nearly tripled in the United States over the last 30 years. Pediatric obesity treatment is a key, as obesity sets youth on a tracjectory for lifetime physical and psychological health complications.[72] Lifestyle modifications (dietary, physical activity, behavior) are the first line of therapy to promote weight reduction in children with obesity. However, successful weight loss with behavioral interventions is still limited, attrition is high, and long-term treatment outcomes are insufficient.[73] Given that treatment outcomes for weight control are limited and most children who participate in weight management programs do not respond sufficiently to the treatment, identification of individual and treatment-level factors associated with weight loss and improved outcomes is critical. It is important to understand the potential predictors as they may explain how children and adolescents respond differently to the same treatment. Identifying children who most likely to succeed in a given program could improve overall success and lead to consideration of alternative approaches based on each patient's characteristics and needs. Moreover, it would be beneficial in allocating existing resources to those who are more likely to benefit from the specific intervention program. A number of characteristics have been related to long-term weight loss treatment outcomes such as age, sex, socioeconomic status, severity of obesity, and cognitive and psychological factors. However, there are no reliable predictors for successful weight reduction in children and adolescents.

More research is needed to examine the variables that predict successful weight reduction in response to lifestyle intervention. This research would be with a large population and evaluate comprehensive variables using a prospective design with a longer follow-up period. Further, there are limitations in some of the studies cited in this review. Since most of these studies have no control group without intervention, there is no information on the change in weight status without intervention. In terms of therapy, some studies have not demonstrated the specific type of diet and exercise that children were following during the intervention for better understanding of the effectiveness of therapy. Also, successful weight loss was only defined based on a decrease in BMI-SDS without considering other body composition measurements, which may be more accurate ways to assess fat mass than BMI. Strengths of these studies include successful treatment by primary care providers in outpatient or academic-based settings. The treatment plan in these studies includes several aspects of lifestyle modification with long-term follow-up. Furthermore, the studies have evaluated a number of factors to identify the predictors of successful weight loss during the intervention. These studies included an acceptable sample size of a representative group of children in different age groups. Collectively there is no evidence of a single factor strongly predicting weight loss; factors interact and models have to be designed to adjust for and incorporate the interdependencies among the factors.

Purpose of Dissertation

Given the complexity of weight loss, there is a clear need to identify both individual- and clinical-level factors of successful weight management. Questions of predictors of successful weight loss in children and adolescents with obesity must be answered to properly develop effective individualized interventions aimed at improving the weight control outcomes.

The aims of this dissertation were the following:

Specific Aim 1: To investigate the impact of the pediatric metabolic syndrome and obesity on the development of type 2 diabetes and cardiovascular diseases.

Specific Aim 2: To identify baseline factors and characteristics associated with successful weight reduction in a medically supervised weight management program among children and adolescents with obesity.

Specific Aim 3: To examine the potential relation between executive function and obesity-related behaviors and the effect of executive function on the treatment outcomes among adolescents with severe obesity seeking surgical options.

Chapter 2: Pediatric Metabolic Syndrome and the Risk of the Development of Type 2 Diabetes and Cardiovascular Diseases: A Retrospective Study

Abstract

Background: The increase in the prevalence of pediatric obesity has led to a rise in associated metabolic complications in pediatric populations. Metabolic Syndrome is a cluster of metabolic abnormalities which increases the risk of developing serious disorders associated with obesity and insulin resistance. The aim of this study is to examine the effect of pediatric metabolic syndrome on being diagnosed with type 2 diabetes, hypertension, stroke, and cardiovascular diseases.

Methods: Retrospective data were obtained from KUMC HERON from 2000 to 2017. Children aged 2 to19 years (defined as a BMI at or above the 95th percentile) with at least three metabolic syndrome factors; obesity, hyperglycemia, elevated triglycerides, low high-density lipoproteins, elevated blood pressure were used to define pediatric metabolic syndrome. Logistic regression and survival analysis were used to evaluate each metabolic syndrome factor on the likelihood of being diagnosed with a disease (type 2 diabetes, hypertension, stroke, or cardiovascular disease) and analyzed the duration of time until the diagnosis.

Results: Among 1979 identified patients, 810 (41.2%) patients presented with at least three of the metabolic syndrome factors. Average age was 14.2$\pm$3.7 years and 44.8% of the sample was female. Nearly 13% of the patients were diagnosed with at least one of the diseases (type 2 diabetes, hypertension, stroke, or cardiovascular disease) after having metabolic syndrome. The analysis revealed that age, and multiple criteria increase the likelihood of being diagnosed with one or more diseases ($p<0.005$). Patients with at least 4 metabolic syndrome factors were diagnosed with diseases sooner than patients with 3 metabolic syndrome factors ($p=0.01$).

Conclusion: Metabolic syndrome may increase the likelihood of diagnosis of certain chronic diseases in children and adolescents with obesity. Early identification and treatment of the children at risk may avoid serious health complications.

Introduction

The prevalence of obesity in children and adolescents is one of the most serious public health issues currently affecting youth. Nearly one of five children aged from 6 to 19 years in the United States has obesity.[4] The alarming nature of obesity centers on its health consequences, typically reserved for adults, including cardiovascular diseases, type 2 diabetes mellitus, sleep apnea, and non-alcoholic fatty liver disease (NAFLD).[8] The adiposity and its endocrine and hormonal actions is responsible for the occurrence of metabolic complications in the body.[74] The combination of dyslipidemia (low high-density lipoprotein cholesterol, hypertriglyceridemia), abnormal glucose regulation, central obesity, and high blood pressure is known collectively as metabolic syndrome.[75]

Metabolic syndrome is a cluster of risk factors that are not only related to the presence of adipose tissue but increase the risk of several co-morbidities such as type 2 diabetes, hypertension, cardiovascular diseases, and many other clinical conditions.[76] Multiple meta-analyses have found that metabolic syndrome increases the risk of cardiovascular diseases by 2-fold and risk of all-cause mortality by 1.5-fold in adults.[77] Morrison et al. found that metabolic syndrome in children ages 6 to 19 years was a significant predictor of adult cardiovascular diseases and type 2 diabetes 25 years later.[78,79]

Metabolic syndrome is common, and its incidence has been increasing for several decades.[80] The National Health and Nutrition Examination Survey (NHANES III) show that the prevalence of the metabolic syndrome was 6.8% among children with overweight and 28.7% among children with obesity.[81] Likewise, a systematic review suggested the prevalence of metabolic syndrome was 11.9% (2.9–29.3%) among children with overweight and 29.2% (10–66%) among children with obesity.[82]

As defined by the US National Heart, Lung and Blood Institute and American Heart Association Consensus Statement, metabolic syndrome describes the presence of three or more risk factors including: 1) central adiposity; 2) elevated blood pressure;3) glucose intolerance; 4) hypertriglyceridemia; and 5) low high-density lipoprotein cholesterol (HDL-C).[83] Although there is no universally accepted definition of metabolic syndrome in the pediatric population, several definitions have been proposed for children and adolescents.[84-87] In general, they share the same common features as adult metabolic syndrome including an obesity estimate (typically body mass index (BMI) or waist circumference), blood pressure measures, blood lipid measures typically including triglycerides and HDL cholesterol and fasting glucose.

The pathogenesis of metabolic syndrome is complex and not completely understood,[88] though several pathophysiological mechanisms are hypothesized to be involved in metabolic syndrome.[85,89,90] Obesity is thought to be a major determinant of metabolic syndrome, causing an increase in triglycerides and blood pressure, and a decrease in HDL.[88] All these factors in addition to inflammation and hormonal factors related to central obesity contribute to the insulin resistance, a hallmark of the metabolic disorder. Prolonged presence of these risk factors is related to the development of altered glucose metabolism and cardiovascular disease.[85]

Lifestyle modification interventions are consistently recommended as the first-line treatment and cornerstone management approach to prevent or control metabolic syndrome.[76,91] Interventions targeting healthy dietary changes, increased physical activity, and behavior modification have been shown to reverse the pathophysiology of the metabolic syndrome, improve biomarkers of risk, and treat comorbidities.[92,93] Encouraging patients and their families through healthy lifestyle changes should be implemented at early stage. Early identification of children at risk of developing metabolic syndrome and referral to specialists as needed is of paramount importance.

The metabolic syndrome has been widely studied in adults; however, there is little research focusing on the impact of pediatric metabolic syndrome on the development of diabetes and cardiovascular diseases. The chronic diseases associated with metabolic syndrome are major causes of morbidity and mortality, therefore, identifying the factors contribute to the development of these diseases has been the focus of much research. A better understanding of childhood obesity and its complications are essential to improve clinical strategies that can reduce or prevent health consequences throughout the life course. The purpose of this study is to investigate the potential impact of the pediatric obesity and metabolic syndrome on future diagnosis of type 2 diabetes, hypertension, stroke, and cardiovascular diseases among children and adolescents. We also investigated the relationship between the risk factors of metabolic syndrome and the temporal trend of disease identification.

Methods

Data Sources

A retrospective study was conducted using the University of Kansas Medical Center's Healthcare Enterprise Repository for Ontological Narration (HERON) system.[94] The HERON database integrates de-identified clinical data from seven different regional sources including hospital electronic medical record systems (e.g., EPIC TM & O2TM), clinical billing system (e.g. IDX), the University of Kansas (KU) Hospital Cancer Registry, KU Biospecimen Repository, Social Security Death Index, University of Kansas Health System (KUHS)

Consortium, and the Research Electronic Data Capture (REDCap) web application.[94] An approval for using this data set was obtained from the Data Request Oversight Committee.

Study Cohort

We reviewed patient records of those who had met the criteria of metabolic syndrome between the years 2000 and 2017 **(Table 1)**. We included patients aged 2 to 19 years with a BMI ≥ 95th percentile for age and sex. We excluded patients with any medical history of type 2 diabetes, hypertension, stroke, and cardiovascular disease. Patients were selected using the i2b2 (Informatics for Integrating Biology and the Bedside) query and analysis tool for HERON.[94,95] We obtained structured data on admission and discharge dates, patient demographics, laboratory values, vital signs, comorbidities and admission diagnosis from the medical chart records.

Table 1. Metabolic Syndrome criteria used in present study

Metabolic Syndrome Criteria	Value
Obesity*	BMI ≥ 95^{th} percentile.
High Blood Pressure	SBP ≥ 135 HH mg.
Elevated Fasting Blood Glucose	FBG ≥ 100 mg/dl.
Elevated Triglyceride	TG ≥ 150 mg/dl.
Low High-Density Lipoprotein	HDL ≤ 40 mg/dl.

Note: Metabolic Syndrome present if ≥3 of the following criteria is fulfilled.
* Obesity is required factor for Metabolic Syndrome inclusion.

Once our sample was identified, we tracked development of new diagnoses of type 2 diabetes, hypertension, stroke, and cardiovascular disease using either the International Classification of Disease, Ninth Revision (ICD-9) or the International Classification of Disease, Tenth Revision (ICD-10) **(Table 2).**

Table 2. Clinical diagnostic codes using ICD-9 and ICD-10

Diagnosis	ICD-9 Codes	ICD-10 Codes
T2D	250.xx	E11
Hypertension	401	I10
Stroke	434.91	I63.9
Cardiovascular Diseases	429.2	I25.10

Abbreviation: **ICD** International Classification of Disease; **T2D** type 2 diabetes.

The timeline of the study was first to identify the patients who have at least three metabolic syndrome criteria, prior to the first diagnosis of the diseases **(**See **Figure 3).** In absence of a consensus pediatric metabolic syndrome definition, we used the definition that has been consistently used in previous studies.[78,79] As waist circumstances was not measured in this cohort, metabolic syndrome definition was modified by using Body Mass Index percentile (age-specific 90th percentile, on the basis of the CDC 2000 Growth Charts) as the measure of adiposity in childhood. BMI cut point has been used instead of the waist circumference as criterion for metabolic syndrome in previous studies.[96-99]

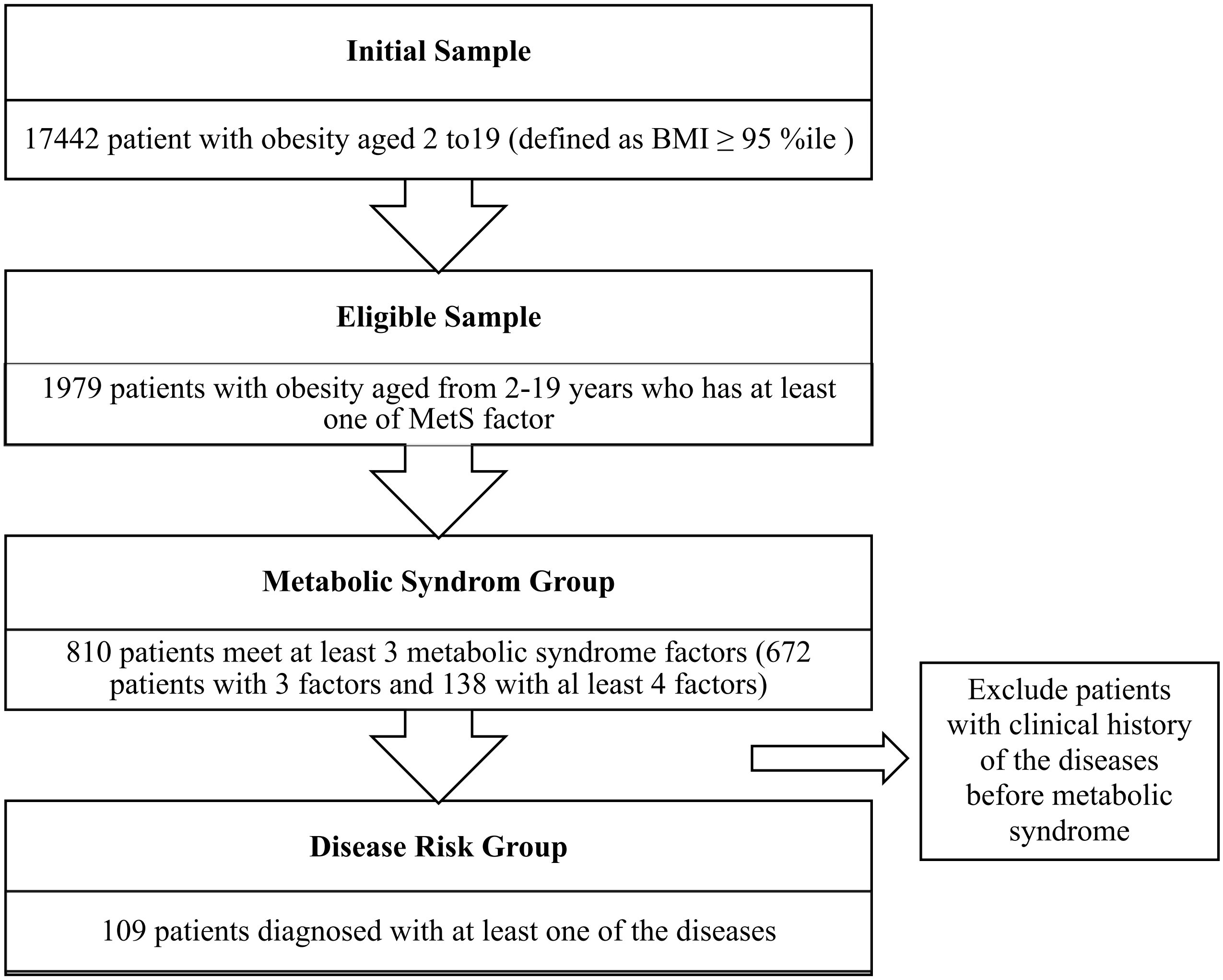

Figure 3. Selection processes flowchart

Statistical Analysis

Statistical analyses included descriptive statistics; frequencies, percentages, and means on the demographic and clinical characteristics of the cohort. The descriptive statistics consisted of means and standard deviations for continuous data and frequencies and percentages for categorical data. Prior to conducting further analyses, assumptions of normality, linearity, and homoscedasticity were examined. Preparing data for analysis also included inspecting outliers and handling missing data through 1) manual data extraction of missing values from the electronic medical records; and 2) case deletion of individual records having missing data on main outcome variables.

Analysis examining differences between two risk groups was conducted to compare baseline patients' characteristics and metabolic syndrome factors using t-test for normally distributed continuous variables, Wilcoxon Analysis tests for continuous variables with skewed distributions, and chi-squared (χ^2) test for categorical variables.

We conducted logistic regression analysis to evaluate the effect of metabolic syndrome factors (BMI percentile, HDL, triglyceride and blood pressure) on the likelihood of developing at least one of the prespecified diseases (type 2 diabetes, hypertension, stroke, and cardiovascular disease) at follow-up (Yes vs. No). We performed Kaplan-Meier survival analysis to analyze time to event data (diagnosis of disease) and to compare two groups of patients. Cox Proportional Hazard Regression analysis further were used to characterize the duration between metabolic syndrome criteria and the disease development.

Statistical significance was assessed at 0.05 level. All data preparations and analyses were performed with IBM SPSS version 20.0 (Chicago, IL, USA) and SAS version 9.2 (SAS institute Inc.) statistical software.

Results

Patient Demographic and Clinical Characteristics

The overall baseline patient characteristics are depicted in **Table 3**. There were 17,442 eligible individuals aged 2 to19 years with obesity (defined as BMI ≥ 95th percentile) from the year 2000 to 2017. Of these, 810 patients satisfied the metabolic syndrome selection criteria and were used to perform subsequent analysis. The average age at the baseline (Metabolic Syndrome were identified) was 14.2 ± 3.7 years, with fairly balanced sex 363 females (44.8%) vs. 447 males (55.2%). The majority of the patients were white race (45.2%).

The average of BMI percentile for age and sex was around the 97th percentile. The average values for triglyceride, HDL-C, and blood pressure were within abnormal levels. The majority of the patients had three metabolic syndrome factors observed (n=672, 83%) while the remainder (n=138, 17%) had at least four metabolic syndrome factors.

Table 3. Baseline demographic and clinical characteristics of the study sample

Characteristics	Overall Sample (N=810)
Age (years)	
Mean (SD)	14.17 (3.65)
Sex, n (%)	
Female	363 (44.8)
Male	447 (55.2)
Race, n (%)	
Black	99 (12.2)
White	366 (45.2)
Other	345 (42.6)
%BMI	
Mean (SD)	96.76 (0.65)

HDL, *mg/dl*	
Mean (SD)	33.55 (5.31)
TG, *mg/dl*	
Mean (SD)	198.90 (96.02)
SBP, *HHmg*	
Mean (SD)	141.09 (6.56)
Number of MetS	
3 factors	672 (83.0)
≥ 4 factors	138 (17.0)

Abbreviation: **MetS** Metabolic Syndrome; %**BMI** body mass index percentile for age and sex**; TG** triglyceride; **SBP** systolic blood pressure; **SD** standard deviation.

The Metabolic Syndrome and Risk of the Disease

After we excluded the patients with clinical history of any of the diseases before meeting metabolic syndrome criteria, the patients were later retrospectively assessed whether they had subsequently been diagnosed with at least one associated disease. Out of 810 patients, a total of 109 patients were diagnosed with at least one of the specified metabolic diseases (hypertension, type 2 diabetes, stroke, and heart disease). The number of patients represent around 13% of our sample with metabolic syndrome. Of those that were diagnosed with a disease, 49 (47%) had hypertension followed by 38 (36.5%) with type 2 diabetes. Heart disease and stroke each had less than 10% incidence. The patients were then stratified into two groups based on their disease status; with disease vs. without disease representing those diagnosed with a disease vs those undiagnosed, respectively **(Table 4)**.

Table 4. Patient stratification by disease diagnosis

	Without disease diagnosis (n=708)	**With disease diagnosis (n=109)**	**p-value**
Age			
Mean (SD)	14.01 (3.62)	15.25 (3.68)	< 0.001
Sex, n (%)			
F	313 (44.2)	50 (49.0)	0.361
M	395 (55.8)	52 (51.0)	
Race, n (%)			
Black	77 (10.9)	22 (21.6)	0.003
White	318 (44.9)	48 (47.1)	
Other	313 (44.2)	32 (31.4)	
Number of MetS, n (%)			
3 factors	597 (84.3)	75 (73.5)	0.007
≥ 4 factors	111 (15.7)	27 (26.5)	
%BMI			
Mean (SD)	96.77 (0.64)	96.75 (0.67)	0.765
HDL, *mg/dl*			
Mean (SD)	33.71 (5.15)	32.27 (6.32)	0.054
TG, *mg/dl*			
Mean (SD)	200.50 (97.63)	185.43 (80.54)	0.120
SBP, *HH mg*			
Mean (SD)	140.76 (6.27)	142.23 (7.39)	0.230

Abbreviation: **MetS** metabolic syndrome; %**BMI** body mass index percentile for age and sex**; TG** triglyceride; **SBP** systolic blood pressure.

Baseline age was found to be significantly associated with the disease diagnosis ($p<0.001$). We also observed association of race with disease risk ($p=0.003$). The number of metabolic syndrome factors, this was also found to be significantly associated with disease risk ($p=0.007$). The multiple logistic regression model was used to answer our study aim of testing for an association between the number of metabolic syndrome factors and disease risk while adjusting for other subject characteristics. Factors that were redundant in the model (BMI, HDL, TG and SBP) were not included since they were used to calculate the number of metabolic syndrome factors. The reference categories for discrete variables were sex (ref. =female), race (ref. =black) and number of metabolic syndrome factors (ref. =3). Test of association between disease risk and number of metabolic syndrome factors while adjusting for other characteristics was assessed at .05 level of significance. Results from the multiple logistic regression are shown on **Table 5**.

Table 5. Multiple logistic regression for predictors of disease diagnosis

Characteristic	Estimate (SE)	Odds Ratio (OR: 95% CI)	p-value
Age	0.08	1.08 (1.01-1.16)	0.03
Gender (Ref: Female)			
Male	-0.26	0.77 (0.50-1.18)	0.23
Race (Ref: Black)			
White	-0.57	0.57 (0.32-1.02)	0.05
Other	-0.75	0.47 (0.25-0.89)	0.06
Number of MetS (Ref. 3 factors)			
≥ 4 factors	0.52	1.68 (1.00-2.77)	0.04

Abbreviation: **MetS** Metabolic Syndrome, **OR** Odds Ratio, **Ref** Reference.

Baseline age and the number of metabolic syndrome factors were the only variables that were found to be statistically associated with disease risk (p=0.027) and (p=0.04) respectively. Patients with at least four metabolic syndrome factors were almost twice as likely to be diagnosed with the disease (type 2 diabetes, hypertension, stroke, or cardiovascular disease) as compared to those with three metabolic syndrome factors (OR:1.68 (1.00 – 2.77)). Increasing age was significantly associated with a greater risk of being with a disease. A unit increase in age increased the likelihood of having a disease diagnosis by 8% (OR: 1.08 (1.01 – 1.16)).

The Relationship between Metabolic Syndrome and Temporal Trend of Disease

Using Cox Proportional Hazard regression model, we investigated the number of metabolic risk factors as the dependent variable and the time to being diagnosed with disease. We used Cox Proportional Hazard regression model to analyze the association between the number of metabolic syndrome factors as predictor and the duration of time until one of the diseases diagnosed. Cox Proportional Hazard provides information about the hazard rate, in this case the risk of getting a disease diagnosis given that the patient has not been diagnosed with a disease at a specific time. An initial Kaplan Meier curve and logrank test was performed on the data **(**See **Figure 4)**.

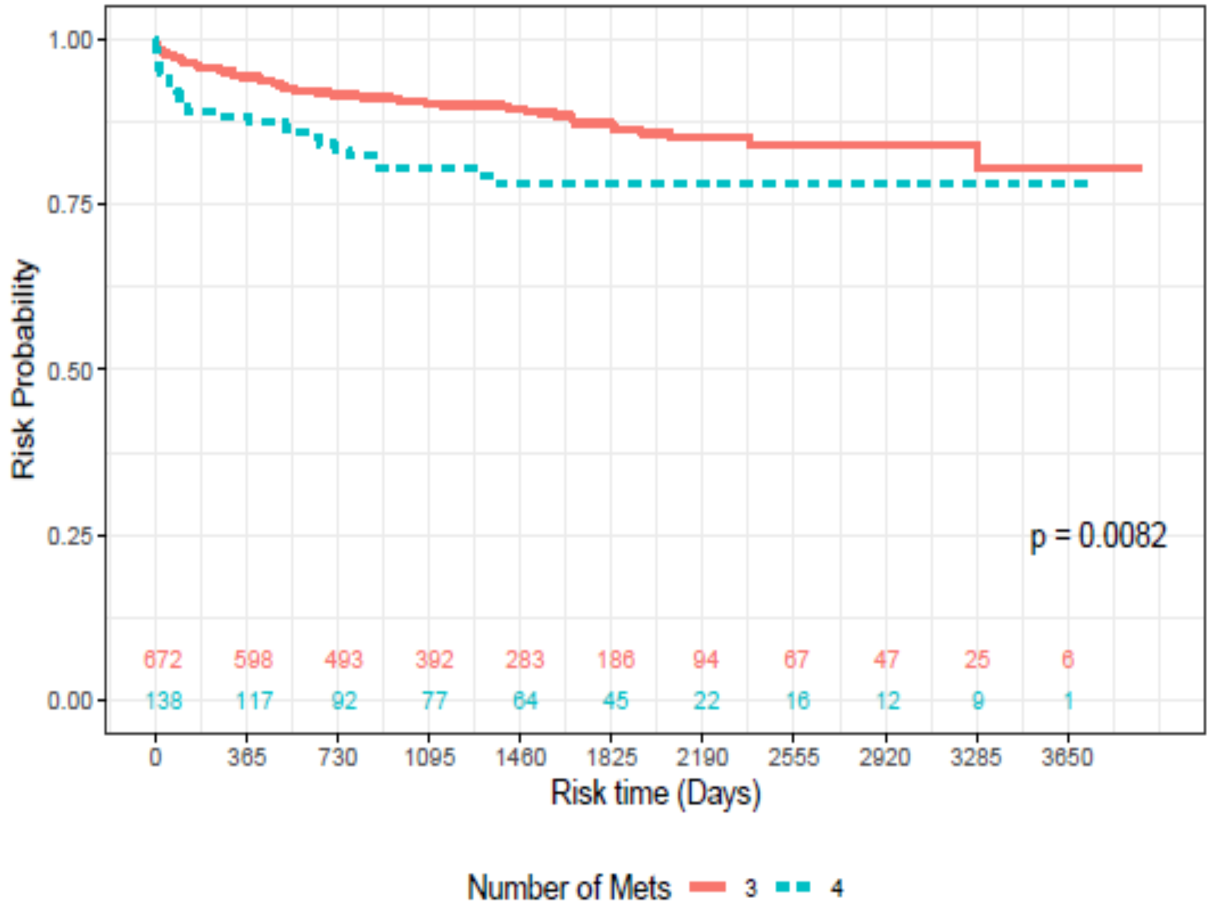

Figure 4. Kaplan–Meier survival curves showing overall survival of the disease risk by number of Metabolic Syndrome factors

Using Kaplan-Meier survival analysis, we observed a statistically significant difference between the two strata; patients with three or at least four metabolic syndrome factors. The probability of being diagnosed with one of the metabolic diseases was significantly higher among patients with at least four metabolic syndrome factors compared with those with three metabolic syndrome factors; p-value associated with disease risk is 0.0082. Patients with at least four metabolic syndrome factors were more likely to receive a diagnosis of disease sooner than those with three metabolic syndrome criteria. For instance, after four years of having Metabolic

Syndrome, at least 25% of patients having at least four metabolic syndrome factors were diagnosed with a disease compared to about 10% of patients with three metabolic syndrome factors.

Further investigation of the time to disease with adjustment of other covariates is performed using Cox Proportional Hazard (PH) regression and results shown on **Table 6**. The expected hazard of getting diagnosis with a disease is nearly 1.6 times higher in patients with at least four metabolic syndrome factors as compared to patients with three metabolic syndrome factors while adjusting for age, sex and gender. **Figure 4** and **Table 6** show the results of the Cox PH Fit analysis.

Table 6. Cox proportional hazard regression results

	Coefficient	SE	Hazard Ratio	2.5%	97.5%	p-value
Number of MetS	0.46	0.23	1.581	1.003	2.49	0.049
Age	0.09	0.03	1.095	1.029	1.17	0.004
Gender	-0.30	0.20	0737	0.498	1.09	0.128

Abbreviation: **MetS** metabolic syndrome

Note: The logrank P value associated with disease risk is 0.0082.

Discussion

As there is an alarming increase in childhood obesity over the past two decades, Metabolic syndrome in children and adolescents has recently become a major public health problem.[100] Metabolic syndrome is one predictor of future risk of cardiovascular disease and type 2 diabetes among children. Therefore, our study addresses the impact of metabolic syndrome and obesity on development of cardiovascular diseases, stroke, hypertension and type 2 diabetes. To our knowledge, it is the first study to assess the contribution of the number of metabolic syndrome criteria on a future diagnosis of disease.

Our findings suggest that metabolic syndrome is associated with an increase of future incidence of both type 2 diabetes and cardiovascular disease among children and adolescents with obesity. A higher frequency of metabolic syndrome factors has been shown to increase the likelihood of being diagnosed with at least one of these chronic diseases after having metabolic syndrome. Children and adolescents with at least four metabolic syndrome factors may be diagnosed with one or more obesity-related comorbidities including type 2 diabetes, hypertension, stroke, and cardiovascular disease sooner than those with three metabolic syndrome factors. These findings suggest that children and adolescents who present with obesity and/or factors associated with metabolic syndrome should receive extra attention toward reducing the potential long-term risks for future chronic diseases.

Traditionally, healthcare providers have evaluated each of the risk factors contributing to metabolic syndrome individually.[83] Rather than a specific phenotype, cluster of metabolic syndrome factors should be considered as a marker for the presence of increased disease risk.[85] Our findings support the importance of early identification of children with multiple metabolic syndrome risk factors. Children who identified with metabolic syndrome risk factor at younger age have lower risk of developing a diagnosed disease later in life. The early identification enables clinicians to apply their most intensive intervention efforts sooner to prevent or reduce the chance of the disease development.[86] The evidence on the rate of metabolic syndrome in the pediatric population and the track of metabolic syndrome from childhood to adulthood should lead to a wider application of screening and intervention programs.[78,79] Further work is needed to explore the potential targets for the prevention of childhood obesity and early onset of metabolic disease.

Metabolic Syndrome Severity Score is a promising new approach that provides additional risk prediction using *z*-score standardized values for all different parameters. These scores are sex- and race-ethnicity specific and reflect the severity of metabolic syndrome.[101] A higher score of metabolic syndrome is associated with long-term risk for type 2 diabetes and cardiovascular disease.[102,103] The clinical use of the severity score would likely benefit from incorporation into the electronic medical record. These scores may help clinicians to stratify patients who need strict monitoring and aid in following their metabolic syndrome status over time. Counseling families on how reductions in metabolic syndrome severity reduce risk of future diseases may assist in motivation toward change and adherence to the intervention.[104]

Our study has a number of limitations. First, the results from this study represent one academic medical center's clinical population, and thus, findings may not generalize. Second, its retrospective nature and the small number of patients limit the validity of the clinical outcomes. Third, data on fasting glucose were only reported for 5% of the patients in our cohort. Thus, we were not able to fully examine the impact of this factors on the disease incidence. Finally, our dataset lacks waist circumference assessment which is an important element of the definition of central obesity as a component of the metabolic syndrome. However, we replaced this criterion with BMI percentile as presented in previous studies.[96-99] Other limitations included that the present study could not provide information on nutrition, physical activity, puberty or other factors that may play mediation roles in this association.

Even with these limitations, we were able to use clinical data obtained in a large database. The use of additional clinical data sets from other facilities would also help with generalizability and allow for more power with the larger sample size. The primary strength of this study is the use of archived clinical data to assess the risk of obesity-related disease progression which reduces costs and time that conducting a large-scale observational trial would otherwise require.

Conclusion

Given the increased obesity prevalence, preventing and treating metabolic syndrome in pediatric patients is becoming an urgent need for public health. Metabolic syndrome and its many consequences may present serious threats to the current and future health of youth. Our findings show that pediatric metabolic syndrome is associated with future diagnosis of obesity-related metabolic diseases. More importantly the number of metabolic syndrome factors are associated with faster development of a disease diagnosis. Evaluating children for metabolic syndrome could identify patients at increased risk of cardiovascular disease and type 2 diabetes and allow for targeted interventions at early stage.

Chapter 3: Early Response Predicts Longer-Term Outcomes in Pediatric Weight Management Program

Abstract

Background: Variability in treatment response is known in pediatric weight management (PWM). The purpose of this study is to examine patient and treatment-specific predictors associated with improvement in weight status in children and adolescents in a medically supervised PWM program.

Methods: We retrospectively analyzed clinical data for youth (2-18 years of age) with obesity enrolled for at least six months in PWM at a large urban center. Weight status (percentage of the 95th percentile for body mass index [%BMIp95]) at 6-months was compared to baseline patient characteristics and program exposure and analyzed using multivariable linear regression modeling.

Results: We included 698 children and adolescents (53.6% female, mean age 10.4 ±3.3 years; mean %BMIp95 132.2±23.2). Compared to the baseline, we observed a reduction in mean%BMIp95 after 6-months (mean difference 2.2 ± 1.5, $p < 0.001$). The strongest predictor of decreased %BMIp95 at 6-months was initial change in %BMIp95 during the first two months of the program ($p < 0.000$). Other characteristics (age, race, sex, socioeconomic status, and psychological diagnosis) were not significant predictors of treatment response.

Conclusion: The present study showed that early weight loss is the strongest unique contribution for predicting treatment outcome as it is significantly associated with greater long-term BMI reduction. The findings highlight the importance of early experience in and response to treatment to increase the likelihood of positive outcomes.

Introduction

Over the last decade, the prevalence of obesity in children and adolescents has increased dramatically, becoming one of the most public health issues.[105] Nearly 18% of children and adolescents aged 2 to 19 years in the United States have obesity.[106] Trends toward increasing obesity prevalence among the pediatric population are not expected to decline. The alarming nature of obesity centers on its serious consequences, rarely seen in children in the past, including asthma, obstructive sleep apnea, orthopedic problems, cardiovascular dysfunction, and type 2 diabetes.[107] In addition to chronic diseases, obesity has been associated with emotional distress and psychological complications. Children with obesity also have greater frequency and higher levels of depression,[108,109] disordered eating,[110,111] and bullying.[112] Furthermore, obesity in childhood and adolescence may continue into adulthood and lead to adverse health outcomes or other obesity-related morbidity.[1]

Successful weight reduction during childhood improves metabolic and cardiovascular outcomes.[113-115] Weight management programs that emphasize lifestyle and behavioral interventions are most likely to produce a significant benefit, but despite the effort and resources that most weight management programs provide, the efficiency and results of such programs are still limited.[14,116,117] It is also understood that in such weight management programs, not all children respond equally to the treatment.[16,118] Many patients fail to achieve meaningful weight loss, and some even gain weight during the treatment. Identification of characteristics that predict success at baseline could contribute to improved intervention efficacy and clinical practice. Recognizing these characteristics could help maximize the effectiveness of existing interventions or develop targeted and personalized interventions. Additionally, identifying factors associated with unsuccessful weight loss outcomes might facilitate alternative treatment approaches when needed and reduce failed experiences.

While identifying factors associated with weight loss could improve interventions, there are currently no reliable predictors of successful weight loss in children and adolescents. Previous studies have considered factors associated with weight loss success in youth. Researchers have shown that several demographic characteristics including age, sex, socioeconomic status (SES), baseline weight and family history of obesity-related comorbidities were all related to the success of the treatment.[14,33,119,120] Early weight loss has also been identified as a factor predicting greater long term treatment outcomes.[37]

Several pretreatment psychological and behavioral factors have been considered barriers to successful weight management, including eating and exercise self-efficacy, binge eating, cognitive eating restraint, and eating disinhibition.[121] Overall, the research on pretreatment predictors of successful weight loss is inconsistent. There are several potential reasons that may account for the inconsistent findings across studies, including differences in the study settings, the number and characteristics of the participants recruited, and the design of weight loss interventions.

Successful intervention for severe obesity in childhood is critical, thus, there is much interest in evaluating the treatment developed specifically for youth with severe obesity. Although most pediatric obesity research has been conducted using changes in BMI-z scores or percentiles to evaluate the treatment outcomes, that approach is not recommended specifically for severe obesity.[122] Extrapolating BMI-z scores or BMI percentiles to determine extreme obesity is problematic since significant changes in weight and BMI are associated with small changes in these metrics.[29,30,123] In addition, the findings emphasize that BMI-z functions poorly as an indicator of adiposity among children with obesity, particularly among those with severe obesity. Alternative measurement has been proposed recently to categorize BMI as "percentage of 95th BMI percentile" (%BMIp95) to define percentiles beyond the 97th percentile. Recent studies suggest that %BMIp95 is more strongly associated with circumferences, triceps skinfolds, and fat mass in children with severe obesity compared with BMI-z scores or percentiles.[30,124] This approach allows classification and tracking of children with severe obesity for both clinical and research purposes. The Pediatric Obesity Weight Evaluation Registry (POWER) study of children with obesity found a 5-point percentile reduction in BMI percentage of the 95th percentile (%BMIp95) to be associated with improved cardiometabolic measures.[31]

Efforts to prevent the obesity crisis have encouraged researchers and health professionals to examine the potential factors related to successful intervention and outcomes. A better understanding of variables that predict weight loss may allow for more effective tailoring of interventions to patient characteristics and increase attendance and success in weight management programs.[22] However, the findings for successful predictors of weight loss are conflicting and mixed in the literature. Taking the inconclusive evidence into consideration, we believe that a study of pretreatment predictors of weight loss is warranted. Therefore, this study aims to determine successful predictors of weight loss at 6-months in children and adolescents with obesity who participated in a medically supervised weight loss program.

Methods

Participants

This project was based on data from Weight Management Clinics (WMC) at Children's Mercy Hospital, Kansas City, Missouri. Patients were referred to the WMC for specialized weight management by primary care providers and subspecialists locally and within approximately a 4-hour region. A retrospective chart review was conducted for all children and adolescents with obesity referred to the WMC from January 2014 through December 2017. We reviewed demographic and clinical data obtained from the patient intake questionnaires, pediatric symptoms checklists, and medical records of patients seen at three different tertiary care-based, structured weight management clinics (WMC). Data collection procedures in the Weight Management Clinic were approved by the Institutional Review Board (IRB) at Children's Mercy Kansas City. A request to rely on the IRB at Children's Mercy Kansas City was approved by the University of Kansas Medical Center.

Inclusion and exclusion criteria

Inclusion criteria included patients aged 2-18 years with a BMI ≥95th percentile for age and sex at their initial visit and availability of an English- or Spanish-speaking parent or caregiver to attend the weight management program with the child. Children with significant intellectual disabilities or genetic conditions (e.g., Down syndrome, Prader-Willi syndrome, Autism spectrum disorder, developmental delay) that prevented age-appropriate participation in therapy sessions were excluded. Patients were included in the analysis if they met the criteria of having baseline and follow-up visit data.

Out of the 1290 patients who attended at least one follow-up visit, 698 patients (54.0%) met the inclusion criteria and were considered for the analysis. A total of 389 patients (30.2%) were excluded for missing a follow-up visit at 6 ± 2 months after the initial visit and 203 patients (15.8%) were excluded for intellectual disabilities or genetic conditions.

Measurements

Electronic medical record data included demographics, anthropometrics, medications, and problem list and diagnoses codes.

Demographic data. Information on age, sex, race, ethnicity, and insurance status was abstracted from the patient medical records and entered into the research database by a trained research assistant. Insurance type groups were public (Medicaid) or private insurance. For socioeconomic status (SES), Census tract median household income was extracted based on patients' home addresses using geocoding as a proxy for SES. The use of area-based SES indicators obtained from address data linked to geocoded census information has been used as an alternative to self-report indicators.[125]

*Clinical Data***.** Medical conditions were identified using *International Classification of Diseases* (ICD)-9 and (ICD)-10 diagnosis codes. Visit documentation and forms collected at the visits were reviewed. Data on nutrition were obtained from registered dietitian documentation notes. Level of program exposure was based on the number of clinical visits that included a height and weight measurement during each time period. Patients on weight loss-promoting medications (metformin, topiramate and phentermine) at the time of the first two visits were identified and included in the study.

Anthropometrics. Child height and weight were measured at each clinic visit by a care assistant or a registered nurse who was trained in standardized procedures to obtain height and weight in youth with obesity. Weight was measured using digital scale, with patients in light clothing and shoes removed, and recorded to the nearest 0.1 kg. Height at visits was measured with patients standing without shoes, and was recorded to the nearest 0.1 cm.

Height and weight measurements were used to calculate BMI-z, BMI percentile, and %BMIp95 percentile for the subject's age and sex using the CDC BMI calculator for statistical analysis software program (www.cdc.gov/nccdphp/dnpao/growthcharts/resources/sas.htm). Obesity class was defined as: 1) obesity class I (BMI between 100% and 119% of the 95th percentile; 2) obesity class II (BMI between 120% to 139% of the 95th percentile or a BMI of 35 whichever was lower); or 3) obesity class III (BMI of ≥140% of the 95th percentile or a BMI of 40 whichever was lower). Those with obesity classes II and III were deemed to have 'severe obesity'.

Weight Management Intervention

The Children's Mercy Weight Management program is a hospital-based clinical treatment program providing interprofessional assessment and treatment for children and adolescents with obesity and their families. The program provides individualized care in the outpatient clinical setting and the interventions are delivered in an interprofessional-based format with all providers participating in the appointments at the same time or over time. The interprofessional team is composed of a specialized medical professional (physician or pediatric nurse practitioner), pediatric psychologist, social workers, and registered dietitians. Patients are scheduled for follow-up visits every 4-6 weeks, but frequency of these visits vary based on clinic availability and patient/family need. At the initial appointment, a complete medical, behavioral, feeding, physical activity, and dietary history is obtained, and treatment goals and recommendations are provided taking into account the unique challenges of the child and the family. All patients are taught balanced eating utilizing MyPlate; behavioral principles of making small, but noticeable changes, environmental controls, and increasing physical activity. At subsequent sessions, response to treatment is assessed, and additional recommendations are provided utilizing a stepwise behavioral approach.

Statistical Analysis

The data are presented as frequencies and percentages for categorical variables and means with standard deviations (SD) for continuous variables. Baseline factors (i.e., medical diagnosis, age, sex, ethnicity, and insurance status) were treated as independent variables and total weight change was treated as a dependent variable. Weight change during the treatment (baseline %BMIp95 minus %BMIp95 at the end of treatment) was the primary outcome and expressed as a change score. Paired t-test or Wilcoxon signed-ranked test were used to compare the change in weight and BMI parameters from baseline and post intervention. Linear regression analyses were conducted to examine the relationship between predictors and weight change outcomes.

In addition to analyzing the weight change as a continues variable, we categorized the change in %BMIp95 into groups. Three groups were identified based on change in %BMIp95 from baseline to the 6-months follow up: 1) gain group increase in %BMIp95 Gain group, 2) lost < 5-point decrease group (%BMIp95 <5-point decrease group) and lost 5 or more points of %BMIp95 (BMIp95 ≥ 5-point decrease group). Analysis examining differences among the groups was conducted to compare baseline patients' characteristics using analysis of variance (ANOVA) test for normally distributed continuous variables, Kruskal-Wallis tests for continuous variables with skewed distributions, and chi-squared (χ^2) test for categorical variables. Logistic regression model was conducted to identify factors significantly associated with a ≥ 5-point decrease in %BMIp95 among patients with 6-month follow-up.

Preliminary tests of the assumptions of the statistical tests, including data normality using Shapiro–Wilk tests (all p values > 0.05), homogeneity of variance (Levene's tests: all p values > 0.05), and homogeneity of regression slopes (all p values > 0.05) were tested and met.

The statistical tests were considered significant if p-value < .05. For statistical analyses we used the software program SPSS 26.0 (Statistical Package for Social Sciences, SPSS for Windows version 13.0, 2019, Armonk, NY, USA).

Results

Patient demographic and clinical characteristics

Data from 698 patients were included in the primary analyses. These patients came from an initial sample of 1290 unique patients with at least one visit recorded in the PWM dataset. For the study cohort, patients had an average initial age of 10.4 years (SD 3.26), with an initial %BMIp95 of 132.2 (SD 23.2). The majority of patients' ethnicity was non-Hispanic (62%) and 36.5% were white. The largest percentage of the sample were enrolled in public insurance (61.3%) and had an annual median household income less than $50,000. Approximately 30% of patients had a BMI ≥140% of the 95th percentile and were classified as severe obesity class 3.

Among all medical conditions, the highest prevalence was found for dyslipidemia (44.8%) and acanthosis nigricans (44.7%), followed by elevated blood pressure (41.3%), and Asthma (23.2%). Twenty percent of the sample had at least one psychological disorder including depression, anxiety, post-traumatic stress disorder (PTSD), attention deficit hyperactivity disorder (ADHD), or bipolar disorder**.** The average number of clinic visits over the six months of the intervention was 3.7 (SD 1.1). Weight loss medications were prescribed for ~11% of patients in our sample. The data from the nutrition note indicated that unhealthy diet and high energy intake are the main contributors for obesity based on an evaluation checklist completed by registered dietitians. Baseline characteristics of the patients included in the study are described in **Table 7**.

Table 7. Demographic and clinical characteristics of patients at baseline visit

Characteristics	All (n=698)
Age, (years) Mean (SD)	10.4 (3.26)
Age Category, n (%)	
2-7	131 (18.8)
8-12	368 (52.7)
13-18	199 (28.5)
Sex, n (%)	
Male	324 (46.4)
Female	374 (53.6)
Race, n (%)	
White	269 (38.5)
Black	135 (19.3)
Hispanic	241 (34.5)
Other	51 (7.6)
Ethnicity, n (%)	
Non-Hispanic/Non-Latino	433 (62.0)
Hispanic/Latino	264 (37.8)
Insurance type, n (%)	
Government	428 (61.3)
Commercial	238 (33.8)
Self-Pay/No Insurance/Other	34 (4.9)
Median Household Income, n (%)	
< $30,000	163 (23.3)
$30,000 - < $50,000	258 (37.0)
$50,000 - < $70,000	139 (19.9)
≥ $70,000	137 (19.6)
Language, n (%)	
English	501 (71.6)
Spanish	187 (26.8)
Other	10 (1.4)

Comorbidities, n (%)	
Acanthosis Nigricans	312 (44.7)
Dyslipidemia	313 (44.8)
Elevated BP	287 (41.1)
Asthma	160 (22.9)
Psychological disorders	141 (20.2)
ADHD	81 (11.6)
Medication, n (%)	73 (10.5)
Number of visits, Mean (SD)	3.8 (1.1)
Obesity Class, n (%)	
Class1	244 (34.9)
Class 2	254 (35.9)
Class 3	215 (29.3)
Weight Status, Mean (SD)	
Weight, (kg)	72.3 (31.2)
BMI, (kg/m2)	31.4 (7.6)
BMI-z	2.4 (0.5)
%BMI	98.7 (1.2)
%BMIp95	132.2 (23.2)
RD identified contributor to obesity, n (%)	
Unhealthy diet	403 (57.7)
High energy intake	388(55.6)
Physical activity concern	300 (43.0)

Abbreviations: **BMI** body mass index, **%BMI**, BMI-for-age percentile, **%BMIp95** BMI expressed as a percentage of the 95th percentile, **BP** blood pressure, **ADHD** Attention deficit hyperactivity disorder, **RD** registered dietitian **SD** standard deviation. **Medication** variable represent number of patients taking weight-loss medication.

The effect of intervention on weight status

The primary study outcome was a change in the %BMIp95 from baseline to six months of the intervention. At six months, 450 patients (64.5%) had decrease in %BMIp95, with overall mean change as -2.1 (SD 6.3). Of those who experienced any decreased %BMIp95, 201 (28.8%

of total sample) patients achieved a decrease in %BMIp95 of ≥5 points with mean %BMIp95 decrease -10.26 (SD 4.6) and 249 patients (35.6%) had a decrease in %BMIp95 of <5 points, with mean BMIp95 decrease -2.2 (SD 1.5). Approximately 35.5% of the sample had a gain in %BMIp95 with an average increase of 4.1(SD 3.8). **Table 8** shows the weight changes at six months of the intervention.

Table 8. Change in outcomes from baseline to 6 months after the intervention

		%BMIp95 change group			
Mean Change	**Total Sample (n=698)**	**≥5-point decrease (n=201)**	**<5-point decrease (n=249)**	**Gain (n=248)**	**p-value**
Weight (kg)	2.2 (4.2)	-2.02 (3.9)	1.91 (2.0)	5.27 (3.3)	<0.001
BMI-z	-0.07 (2.4)	-0.28 (0.25)	-0.051 (0.05)	0.06 (0.12)	<0.001
%BMI	-0.3 (0.9)	-0.64 (0.73)	-0.23 (0.34)	0.2 (0.7)	<0.001
%BMIp95	-2.1 (6.3)	-10.26 (4.6)	-2.2 (1.5)	4.1 (3.87)	<0.001

Abbreviations: **BMI** body mass index, **%BMI**, BMI-for-age percentile, **%BMI95** BMI expressed as a percentage of the 95^{th} percentile.

We next examined the patient characteristics based on the %BMIp95 change groups (See **Table 9**). Four variables reached the significance of p ≤ .05 for consideration in regression modeling process. Patients in ≥5-point decrease group attended more visits compared with other groups (p= 0.033). Among the obesity-related comorbidities, patients in ≥5-point decrease group less often had a diagnosis of acanthosis nigricans. Other comorbidities or medical concerns did not significantly differ among the three groups. The early change in %BMIp95 from baseline to the first two months of treatment was significantly different among the groups (<0.001). Average change was -4.0 (SD 3.7) in the ≥5-point decrease group compared with the average change in

<5-point decrease -0.83 (SD 2.9) and Gain group 1.1 (SD 3.6). **Figure 5** shows boxplots of the change in %BMIp95 at 1 to 2 months based on the three %BMIp95 change groups at 6-months.

No statistically significant differences were found among the patients in the three %BMIp95 change groups for age, sex, race, ethnicity, insurance type, household income, language, obesity class, or medication. **Table 9** shows differences among the %BMIp95 change groups for demographic and clinical characteristics.

Table 9. Characteristics of patients based on the weight change groups at 6-month

	%BMIp95 change group			
Characteristics	**≥5-point decrease (n=201)**	**<5-point decrease (n=249)**	**Gain (n=248)**	**p-value**
Age, Mean (SD)	10.4 (3.5)	10.7 (2.9)	10.2 (3.4)	0.19
Age Category, n (%)				0.33
2-7	47 (23.3)	38 (15.2)	46 (19.7)	
8-12	101 (50.2)	137 (55.0)	130 (52.4)	
13-18	53 (26.3)	74 (29.7)	72 (29.0)	
Sex, n (%)				0.44
Male	100 (49.5)	103 (41.9)	119 (48.0)	
Female	102 (50.5)	143 (58.1)	129 (52.0)	
Race, n (%)				0.447
White	86 (42.6)	85 (34.6)	99 (39.9)	
Black	30 (14.9)	56 (22.8)	49 (19.8)	
Hispanic	70 (34.7)	86 (35.0)	82 (33.1)	
Other	16 (7.9)	19 (7.7)	18 (7.3)	
Ethnicity, n (%)				0.68
Non-Hispanic/Non-Latino	121 (60.2)	158 (64.2)	155 (62.5)	
Hispanic/Latino	80 (39.8)	88 (35.8)	93 (37.5)	
Insurance type, n (%)				0.88
Government	120 (59.4)	150 (61.0)	156 (62.9)	

Commercial	72 (35.6)	82 (33.3)	82 (33.1)	
Self-Pay/No insurance/other	10 (5.0)	14 (5.7)	10 (4.0)	
Median Household Income, n (%)				0.49
< $30,000	44 (21.8)	57 (23.3)	62 (25.0)	
$30,000 - < $50,000	69 (34.2)	92 (37.6)	95 (38.3)	
$50,000 - < $70,000	46 (22.8)	42 (17.1)	51 (20.6)	
≥ $70,000	43 (21.3)	54 (22.0)	40 (16.1)	
Language, n (%)				0.93
English	146 (72.3)	175 (71.1)	181 (73.0)	
Spanish	52 (25.7)	68 (27.6)	64 (25.8)	
Other	4 (2.0)	3 (1.2)	3 (1.2)	
Comorbidities, n (%)				
Acanthosis Nigricans	75 (37.1)	120 (48.8)	115 (46.4)	0.037
Dyslipidemia	98 (48.8)	110 (44.2)	105 (42.3)	0.38
Elevated BP	94 (46.5)	95 (38.6)	98 (39.5)	0.18
Asthma	43 (21.3)	60 (24.4)	58 (23.4)	0.74
Psychological disorders	49 (242)	42 (17)	50 (20.2)	0.14
ADHD	30 (14.9)	23 (9.3)	27 (10.9)	0.18
Number of visits, Mean (SD)	4 (1.1)	3.72 (1.1)	3.64 (1.1)	0.033
Medication, n (%)	32 (14.8)	20 (8.0)	21 (10.4)	0.21
Obesity Class, n (%)				0.02
Class1	58 (28.7)	102 (41.5)	83 (33.5)	
Class 2	85 (42.1)	83 (33.7)	81 (32.7)	
Class 3	59 (29.2)	61 (24.8)	84 (33.9)	
Baseline %BMIp95, Mean (SD)	133.4 (21.4)	128.8 (21.2)	134.8 (26.3)	0.01
Change in %BMIp95 at 1-2 months, Mean (SD)	- 4.0 (3.7)	-0.83 (2.9)	1.1 (3.7)	<0.001

Abbreviations: **BMI** body mass index, BMI95 BMI expressed as a percentage of the 95th percentile, **BP** blood pressure, **ADHD** Attention deficit hyperactivity disorder, **SD** standard deviation.
Note: **Medication** variable represent participants taking weight-loss medication.

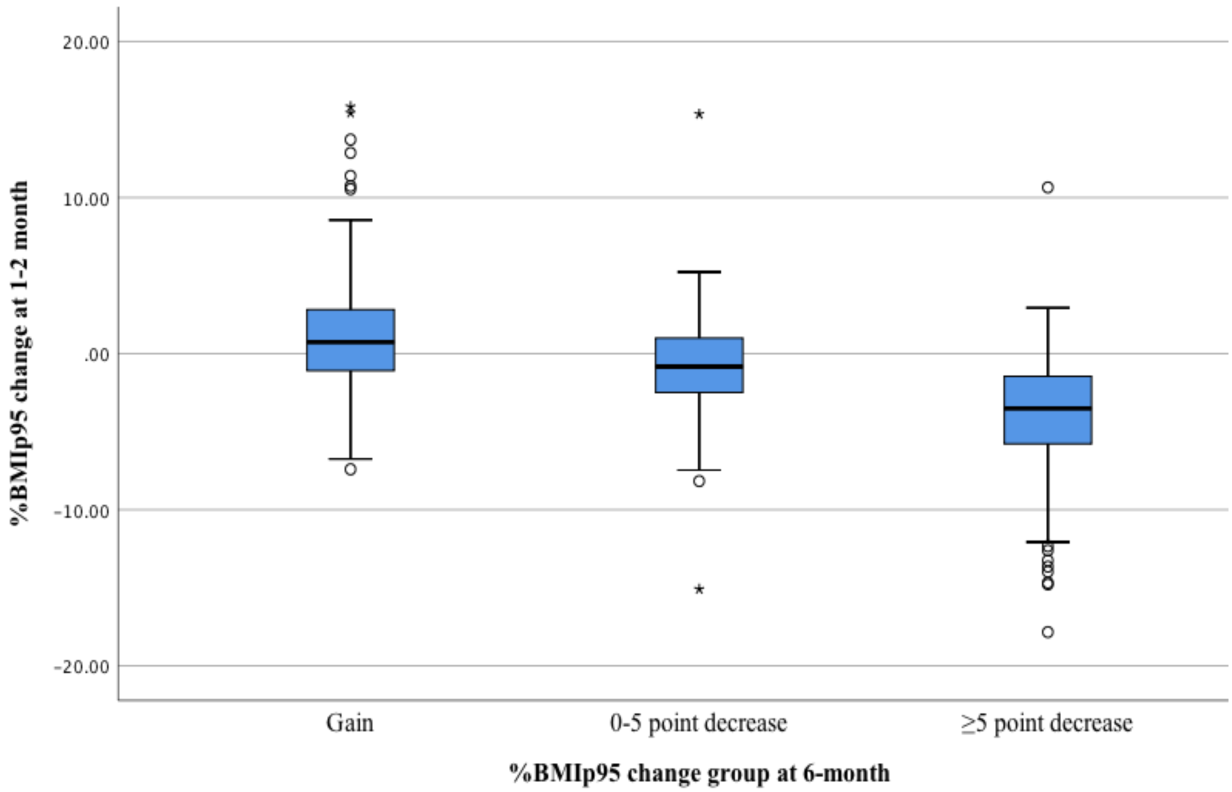

Figure 5. Percentage change in %BMIp95 at 1 to 2-months categorized by change in %BMIp95 at 6-months

Demographics and clinical predictors of weight loss outcomes

Regression model was conducted to examine the relation between baseline variables and successful weight reduction at 6-months. The strongest predictor of treatment outcomes was initial change in %BMIp95 at 1 to 2 months of the program (See **Table 10**). Early change in %BMIp95 was positively associated with change in %BMIp95 at 6-months of the intervention (R2=0.38, P<0.001). Early change in BMIp95%ile explained 38% of variance in the ultimate change at 6 months. Children who lost weight during the first two months of the program were more successful in losing weight at 6-months of the program. The overall mean changes in

%BMIp95 was -1.14 (SD 4.0) after the first two months, with178 patients (25.5%) achieving an early response to the weight management intervention of ≥3 %BMIp95 reduction after the first two months of the intervention. **Figure 6** shows scatterplots of the change in BMI at 6-months based on BMI change at 1- to 2-months. No other demographic or clinical characteristics were significant predictors for weight loss at 6 months.

Table 10. Multiple linear regression analysis with change in %BMIp95 at 6-month as the dependent variable

Predictors	**Regression Coefficient**	**95% CI**	**p-value**
Age	-0.029	-0.15 to 0.093	0.64
Gender	0.412	-0.40 to 1.23	0.32
Race	0.103	-0.316 to 0.52	0.63
Acanthosis Nigricans	0.465	-1.33 to 0.40	0.29
Number of visits	-0.161	-0.53 to 0.21	0.39
Baseline %BMIp95	0.004	-0.023 to 0.02	0.66
%BMI95 change at 1-2 months	0.939	0.84 to 1.04	<0.001

Abbreviation: **CI** confidence interval **%BMIp95** BMI expressed as a percentage of the 95^{th} percentile.
Model was controlled for participant's age, race, gender, and ethnicity, Baseline %BMIp95.

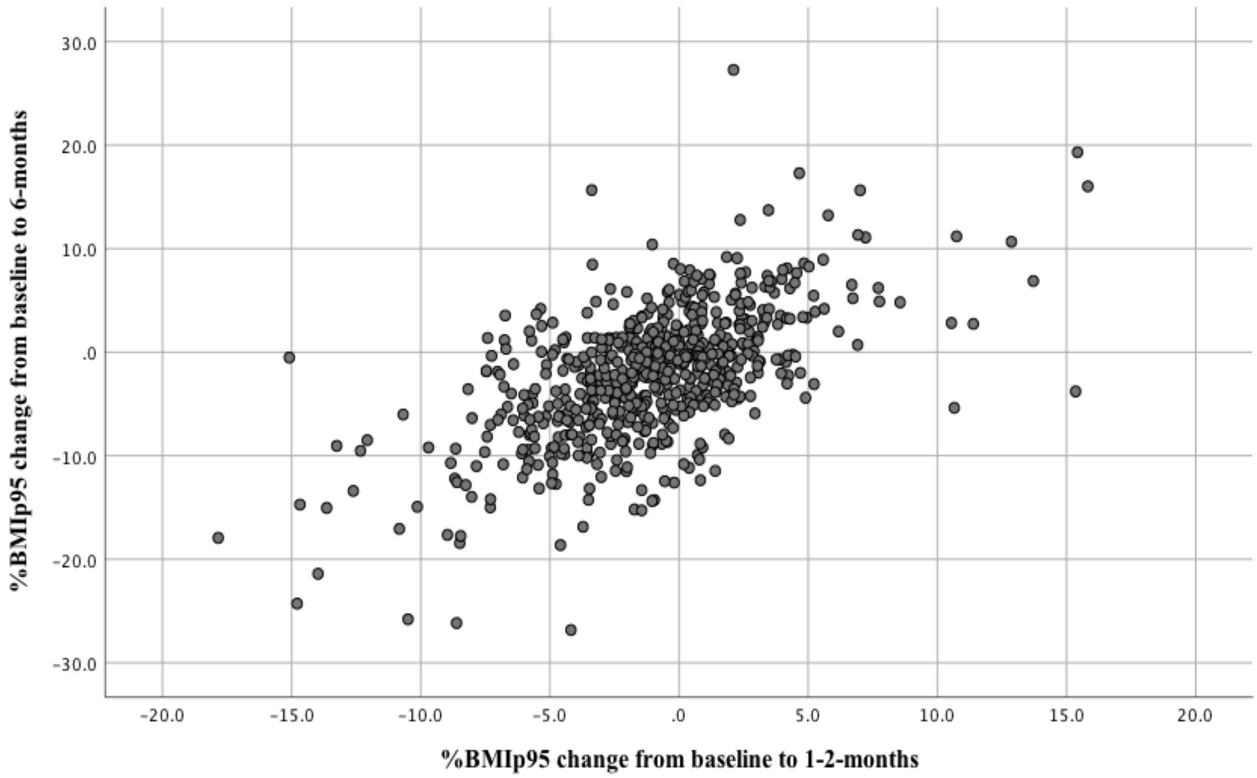

Figure 6. Association between early change in %BMIp95 at 1-2 month and change in %BMIp95 at 6-months

Discussion

The findings from this study support that early treatment response is significantly and strongly associated with greater long-term response in youth participating in a medically supervised weight management program. Patients who showed reduction in %BMIp95 during the initial two months of treatment were significantly more successful in losing weight later at six months. These data are consistent with previous studies showing that patients with early improvement in weight continued to show significant difference in ongoing weight loss.[17,37,126,127] Our study is unique in its utilization of %BMIp95 as the primary metric of response using clinical data. These results a reflect real-life situations in the management of children and adolescents with obesity in a clinical setting.

Identifying factors that predict who will successfully lose weight in weight management programs may provide insight that could improve the programs' success rates. This study suggests that early weight change may be a useful indicator of long-term success. The results generally support the recommendation to modify an individual's treatment as soon as a low early response to the treatment is identified. The clinicians may then use initial weight loss as criterion to decide whether continuing a specific treatment is beneficial for the patient. If early weight loss is not attained, it may be prudent to transition the patient to an alternative treatment plan rather than continuing in an intervention where long-term success is unlikely. Alternative treatment approaches could be considered including different diet plans, pharmacotherapy, or targeting additional behaviors. With the current focus on cost-effective treatments, it could be beneficial to tailor interventions depending on how a patient initially responds. This strategy allows health providers to start with a less intensive and lower-cost treatment and only provide additional intensive treatment to those who are non-responsive. Certainly, new research studies should attempt to develop new treatments to maximize long-term weight benefits for less responsive patients.

It is still unclear why early treatment response is a strong predictor of long-term treatment outcomes in weight management interventions. One hypothesis is that physiological differences, including circulating hormones and metabolism rates cause some to lose weight more consistently than others.[128] Another possibility is that an initial success may serve as a reinforcer, generating more self-confidence and greater self-efficacy for adhering to recommendations, and thus, patients continuing with changes made to diet and physical activity throughout the treatment.[127] This in turn may lead to successful weight loss and maintenance. It is also possible that children and adolescents who lose weight early in the intervention then have greater motivation and commitment to adhere to the recommendations, leading to better outcomes. Conversely, failure to achieve weight loss early in the intervention may indicate that the patients may have additional physiologic, behavioral, or psychosocial barriers to successful weight reduction. Moreover, continued participation in an intervention program that is not working may lead to feelings of frustration and decreased interest and confidence in future weight control efforts.[129] Emerging evidence suggests that failure to achieve weight loss during the first weeks of treatment is important predictor of drop-out from the obesity program.[130] Therefore, it is important to provide additional support and encouragement to children and adolescents who struggle at the beginning of the intervention to help maintain participation in program components. Taken together, consideration of factors that promote early weight change, especially at beginning of the intervention helps promote better early treatment response. An in-depth examination of factors contributing to early weight change will be vital for future research.

The current study has multiple strengths. First, clinical databases such as this have the advantage of reporting predictors of clinically implemented weight management programs, which have a higher treatment outcome, which have a high degree of relevance to clinical care and generalizability. Second, the large sample size allowed for the evaluation of several patient-level variables and program characteristics in relation to BMI reduction. Finally, the generalizability of the results is supported by the relatively diverse cohort of the clinical sample.

Conversely, our study has a number of limitations that should be acknowledged. First, due to the retrospective nature of our study design, our findings cannot imply causation. Randomized clinical trials are needed to confirm the findings. Second, we studied a clinical sample of patients referred for obesity treatment at a specialty clinic and therefore, our study population does not necessarily represent all children and adolescents in the community. Finally, there are many other factors that we did not assess which may have an effect on weight loss outcomes such as family history, eating behaviors, personality and physical health.

Conclusion

The study reinforced the importance of early weight loss as the strongest unique contributor for predicting positive treatment outcomes and should be recognized in clinical practice. The findings highlight the importance of early intensive weight loss treatment to increase the likelihood of positive outcomes in the longer term, and intensification of treatment early for those not responding with a change in BMI percentile in the first 4-8 weeks of treatment. Assessing presenting characteristics and factors associated with treatment outcome may allow practicing clinicians to individualize a weight management program or determine the 'best-fit' treatment for youth with obesity.

Chapter 4: The Role of Executive Function on Obesity-Related Behaviors and Treatment Outcomes in Adolescent Candidates for Bariatric Surgery

Abstract

Objective: The understanding of the role of executive function on weight loss and obesity-related behaviors in adolescents preparing for bariatric surgery has been limited. The aim of this study was: 1) to examine the association between executive function and weight loss; 2) and second to investigate the relationship between executive function and obesity-related behaviors among adolescents enrolled in a bariatric surgery preparation program.

Methods: Participants were adolescents with severe obesity, aged 13 to 18 years enrolled in a hospital-based program to prepare for bariatric surgery. Behavioral Rating Inventory of Executive Functioning (BRIEF2) was used to assess executive function in daily life. Participants completed eating behaviors, physical activity and self-efficacy questionnaires at the baseline visit. The primary outcome measure was a change in %BMIp95 from baseline to 3 and 6 months. Multiple linear regression analysis was conducted, and demographic variables and baseline body mass index were controlled for in the analysis.

Results: Participants were 67 adolescents (age 16 ± 1.5 years, %BMIp95 170.1± 38, 74.6% female, 52.2% White) Participants lost an average of 5.23 points on %BMIp95 (<0.001) at 3-months of follow-up. Executive function was significantly associated with disinhibited eating behaviors (uncontrolled eating and emotional eating), physical activity levels, and eating self-efficacy ($p<0.05$). Self-reported executive function was not significantly associated with change in %BMIp95 at 3 months or at 6 months ($p>0.05$).

Conclusion: Our study indicates that executive function may play a role in multiple obesity-related behaviors in adolescent preparing for bariatric surgery. This finding suggests that executive function in the preoperative period deserves extended research and clinical focus. Pre-treatment assessment of executive function may be useful in identifying individuals at risk for suboptimal treatment outcomes and further tailoring of interventions.

Introduction

Severe obesity (defined as a BMI ≥120% of the 95th percentile) is estimated to affect nearly 9% of youth in the United States and has both immediate and long-term physical and psychological consequences.[131] Despite the alarmingly high rate of severe obesity and its serious complications in youth, current treatments for children and adolescents including behavioral and pharmacological interventions are limited in effectiveness and not widely available.[11,132] As a result, bariatric surgery is generally accepted as the most effective treatment option for adolescents who have not achieved adequate weight loss through nonsurgical therapy. Bariatric surgery has consistence evidence supporting it as an effective treatment for long-term weight reduction and for achieving remission of medical comorbidities.[133,134] However, weight loss following surgery is highly variable and predictors of outcomes are not fully understood.[133,135]

While it is clear severe obesity is associated with poor physical and psychological health, emerging evidence has linked severe obesity with poor cognitive function in several domains, especially in the area of executive function.[51,70] Recent studies found that executive dysfunctions are linked to excess weight in children and adolescents. The evaluation of executive function performance in a sample of adolescents with severe obesity reveals deficits in attention, inhibitory control, working memory, and reward sensitivity.[51,136] Moreover, there is a connection between executive functioning and poor weight loss outcomes following both lifestyle intervention and bariatric surgery.[55,137] Currently, evidence for the role of executive function in the prediction of weight loss during treatment is insufficient.

Executive functions are cognitive processes that contribute to self-control and goal-directed behaviors.[49] Executive function plays a critical role in the self-regulatory process that is essential to manage healthy lifestyle habits to respond effectively to the obesogenic environment such as inhibitory control of food intake, planning for physical activity, and managing high-risk situations.[48,51,138] Deficits in executive function can influence youth's ability to follow treatment recommendations, and thus impact weight-loss outcomes.[139]

Evidence supports the relationship between executive function and obesity-related behaviors. Adolescents who demonstrated greater impairments in executive functions had more eating disorders[140], physical inactivity[59], and consumption of high-calorie foods.[141] It may be a contributing factor in youth with obesity to be unable to regulate their weight and may be related to their difficulty in changing their unhealthy behaviors. Evaluation of executive function and its association with obesity-related behaviors is especially important during preoperative intervention for bariatric surgery. Early identification of these deficits may have important clinical implications, as they have been identified as predictors of poor post-surgery outcomes and less adherence to the post-operative guidelines for diet and physical activity in adolescents and adults.[137,142,143]

Few studies have examined the relationship between multiple obesity-related behaviors and executive function in adolescents. Furthermore, there are limited data regarding the role of executive function prior to bariatric surgery when adopting a healthy lifestyle is critical. Preoperative executive dysfunction can be indicative of postoperative difficulties in weight loss outcomes and treatment adherence. Determining whether baseline executive function predicts treatment success would provide additional targets for intervention. To our knowledge, no study has investigated the role of executive function in daily life on the treatment outcomes in adolescents seeking surgery surgical weight management. In this study, we first examined the association between executive function and weight loss in the preoperative period. Second, we investigated the relationship between executive function and obesity-related behaviors. We hypothesized that executive function would be related to preoperative weight loss, as poorer executive function at the start of treatment would predict suboptimal weight loss outcomes at 12 weeks. We also hypothesized that poorer executive function would be associated with multiple obesity-related behaviors in bariatric candidates.

Methods

Study design and participants

Participants were adolescent bariatric surgery candidates recruited within the routine preoperative clinical evaluation.

Inclusion criteria were adolescents aged 13 to 18 years old with severe obesity BMI ≥120% of the 95th percentile and the ability to speak in English. Adolescents who suffered from neurological disorders (e.g., autism spectrum disorders, Down syndrome), had learning disabilities, developmental delays, or a history or presence of traumatic brain injuries were excluded from this study.

Patients were screened through their medical records to determine whether they met the eligibility criteria for the study.

Measurements

Self-report questionnaires on executive function and obesity-related behaviors were assessed at baseline. All measurements were built as data collection instruments and were administered through REDCap (Research Electronic Data Capture) software. Anthropometric assessment time points were 0 months (baseline), 3 months (mid-treatment), and 6 months (post-treatment).

The research protocol, and any subsequent modifications, were reviewed and approved by the Institutional Review Board (IRB) at Children's Mercy Kansas City. A request to rely on the IRB at Children's Mercy Kansas City was approved by the University of Kansas Medical Center.

1. Anthropometric measures

Weight and height were measured in duplicate. BMI (kg/m^2) was calculated using the mean height and weight values. Age- and sex-specific BMI percentiles and z scores were calculated using SAS (SAS Institute, Inc, Cary, NC) code provided by the Centers for Disease Control and Prevention (available at www.cdc.gov/nccdphp/dnpao/growthcharts/resources/sas.htm). We used percent of the 95th percentile (%BMIp95) to present the weight status as it is the practical approach to express high BMI values for children and adolescents with severe obesity.[144] Obesity class I was defined as a BMI between 100% and 119% of the 95th percentile. Severe obesity was defined as a BMI between 120% and 139% of the 95th percentile or a BMI of 35, whichever was lower (class 2), or patients with a BMI of ≥140% of the 95th percentile or a BMI of 40, whichever was lower (class 3).[144]

2. Executive Function

Behavioral Rating Inventory of Executive Functioning ® (BRIEF2 -Self Report)

The Behavior Rating Inventory of Executive Functioning, Second Edition, Self-Report Version (BRIEF-2) is a standardized inventory assessing youth's perception of their own executive functions, and purposeful, goal-directed, and problem-solving behavior in their daily life. The BRIEF-2 contains 55 items that yields seven non-overlapping clinical subscales including Inhibit, Self-Monitor, Shift, Emotional Control, Task Completion, Working Memory, and Plan/Organize. Theoretically and statistically derived scales measure the adolescent's ability to regulate and monitor behavior (Behavior Regulation Index, BRI), emotional responses (Emotion Regulation Index, ERI), and cognitive processes (Cognitive Regulation Index, CRI). These scales can also be combined into a summary measure Global Executive Composite (GEC) score. (See **Figure 7**).

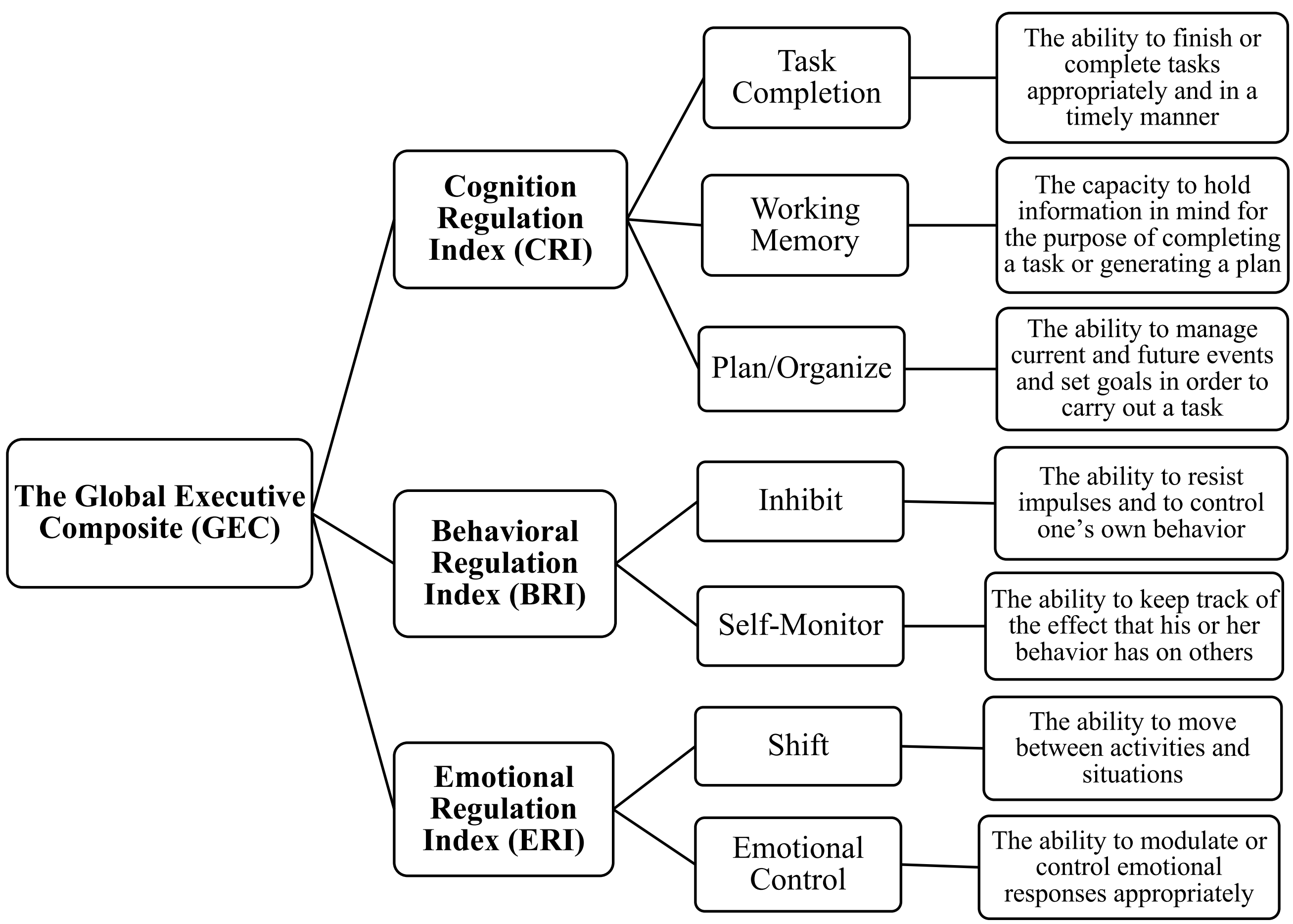

Figure 7. BRIEF2 self-report clinical scales, indexes, and composite[145]

Participants indicated on a 3-point Likert scale for each item whether the statement applied to them, with the options 'never', 'sometimes' or 'always'. All scores are on a *T* score scale ($M = 50$, standard deviation (SD) = 10), with higher *T*-values reflecting weaker executive function and scores ⩾65 considered clinically significant[146] (See **Table 11**). Internal consistency was excellent for the Global Executive Composite (α = 0.90).

Table 11. BRIEF2 self-report score profile[146]

Classification	Scoring
Normal	T score less than 60
Mildly elevated	T score of 60-64
Potentially clinically elevated	T score 65 to 69
Clinically elevated	T score of 70 or greater

Note: Scores ⩾ 65 considered clinically significant, with higher *T*-scores reflecting weaker executive function.

3. Eating Behaviors

Three-Factor Eating Questionnaire-R18

The revised 18-items version of the 'Three-Factor Eating Questionnaire' was used to assess eating behaviors. This instrument is a shortened and revised version of the original 51-item Three-Factor Eating Questionnaire. The questionnaire measures three different eating patterns: (1) cognitive restraint, which is the conscious control of food intake with concerns about body shape and weight; (2) uncontrolled eating, which is the overconsumption of food due to a variety of stimuli, associated feelings of being out of control, and subjective feelings of hunger; and (3) emotional eating, which is a tendency to eat in response to negative emotional feelings or moods such as depression, anxiety, or sadness. The responses were coded on a 4-point Likert scale (e.g., 1 = never, 2 = rarely, 3 = sometimes, 4 = always). Item scores are summated into scale scores for cognitive restraint, uncontrolled eating, and emotional eating. The raw scale scores are transformed to a 0–100 scale [((raw score − lowest possible raw score)/possible raw score range) × 100]. Higher values indicate greater presence of cognitive restraint, uncontrolled, or emotional eating.[147] The internal-consistency of subscales was estimated using Cronbach's alpha for each scale (cognitive restraint = 0.84, uncontrolled eating = 0.88, emotional eating = 0.90).

4. Physical Activity Levels

Physical Activity Questionnaire for Adolescents

Physical Activity Questionnaire for Adolescents (PAQ-A) was used to assess the physical activity levels. PAQ-A is a validated self-report seven-day recall for adolescents aged 13 to 18 years old. It consists of nine items using a 5-point Likert scale that are used to calculate summary activity scores. Items assess physical activity performed at school (physical education, recess, lunchtime), right after school, and at home (organized and recreational). Each PAQ-A item was scored on a five-point scale (1-5), with '1' indicating low and '5' a high level of physical activity levels. The end result is the average value of the points obtained, with higher scores corresponding to a higher level of PA.[148,149] The internal consistency for PAQ-A using Cronbach alpha ranges from 0.72 to 0.88.

5. Self-Efficacy

Weight Efficacy Lifestyle Questionnaire.

Eating self-efficacy was measured by the Weight Efficacy Lifestyle Questionnaire Short-Form (WEL-SF). WEL-SF is validated self-reported questionnaire assessing the individual's "confidence in the ability to resist overeating in the presence of challenging situations" related to emotional situations, availability of food, social pressure, positive activities, and physical discomfort. It consists of eight items and each item scored from 0 (not confident) to 10 (very confident). Summed scores range between 0 and 80, with higher scores indicating higher eating self-efficacy.[150] Internal consistency for WEL-SF using Cronbach's alpha is 0.92.

6. Sleep Pattern

Sleep Duration and Quality

Sleep duration was assessed by asking about bedtime/wake-time on both weekday and weekend "on an average weekday, what time do you usually fall asleep/wake up" and "on an average weekend, what time do you usually fall asleep/wake up". These items were adapted from the Sleep Habits Survey, which was developed and validated for use in adolescents.[151] Both on weekdays and weekend days, as assessed in other studies, sleep durations (hours) is calculated as the difference between self-reported bedtime and wake time. The mean daily sleep time was calculated by adding the weekday sleep time and weekend sleep time and by assigning them 5/7 weight and 2/7 weight, respectively.

Sleep quality was assessed using the question, "overall on average during the last 30 days, how much of a problem did you have during sleeping, such as falling to sleep, waking up frequently or waking up early in the morning?". The frequency of sleep problems was rated using a scale of 1 (none), 2 (sometimes) or, 3 (most of the times), with higher scores indicating poor sleep quality.

7. Clinical and Demographic Characteristics

Age, sex, race, ethnicity, and educational attainment, and medical insurance were measured by a questionnaire administered at baseline. Obesity-related comorbidities were assessed by medical chart review at the baseline.

Pre-surgery Preparation Intervention

All potential bariatric surgery candidates were required to enroll in a minimum six-month preoperative preparation treatment before the interprofessional team decision for their eligibility. The intervention was a medically supervised clinical weight loss program targeting weight loss and lifestyle changes. Participants attended monthly visits led by an interprofessional team specializing in pre- and post-bariatric care in adolescents including physician, registered dietitian, exercise physiologist, social worker, and psychologist. The team members work with the patients collaboratively and set goals for diet, physical activity or exercise, and other lifestyle changes tailored to the need of each child and family. Patients were encouraged to self-monitor food intake and physical activity using paper and pencil or an app of their choice. The team worked with patients to educate them about the treatment guidelines and to adopt behaviors related to a healthy lifestyle before and after bariatric surgery. Patients are provided with a print manual outlining the nutritional curriculum and asked to bring it with them to the monthly visits. Healthcare providers discussed patient status at monthly team meetings based on clinic notes and the bariatric checklist to determine progress towards surgery and additional needs.

Statistical Analysis

Descriptive statistics were conducted for the main variables to describe the sample. Continuous variables are presented as means ± standard deviation or 95% confidence intervals (CI). Categoric variables are presented as counts and percentages. Correlation analysis was conducted to explore the association between executive function and obesity-related behaviors.

We used Pearson's correlation coefficient for normally distributed variables, Spearman's correlation coefficient for non-parametric variables and Kendall's tau correlation coefficient for categorical variables. Weight change during the treatment (baseline %BMIp95 minus %BMIp95 at post treatment) was the primary outcome of the study and was expressed as a change score. Paired t-test and Wilcoxon signed-ranks test were used to compare the change in weight and BMI parameters from baseline and post intervention. Linear regressions were then conducted to examine the contribution of executive functions to weight loss at 3-month after controlling for potential covariate variables (age, race, sex, and baseline %BMIp95).

Preliminary tests of the assumptions of the statistical tests, including data normality using Shapiro–Wilk tests (all p values > 0.05), homogeneity of variance (Levene's tests: all p values > 0.05), and homogeneity of regression slopes (all p values > 0.05) were evaluated.

Two-sided p values $\leq .05$ were considered statistically significant. For statistical analyses we used the software program SPSS 26.0 (Statistical Package for Social Sciences, SPSS for Windows version 13.0, 2019, Armonk, NY, USA).

Results

Baseline Demographic and clinical Characteristics

Executive function data were collected from 67 adolescents at the baseline, 56 of patients completed all the study measurements at the baseline, and 48 participants completed followed up at 3 months (± 2 weeks) of the treatment.

Participants were, on average, 16 years of age (SD 1.54) and around 75% were females. Approximately 85% of participants had a BMI ≥140% of the 95th percentile and were classified as severe obesity class 3, with an initial %BMIp95 of 170.2 (SD 37.9). The majority of the sample identified as non-Hispanic (83.6%) and white (52.2%). Participants who were enrolled in government insurance (Medicaid) as their primary insurance were 62.7% of the sample. The prevalence of any medical conditions in the sample was 92.5% with a mean number of comorbidities of 2.5 (SD =1.7, range 0–8). Among all diseases, the highest prevalence was found for depression or anxiety (55.2%) followed by prediabetes (53.7%), elevated blood pressure (22.4%), obstructive sleep apnea (22.4%), and asthma (20.9%). **Table 12** presents demographic and clinical characteristics of the sample.

Table 12. Demographic and clinical characteristics of participants

Characteristics	**All (n=67)**
Age, (years) Mean (SD)	16 ± 1.54
Age Category, n (%)	
13-15 years	23 (33.8)
16-18 years	45 (66.2)
Sex, n (%)	
Male	17 (25.45)
Female	50 (74.6)

Race, n (%)	
White	35 (52.2)
Black	18 (26.9)
Other	14 (21)
Ethnicity, n (%)	
Non-Hispanic	56 (83.6)
Hispanic	10 (14.9)
Insurance Type, n (%)	
Government	42 (62.7)
Commercial	22 (32.8)
Other	3 (4.5)
Current Education, n (%)	
Middle	12 (19)
High school	50 (70)
College	4 (6)
Comorbidities, n (%)	
Anxiety/Depression	37 (55.2)
Prediabetes	36 (53.7)
Acanthosis Nigricans	26 (38.8)
ADHD	17 (25.4)
Elevated BP	15 (22.4)
OSA	15 (22.4)
Asthma	14 (20.9)
Dyslipidemia	12 (17.9)
PCOS	12 (17.9)
Type 2 Diabetes	11 (16.4)
Obesity Class, n (%)	
Class 2	10 (15.0)
Class 3	56 (85)
Weight Status, Mean (SD)	
Weight (kg)	139.0 ± 29.6
BMI (kg/m2)	48.8 ±11
BMI-Z	2.68 ± 0.31
%BMI	99.4 ± 0.43
%BMIp95	170.2 ± 37.9
Blood Pressure, Mean (SD)	
BP Systolic (mmHg)	127.3± 13.8
BP Diastolic (mmHg)	72.6 ± 8.8

Abbreviation: **OSA** Obstructive Sleep Apnea; **PCOS** Polycystic Ovary Syndrome: **ADHD** Attention Deficit Hyperactivity Disorder; **BP** Blood Pressure; **SD** Standard deviation; **%BMIp95** BMI expressed as a percentage of the 95^{th} percentile.

In this study, we used Global Executive Composite (GEC) to represent the overall BRIEF-2 Score. At baseline, self-report on BRIEF for Global Executive Composite (GEC) suggested that nearly 27% of adolescents in the sample exhibited clinically significant executive dysfunction in everyday life (T-scores greater than 65), with comparable functioning across domains of cognition behavioral, and emotional regulation. Detailed results for self-report BRIEF2 scales and indexes are displayed in **Table 13.**

The patient demographic characteristics were not significantly associated with any of the executive function domains. Among the obesity-related comorbidity, Global Executive Composite (GEC) was only significantly associated with Attention Deficit Hyperactivity Disorder (ADHD) (r=0.31, p=0.002).

Table 13. Description data for self-report of executive function

BRIEF-2 Scales and indexes All (n=67)	**Mean (SD)**	**Mildly elevated n (%)**	**Clinically impairment n (%)**
Task Completion	57.5 ± 10.9	11 (16.4)	19 (28.3)
Working Memory	57.5 ± 12.4	9 (13.)	17 (25.4)
Plan/Organize	54.4 ± 10	4 (6.0)	13 (19.4)
Cognition Regulation Index (CRI)	56.8 ± 11.8	4 (6.0)	17 (25.4)
Inhibit	56.5 ± 11.3	8 (11.9)	17 (25.4)
Self-Monitor	55.7 ± 10.8	6 (9.0)	17 (25.4)
Behavioral Regulation Index (BRI)	57.7 ± 11.3	12 (17.9)	16 (24.8)
Shift	56.0 ± 12.7	8 (11.9)	17 (25.4)
Emotional Control	58.6 ± 11.3	11 (16.4)	17 (25.4)
Emotional Regulation Index (ERI)	57.7 ± 11.7	9 (13.4)	16 (23.9)
Global Executive Composite (GEC)	57.6 ± 10.9	9 (13.4)	18 (26.8)

Abbreviation: **BRIEF** Behavior Rating Inventory of Executive Function.
For BRIEF-2, T score of 60-64 are considered mildly elevated; T score (M=50, SD=10) of ⩾65 is considered clinically significant; higher scores indicate higher impairment.

Correlations of Obesity-Related Behaviors and Executive Function

See **Table 14** for the baseline descriptive of obesity-related behaviors in the sample. We conducted correlation analysis to examine the association between executive function and obesity-related behaviors.

Table 14. Baseline descriptive of obesity-related behaviors in the sample (n=56)

Behavior	**Range (Min-Max)**	**Mean ± SD**
Eating Behaviors		
Uncontrolled Eating	0-75	31 ± 17.2
Cognitive Restraint	4.2-62.5	34 ± 14.3
Emotional Eating	0-75	30.5 ± 23.2
Physical Activity (score)	1-3.2	1.9 ± 0.68
Weight Self-Efficacy	7-80	53.4 ± 17.6
Sleep Duration (hr.)	4.3-11.0	8.3 ± 1.4
Sleep Quality (score)*	1-3	1.7 ± 0.8

Abbreviation: **SD** Standard Deviation.
Higher scores in sleep quality indicated poor sleep quality. For all the other behaviors, higher score indicates higher level of behavior.

Self-report executive function was significantly associated with multiple obesity-related behaviors (see **Table 15**). Adolescents with higher GEC scores, indicating poorer executive function, reported higher levels of uncontrolled eating (r=0.54, p<0.001) and emotional eating (r=0.44, p=0.001). There were no significant associations between executive function and subscales of cognitive restraint (r= - 0.13, p=0.31). Moderate correlation emerged between GEC scores and weight self-efficacy among the total sample (r=-0.37, p=0.001), indicating poorer executive function was associated with lower eating self-efficacy. Physical activity trended towards a negative correlation with GEC *(r* =-0.27, p=0.048)*,* but it was a weak correlation. Adolescents with a higher score on GEC tended to have lower physical activity levels.

Sleep quality was also correlated with executive function (r = 0.23, p<0.035). Adolescents with higher GEC scores, reflecting worse executive function reported poorer sleep quality. Nevertheless, there was no significant correlation detected for sleep duration with GEC or any BRIEF2 indexes (*r*= -0.15, p=0.29).

Table 15. Correlation between baseline executive function and obesity-related behaviors among adolescent bariatric candidates (n=56)

Obesity-Related Behaviors	**BRIEF-2 Indexes and Composite Scores**							
	Cognition Regulation Index (CRI)		**Behavioral Regulation Index (BRI)**		**Emotional Regulation Index (ERI)**		**Global Executive Composite (GEC)**	
	r	**p**	**r**	**p**	**r**	**p**	**r**	**p**
Eating Behaviors								
Cognitive Restraint	-0.08	0.557	-0.15	0.261	-0.16	0.223	-0.13	0.312
Uncontrolled Eating	0.48	<0.001	0.51	<0.001	0.49	<0.001	0.54	<0.001
Emotional Eating	0.33	0.011	0.53	<0.001	0.43	0.001	0.44	0.001
Weight Self-efficacy	-0.27	0.042	-0.42	0.001	-0.35	0.006	-0.37	0.005
Physical Activity	-0.290	0.030	-0.16	0.227	-0.25	0.061	-0.27	0.048
Sleep Pattern								
Sleep Duration	-0.184	0.18	-0.14	0.32	-0.07	0.60	-0.15	0.29
Sleep Quality	0.23	0.039	0.20	0.068	0.23	0.041	0.23	.035

Abbreviation: **BREIF-2** Behavioral Rating Inventory of Executive Functioning.
Note: **r** represents correlation coefficient and **P** represents p-value; Pearson’s correlation coefficient for normally distributed variables, Spearman’s correlation coefficient for non-parametric variables and Kendall’s tau correlation coefficient for categorical variables.

Relationship of Executive Functions with BWL Program Outcomes

The intervention outcome was a change in the %BMIp95 from baseline to 3-month and 6-month of the intervention We examined whether executive function difficulties on the BRIEF2 were associated with lower weight loss at 12 weeks **(**see **Table 16).** Participant's weight status decreased an average of 5.23 (SD 8.4) percentile points %BMIp95 ($p<0.001$) at 3-month follow-up and 4.62 (SD 6.6) percentile points on %BMIp95 ($p<0.001$) at 6-month follow-up. The linear regression analysis showed no significant associations between %BMIp95 change and BRIEF subscales scores at 3-months or 6-months (p's>0.05). There was a negative association between GEC score and number of clinical visits ($r=-0.27$, $p=0.023$), indicating that participants with poorer executive functions attended fewer number of visits. The association of number of visits were significantly associated with behavioral regulation index (BRI) Scores ($r=-0.32$, $p=0.008$).

The average number of visits was 3.84 (SD 1.8). **Table 17** shows the contribution of executive functions to weight loss following the intervention and the number of visits.

Table 16. Weight change from baseline to (1, 3, and 6) months following the intervention

Mean change (p-value)	**1-mon follow-up (n=48)**	**3-mon follow-up (n=48)**	**6-mon follow-up (n=40)**
Weight (kg)	-0.65 (0.21)	-2.02 (0.03)	-2.05 (0.07)
BMI (kg/m2)	-0.34 (0.09)	-1.10 (0.005)	-0.89 (0.022)
BMI-Z	-0.02 (0.004)	-0.05 (<0.001)	-0.04 (<0.001)
%BMI	-0.032 (0.001)	-0.12 (<0.001)	-0.10 (<0.001)
%BMIp95	-1.64 (0.01)	-5.23 (<0.001)	-4.63 (<0.001)

Abbreviation: **BMI** body mass index; **%BMIp95** BMI expressed as a percentage of the 95^{th} percentile.
Note: tested the mean change using Independent t-test for normal distributed variables and Wilcoxon signed-ranks for non-normal distributed variables.

Table 17. The association between executive function indexes and the intervention outcomes

BRIEF-2 Indexes* Regression Coefficient (p-value)	%BMIp95 Change 3-mon follow-up	 6-mon follow-up	Number of visits
Cognition Regulation Index (CRI)	-0.13 (0.81)	-0.16 (0.37)	-0.24 (0.048)
Behavioral Regulation Index (BRI)	-0.13 (0.38)	-0.18 (0.29)	-0.32 (0.008)
Emotional Regulation Index (ERI)	-0.12 (0.40)	-0.13 (0.46)	-0.23 (0.070)
Global Executive Composite (GEC)	-0.14 (0.31)	-0.16 (0.32)	-0.27 (0.023)

Abbreviation: **%BMIp95** BMI expressed as a percentage of the 95th percentile; **BRIEF-2** Behavioral Rating Inventory of Executive Functioning.
*Regression coefficient (p-value); the model was controlled for age, sex, race and baseline %BMIp95; Number of visits range from 1-6 visits during the period of the study, change in %BMIp95 from baseline to 3-month and 6-month follow up.

Discussion

The present study aimed to examine whether aspects of executive function, using a comprehensive assessment of self-reported executive functions, were associated with obesity-related behaviors and 3- and 6-month weight loss outcomes of a medically supervised weight management program in adolescent bariatric surgery candidates. This study is one of the first to explore the role of a self-report measure of executive function skills on multiple obesity-related behaviors and weight loss outcomes in adolescents seeking surgery options.

Our findings showed that ~27% of the bariatric surgery candidates reported problems experienced in daily life by exhibiting clinically meaningful levels of executive function impairment. However, 60% of candidates had executive functioning in the normal range. The high proportion of youth with executive function impairment highlights the heterogeneity of candidates enrolled in obesity treatment. Studies have suggested that executive function difficulty can increase the challenges of adhering to weight management recommendations and thereby may be linked to poor outcomes and attrition, if left unaddressed. This knowledge emphasizes the significance of understanding how these various phenotypes can help predict treatment outcomes, with treatment strategies personalized accordingly. Pre-operative evaluation of executive function deficits is critical, as executive functioning has been identified as being predictive of postoperative outcomes. Previous studies show that baseline executive dysfunction is positively associated with poorer adherence and reduced weight loss post-surgery in both adolescents and adults.[137,152]

Consistent with our hypothesis, executive functions were significantly correlated with eating behaviors. The results demonstrated that poorer executive function is linked to dysregulated eating behaviors including emotional and uncontrolled eating, both thought to reflect an individual's level of disinhibited eating. Adolescents with a greater self-report of disinhibited eating had significantly higher scores on all BRIEF2 subscales, indicating higher levels of impairment. It is possible that executive dysfunction (i.e., inhibitory control) could contribute to less control of eating behavior and difficulty avoiding tempting foods.[153,154] Our findings suggest that controlling such behaviors may utilize a unique set of executive functions. This is consistent with previous studies that have demonstrated associations between executive dysfunction and dysregulated eating behaviors in children or adolescents with obesity.[64] Our study represents the first study to examine the relationships between executive function and disinhibited eating behaviors in adolescent bariatric candidates. Our finding contributes to the literature

Physical inactivity also emerged as another obesity-related behavior associated with executive function. Adolescents with higher executive function scores, indicating greater executive function impairment, reported lower physical activity levels. Higher cognition regulation index (CRI) scores that reflect poorer task completion, planning, and working memory skills, were significantly associated with physical inactivity compared with other sub-components of executive function. These executive function skills may be necessary to form intentions to engage in physical activity and to hold information in mind to complete or generate an exercise plan. These findings are consistent with previous studies indicating that individuals with impaired executive functioning are less likely to follow physical activity guidelines.[155,156]

The associations between executive function and obesity-related behaviors, such as eating and physical activity patterns, can provide a better understanding of why youth with executive function impairments may be less likely to achieve successful weight outcomes in behavioral obesity intervention programs. Our study adds to the growing body of knowledge about the relationship between executive function skills and obesity-related behaviors during the pivotal period of adolescence.[51,141,157] Our findings provide further evidence for an association between poor executive function and multiple obesity-related behaviors for those seeking bariatric surgical treatment options. Greater difficulty in executive function could play a role in unhealthy behaviors that may have the potential to undermine bariatric surgery outcomes.[158,159] The findings reinforce the importance of early evaluation of executive function and targeted interventions that potentially facilitate improved healthy behaviors, and ultimately, lead to better treatment outcomes.

Self-efficacy is a key concept of social cognitive theory and an important predictor of behavioral change. Eating efficacy specifically plays a crucial role in healthy dietary decisions and healthy eating behaviors.[160] Previous studies found significant associations between preoperative eating self-efficacy, and weight loss after bariatric surgery in adults.[161,162] Our results suggest that executive function was negatively associated with preoperative levels of eating self-efficacy. Adolescent bariatric candidates with poorer executive function exhibited lower confidence in their ability to control their eating behavior in challenging situations. The findings highlight the importance of executive function and self-efficacy in youth’s ability to self-regulate eating behaviors in challenging situations. In addition, our results suggest that the baseline executive function assessment during preoperative interventions may identify individuals with limited confidence in making healthy behavior changes, and thus potential for poor adherence to guidelines. These findings underscore the importance of integrating both cognitive and motivational aspects of self-regulation during the initial phase of behavior changes, such as physical activity or eating habits.

Contrary to our hypothesis, self-reported executive function measured at baseline was not associated with short-term weight change outcomes in our sample. We found that executive function skills in daily life did not predict weight loss during the first 12 weeks of treatment in a presurgical weight loss program. This is not in line with previous research that suggests executive function is a predictor of obesity treatment outcomes in children.[54,139,163] Possible differences in study duration, age range, setting, and cognitive tasks potentially explain the discrepant findings with the studies. In addition, most of these studies relied on objective performance of executive function. Some evidence suggests that self-reported measures of executive function do not correlate with objective neuropsychological tasks.[164] Thus, the self-report measurement may underestimate true levels of cognitive deficits in this population. The correlation between enhanced executive functioning and increased weight loss during treatment may also not represent a direct impact on weight loss, but rather an effect on adherence to a treatment regime in everyday life.[165] Future work should consider assessing adherence to recommendations as mediation of this association. Interestingly, we observed that executive dysfunction was associated with poorer adherence as measured by the number of visits during the interventions. Adolescents with better executive function skills, particularly self-monitor and inhibit skills, might attend more clinical visits. Previous studies have linked impulsivity to attrition in behavioral weight management treatment among adults.[166,167]

The present study is limited in several ways that should be considered when interpreting these findings. First, the present sample size was small and confirmation of the current findings in larger samples is much needed. Second, the association between executive function and obesity-related behaviors was a cross-sectional analysis and that does not allow for comment on causality. Also, it was an exploratory correlational study conducted in a clinical setting with no control group, which limits the overview of potential confounding factors and conclusions of causality. Third, the self-reported measurements may be influenced by common self-report biases. This problem can be resolved by complementing the study with objective measures. The objective measures may have strengthened the theoretical links that were examined in the present study. Lastly, self-selection to participate in the study may limit the generalizability of our findings.

Clinical Implications

Executive Function Training

Currently, most of the behavioral weight management programs do not typically involve executive function training components that may theoretically enhance intervention outcomes in terms of weight loss and maintenance.[139] However, the evidence suggests that structured behavioral weight management treatment may indirectly support children and adolescents in strengthening and enhancing executive function through a broad range of self-regulatory skills training.[50] Such programs improved specific domains of executive functions, such as inhibitory control skills and delay discounting across the course of the intervention, indicating its efficacy in improving weight loss outcomes. The self-regulatory strategies learned in these weight management programs including goal setting, self-monitoring, and mental controlling help in recruiting and challenging the executive system and thus, leading to executive function development.[50]

Executive function training could be integrated into weight management programs with an emphasis on including self-regulatory cognitive and behavioral strategies. These strategies could target certain obesity-related behaviors. For example, the training could use food as a target and support children practicing inhibiting response to obesogenic food items. Working memory training can also hold promise for dietary behavior changes necessary for long-term weight loss.[168] Comprehensive executive function assessment prior to enrollment in pediatric obesity treatment may provide an understanding of the adolescent's perspective with respect to difficulties in self-control and self-regulatory behavior. This is critical when considering intervention strategies. Thus, the intervention could be tailored to meet the needs of children who are deficient in certain executive function domains.

Conclusion

The current study explored the impact of executive function on obesity-related behaviors and weight reduction outcomes in adolescent seeking surgical weight management. Obesity-related behaviors including disinhibited eating behaviors, lower levels of physical activity and poorer sleep quality and lower eating self-efficacy were associated with weaker executive function in everyday life in the adolescents with severe obesity. Further studies are required to establish the clinical significance of executive function before bariatric surgery. If confirmed in future studies, such findings raise the possibility that executive function in this population may be linked to a wide range of poor treatment outcomes.

Chapter 5: General Discussion

Summary of Results and Future Implications

Pediatric obesity is a major health concern of the developed world. The prevalence of obesity has tripled among children and adolescents in the United States over the last three decades reaching epidemic proportions. According to the Centers for Disease Control and Prevention, obesity affects nearly 18.5% of children and adolescents ages 2 to 19 years in the United States.[1] On converting the 18.5% into actual numbers, the result is quite alarming. Obesity now affects about 13.7 millions youth in the United States.[3] Due to the severity of the physical and psychological consequences associated with pediatric obesity, health care professionals have received a call to action to address this problem.

Currently, weight management prevention and intervention programs have targeted this population, providing several options for treatment. Treatments that involved dietary, physical activity, behavioral, environmental, and pharmacological approaches are recommended to achieve a healthy weight.[169] To date, however, interventions to address pediatric obesity had limited efficacy and results have been modest.[116] The evidence demonstrated that only a small proportion of children and adolescents with obesity achieve clinically significant weight loss following the intervention. Therefore, it is important to identify factors associated with treatment success to guide treatment development and identify children who may need additional support or an alternative approach for weight loss.

A comprehensive evaluation of demographic, biological, cognitive, and behavioral predictors of successful weight loss is limited, especially for children with severe obesity participating in medically-supervised intervention. Questions of predictors of successful weight loss in children and adolescents with obesity must be answered to properly develop effective individualized interventions aimed at improving weight control outcomes. This series of studies aimed to (1) investigate the impact of pediatric metabolic syndrome and obesity on the development of type 2 diabetes and cardiovascular diseases, (2) identify the factors that may influence weight management interventions for successful weight reduction among children and adolescents with obesity, and 3) examine the potential relationship between executive function and obesity-related behaviors and the effect of executive function on the treatment outcomes among adolescents with severe obesity seeking surgical options. The ultimate goal of this dissertation was to investigate the factors associated with better treatment outcomes and to create awareness among healthcare professionals regarding the need for individualized weight management interventions for treating youth with severe obesity. Below a general discussion of the findings for the three studies and potential implications is provided.

Pediatric obesity seriously threatens the future health of children and adolescents. Our first study's findings highlight the seriousness of pediatric obesity in the context of metabolic syndrome and its impact on developing future diseases. Around 13% of children and adolescents with obesity who met at least three factors of metabolic syndrome developed at least one of the associated diseases later in childhood/adolescence life including hypertension, heart diseases, or type 2 diabetes. We found age, when Metabolic syndrome developed was positively associated with the risk of developing the diagnosed disease. Older children with Metabolic Syndrome were more likely to receive the diagnosis. These findings support the need for early detection and preventive measures of the metabolic factors as younger age at detection is related to a lower likelihood of developing the diagnosed disease later in life. We also found the number of metabolic syndrome factors was significantly associated with the risk for future type 2 diabetes, cardiovascular diseases, hypertension, and stroke diagnosis. Youth with at least four metabolic syndrome factors were twice as likely to be diagnosed with a chronic disease compared to those with three metabolic syndrome factors. Also, those with at least four metabolic syndrome factors were more likely to receive a diagnosis of the disease sooner than those with three metabolic syndrome factors. Identification of children with multiple component risks is critical for addressing chronic diseases such as heart disease and type 2 diabetes. It also allows healthcare professionals to concentrate resources and to target focused and intensive intervention efforts. Treatment of metabolic syndrome should focus on a combination of diet, exercise, and other behavioral changes for improving weight and metabolic syndrome status.[170] Future research is needed to provide more insightful and concrete recommendations for clinicians and families as we face the increasing burden of childhood obesity and other associated morbidities.

Targeting weight-related behaviors as part of behavioral weight-loss treatment is the first line of treatment for pediatric obesity. Previous studies suggest significant variability in weight loss for children and adolescents with obesity receiving the same standardized intervention.[127] Most children who participate in weight management programs do not respond favorably to the treatment.[16] Several studies have evaluated the factors associated with treatment response to find early predictors of success or failure among individuals with obesity. However, it is a challenge to determine the predictors for successful weight control interventions, as the findings have been inconsistent. Therefore, the second study aimed to explore the characteristics that predicted successful weight loss following a medically supervised obesity intervention for children and adolescents with obesity. With inconclusive evidence regarding which variables are predictive or associated with successful treatment outcomes, this study was developed with hopes of adding to the current literature on predictors of weight loss among youth with obesity. We specifically identified the clinical and demographic-related factors associated with a reduction of body mass index percent of the 95th percentile (%BMIp95) at 6-months for children and adolescents receiving care at a tertiary care obesity management clinic. Among all the potential factors, early weight loss response was the strongest predictor of treatment response for further weight reduction. We found that weight loss during the first two months of the intervention was significantly associated with weight loss after six months, accounting for approximately 38% of the variance. The findings suggest that children and adolescents who lose more weight initially during treatment will continue to lose significantly more weight. Closer examination of factors related to early weight loss also will be important for future research. Thus, the clinicians may potentially provide interventions targeting these factors to enhance early weight loss, which may then contribute to long-term weight loss.

This study also offers insight into the potential importance of the initial stages of lifestyle intervention. It suggests that early weight loss may be considered as a marker of success and could be a valuable tool for predicting treatment outcomes in the clinical setting. Clinicians should facilitate early behavior changes to enhance early weight loss, thus improving the overall treatment outcomes. Although the ideal early weight loss is not well documented in the previous studies, Goldschmidt et al. suggested that 4 to 8% reduction of initial weight at 2-months was necessary to achieve successful long-term treatment outcomes.[171]. Furthermore, early non-response to treatment may be a signal for changing the treatment approach. Future studies should investigate whether children who fail to achieve early weight reductions would benefit from an alternative treatment approach.

To improve the effectiveness of the interventions, more research is needed to understand why some children are successful in these programs while others are not, with the goal to reduce the burden of obesity. Future studies may examine whether alternative treatment strategies can be employed to improve treatment outcomes among those with low initial weight loss.

Lifestyle management alone is rarely sufficient to bring severe obesity into remission and allow attainment of a normal BMI.[172,173] Thus, severe obesity has led to the acceptance of more aggressive weight management interventions, including bariatric surgery. The evidence has supported bariatric surgery as currently the most successful approach for significant and sustained weight loss and improvement of associated comorbidities in adolescents with severe obesity.[133,174] However, the pre-surgery preparation process is long and difficult due to the intensity of lifestyle changes required.[174] Patients undergoing bariatric surgery are strongly encouraged to follow healthy patterns to achieve preoperative weight loss, primarily to improve surgical results by stabilizing any preoperative patient comorbidities.[175] Patients, especially adolescents, often face challenges adhering to the recommendations related to eating and physical activity habits prior to and after surgery, which are associated with poorer weight loss outcomes.[176]

Emerging evidence links executive function to weight loss outcomes in adolescents with obesity.[50] Given that executive functions includes higher-order cognitive abilities such as inhibition, attention, planning, and working memory, deficits in these functions could lead to poor adherence to lifestyle changes. We have limited knowledge about the executive functions that influence weight loss and weight-related behaviors that may contribute to obesity in youth, with severe obesity preparing for bariatric surgery. Therefore, the objective of the third study was to examine the relationship between weight loss and multiple obesity-related behaviors with executive function among bariatric surgery candidates. Our study indicated that the presence of clinically significant baseline executive function impairment in around 27% of bariatric surgery candidates. Although we did not find an indication of a relationship between executive function and weight loss in our sample, the study revealed other significant findings.

Eating behaviors, physical activity, and eating self-efficacy were associated with executive function in daily life. We found that executive function was linked to dysregulating eating behaviors, as measured by the Three-Factor Eating Questionnaire (TFEQ-18). Poorer self-reported executive function skills were also associated with higher ratings of emotional and uncontrolled eating. Because executive function is critical in inhibitory and emotional control, individuals with poorer executive functioning might have lower utilization of these skills required for eliminating food cues in the environment. Executive function was also associated with physical activity levels as measured by a self-reported 7-day recall questionnaire. Adolescents with poorer executive function, particularly within the cognition regulation domain, reported lower levels of daily physical activity. Weaker cognition regulation that reflects poorer working-memory, planning, and task completion abilities may present a barrier to adopt or maintain physical activity among adolescents with obesity Another behavior, eating self-efficacy, has been found to be correlated with executive functions. Adolescents with weaker executive function skills were less confident in resisting overeating in challenging situations. Self-efficacy plays a crucial role in healthy dietary decisions and promote the necessary confidence to engage in healthy behaviors.[177] Low eating self-efficacy may contribute to poor adherence to dietary recommendations, and thus difficulty in achieving successful outcomes.

In this study, we proposed to assess the relationship between diet quality and executive function. We evaluated the adolescents' diet intake using the Diet History Questionnaire III *(*DHQ III*)* at the baseline. DHQ III is a validated semi-qualitative food frequency questionnaire developed to assess food and dietary supplement.[178] The web-based questionnaire consists of 135 food and beverage line items and 26 dietary supplement questions, and it includes an assessment of portion size. The questionnaire usually takes up to 45 minutes to complete. However, due to some barriers including lack of time and clinic flow, patients were not able to complete the questionnaire at clinic. Therefore, patients had access to the questionnaire two days before the baseline visit and they were advised to complete it within one to two weeks from the baseline visit. We followed up with patients several times to make sure they successfully completed it. Unfortunately, only 55% (30 out of 54) of patients were able to complete the questionnaire. Moreover, approximately half of those completers provided implausible data. The energy intake was underestimated by 45% as they reported their daily calorie intake less than 600 calories. The misreporting of the energy intake among adolescents is well-documented in the literature.[179,180] Evidence shows that children and adolescents with overweight or obesity are more likely to underestimate their calorie intake compared with their normal weight counterparts.[180,181] It is uncertain whether underreporting was due to reporting errors, recall challenges, or other factors such as socially desirable reporting, day-to-day variation in energy intake, or inaccurate portion size estimation. These results suggest that feasible and valid dietary assessment methods are needed to accurately assess the dietary intake and diet quality of adolescents with obesity in clinical setting. Feasible and accurate dietary assessment are needed not only to establish the reliability of collected dietary data for research purposes but also to evaluate the diet intake in the clinical settings. Accurate dietary assessments can help clinicians and other members of the healthcare team engage patients in diet education and evidence-based behavior counseling. Future research is needed to investigate which foods are misreported, and more fundamentally, why individuals underreport their intake. Future research should also focus on improving dietary assessment methodologies and developing ways of using new technologies to make it more practical and feasible for youth to accurately report their food consumption.

Overall, the findings reinforce the importance of early evaluation of executive function in the treatment course, with follow-up support throughout the intervention period to address these eating behaviors. Pre-treatment detection of executive deficits may have important clinical implications in bariatric surgery patients, as executive function was identified as a predictor of poor postoperative outcomes.[137] Specifically, research shows that pre-operative executive function impairment is associated with poorer adherence and reduced weight loss at post-surgery follow-up.[137] The present study may help to explain this proposed relationship by demonstrating a link between executive dysfunction and disordered eating behaviors (i.e., uncontrolled and emotional eating). Because of their difficulties inhibiting and controlling eating impulses, individuals with executive dysfunction may be predisposed to worse weight loss outcomes. Recognizing executive function as a potential factor of disordered eating may assist in designing and developing more effective programs to promote weight loss and successful healthy eating. Future research should examine whether improvement in executive function would lead to reduced dysregulated eating behaviors or other weight-related behaviors.

This dissertation sought to provide additional insight into the health complications associated with obesity and metabolic syndrome and factors that may influence intervention outcomes in children and adolescents. The study contributes to the literature supporting that early weight loss success is associated with long-term weight loss success. Moreover, it demonstrates the role of pretreatment executive functions on obesity-related behaviors in adolescents seeking surgical options. The study also highlights the importance of evaluating and intervening on executive function in conjunction with an obesity intervention. Taken together, these data show the importance of early comprehensive assessment of each child to identify factors that contribute to positive outcomes and provide the most effective tailored treatment approach.

Conclusion

Given that treatment outcomes for pediatric weight control programs is not effective, it is important to identify what factors determine treatment success and successful weight loss in this population. Early assessment of individuals and treatment-level factors associated with weight loss could facilitate individualized intervention. Using pretreatment characteristics can be an effective strategy to identify patients at risk for failure and allow for individualized tailoring of treatments program accordingly. Future research should be directed toward confirming our findings, as well as identifying additional strategies to improve the effectiveness of behavioral interventions for children and adolescents with obesity.

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Appendices

Appendix 1: Behavior Rating Inventory of Executive Function2®-Self-Report

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BRIEF®2

Behavior Rating Inventory of Executive Function®, Second Edition

Gerard A. Gioia, PhD, Peter K. Isquith, PhD, Steven C. Guy, PhD, and Lauren Kenworthy, PhD

PARENT FORM

	N = Never S = Sometimes O = Often			
1.	Is fidgety	N	S	O
2.	Resists or has trouble accepting a different way to solve a problem with schoolwork, friends, tasks, etc.	N	S	O
3.	When given three things to do, remembers only the first or last	N	S	O
4.	Is unaware of how his/her behavior affects or bothers others	N	S	O
5.	Work is sloppy	N	S	O

TEACHER FORM

	N = Never S = Sometimes O = Often			
1.	Is fidgety	N	S	O
2.	Resists or has trouble accepting a different way to solve a problem with schoolwork, friends, tasks, etc.	N	S	O
3.	When given three things to do, remembers only the first or last	N	S	O
4.	Is unaware of how his/her behavior affects or bothers others	N	S	O
5.	Work is sloppy	N	S	O

SELF-REPORT FORM

	N = Never S = Sometimes O = Often			
1.	I have trouble sitting still	N	S	O
2.	I have trouble accepting a different way to solve a problem with things such as schoolwork, friends, or tasks	N	S	O
3.	When I am given three things to do, I remember only the first or last	N	S	O
4.	I am not aware of how my behavior affects or bothers others	N	S	O
5.	My work is sloppy	N	S	O

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SAMPLE SAMPLE SAMPLE SAMPLE SAMPLE SAMPLE SAMPLE SAMPLE

Appendix 2: Diet History Questionnaire III (DHQ III)

DHQ III Diet History Questionnaire

Appendix 3: Children Mercy Hospital Bariatric Nutrition Guide