Resting Energy Requirements in Overweight and Obese Adolescents: Do Prediction Equations Accurately Estimate Needs?

By

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Abstract

Background: Resting energy expenditure (REE) accounts for the largest portion of total energy expenditure (TEE) and is a valuable tool for clinicians to provide individualized energy needs recommendations. Accurate recommendations are important in light of the current childhood obesity epidemic. Highly accurate measures of REE, such as indirect calorimetry, are costly and impractical for use in a clinical setting. Prediction equations have been developed for quick and easy use by clinicians. While various prediction equations exist, few have been validated for use in overweight and obese adolescent populations.

Objective: The objective of this thesis project is to investigate the accuracy of prediction equations against resting metabolic rate (RMR) measured by indirect calorimetry in overweight and obese adolescents in comparison to normal weight adolescents. In addition, this project will examine the factors of measured RMR that account for the largest amount of variance.

Methods: Data from 111 adolescent male and female subjects across all body mass index (BMI) groups from three previous Energy Balance Research studies was used. Measured RMR was compared to REE predicted by equations. Age, sex, race, fat mass, and fat-free mass were used as variables in linear regression modeling to determine factors accounting for the most variance in measured RMR.

Results: In terms of significant differences from measured RMR, the Muller-1 equation was the most accurate prediction equation, ($p>0.05$ for overweight, obese, and combined overweight and obese groups), followed by the Molnar equation ($p>0.05$ for overweight and combined overweight and obese groups). The addition of age, sex, race, fat mass, and fat-free mass to the unadjusted model of measured RMR resulted in non-significant differences ($p>0.05$) between all BMI groups, accounting for 75% of variance. The addition of fat-free mass to the linear regression model resulted in the largest increase in RMR variance explanation, accounting for an additional 23%.

Conclusions: This data confirms that prediction equations overestimate measured RMR in overweight and obese adolescents. Equations developed with the specific addition of overweight and obese subjects, such as the Muller-1 and Molnar equation, prove to be better tools to accurately estimate RMR.

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Chapter I: Introduction

Childhood obesity continues to rise in prevalence. With this rise comes an increased need for researchers and clinicians to determine better strategies for preventing and treating childhood obesity. Prior to implementing interventions aimed at weight loss or weight maintenance, it is important to first assess energy needs. Having an accurate assessment of energy expenditure can help clinicians to provide more individualized and effective recommendations and, in turn, slow the rise in childhood obesity and obesity related co-morbidities.

Resting energy expenditure accounts for 50-70% of total energy expenditure (1). Resting energy expenditure can be measured in various ways. The most accurate methods of measurement are costly, require highly-trained users, and are not practical for use in a clinical setting. Databases of individual resting energy expenditure values from highly accurate methods of measurement, such as indirect calorimetry, have been used to develop prediction equations that are easily accessible and simple to use (2-4). Over 200 prediction equations have been developed over the past century (5). The Harris-Benedict equation, which was developed in 1918, is still utilized by many clinicians in practice today, over 100 years later, to predict individual energy needs (2).

Although many prediction equations exist, most have been developed from measured resting metabolic rate (RMR) data on large samples of healthy weight adults (2, 4). Equations that have been developed on adolescents tend to have smaller samples sizes than those of adults. Very few equations have been developed for and validated on overweight and obese adolescents (6-11). In addition, characteristics of the cohort used in the development of equations published in the early-to-mid twentieth century may not reflect the anthropometrics, physical activity level, and overall body composition of individuals in the twenty-first century (12).

Developed equations use variables such as height, weight, age, sex, fat mass (FM), and fat-free mass (FFM) to predict an individual's energy needs. Differing values for each of these variables account for differences observed between individuals in metabolic rate. For example, it is generally observed that males have a higher absolute RMR than women, with one proposed explanation being differences in FFM between genders (13). In addition, it is generally observed that RMR decreases with age, with the exact mechanism largely up-for-debate (14). It is also commonly observed that obese individuals have a higher absolute RMR than non-obese individuals, however, when comparing RMR per kilogram of body mass, the obese individuals actually have a lower RMR than non-obese individuals (15).

A previous study evaluating the primary determinants of RMR in a reference 70 kg, adult male found that vital organs (brain, heart, liver, and kidneys), skeletal muscle, miscellaneous tissue (bone, skin, and intestines), and adipose tissue accounted for respectively 58%, 22%, 16%, and 4% of RMR (16). However, this example may not accurately reflect the determinants of RMR in an individual with a differing body composition including greater amounts of adiposity than a reference 70 kg, healthy, adult male. Furthermore, this example may not accurately reflect adolescents, a population younger than the reference whose body composition is changing rapidly throughout puberty (17). A small number of studies exist that examine RMR determinants related to differing amounts of FFM and FM in adolescent populations (17, 18).

The proposed differences in RMR of overweight and obese adolescents compared to healthy weight adolescents may indicate that commonly used predictive equations developed on healthy weight subjects will not be adequate. There is a need for evaluation and validation of previously developed predictive equations on overweight and obese adolescents in a current, diverse population.

Research Question

Which predictive equations, if any, will most accurately estimate measured RMR in overweight and obese adolescents as compared to normal weight adolescents?

Aim 1**:** To investigate the accuracy of energy needs predicted by equations against measured RMR in both normal and overweight/obese adolescents.

Hypothesis 1: Commonly used prediction equations will overestimate RMR in overweight and obese adolescents in comparison to normal weight adolescents. Equations developed with the specific addition of overweight and obese adolescents will more accurately predict RMR than those developed for general, non-weight specific use.

Aim 2: To determine the variables that account for the largest amount of variation in measured RMR of overweight and obese adolescents as compared to normal weight adolescents.

Hypothesis 2: Fat mass will account for a larger amount of variation in measured RMR of overweight and obese adolescents as compared to normal weight adolescents.

Chapter II: Review of Literature

Childhood Obesity

Over the past few decades, the prevalence of childhood obesity has significantly increased. A body mass index (BMI) at the 85th percentile up to the 95th percentile on the Center for Disease Control (CDC) growth chart is classified as overweight and greater than or equal to the 95 percentile is classified as obese (19). According to the 2011-2012 National Health and Nutrition Examination Survey (NHANES) data, 31.8% of children ages 2-19 were found to be either overweight or obese with 16.9% classifying as obese (20).

The long-term metabolic consequences of childhood obesity encompass every major system of the body (21). Non-alcoholic fatty liver disease (NAFLD) is the leading cause of chronic liver disease in children (22). The mortality of NAFLD in obese children ranges between 1.7%- 85% (21). Childhood obesity is also correlated with hypertension (21), and increases in BMI are associated with an increased risk of developing hypertension (23). Other co-morbidities associated with childhood obesity include dyslipidemia, type 2 diabetes mellitus, and obstructive sleep apnea (24). Childhood obesity is an independent predictor of adult obesity despite parental obesity, however, parental obesity more than doubled the risk of adult obesity in children of all BMI categories (25).

Core Concepts of Energy Expenditure

Excessive weight gain, and furthermore obesity, is a result of positive energy balance. In order to assess energy balance patterns in relation to obesity, it is important to understand the basic concepts and terminology surrounding energy expenditure. Total energy expenditure (TEE) is the sum of basal energy expenditure (BEE), the thermic effect of food (TEF), physical activity (PA), and thermoregulation, and it is expressed in terms of kilocalories (kcal)/ 24 hours (26).

Basal energy expenditure encompasses all energy needed to carry out basic metabolic functions of the body on a cellular level in addition to the energy needed to maintain blood circulation, respiration, and gastrointestinal and renal processing. Basal energy expenditure includes the energy needed to remain aroused and is higher than sleeping energy expenditure. (26)

The thermic effect of food increases basal metabolism between 0-5% for fat, 5-10% for carbohydrate, and 20-30% for protein. The degree to which physical activity increases total energy expenditure is dependent on the activity level of the individual, but could nearly double BEE in highly active individuals. Thermoregulation is not of great importance in determining TEE as humans are able to self-regulate body temperature though clothing and environment. Total energy expenditure in children also includes the energy associated with tissue deposition for growth. The energy needed for tissue deposition is highest at birth, declines in early childhood, and increases again at the time of puberty. (26)

It should be noted that basal metabolic rate (BMR) and resting metabolic rate (RMR) as well as basal energy expenditure (BEE) and resting energy expenditure (REE) are often times used interchangeably. BMR represents a situation in which only basal energy needs are measured, while RMR measurements tends to be higher and may reflect recent food intake or delayed effects of physical activity. BMR and RMR are rates expressing a unit of energy over a specified amount of time, such as milliliters of oxygen per minute. These rates are converted into a more useful value expressing kcal/ day, referred to as BEE and REE. For the purposes of this study, RMR and REE will be used interchangeably.

Measuring Energy Expenditure

There are three categories of techniques to measure energy expenditure: direct calorimetry, indirect calorimetry, and non-calorimetric techniques (27). Direct calorimetry measures heat losses from the body in a closed chamber to provide exact energy expenditure in the form of heat. While direct calorimetry is effective at determining energy expenditure, it is extremely costly, labor intensive to maintain, and not readily available for use in research except for a select few locations around the world (27).

The next category of tools in estimation is indirect calorimetry. This method measures an individual’s RMR by analyzing the rate of oxygen consumption and carbon dioxide exhalation using a formula to convert the rates into REE, expressed as kcals/ day (27). Indirect calorimetry is more widely available for use in research and clinical practice, and it is a cheaper method to accurately determine energy expenditure in comparison to direct calorimetry. Both calorimetry methods are used as a comparative standard for other predictive and less accurate non-calorimetric methods.

The third category of determining energy expenditure is through non-calorimetric methods. This category uses metabolic and physiologic measures that correspond to energy expenditure, all of which vary in accuracy and feasibility (27). Some of these methods include doubly labeled water, heart rate monitoring, and activity monitoring (27). The details of each of the non-calorimetric methods is beyond the focus of this paper.

While the above methods of assessing energy expenditure provide accurate results, they are often not useful in a clinical setting as they are not practical. Over time, many predictive equations have been created to quickly and easily determine REE and TEE. Over 200 equations have been developed, each one which vary slightly (5).

Development of Predictive Equations

The rise in interest and utilization of BMR occurred during the early twentieth century from clinicians using BMR as a way to diagnose thyroid diseases (28). Harris and Benedict published a landmark study in 1918 from the measured RMR data on 236 male and female subjects that highlighted the importance of strict testing conditions (2, 28). Harris and Benedict also found that both height and weight are independent determinants of RMR, and from this finding they developed the first REE prediction equation (2, 28). The Harris-Benedict study subjects were between the ages of 21-70 years old and between 25kg-129.4kg (2). The original study subjects may not represent the populations that this equation is used on today such as adolescents and overweight and obese populations, despite the frequent use of this equation in the twenty-first century (29).

The later development of prediction equations came from the analysis of databases of compiled RMR values from studies over previous decades (3, 4). Statistical regression analysis of factors that contribute to measured RMR such as weight, height, age, sex, fat mass, fat-free mass, and physical activity level is the basis for the development of these equations. The 1985 combined report from the

Food and Agriculture Organization (FAO), World Health organization (WHO), and United Nations University (UNU) on *Energy and Protein Requirements* proposed equations for various age ranges from a database with over 7000 data points from studies all over the world (4). Further review of the FAO/WHO/UNU report found that 57% of the data points for males came from Italian subjects (30). It was found that the Italian subjects had a higher RMR per kilogram of body weight, leading to overestimation of energy needs for other non-Italian populations (31). It is important to note the characteristics of the subjects that equations were developed on, such as age, gender, ethnicity, and weight status, as these factors may influence practical implications for widespread use.

Predictive Equations in Adolescents

Many predictive equations have been developed for use in adolescents, but only a few of these equations have been developed with the inclusion of overweight and obese adolescents. Of the select few equations that have been developed specifically on overweight and obese adolescents, each use different variables to predict RMR. (6-11)

In the 2005 publication of the *Dietary Reference Intakes*, the Institute of Medicine (IOM) published BEE and TEE equations for use in the general pediatric population as well as separate BEE and TEE equations for use in exclusively overweight and obese pediatric populations (26). The IOM developed these equations from a database of TEE values measured with doubly labeled water (DLW), which is a highly accurate, direct measurement of energy produced by the oxidation of nutrients into carbon dioxide and water (26). The IOM equations, also known as the Estimated Energy Requirement Equations (EER), are the most commonly used equations in the pediatric clinical settings, and they are recommended for use by the Academy of Nutrition and Dietetics Pediatric Weight Management guidelines (32).

Despite these recommendations, there is a lack of agreement in the literature as to which equation is best validated and appropriate for use in overweight and obese adolescents. The Academy of Nutrition and Dietetics Evidence Analysis Library gives a “consensus” rating for the predictive equations recommended to use in this population as there is a lack of evidence analysis (33). Recommendations are assigned a rating by an expert work group based on the grade of the supporting evidence and the balance of benefit versus harm. Recommendation ratings are Strong, Fair, Weak, Consensus or Insufficient Evidence (33).

With the childhood obesity epidemic on the rise, it is important for clinicians to be able to accurately estimate energy requirements in order to provide evidenced-based recommendations for intervention and prevention of future co-morbidities. Validation of predictive equations on overweight and obese adolescents can help to improve estimation of energy needs. The purpose of this literature review is to compare studies evaluating predictive equations to the results of indirect calorimetry in order to determine the most validated equations for overweight and obese adolescents.

Relevant Research

After a comprehensive database search for relevant research and narrowing down selections to best fit the criteria for this review, four original research articles with similar methodology have been selected. The following research is specific to overweight and obese children under the age of 21 in comparing predictive energy equations to measured resting energy expenditure through indirect calorimetry.

The data collection and analysis methods between the studies were consistent. Of note, both Henes et al. and White et al. used portable indirect calorimetry, which has yet to be validated for use in an obese youth population (1, 34). Standard procedures were used to collect height, weight, body composition if applicable, and measured RMR. Both Hofsteenge et al. and Zhang et al. analyzed equations with FM and FFM mass as variables, and they measured body composition through dual energy X-ray absorptiometry (DXA) and bioelectrical impedance analysis (BIA), respectively (35, 36).

There were slight differences in the demographics of each study's subjects. All studies included both males and females. Hofsteenge et al. examined 121 overweight and obese adolescents between the ages of 12-18 years old in the Netherlands (35). Henes et al. examined 80 overweight and obese youth between the ages of 7-18 years in the United States (34). Zhang et al. examined 248 non-specified obese and non-obese youth between the ages of 7-13 in China (36). White et al. examined 53 youth across normal, overweight, and obese BMI categories between the ages of 6-21 years old in the United States (1).

A variety of equations were used across the 4 studies; however, all studies had a small number of equations in common. Hofsteenge et al. compared the results of standard indirect calorimetry to 43 total equations of which 31 were weight-based equations and 12 were FFM-based equations (35). Henes et al. compared the results of portable indirect calorimetry to nine predictive equations (34). Zhang et al. compared the results of standard indirect calorimetry to 11 predictive equations, one of which was a new equation developed from study data as a stepwise regression analysis in children with obesity (36). White et al. compared the results of both standard indirect calorimetry and portable indirect calorimetry to nine predictive equations (1).

Hofsteenge et al., Henes et al., and Zhang et al. measured accuracy of each equation as subjects within +/- 10% of the measured RMR (34-36). White et al. measured accuracy of each predictive equation as a concordance correlation coefficient (1).

Hofsteenge et al. found the Molnar equation to have an accuracy of 74%, with 16% underprediction and 9% overprediction. Interestingly, this study also found the Schofield weight and height 18-30-year-old equation to be 74% accurate, with 8% underprediction and 17% overprediction. While the Schofield (3) weight and height 10-18-year-old equation was only 50% accurate. This is believed to be because the Schofield 18-30-year-old equation is based on adults with larger body mass who have a more similar body composition to the overweight and obese adolescents measured in this study. This study preformed a secondary analysis on the accuracy of the predictive equations when removing the individuals that classified as overweight but not obese, and the results proved no significant differences in accuracy. This study also measured body composition using a DXA and examined the results of predictive equations that take into account FFM%. The FFM-based equations did not prove to be any more accurate than the weight and height-based equations in this population. (35)

Henes et al. distinguished the accuracy of predictive equations between genders. The Harris-Benedict equation was found to have an accuracy of 65% in both males and females, while the Molnar equation was found to have an accuracy of 65% in females and 54% in males. This study also compared measured RMR to TEE equations using a physical activity coefficient of 1 to indicate a sedentary lifestyle, and the results substantially overpredicted measured RMR. (34)

Zhang et al. predicted found that the Harris-Benedict equation had the highest percentage of accuracy in both the obese population at 68% and the non-obese population at 47%. This study also found that the obese children had a lower REE/kg body weight than the non-obese children. (36)

White et al. found that the Molnar equation has the strongest correlation across all BMI categories to standard indirect calorimetry. However, the Molnar equation had a higher mean bias, or overestimation of RMR, for overweight and obese individuals than those of normal weight status, 14.3% $\pm$ 8.8% and 7.8% $\pm$ 7%, respectively. This study also found that REE/kg body weight was lower in overweight and obese individuals than non-obese individuals using both standard and portable indirect calorimetry. (1)

Discussion

Based on this review of literature, the Harris Benedict and Molnar equations prove to be the most accurate predictive equations in overweight and obese adolescents. The development of the Harris-Benedict equation was previously discussed. The Molnar equation was developed in 10-16 year old male and female adolescents of normal weight, overweight, and obese BMI categories (6).

Zhang et al. pointed out that the generalizability of predicative equations to various ethnicities, such as the group of Chinese subjects being studied, is limited due to many equations being developed in Caucasian populations. Another limitation to Zhang’s study is the fasting protocol for indirect calorimetry. The protocol only included a 2-hour required fasting period, while the other studies followed a 10-12-hour standard fasting protocol. This is significant as a 2-hour fasting period does not represent a true fasted state and could lead to increased RMR due to the thermic effect of food. (36)

Henes et al. pointed out that accuracy of predictive equations in overweight and obese children varies between genders and are less accurate in males (34). Predictive equations are created with the assumption that males have higher FFM% than females and therefore higher energy requirements (37). However, overweight and obese males have a lower ratio of FFM to FM compared to normal weight males which may decrease the accuracy of the predictive equations (38).

It should be noted that most predictive equations are developed on healthy weight subjects with lower levels of adiposity compared to overweight and obese individuals (3). It is unclear how significantly FFM differs between obese and non-obese adolescents (18), however, as adiposity continually increases, as seen in obesity, significant differences exist in FM between obese and non-obese adolescents. It has been found that FM accounts for a small percentage of RMR compared to FFM in a reference healthy male (16). It is of interest as to how RMR changes with increasing FM. A previous study comparing non-obese adolescents to obese adolescents with an average of 16kg of additional FM found that controlling for FFM alone in an analysis of covariance still resulted in significant differences in RMR between groups (18). It was found that upon adding FM to the model and controlling for both FFM and FM, no significant differences remained between groups (18). This study supports other research suggesting that both FMM and FM account for significant differences in RMR between non-obese and obese adolescents (17, 39).

Although the previous studies discussed did not find equations using FM and FFM as variables to be the most accurate, it is of interest to continue to study FM in relation to differences in RMR with the current childhood obesity epidemic. Prediction equations that take into account FM and FFM, such as a version of the Muller equation (7), which was developed on normal weight, overweight, and obese adolescents, may be a beneficial tool in predicting RMR.

Conclusions

Both the White et al. and Zhang et al. studies converted measured RMR values into REE/kg of body weight as a standard way to compare results between subjects of all BMI categories (1, 36). Both found REE/kg to be lower in overweight and obese subjects than in normal weight subjects. This suggests that the use of predictive equations developed on normal weight adolescents may overestimate energy expenditure in overweight and obese adolescents.

These studies have indicated that the Harris-Benedict and Molnar equations prove to be accurate predictive tools as compared to indirect calorimetry in their respective groups of subjects. However, there is still a need to validate these two equations as well as other commonly used equations in a group of subjects that best represent the population of interest for which they will be used. Research subject characteristics for the population of interest should be diverse and represent the increasing proportion of overweight and obese adolescents in the twenty-first century.

Chapter III: Methods

Overview

This thesis project used pre-existing data from the following three studies at the Center for Children's Healthy Lifestyles and Nutrition (Kansas City, MO):

- A study of Activity, Adiposity, and Appetite in Adolescents (AAAA)
- The Brain, Appetite, Teenagers, and Exercise (BATE)
- Sable Indirect Calorimetry Device Validation Study (Sable)

Each study's respective setting, subject inclusion criteria, recruitment process, and pertinent subject characteristics will be detailed below. The data collection of height, weight, DXA scans, and measured RMR values followed the same standard operating procedure across all three studies with only minimal protocol differences that will be noted in the *procedures* subsection. RMR data collected from these three studies was compared to specified predictive equations. Subjects' height measurements, weight measurements, and body composition measures obtained from the DXA scan, such as fat mass and fat-free mass, were used as variables in these various predictive equations. In addition, body composition data collected from these three studies was used in a linear regression to determine variables accounting for the most significant variations in measured RMR.

Ethics

The Institutional Review Board at Children's Mercy Hospital approved all three study protocols. Subjects enrolled in all three studies completed informed consent. This thesis project is covered under existing study protocols and consent forms (AAAA: IRB #16120865, BATE: IRB # 00000096, Sable: IRB #00000654).

AAAA

AAAA was a pilot study with a cross-sectional design that began recruitment in September of 2017 and competed all study-related visits by November of 2018. Subjects were recruited primarily from Children's Mercy Hospital and The University of Kansas Health Systems. Subjects included healthy, adolescent males between the ages of 14-18. Participants were stratified into one of four study sub-groups based on both BMI status (normal weight or overweight/ obese) and physical activity level (sedentary or active).

BATE

BATE was a pilot study with a randomized intervention that began recruitment in December of 2018 and completed all study-related visits by August of 2019. Subjects were recruited primarily from Children's Mercy Hospital and The University of Kansas Health Systems. Subjects included adolescent males and females between the ages of 14-17. Additionally, subjects were to be between the 85th and 99th BMI percentile for age and sex, weight stable, at risk for type 2 diabetes according to the American Diabetes Association criteria (40), sedentary as classified by less than 20 minutes of exercise per day, willing to participate in an exercise program, and not taking any medication that may alter metabolism.

Sable

The Sable study was a validation study of a new RMR measurement device against an industry research standard. Sable began recruitment in October of 2019 and completed all study-related visits by December of 2019. Subjects included adolescent males and females between the ages of 13-18. Additionally, subjects were to be between the 5th and 95th BMI percentile for age and sex.

Procedures

Height was measured with a mounted stadiometer. Height was assessed while the subject was wearing provided surgical scrubs and non-slip socks. Measurements were recorded to the nearest tenth of a centimeter and taken at least twice until two values were within 4 millimeters. Weight was measured on an electronic scale. Weight was assessed while the subject was wearing provided surgical scrubs and non-slip socks. Measurements were recorded to the nearest tenth of a kilogram and taken at least twice until two values were within 0.1 kilogram.

Fat mass and FFM were measured using a GE Lunar whole-body dual energy X-ray absorptiometer. Prior to starting the DXA scan, subjects were asked to remove all items that may attenuate the X-ray beam such as jewelry, watches, and undergarments affixed with metal. Additionally, each female subject was required to provide a urine sample for a pregnancy test as a standard precaution prior to the scan. Female subjects with a positive pregnancy test reading were not able to proceed with the scan. All subjects were scanned while wearing provided surgical scrubs and non-slip socks. Subjects were positioned onto the DXA table and asked to remain completely still for the duration of the scan. Each subject received a total body scan. Upon completion of the scan, the regions of interest were adjusted per protocol to ensure correct positioning at certain anatomical markers on the DXA enCORE software before finalizing the report. Fat mass and FFM values were reported in grams.

Resting metabolic rate was measured via indirect calorimetry using a Parvo Medics TrueOne 2400 ventilated hood system. All subjects were asked to fast from food and beverages other than water and to refrain from exercise for 12 hours prior to their visit. All RMR tests took place in the morning. Prior to the test, each subject was given a chest-strap heart rate monitor to wear. All subjects were tested while lying in a supine position on top of a hospital bed and were provided with a blanket and pillow. Subjects were asked to remain still and awake for the entirety of the test. The test exam room was kept at a consistent, comfortable temperature with quiet surroundings for all study visits.

Prior to each RMR test, the gas and flowmeter were calibrated per protocol. Upon starting the test, stable measurements were to be attained within the first 10 minutes. Both AAAA and BATE tested RMR for 45 minutes, while Sable only tested RMR for 33 minutes. Despite the differences in total test time, all three studies analyzed data for the 10-minute window with the lowest coefficient of variation of each test. The 10-minute window could not include the first 10 minutes that were used to stabilize subject measurements. Resting metabolic rate was expressed as kcal/day and was calculated as the average of the data points in the 10 minutes with the lowest coefficient of variation.

All data were collected by staff, primarily graduate research assistants, on the Energy Balance Research team. Staff were required to be trained and approved by a supervisor prior to collecting data for each of the previously mentioned procedures.

Analysis of Data

Secondary data analysis of AAAA, BATE, and Sable participants were conducted using SAS statistical software. All subjects were stratified into one of three BMI groups, normal weight, overweight, or obese, based on CDC growth charts for age and sex (41). For all tests, statistical significance was set at $P \leq 0.05$.

Differences between BMI groups for quantitative participant characteristics were presented as least square means. Differences between the frequency of race categories were presented as a chi-squared probability. Participant characteristics, with the exception of race and male sex, were presented as a mean ± standard deviation. Race and male sex were presented as a percentage of frequency.

Measured RMR and predicted RMR were compared using the student's t-test method. Measured and predicted RMR data was expressed as a mean kcal/day ± standard deviation. Below is a list of all prediction equations utilized in data analysis. All equations are specified for use of individuals within the age-range of subjects in all three studies.

Predictive Equations for Resting Energy Expenditure (REE)

Equations Developed for General Use	
Harris-Benedict (2)	M: (kcal/day) = 66.4730 + 13.7516W(kg) + 5.0033H(cm) - 6.7550A(yr) F: (kcal/day) = 655.0955 + 9.5634W(kg) + 1.8496H(cm) - 4.6756A(yr)
WHO-1 (4)	M: (kcal/day) = 17.5W(kg) + 651 F: (kcal/day) = 12.2W(kg) + 746
WHO-2 (4)	M: (kcal/day) = 16.6W(kg) + 77H(m) + 572 F: (kcal/day) = 7.4W(kg) + 482H(m) + 217
Schofield-1 (3)	M: (MJ/day) = 0.074W(kg) + 2.754 F: (MJ/day) = 0.056W(kg) + 2.898
Schofield-2 (3)	M: (MJ/day) = 0.068W(kg) + 0.574H(m) + 2.157 F: (MJ/day) = 0.035W(kg) + 1.948H(m) + 0.837
IOM-1 (26)	M: (kcal/day) = 420 – 33.5A(yr) + 418.9H(m) + 16.7W(kg) F: (kcal/day) = 516 – 26.8A(yr) + 347H(m) + 12.4W(kg)
Equations Developed with the Specific Inclusion of Overweight and Obese Subjects	
Molnar (6)	M: (kJ/day) = 50.9W(kg) + 25.3H(cm) - 50.3A(yr) + 26.9 F: (kJ/day) = 51.2W(kg) + 24.5H(cm) - 207.5A(yr) + 1629.8
Muller-1 (7)	(MJ/day) = 0.02606W(kg) + 0.04129H(cm) + 0.311(sex) - 0.08369A(yr) - 0.808
Muller-2 (7)	(MJ/day) = 0.07885FFM(kg) + 0.02132FM(kg) + 0.327(sex) + 2.694
IOM-2 (26)	M: (kcal/day) = 79 – 34.2 A(yr) + 730H(m) + 15.3W(kg) F: (kcal/day) = 322 – 26.0A(yr) + 504H(m) + 11.6W(kg)

M, male; F, female; W, weight; H, height; A, age; sex (M=1, F=0); FM, fat mass; FFM, fat free mass

A multivariate linear regression was used to explain the variance between variables influencing measured RMR. Age, race, and sex were initially added to the unadjusted model. Following models included the addition of fat-free mass and, lastly, fat-mass. Measured RMR data adjusted throughout the linear regression was presented as a mean ± standard deviation. Differences between BMI groups in each model were presented as least square means.

Chapter IV: Results

The purpose of this thesis was to determine the accuracy of predictive equations in estimating measured RMR of overweight and obese adolescents as compared to healthy weight adolescents. A secondary aim of this thesis was to determine the factor or factors that account for the largest amount of variance in measured RMR. All tables and figures are given in the section labeled Tables and Figures.

Group Characteristics

Table 1 summarizes participant characteristics. The mean age of the 111 participants was 15.4 years old. Of those participants, 69% were males. The participants were divided into three BMI groups: healthy (n=69), overweight (n=14), and obese (n=28). There was not a significant difference between BMI groups for sex, age, or height. There was a significant difference within race subcategories ($p=0.004$), with 66.7% of participants being classified as white.

Differences in weight, BMI, BMI-for-age z-score, fat mass, and body fat percentage were statistically significant ($p \leq 0.05$) between each group. Of note, there was not a significant difference between the overweight and obese groups for measured RMR (kcal/day). In addition, there was not a significant difference between the overweight and obese groups for BMI-for-age (percentile) or fat-free mass (kg).

Measured RMR vs Predictive Equations

Table 2 summarizes RMR (kcal/day) measured by the Parvo system and REE (kcal/day) predicted from equations by four BMI groups: healthy, overweight, obese, and combined overweight and obese. The fourth BMI category of combined overweight and obese was added to this analysis as it was found that the measured RMR for both groups was not significantly different ($p=0.997$). Data are presented as a mean ± standard deviation.

The Muller-1 equation, using weight (kg), height (cm), sex, and age as variables, proved to be the most accurate equation tested against measured RMR. Differences between the Muller-1 equation and measured RMR were not statistically significant ($p>0.05$) when comparing all subjects as well as the overweight, obese, and combined overweight and obese groups. The Muller-1 equation was highly accurate for the obese group in particular, with a mean overprediction of only 1.362 kcal/day. In addition, there were not statistically significant differences between measured RMR and the Molnar equation in all subjects, as well as both the overweight and combined overweight and obese groups.

The IOM-1 equation was the only equation that did not have statistically significant differences from measured RMR in the healthy weight group. In the overweight group, there were not statistically significant differences between measured RMR and the Harris-Benedict, Molnar, Muller-1, IOM-1, Muller-2, and WHO-2 equations, listed in order of proximity to measured RMR. However, when combining the overweight subjects with the obese subjects, only the Molnar and Muller-1 equations did not have statistically significant differences from measured RMR.

Figure 1 displays each equation and measured RMR by BMI group and includes standard error bars in both directions. In general, prediction equations overestimated measured RMR for each group analyzed. The equations that underestimated measured RMR were the Molnar equation for all, healthy, and overweight groups and the Muller-1 equation for the overweight and combined overweight and obese groups. Of note, standard error was higher for all equations in the overweight group compared to equations in the other BMI groups.

Variables Determining RMR

Table 3 summarizes the measured RMR linear regression model, separated by three BMI groups: healthy, overweight, and obese. Unadjusted, there were statistically significant differences between the healthy weight group and both the overweight ($p=0.001$) and obese ($p<0.001$) groups, with only 23% of variance in RMR explained. An additional 28% of variance was explained when age, sex, and race were added to the unadjusted model. However, statistically significant differences in RMR remained between the healthy group and both the overweight ($p<0.001$) and obese ($p<0.001$) groups. Upon adding FFM (kg) to the model, an additional 23% of RMR variance was explained, with significant differences only remaining between the healthy weight and obese groups (p=0.001). Lastly, FM (kg) was added to the model to explain an additional 1% of RMR variance and result in no significant differences between all three BMI groups. Figure 2 displays the increase in variance explanation as RMR variables are added to the model. Fat-free mass was the single variable that explained the largest amount of variance when added to the model.

Tables and Figures

Table 1. Participant Characteristics Overall and by BMI Groups

Characteristic	All *(n=111)*	BMI Groups Healthy *(n=69)*	Overweight *(n=14)*	Obese *(n=28)*	Between-group differences (p-value < 0.05)
Male sex (%)	69%	71%	79%	61%	NS
Race (%)					*0.004
Asian/ Pacific	3.6%	0.0%	7.1%	10.7%	
Black	27.9%	23.2%	28.6%	39.3%	
Indian/ Alaskan	1.8%	0.0%	0.0%	7.1%	
White	66.7%	76.8%	64.3%	42.9%	
Age (y)	15.4 ± 1.2	15.3 ± 0.1	15.4 ± 0.3	15.5 ± 0.2	NS
Height (cm)	170.7 ± 9.0	170.1 ± 9.0	172.9 ± 8.8	170.9 ± 9.1	NS
Weight (kg)	69.0 ± 16.7	58.6 ± 8.6	75.8 ± 8.0	91.4 ± 10.1	1 vs 2,3; 2 vs 3
Body mass index	23.7 ± 5.3	20.2 ± 1.8	25.4 ± 1.4	31.4 ± 3.2	1 vs 2,3; 2 vs 3
BMI-for-age (percentile)	66.6 ± 27.5	49.2 ± 20.1	90.4 ± 2.8	97.6 ± 1.2	1 vs 2,3
BMI-for-age (Z-score)	0.66 ± 1.0	-0.03 ± 0.6	1.3 ± 0.2	2.0 ± 0.2	1 vs 2,3; 2 vs 3
Fat-free mass (kg)	50.0 ± 10.1	46.8 ± 9.1	55.9 ± 10.6	55.6 ± 8.7	1 vs. 2,3
Fat mass (kg)	18.8 ± 11.4	12.0 ± 4.1	20.1 ± 5.8	36.2 ± 7.6	1 vs 2,3; 2 vs 3
Body fat (%)	25.9 ± 10.5	20.8 ± 7.2	26.7 ± 8.2	39.2 ± 6.5	1 vs 2,3; 2 vs 3
RMR (kcal/day)	1637.8 ± 256.6	1543.0 ± 203.9	1789.5 ± 302.9	1795.5 ± 242.1	1 vs 2,3

*Result represents p-value for differences between race sub-categories
Data is presented as a percent or a mean ± standard deviation.
1, Healthy; 2, Overweight; 3, Obese; NS, Not Significant (P ≥ 0.05)

Table 2. Energy Needs (kcal/day) - Measured vs. Predictive Equations Overall and by BMI Groups

	BMI Groups				
	All *(n=111)*	Healthy *(n=69)*	Overweight *(n=14)*	Obese *(n=28)*	Overweight & Obese *(n=42)*
Direct Measure of RMR (kcal/day)					
Parvo System	1637.8 ± 256.6	1543.0 ± 203.9	1789.5 ± 302.9	1795.5 ± 242.1	1793.5 ± 260.2
Predictive Equations - General Use (kcal/day)					
Harris-Benedict	*1711.4 ± 256.5	*1581.2 ± 173.2	1830.7 ± 198.8	*1967.9 ± 231.9	1922.1 ± 228.6
WHO-1	*1780.7 ± 302.5	*1622.1 ± 196.2	*1920.0 ± 219.3	*2102.1 ± 266.8	2041.4 ± 263.9
WHO-2	*1756.5 ± 294.4	*1622.0 ± 194.1	1893.6 ± 239.5	*2019.6 ± 320.7	1977.6 ± 299.2
Schofield-1	*1801.7 ± 308.3	*1637.3 ± 200.9	*1942.2 ± 217.9	*2136.5 ± 259.0	*2071.7 ± 260.5
Schofield-2	*1778.4 ± 296.2	*1642.3 ± 201.6	*1915.0 ± 239.8	*2045.5 ± 310.6	*2002.0 ± 292.7
IOM-1	*1710.6 ± 295.9	1549.4 ± 188.4	1846.6 ± 219.9	*2024.3 ± 255.7	*1965.1 ± 256.1
Predictive Equations - Specific Inclusion of Overweight and Obese Subjects (kcal/day)					
Molnar	1626.4 ± 265.4	*1498.3 ± 202.8	1743.8 ± 203.7	*1878.8 ± 218.8	1833.8 ± 221.0
Muller-1	1662.8 ± 172.1	*1593.0 ± 144.1	1733.8 ± 150.4	1796.8 ± 153.8	1775.8 ± 153.8
Muller-2	*1737.1 ± 226.4	*1640.9 ± 188.3	1859.8 ± 204.3	*1926.5 ± 178.6	*1903.2 ± 188.1
IOM-2	*1780.3 ± 306.3	*1630.2 ± 219.0	*1917.8 ± 249.2	*2064.8 ± 281.5	*2015.8 ± 277.1

*Indicates significant difference (p-value ≤ 0.05) in kcal/day between predictive equation and Parvo System within BMI group.
Data is presented as a percent or a mean ± standard deviation.

Figure 1.

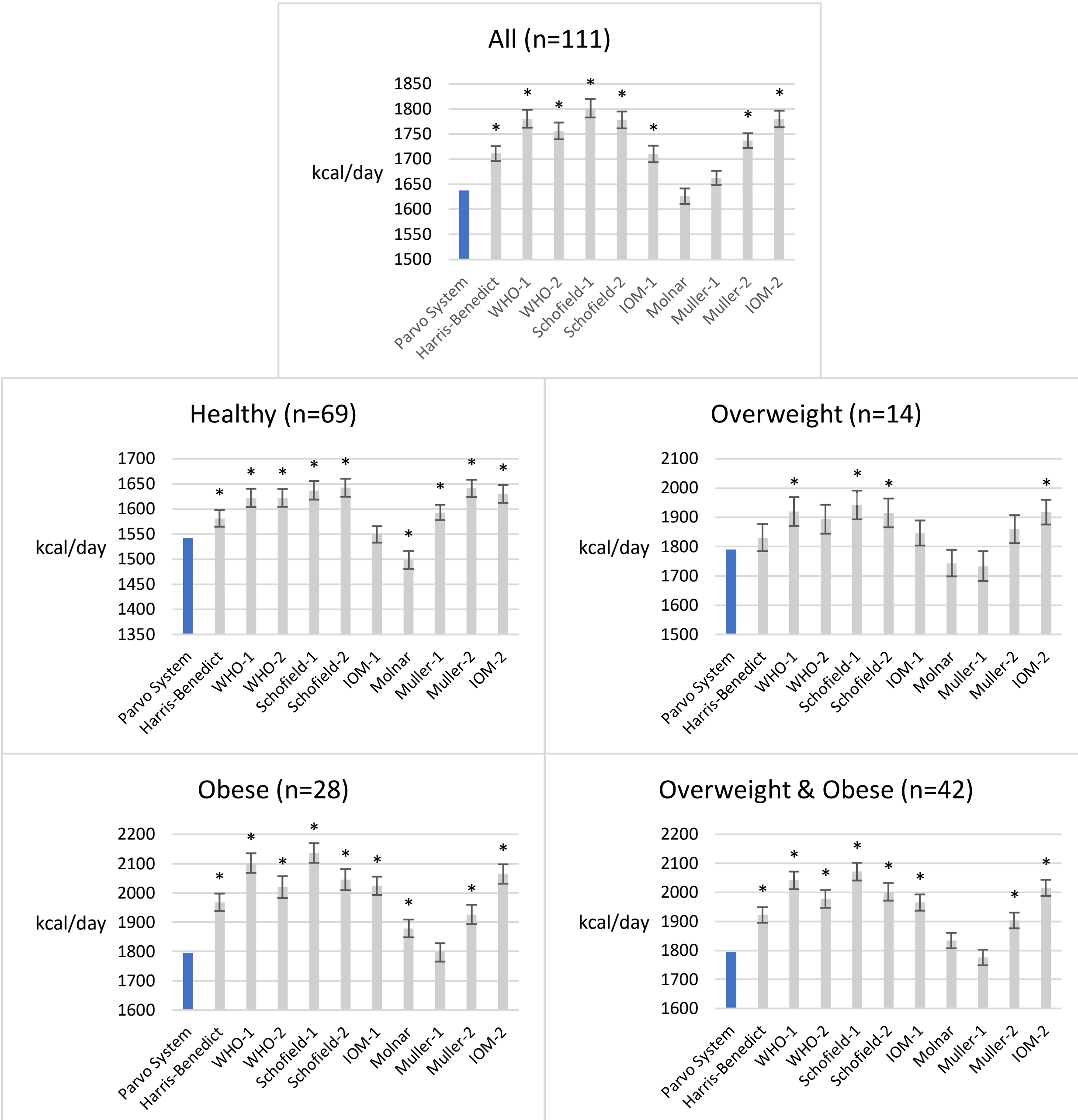

Figure 1. Parvo System vs Predictive Equations Overall and by BMI groups.
*Indicates significant difference (p-value $\leq$ 0.05) in kcal/day between Parvo System and predictive equation. Standard error bars are shown in both positive and negative direction for each equation.

Table 3. Analysis of Covariance Assessing Resting Metabolic Rate Controlling for Age, Sex, Race, Fat-Free Mass, and Fat Mass

	BMI Status				
Variable (kcal/day)	Healthy *(n=69)*	Overweight *(n=14)*	Obese *(n=28)*	Between-group differences (p-value ≤ 0.05)	R_2
Unadjusted	1543.0 ± 27.4	1789.5 ± 60.9	1795.5 ± 43.0	1 vs 2,3	0.23
Age + Sex + Race	1521.2 ± 22.6	1770.1 ± 49.2	1842.8 ± 35.9	1 vs 2,3	0.51
Age + Sex + Race + FFM	1583.7 ± 17.8	1683.6 ± 37.4	1743.8 ± 29.6	1 vs 3	0.74
Age + Sex + Race + FFM + FM	1616.2 ± 27.7	1673.2 ± 37.8	1664.3 ± 60.0	NS	0.75

Data is presented as a mean ± standard deviation.
1, Healthy; 2, Overweight; 3, Obese; NS, Not Significant (p > 0.05)

Figure 2.

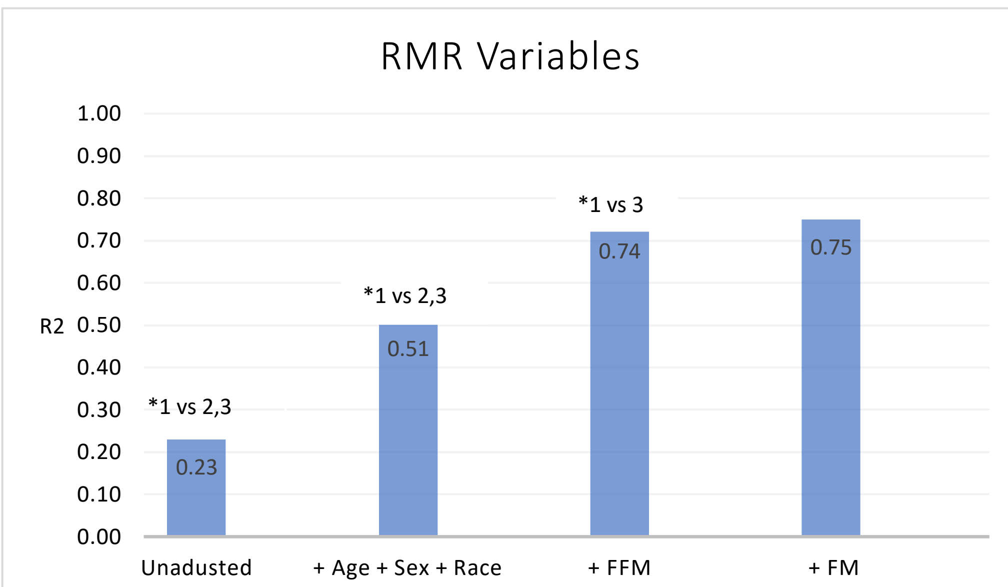

Figure 2. Factors explaining variation in measured RMR.
The addition of age, sex, and race to the unadjusted model explained 28% of RMR variance with significant differences remaining between all groups (p≤ 0.05). The addition of FFM resulted in the largest single-variable increase by explaining an additional 23% of variance, with significant differences only remaining between groups 1 and 3 ($p \leq 0.05$). The final addition of FM explained 1% of variance and resulted in non-statistically significant differences (p> 0.05) between all groups.

Chapter V: Discussion

This thesis was focused on answering the question: which predictive equations, if any, will most accurately estimate measured RMR in overweight and obese adolescents as compared to normal weight adolescents? It was hypothesized that prediction equations will overestimate measured RMR in overweight and obese adolescents. Additionally, it was hypothesized that equations developed with the specific addition of overweight and obese adolescents will more accurately predict RMR than those developed for general, non-weight specific use. The results of this set of data did confirm the hypothesis by showing that all equations analyzed, with the exception of the Molnar and Muller-1 equation, overestimated measured RMR. Interesting, the only two equations that underestimated RMR in any group proved to be the two equations that most accurately estimated measured RMR for the overweight, obese, and combined overweight and obese groups.

The results of this data also confirm the hypothesis, as both the Muller-1 equation and Molnar equation were developed with the specific addition of overweight and obese subjects. However, other equations used in analysis that were developed with the addition of overweight and obese adolescent subjects such as the Muller-2 and IOM-2 equations significantly ($p \leq 0.05$) overestimated measured RMR in the overweight, obese, and combined overweight and obese groups, with the exception of the Muller-2 equation in the overweight group. The overweight group had a greater number of equations that predicted non-significantly different ($p>0.05$) measured RMR values, with the most accurate equation being the Harris-benedict equation. However, upon combining the overweight participants with the obese participants, the only equations that remained non-significantly different ($p>0.05$) from measured RMR values were the Muller-1 and Molnar equation. This may be due to the small sample size of the overweight group (n=14) compared to the healthy weight group (n=69) and the obese group (n=28).

A secondary aim of this thesis was to determine the variables that account for the largest amount of variation in measured RMR. It was hypothesized that FM will account for a larger amount of variation in measured RMR of overweight and obese adolescents as compared to normal weight adolescents. This set of data showed that FFM was the single variable that explained the largest amount of variance in measured RMR upon addition to the previous model, accounting for an additional 23% of variance. Despite the large increase in explanation of RMR variance, the addition of FFM did not complete the model, as there were still significant RMR differences between the healthy weight and obese groups (p=0.001) but not overweight group. The final addition of FM to the model resulted in non-significant differences between all BMI groups, although only explaining an additional 1% of variance in RMR. The significant difference that remained between the healthy weight and obese groups after controlling for FFM was likely due to the increased contribution to RMR that the obese group's fat mass had (24.2kg more than heathy weight group) in contrast to the fat mass of the overweight group (8.1kg more than healthy weight group.) Of note, despite significant differences between all three groups in fat mass, there were not significant differences between the overweight and obese groups in fat-free mass.

Comparison to the Literature

Previous studies have found the Molnar equation to be the most accurate equation to estimate RMR in overweight and obese adolescents (1, 35), and the current data supports the accuracy of the Molnar equation in this population. Fewer studies have found the Muller-1 equation to be the most accurate equation for overweight and obese adolescents (1), however, this set of data found the Muller-1 equation to be the best equation to predict measured RMR for overweight and obese adolescents. This set of data also found that the Muller-2 equation, which uses FFM and FM as variables, was no more accurate than weight-based equations, and this is supported by the findings of previous studies (35, 36).

Strengths and Limitations

One strength of this study design is the consistency of data collection. All tests performed and data collected were executed and recorded by trained staff who followed the same protocols for all three studies. Another strength of this study design includes the use of DXA body composition testing as opposed to other forms of measurement such as skin-folds or bioelectrical impedance analysis that rely on precise measurements of a trained technician and vary with hydration status, respectively. In addition, all RMR tests were performed on a standard ventilated-hood metabolic cart as opposed to portable indirect calorimetry which has yet to be validated for use in overweight and obese youth (1, 34). Strengths of this data set include the addition of a healthy weight group as a control. Previous literature of similar study design does not consistently include a control group and therefore is unable to determine the extent of accuracy of prediction equations for overweight and obese adolescents compared to those of a healthy weight.

Limitations of this set of data include a relatively small sample of overweight subjects compared to the number of healthy weight and obese subjects. This small sample of subjects limited the ability to determine accuracy of prediction equations within the overweight group and limited the ability to differentiate accuracy of equations specifically between overweight and obese subjects. Additional limitations include the disproportionate number of males in the sample (69% of total), and this is likely due to the AAAA study only enrolling male participants. Previous research has found equations to have differing accuracy between males and females (34). Therefore, the prediction equations found to be the most accurate in this research may not be as generalizable to females. Future research of similar methodology including a larger sample of females and data analyzed separately by sex may be beneficial. Finally, this research did not look at RMR in terms of kcal/kg/day, which is a commonly used measure in clinical settings and may be more useful for clinicians and dietitians.

Clinical Significance

This thesis only defined accuracy of an equation by lack of significant differences from measured RMR across BMI groups. Statistically significant differences, or lack of differences, between predictive equations and measured RMR does indicate the extent to which one predictive equation is more accurate than another. This poses the question: what extent of overestimation of RMR would further excessive weight gain to a clinically significant level, contributing to the rise in childhood obesity? In addition, the Parvo ventilated hood system has differing accuracy from the criterion Douglas Bag method of indirect calorimetry (1). Further research is needed to compare the differences in standard error between the Parvo ventilated hood system and criterion Douglas Bag system and between the Parvo system and prediction equations.

Implications

This research found that commonly recommended prediction equations significantly overestimated measured RMR in overweight and obese adolescents. Continued use of these equations by clinicians may lead to inaccurate energy recommendations, potentially contributing to further weight gain. The findings of this research are important in light of the current obesity epidemic. This research also proves that there is a need to re-evaluate equations recommended for use by clinicians on overweight and obese adolescents.

Conclusions

The goal of this research was to find the most accurate equations to estimate RMR in overweight and obese adolescents so that clinicians can provide better recommendations and, ultimately, slow the progression of the childhood obesity epidemic. Although previous research has been conducted aiming to determine the best predictive equations for use on overweight and obese adolescents, there still remains no consensus. The strength of this research adds to the current literature to help health professionals come to a consensus.

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