Comparison of Prediction Equations for Resting Energy Expenditure vs the KORR ReeVue Indirect Calorimeter in Obesity

By

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Abstract

An increasing number of institutions and community settings are assessing resting energy expenditure (REE) to tailor weight loss interventions. Resting energy expenditure can be assessed using an indirect calorimeter or from prediction equations. Portable indirect calorimeters are not widely available and have associated equipment and operating costs, whereas assessment of REE using prediction equations is cost-effective and simple to use. Data are lacking to assess the agreement for the measurement of REE between portable indirect calorimeters and prediction equations to help inform institutions and community settings on the best option to assess REE in an obese population. The purpose of this study was to compare the seven most common prediction equations for estimation of resting energy expenditure (REE) – Mifflin St. Jeor (MSJ), Harris Benedict (HB), Owen, American College of Chest Physicians (ACCP) 21, ACCP 25, World Health Organization/Food and Agriculture Organization/United Nations University (WHO/FAO/UNU; using weight only), and WHO/FAO/UNU (using both weight and height) – to measured REE (MREE) using the KORR ReeVue indirect calorimeter in free-living obese adults. Statistical analyses were completed to understand if age, sex, race, or obesity grade influenced the agreement between the estimated REE for the prediction equations and MREE for the KORR ReeVue indirect calorimeter. The study found the prediction equations of MSJ, HB, WHO/FAO/UNU (using weight only), and WHO/FAO/UNU (using both weight and height) accurately estimated REE in obese adults within ±150 kcal/day of MREE. Of these four equations, Harris Benedict had the least amount of contributing variables that influenced the estimation of MREE (only race contributed) and Mifflin St. Jeor had the second least amount (race and sex contributed) of contributing variables. Therefore, these prediction equations would be appropriate to use in clinical practice if an institution did not have access to an indirect

calorimeter. The prediction equations of Owen and American College of Chest Physicians; however, under- and overestimated MREE, respectively, and should be avoided in clinical practice.

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<u>Chapter 1: Introduction</u>

The primary objectives for this study were to build upon previous research comparing prediction equations for estimating resting energy expenditure (REE) to measured REE (MREE) and provide guidance for clinicians regarding utility of a portable indirect calorimeter. Obesity is a prevalent problem in today's society, with over one-third (36.5%) of the population of the United States being obese [1]. Many preventable health issues stem from obesity, including heart disease [2], diabetes [3, 4], non-alcoholic fatty liver disease [5], and certain types of cancer [6]. Obesity results from an energy imbalance. Energy metabolism differs among obese individuals [7]. Determining accurate energy expenditure for obese adults is imperative in order to develop personalized nutrition recommendations to promote weight loss and reduce obesity-related disease risk.

Traditional indirect calorimetry using a ventilated hood is considered the gold standard for quantification of resting energy expenditure and calculation of energy needs [8, 9]. Indirect calorimetry works by measuring the amount of oxygen consumed and carbon dioxide expired in real-time [8]. Energy expenditure is then calculated based on the Weir equation [10] REE (kcal/day) = $1.44\ (3.94\ VO_2 + 1.1\ VCO_2)$, in which REE = resting energy expenditure, VO_2 = volume of oxygen, and VCO_2 = volume of carbon dioxide.

The majority of published previous research compares the prediction equations for resting metabolic rate to traditional indirect calorimeters (i.e., metabolic carts) [11-13]. However, it is not always feasible to have a traditional indirect calorimeter in a clinical setting due to high cost, size of the machine, limited locomotion, and level of operator training required. Portable indirect calorimeters are a less expensive option than traditional indirect calorimeters that still provide valid and reliable results [14, 15]. One particular portable indirect calorimeter, the

KORR ReeVue indirect calorimeter, has become increasingly used in outpatient institutions and community settings [16-18]. The KORR ReeVue indirect calorimeter is an accurate, portable, simple system to assess REE. The KORR ReeVue indirect calorimeter was compared to the Cosmed Quark CPET metabolic cart [14]. No difference between the two devices was found for the measured resting metabolic rate (P=0.22). The researchers found a test-retest intraclass correlation coefficient of 0.91 (95% confidence interval, 0.76-0.97) indicating reliability for the KORR ReeVue system. Bland-Altman tests found a mean bias of -32.1 kcal/day with limits of agreement -222 and 161 kcal/day [14]. Another study compared the KORR ReeVue indirect calorimeter and CardioCoachCO_2 to the MedicalGraphics CardiO_2/CP and found no differences between the KORR ReeVue (202±45 mLO_2/min), the CardioCoachCO_2 (209±51 mLO_2/min), and the MedicalGraphics CardiO_2/CP (226±57 mLO_2/min) in a sample of thirty subjects [19].

Many facilities do not have access to a device that measures REE and must determine if a device is worth the investment or instead rely on prediction equations. The KORR ReeVue indirect calorimeter requires a private space within a facility designated to conducting the test, operator training to use the machine, a one-time cost of $5000 to purchase the machine, and recurring costs of $335 plus shipping every two years for maintenance and $7.25 for each KORR factory authorized MetaBreather™ (which includes a nose clip, 5-foot expandable hose, and filter) to be used for each individual REE test [20]. It was important to assess the agreement between the estimated REE for each validated prediction equation and the MREE for this particular indirect calorimeter to provide guidance to clinicians regarding utility of the machine and ensure accurate recommendations are given to patients that enable restoration of energy balance.

The purpose of this study was to compare the seven most common prediction equations for estimating REE – Mifflin St. Jeor (MSJ) [21], Harris Benedict (HB) [22], Owen [23, 24], American College of Chest Physicians (ACCP) 21, ACCP 25 [25], World Health Organization/Food and Agriculture Organization/United Nations University (WHO/FAO/UNU; using weight only), and WHO/FAO/UNU (using both weight and height) [26] – to the measured REE (MREE) of the KORR ReeVue indirect calorimeter [27]. In addition to comparing overall agreement, statistical analyses were completed to understand if age, sex, race, or obesity grade influenced the agreement between the estimated REE for the prediction equations and MREE for the KORR ReeVue indirect calorimeter. An increasing number of institutions and community settings are investing in this indirect calorimeter to determine MREE and give recommendations to patients. Published studies are lacking that compare this commonly used indirect calorimeter to validated prediction equations and provide guidance if the purchase of this calorimeter is worthwhile. This study was designed to provide guidance for institutions and community settings who are deciding to invest in the KORR ReeVue indirect calorimeter and if the cost is necessary based on agreement between the MREE of the indirect calorimeter and the estimated REE using the prediction equations.

Research Questions

1. In obese adults (BMI ≥30 kg/m^2 and age ≥18 years), what is the agreement of seven REE predictive equations (MSJ, HB, Owen, ACCP 21, ACCP 25, WHO/FAO/UNU (using weight only), and WHO/FAO/UNU (using both weight and height) compared to the MREE of the KORR ReeVue indirect calorimeter?

2. Does age, sex, race, or obesity grade influence the agreement between the estimated REE from the prediction equations and the MREE from the KORR ReeVue indirect calorimeter?

Chapter 2: Review of Literature

I. The problem of obesity

Obesity is a prevalent problem in today's society, with over one-third (36.5%) of the population of the United States obese [1]. Many preventable health issues stem from obesity, including heart disease [2], diabetes [3, 4], non-alcoholic fatty liver disease [5], and certain types of cancer [6]. The 2013 AHA/ACC/TOS Guideline for the Management of Overweight and Obesity in Adults reported a sustained weight loss of 3-5% of body weight is enough to produce clinically meaningful health benefits, including reduction of triglycerides, blood glucose, hemoglobin A1C, and the risk of developing type 2 diabetes [28].

II. Total energy expenditure

In order to induce weight loss, a precise measure of energy expenditure is required. Total energy expenditure is comprised of three main components: basal metabolic rate, physical activity, and the thermic effect of food [29]. Basal metabolic rate is the largest contributor to total energy expenditure and is a measurement of how many calories or energy the body requires to maintain and preserve basic vital functions such as heartbeat, breathing, and body temperature maintenance. Basal metabolic rate involves strict measurement requirements with a metabolic chamber and is therefore difficult to measure in free-living individuals. Instead, resting energy expenditure (REE) is typically measured when an individual is at rest in a comfortable position. REE is typically up to 10% higher than basal metabolic rate [30].

III. Measurement of energy expenditure

A. Doubly labeled water

There are several methods used to measure energy expenditure including doubly labeled water, direct calorimetry (metabolic chamber), or indirect calorimetry. Doubly labeled water is a valid measurement of energy expenditure in free-living animals and humans [31]. It involves free-living subjects drinking a known amount of water containing two different stable isotopic forms of water: $H_2{}^{18}O$ and $^{2}H_2O$ [30]. The two isotopic forms of water mix with the body's water and are gradually eliminated from the body. Body water samples including blood, saliva, or urine are collected periodically to determine the rate at which the two isotopes are eliminated from the body. The hydrogen isotope (^{2}H) is lost as water only, while the oxygen isotope (^{18}O) is lost as both water and carbon dioxide [29, 31]. The rate of disappearance for the oxygen isotope is faster than for the hydrogen isotope and the difference between the two represents carbon dioxide production. The rate of carbon dioxide production can then be used to calculate energy expenditure [32].

B. *Direct calorimetry*

Direct calorimetry is another method used to measure energy expenditure. It involves a metabolic chamber that measures the amount of heat given off an individual's body through evaporation, convection, and radiation [30]. The three main types of direct calorimeters include isothermal, heat sink and convection systems [33]. Isothermal systems consist of a chamber lined with a layer of insulating material and is maintained at a constant temperature using circulating fluid. Heat sink systems (which include a suit calorimeter) consist of a chamber or suit in which water is circulated through tubes in the insulating garment and the heat lost by the subject is extracted by a liquid-cooled heat exchanger. Lastly, convection systems consist of an insulated chamber ventilated with an air flow at a known rate. Heat lost by the subject is calculated from the difference in temperature of ventilated air leaving the chamber. Overall, direct calorimeters are typically large in size, very expensive and require a high degree of operator expertise [30, 33].

C. Indirect calorimetry

Indirect calorimetry is the most common method of measuring REE [30]. Indirect calorimetry works by measuring the amount of oxygen consumed and carbon dioxide expired and provides an accurate and practical measure for calories burned in an individual at rest [29]. Energy expenditure is then calculated from the gaseous exchange based on the Weir equation [10] REE (kcal/day) = 1440 (3.941 VO_2 + 1.11 VCO_2), in which REE = resting energy expenditure, VO_2 = volume of oxygen, and VCO_2 = volume of carbon dioxide.

The use of indirect calorimeters is advantageous in an outpatient or community setting because it allows health professionals to recommend an individualized daily caloric intake for each patient to promote safe and effective weight loss. The portable indirect calorimeters are smaller in size, more affordable than a traditional indirect calorimeter, and typically easier to operate [8]. Patients are also able to learn the status of their metabolic rate (slow, normal, fast). It can be useful for a patient to learn their current obese state was not due to an altered metabolism and therefore empower the patient to make healthy behavioral changes and improve treatment outcomes.

Various types of indirect calorimeters exist including Douglas bag, metabolic cart, or portable indirect calorimeters [9]. The Douglas bag is a flexible total collection system comprised of a leak-proof bag. A three-way valve connected to the top of the bag can be rotated to allow atmospheric air or expired air into the bag. A subject breathes through the mouthpiece and expired air is collected. Following the timed collection period of 10-20 minutes, the valve is rotated to seal the bag and the volume of expired air in the bag is measured [9].

Metabolic carts, such as the Deltatrac or Cosmed Quark, are another type of indirect calorimeter that has been demonstrated to be a reliable method of measuring REE [34]. When using a metabolic cart, a subject breathes into a canopy-like mask or mouthpiece connected to the metabolic cart. The inspired and expired air are continuously collected and analyzed in the mixing chamber [9]. The Deltatrac and Cosmed Quark metabolic carts are open-circuit calorimeters with a canopy hood and are used for both mechanically ventilated and spontaneously breathing patients. Longitudinal analysis showed no difference between the results obtained with Deltatrac and Cosmed Quark REE. [35]

Portable (or sometimes referred to as handheld) indirect calorimeters, such as MedGem or KORR ReeVue, are the last type of indirect calorimeters used to measure REE. Bland–Altman analysis comparing the Deltatrac metabolic cart to the MedGem indirect calorimeter derived a mean bias of +162.3 kcal/day, with limits of agreement +577 to -253 kcal/day, in a study of twenty-four nutrition support patients [36]. Another study of thirty-six obese inpatients compared the MedGem indirect calorimeter and metabolic cart to various prediction equations [37]. The subjects were predominately female and Caucasian with ages ranging from 20 to 80 years old. The intra-class reliability for the MedGem indirect calorimeter ranges between r = 0.97–0.98 and the inter-class reliability for the device ranges between r = 0.91–0.97 [38].

The KORR ReeVue indirect calorimeter is another example of a portable indirect calorimeter and was the system used in the present study to determine measured REE. The KORR ReeVue system uses a mixing chamber, in which the concentration of oxygen expired by each patient is collected and analyzed [27]. A one-way valve is built into the MetaBreather™ mouthpiece which allows room air to enter during inspiration and closes during expiration to ensure all expired air is passed through the KORR ReeVue system. It self-calibrates between each test and adjusts to standard conditions for barometric pressure, temperature, and humidity.

The system uses the equation 4.813 kcal for every milliliter of oxygen consumed to calculate calories burned.

The KORR ReeVue system has been found to be an accurate and reliable method for measuring REE [14, 27, 39-41]. One study compared the KORR ReeVue indirect calorimeter and CardioCoachCO_2 to the MedicalGraphics CardiO_2/CP and found no differences between the KORR ReeVue (202±45 mLO_2/min), the CardioCoachCO_2 (209±51 mLO_2/min), and the MedicalGraphics CardiO_2/CP (226±57 mLO_2/min) in a sample of thirty subjects [19]. A pilot study (n=19) indicated the system is a valid and precise machine for calculating resting metabolic rate, as there was no difference between REE when comparing the KORR ReeVue portable indirect calorimeter with the traditional indirect calorimeter (p=0.22) [14]. The test retest correlation coefficient was 0.91 (95% confidence interval, 0.76-0.79). However, this study was conducted in an overweight and obese adolescent population, not adults.

Another study compared five indirect calorimetry systems including the KORR ReeVue system to the Deltatrac Metabolic Monitor (VIASYS Healthcare Inc., SensorMedics, Yorba Linda, CA), and found none of the systems were truly reliable in a clinical setting [40]. A paired t test indicated no difference in REE between the KORR ReeVue indirect calorimeter and the Deltatrac (p=0.89). The KORR ReeVue indirect calorimeter had one of the smallest within-subject coefficient of variation of the five systems at 11.9% (p<0.01) in a sample of seventeen subjects. Limitations of this study included site-to-site variations in study protocol, subject characteristics, as well as limited sample size with each calorimeter leading to low statistical power.

The KORR ReeVue indirect calorimeter is becoming increasingly used by various institutions and community settings [16-18]. Although portable indirect calorimeters are smaller in size, less expensive, and easier to operate than a traditional indirect calorimeter, facilities must still determine if they have the resources available to sustain the machine. The KORR ReeVue indirect calorimeter requires a private space within a facility designated to conducting the test, operator training to use the machine, a one-time cost of $5000 to purchase the machine, a recurring cost of $335 plus shipping every two years for maintenance, and a recurring cost of $7.25 for each KORR factory authorized MetaBreather™ (which includes a nose clip, 5-foot expandable hose, and filter) to be used for each individual REE test [20]. This study was designed to provide guidance for institutions and community settings who are deciding to invest in the KORR ReeVue indirect calorimeter and if the cost is necessary based on agreement between the measured REE of the indirect calorimeter and the estimated REE using the prediction equations.

IV. Physiological variables that impact REE measurement

Several variables affect REE including lean body mass, fat mass, sex, body temperature, age, race, genetics, and various medical conditions/disease states [30, 42-46]. Lean body mass contributes the largest amount to resting energy expenditure, as 60-85% of inter-individual differences in REE can be explained by lean body mass [42-44]. Fat mass and age also contribute to variability in REE in both males and females. Males tend to have a greater percentage of lean body mass than females and therefore have a higher energy expenditure [45]. Individuals with a fever or elevated body temperature have an increased energy expenditure [44]. Age is also a factor, as resting energy expenditure decreases 2% for every decade after 30 years [44, 46]. Some individuals can inherit a lower or higher energy expenditure due to genetic predisposition [30]. The majority of research regarding energy expenditure uses a primarily Caucasian, female population [12, 43, 47, 48] or race/ethnicity is not specified, creating difficulty to generalize to other populations. One study did find the predictive equations of Owen and Mifflin St. Jeor underestimated REE in non-Hispanic individuals, but found no differences in prediction equation accuracy in non-Hispanic Black, Hispanic, Asian, and Others participants [38]. Last, medical conditions can impact REE. Endocrine disorders such as hypothyroidism can lead to decreased energy expenditure and hyperthyroidism can lead to increased energy expenditure [9, 44].

When stratified for sex and BMI level, accuracy of predictive equations for estimated REE was found to be very low, particularly among Caucasian females and a BMI greater than 40 kg/m^2 [43]. Majority of studies exploring the accuracy and over/underestimation of predictive equations fail to take different ages into consideration, and instead combine all individuals above the age of eighteen and then stratify by variables such as sex and BMI level [12, 43, 49-51]. Lean body mass typically declines with age and chronic illness also tends to become more prevalent [45, 48], so accuracy of predictive energy expenditure equations may also vary.

Due to the number of factors that impact metabolic rate, REE is typically performed in an inpatient setting where a strict protocol is followed. However, REE measurements can also be sufficiently reproduced when subjects are given careful instructions and follow them accordingly in an outpatient setting [29]. The measurement protocol includes restrictions on the testing environment, energy intake, physical activity, use of stimulants, nicotine, alcohol, and various medications/supplements [9]. The requirements provided by KORR Medical Technologies, Inc., regarding use of its portable indirect calorimeter align with scientific reviews of indirect calorimetry protocol for clinicians. Measurements should be taken in a quiet environment with the individual in a relaxed position [27, 52], the individual should abstain from eating any meals or snacks for at least 4-5 hours prior to the test [9, 27, 52], the individual should avoid exercise at least 4 hours [9] (or 2 hours for moderate activity and 14 hours for vigorous activity [52]) or on the day of testing [27], caffeine should be avoided at least 4 hours prior to testing [9, 27, 52, 53], and nicotine should be avoided at least 1-2 hours prior to testing [9, 52, 54]. Other factors have also been found to impact metabolic rate including the use of stimulants, sedatives, and neuromuscular blocking agents [9], hypothyroidism [9], HIV/AIDS [9, 55], sleep apnea [56], cancer [57, 58], those undergoing hemodialysis [9] or those who previously had bariatric surgery [59]. Therefore, these individuals were excluded from the present study.

V. Equations to predict REE

Multiple prediction equations exist to estimate REE in adults and can be used when special equipment such as an indirect calorimeter is not available. The Academy of Nutrition and Dietetics position on determining energy needs in adult weight management states "Estimated energy needs should be based on RMR. If possible, RMR should be measured (eg, indirect calorimetry). If RMR cannot be measured, then the Mifflin-St. Jeor equation using actual weight is the most accurate for estimating RMR for overweight and obese individuals." [44]. In addition to the Mifflin-St. Jeor, there are other commonly used prediction equations.

Seven common prediction equations for estimating REE include Mifflin St. Jeor (MSJ) [21], Harris Benedict (HB) [22], Owen [23, 24], American College of Chest Physicians (ACCP) 21, ACCP 25 [25], World Health Organization/Food and Agriculture Organization/United Nations University (WHO/FAO/UNU; using weight only), and WHO/FAO/UNU (using both weight and height) [26]. These prediction equations are based on anthropometric variables including height, weight, sex, and age. One study indicates the accuracy of predictive equations does not improve when body composition data, such as fat mass or lean body mass, is also used [12]. See Appendix B: Table 1 for comparisons of the equations and predictor variables.

A. Mifflin St. Jeor (MSJ) equation

The Mifflin St. Jeor equation was developed in 1990 from a sample of all BMI levels (normal weight, overweight, obese, and morbidly obese) with individuals ranging in age from 19 to 78 years old. It yielded an accurate measure of energy expenditure in overweight and obese adults [13, 45, 48, 60].

Garrel and colleagues found the MSJ equation predicted values within 10% of MREE in 62±102% of men and 39±137% of women [61]. Frankenfield and colleagues found MSJ as the most accurate prediction equation for a sample of 130 non-hospitalized individuals [13]. The predicted values fell within ±10% of MREE in 82% of non-obese (BMI<30 kg/m^2) subjects (n=83) and 70% of obese (BMI≥30 kg/m^2) subjects (n=47). Ten percent of non-obese subjects had a predicted REE above the range of agreement (±10% of MREE) and 8% had a predicted REE below the range of agreement. Nine percent of obese subjects had a predicted REE above the range of agreement and 21% had a predicted REE below the range of agreement. In another study [38], Bland Altman plots displaying bias and agreement of each prediction equation indicated 56.4% of the participants' predicted REE values were within ±10% of the MREE for the MSJ equation (29.0% were under-predicted and 14.6% were over-predicted).

Another study of thirty-six obese inpatients compared the metabolic cart MREE to the MSJ prediction equation [37]. The subjects were predominately female and Caucasian with ages ranging from 20 to 80 years old. The MSJ equation had a coefficient of 0.41 (p=.0135) and predicted REE within ±10% of MREE in 14.8% of ventilator-dependent patients and 33.3% of spontaneously breathing patients. See Appendix B: Table 2 for studies validating the Mifflin-St. Jeor prediction equation.

B. Harris Benedict (HB) equation

The Harris Benedict equation was developed in normal-weight individuals aged 16 to 74 years old in 1918, making it the oldest prediction equation still in clinical use [22]. Adjusted body weight is sometimes preferred in the HB equation, as it reduces the amount of overestimation of resting energy expenditure in obese adults [13]. Most predictive equations use actual body weight in their calculations, but the use of adjusted body weight may be warranted for obese individuals to minimize the effect of the large amount of adipose tissue that is metabolically-inactive compared to lean body mass [62]. However, adjusted body weight has several limitations, as prediction equations were developed using actual body weight and there is finite data supporting the substitution of adjusted body weight for actual body weight to improve the accuracy of REE equations [63, 64]. Due to poor scientific evidence, adjusted body weight was not used in this study.

Garrel and colleagues [61] found the HB equation predicted values within ±10% of MREE in 73±116% of men and 31±91% of women. The mean overestimation of the MREE was 11.7% in 67 subjects for the HB equation. Frankenfield and colleagues [13] found the predicted values using the HB equation with adjusted body weight fell within ±10% of MREE in 26% of obese (BMI≥30 kg/m^2) subjects (n=47). Two percent of subjects had a predicted REE above the range of agreement (±10% of MREE) and 72% had a predicted REE below the range of agreement. In morbidly obese subjects with a BMI≥40, predicted REE using the HB equation with adjusted body weight underestimated MREE in 100% of subjects (n=27). In another study [38], Bland Altman plots displaying bias and agreement of each prediction equation indicated 57.6% of the participants' predicted values were within ±10% of the MREE for the HB equation (18.0% were under-predicted and 24.5% were over-predicted).

Another study of thirty-six obese inpatients compared the metabolic cart MREE to the HB prediction equation [37]. The subjects were predominately female and Caucasian with ages ranging from 20 to 80 years old. This study indicated the HB equation using adjusted body weight with a stress factor and the HB using average body weight with a stress factor had the highest correlation between predicted REE and MREE with coefficients of 0.59 (p=0.0002) and 0.57 (p=0.0003), respectively. See Appendix B: Table 3 for studies validating the Harris Benedict prediction equation.

C. Owen equation

Actual body weight is used in the Owen equation [23, 24]. The men's equation was developed in 1986 based on a sample of n=60 with ages ranging from 18 to 82 years old and included all BMI levels. The women's equation was developed in 1987 based on 44 subjects aged 18 to 65 years old and also included all BMI levels.

Garrel and colleagues [61] found the Owen equation predicted values within ±10% of MREE in 95±69% of men and 82±9% in women, and had a mean overestimation of the MREE in 7.4% of subjects. Frankenfield and colleagues [13] found the predicted values using the Owen equation fell within ±10% of MREE in 73% of non-obese (BMI<30 kg/m^2) subjects (n=83) and 51% of obese (BMI≥30 kg/m^2) subjects (n=47). Six percent of non-obese subjects had a predicted REE above the range of agreement (±10% of MREE) and 21% had a predicted REE below the range of agreement. Six percent of obese subjects had a predicted REE above the range of agreement and 43% had a predicted REE below the range of agreement. In another study [38], Bland Altman plots displaying bias and agreement of each prediction equation indicated 8% of the participants' predicted REE values were within ±10% of the MREE for the

Owen equation (39.2% were under-predicted and 51.9% were over-predicted). See Appendix B: Table 4 for studies validating the Owen prediction equation.

D. American College of Chest Physicians (ACCP) equations

The ACCP equation was developed in 1997 for critically ill patients [30]. Actual body weight is used if body mass index (BMI) is 16-25 kg/m^2 and ideal body weight is used if BMI is >25 kg/m^2 in the American College of Chest Physicians equations [25, 30, 37]. However, ideal body weight has several limitations, as these weights vary by population and there is no single weight that applies universally to all demographic factors or comorbidities [65, 66]. Due to poor scientific evidence, ideal body weight was not used in this study.

One study of thirty-six obese inpatients compared the metabolic cart MREE to the ACCP prediction equations of 21 kcal per kg of actual body weight and 25 kcal per kg of adjusted body weight [37]. The subjects were predominately female and Caucasian with ages ranging from 20 to 80 years old. The ACCP equation of 21 kcal per kg of actual body weight was found to predict REE within ±10% of MREE in 48.2% of ventilator-dependent patients and 22.2% of spontaneously breathing patients. The ACCP equation of 25 kcal per kg of adjusted body weight was found to predict REE within ±10% of MREE in 37.0% of ventilator-dependent patients and 44.4% of spontaneously breathing patients [37]. Another researcher found the ACCP equation of 25 kcal per kg of actual body weight estimated REE within 80-110% of MREE in 64.6% of subjects (n=27) and the ACCP equation of 25 kcal per kg of adjusted body weight estimated REE within 80-110% of MREE in 63.5% of subjects [67]. Predicted REE was less than 80% of MREE in 22.9% of subjects using actual body weight and 27.1% of subjects using adjusted body weight. Predicted REE was greater than 110% of MREE in 12.5% of subjects using actual body weight and 9.4% of subjects using adjusted body weight. See Appendix B: Table 5 for studies validating the ACCP prediction equation.

E. The World Health Organization/Food and Agriculture Organization/United Nations University (WHO/FAO/UNU) equation

The WHO/FAO/UNU equation was developed in 1985 from a sample of majority men of Italian descent with ages ranging from 19 to 82 years old [21]. Actual body weight is used in the World Health Organization/Food and Agriculture Organization/United Nations University (WHO/FAO/UNU) equation.

The WHO/FAO/UNU equation predicted values within ±10% of MREE in 100±77% of men and 100±46% of women [61]. Bland Altman plots displaying bias and agreement of each prediction equation indicated 55.5% of participants' predicted REE values were within ±10% of the MREE for the WHO/FAO/UNU equation (17.4% were under-predicted and 27.1% were over-predicted) [38]. Another study found the WHO/FAO/UNU prediction equation was accurate (within ±10% of MREE) in 65.6% of males (n=64) and 61.8% of females (n=55) over the age of 70 years. Predicted REE was less than 10% of MREE in 9.4% of males and 5.5% of females. Predicted REE was greater than 10% of MREE in 25.0% of males and 32.7% of females [68]. See Appendix B: Table 6 for studies validating the WHO/FAO/UNU prediction equation.

VI. Conclusion

In conclusion, the purpose of this study was to compare the seven most common prediction equations for estimating REE – Mifflin St. Jeor (MSJ) [21], Harris Benedict (HB) [22], Owen [23, 24], American College of Chest Physicians (ACCP) 21, ACCP 25 [25], World Health Organization/Food and Agriculture Organization/United Nations University

(WHO/FAO/UNU; using weight only), and WHO/FAO/UNU (using both weight and height) [26] – to the MREE of the KORR ReeVue indirect calorimeter [27]. In addition to comparing overall agreement, statistical analyses were completed to understand if age, sex, race, or obesity grade influenced the agreement between the estimated REE for the prediction equations and MREE for the KORR ReeVue indirect calorimeter. An increasing number of institutions and community settings are investing in this indirect calorimeter to determine MREE and give recommendations to patients [16-18]. Although portable indirect calorimeters are smaller in size, less expensive, and easier to operate than a traditional indirect calorimeter, facilities must still determine if they have the resources and funds available to sustain the machine. This study was designed to provide guidance for institutions and community settings who are deciding to invest in the KORR ReeVue indirect calorimeter and if the cost is necessary based on agreement between the MREE of the indirect calorimeter and the estimated REE using the prediction equations. Published studies are lacking that compare this commonly used indirect calorimeter to validated prediction equations and provide guidance if the purchase of this calorimeter is worthwhile.

<u>Chapter 3: Methods</u>

I. Overview

The purpose of this study was to compare the seven most common prediction equations for estimating REE – MSJ, HB, Owen, ACCP 21, ACCP 25, WHO/FAO/UNU (using weight only), and WHO/FAO/UNU (using both weight and height) – to the MREE of the KORR ReeVue indirect calorimeter. In addition to comparing overall agreement, statistical analyses were completed to understand if age, sex, race, or obesity grade influenced the agreement between the estimated REE for the prediction equations and MREE for the KORR ReeVue indirect calorimeter.

Study data were retrospectively collected from existing medical records via Vanderbilt University Medical Center's StarPanel and entered into a password-protected Excel spreadsheet on an encrypted USB drive. De-identified information was exported from Excel into R (Version 3.3.0) for data analysis. Data analyses were conducted by the principal investigator and Vanderbilt Department of Biostatistics.

II. Sample

More than 4000 free-living obese (defined as BMI $\geq$ 30 kg/m^2) adults (age 18 years and older) established care at the Center for Medical Weight Loss (MWL) outpatient clinic at Vanderbilt University Medical Center from the establishment of the clinic in 2012 to present date. The Vanderbilt Center for Medical Weight Loss is a comprehensive weight loss program comprised of doctors, nurse practitioners, registered dietitians, exercise physiologists, and psychologists dedicated to providing support and medically-proven care to assist individuals with weight loss. When establishing care at a Vanderbilt University Medical Center outpatient clinic, all patients were presented with the following statement to sign: "I agree to donate my left over blood or tissue samples and share my de-identified health information with BioVU and approved researchers. I understand that I will not receive compensation or test results." Since this retrospective study collected existing health information, a separate consent form was not necessary. Upon entry into the MWL clinic for treatment, all patients underwent a REE test using the KORR ReeVue indirect calorimeter. Starting with a sample of 4323 subjects, data were collected on all subjects remaining following exclusion criteria. Subjects were excluded if any of the following applied: BMI <30 kg/m^2, age <18 years, pregnant, lack of health insurance, current treatment of chemotherapy/radiation, consumption of caffeine, tobacco, stimulant medications, inhalers, herbal supplements or nasal sprays <12 hours of REE test, consumption of food or beverages (besides water) <12 hours of REE test, exercise on the day of REE test, presence of hypothyroidism, hyperthyroidism, cancer, HIV/AIDS, or sleep apnea, currently undergoing hemodialysis, previously undergone bariatric surgery, or REE test duration >10.1 minutes.

III. Setting

Data collection occurred from the date of IRB approval on September 5, 2017 to October 30, 2017. The principal investigator (student) completed all data collection. Information was collected from Vanderbilt University Medical Center's EMR system StarPanel and entered into a password-protected Excel spreadsheet on an Integral® Crypto Drive FIPS 197 Encrypted USB drive. De-identified data were then shared with Vanderbilt's Department of Biostatistics for data analysis.

IV. Ethics

Vanderbilt University Medical Center's Human Subjects Committee reviewed the research proposal. This research qualified for exempt status due to negligible risks to subjects. All existing data collected from StarPanel and entered into the password-protected Excel spreadsheet on the Integral® Crypto Drive FIPS 197 Encrypted USB drive were de-identified to protect patients' information. Thesis committee members from both Vanderbilt and University of Kansas Medical Center only had access to de-identified information.

V. Procedures

This study was a cross-sectional study using retrospective data collected by the Center for Medical Weight Loss at Vanderbilt University Medical Center. Existing patient charts from 1/01/2013 to 12/31/2016 were reviewed. Exclusion criteria to establish care at the MWL clinic included BMI < 30 kg/m^2, pregnancy, age <18 years, lack of health insurance, and current treatment of chemotherapy/radiation. All new patients who established care were routinely required to complete a REE test using the KORR ReeVue indirect calorimeter at the time of their initial assessment. All patients had fasted 12 hours prior to the REE test. Other controlled factors which excluded patients from completing the test included consumption of caffeine, stimulant medications, inhalers, herbal supplements, nasal sprays, or any other substances that may increase metabolic rate within 12 hours prior to the REE test. Patients were instructed to lie down in a semi recumbent position on the exam table in a quiet, private room with an average temperature of 68 degrees Fahrenheit [27]. A nose clip was affixed to the patient's nose to block airflow through the nostrils and they were instructed to breathe normally through the 5-foot mouth hose for ten minutes. Two medical assistants trained in using the KORR ReeVue indirect calorimeter completed the tests to reduce operator error. Instructions given by the company who manufactures the indirect calorimeter, KORR Medical Technologies, Inc., were followed to reduce measurement error and ensure accuracy of the REE test results. These instructions included avoidance of eating 4 hours prior to the test, avoidance of exercise on the day of the test, avoidance of the use of stimulants prior to testing, advice for participants to get into a comfortable position and relax prior to testing, and instruction to keep lips sealed tightly around the mouthpiece [27]. Measured resting energy expenditure was collected from each REE test. A print-out of this measurement occurred immediately following the completion of the REE test. Photocopies of the REE results were scanned into each patient's chart.

Calibration and routine maintenance was performed prior to each testing cycle to adjust for barometric pressure, temperature and humidity in the testing environment. Results indicating poor test quality, such as air leaks in the mixing chamber or around the mouthpiece were excluded. The minimum duration of each REE test was ten minutes, however, the KORR ReeVue indirect calorimeter may have continued the test until a steady state was reached with a maximum test duration of thirty minutes [20]. If the REE test continued past the ten-minute mark, the medical assistants manually ended the tests prematurely between minutes ten and eleven. Due to the manual conclusion of the test after its minimum duration yet prior to reaching a steady state, results with a test duration greater than 10.1 minutes were excluded from the study.

Following IRB approval, the following information was retrospectively gathered by the principal investigator (student) from each patient's chart from the date they completed the REE test: age, sex, height, body weight, BMI, race/ethnicity, tobacco status, MREE, medical diagnosis of hypothyroidism, hyperthyroidism, cancer, HIV/AIDS, sleep apnea, currently undergoing hemodialysis, and history of bariatric surgery. BMI 30-34.9 kg/m^2 was defined as Class I obesity, BMI 35-39.9 kg/m^2 was defined as Class II obesity, and BMI ≥40 kg/m^2 was defined as Class III obesity. The researcher used the "dump data" option in StarPanel from the panel of 4323 patients into a password-protected Excel spreadsheet. This password-protected Excel spreadsheet was stored on the Integral® Crypto Drive FIPS 197 Encrypted USB drive.

Within this data dump, race/ethnicity, sex, tobacco status, and medical diagnoses were collected. Next, the researcher individually entered each patient's medical record and collected the following information from the scanned REE test results page: age, height, weight, BMI, and MREE.

Using each patient's height, weight, sex, and age, REE was calculated using the MSJ, HB, Owen, ACCP 21, ACCP 25, WHO/FAO/UNU (using weight only), and WHO/FAO/UNU (using both weight and height) prediction equations. The prediction equations are listed in Appendix B: Table 1.

VI. Materials

The KORR ReeVue indirect calorimeter was used to measure REE (Appendix A). The KORR ReeVue system used a mixing chamber, in which the concentration of oxygen expired by each patient was collected and analyzed [27]. A one-way valve was built into the MetaBreather™ mouthpiece which allows room air to enter during inspiration and closes during expiration to ensure all expired air was passed through the KORR ReeVue system. It self-calibrated between each test and adjusted to standard conditions for barometric pressure, temperature, and humidity. The system uses the equation 4.813 kcal for every milliliter of oxygen consumed to calculate calories burned.

VII. Analysis of Data

The relevant information was extracted from the EMR and entered into the password-protected Excel spreadsheet on an encrypted USB drive. Patient identifiers were immediately removed by the principal investigator (student) upon completion of data collection. The data files did not contain any individually identifying information and adhered to the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule.

Statistical analyses were performed using R (Version 3.3.0; Appendix A) by the Department of Biostatistics at Vanderbilt University. Means and standard deviations were calculated for continuous variables, and percentages were calculated for categorical variables. Spearman correlation coefficients were calculated for raw data. Bland-Altman plots were used to estimate agreement between each prediction equation and MREE. The confidence limit for clinical agreement was pre-specified at ±150 kcal/day. Linear regression was used to assess the relationship between the MREE from the KORR ReeVue indirect calorimeter and then estimated REE from each of the prediction equations, using MREE as the outcome variable and each prediction equation as the independent variable. The prediction errors were then evaluated against age, sex, race, and obesity grade. Wald Chi-Squared tests were used to determine the significance of explanatory variables (age, sex, race, and obesity grade) and if they influenced the agreement between the estimated REE and MREE. Partial R-squared (R^2) was used to determine the percentage of variance explained by each significant explanatory variable to the overall model R^2. MREE served as the benchmark for comparison of all prediction equations. Statistical significance was set at $p \leq 0.05$.

Chapter 4: Results

The purpose of this study was to compare several prediction equations for estimating REE to the MREE of the KORR ReeVue indirect calorimeter. In addition to comparing overall agreement, statistical analyses were completed to understand if age, sex, race, or obesity grade influenced the agreement between the estimated REE for the prediction equations and MREE for the KORR ReeVue indirect calorimeter. This study was designed to provide guidance for institutions and community settings who are deciding to invest in the KORR ReeVue indirect calorimeter and if the cost is necessary based on agreement between the MREE of the KORR ReeVue indirect calorimeter and the estimated REE using the prediction equations.

Sample

The total number of patient charts reviewed was n=4323 (see Appendix C: Figure 1). Patients with no REE tests were excluded (n=901). We also excluded patients with a presence of hypothyroidism, hyperthyroidism, cancer, HIV/AIDS, sleep apnea, undergoing hemodialysis, or had previously undergone bariatric surgery (n=2001). If patients' REE test had a duration of ≥10.1 minutes, they were also excluded from the study (n=605). Therefore, the final analysis data set included 816 unique subjects.

Descriptive characteristics of the sample are listed in Appendix C: Table 7. The sample was comprised of 83% female (n=681) and 17% male (n=135) subjects. The average age was 43.2 years and 46.1 years for females and males, respectively. The average weight was 110.2 kg for females and 133.3 kg for males, while the average height was 163.9 cm for females and 178.3 cm for males. This yields an average BMI of 41.0 kg/m^2 for females and 41.9 kg/m^2 for males. The sample was 64% white (including n=420 females and n=101 males), 29% black (including n=215 females and n=24 males), and 7% other. Regarding ethnicity, only 4% of subjects (including n=25 females and n=5 males) were Hispanic/Latino, with the remaining 96% not Hispanic/Latino (including n=656 females and n=130 males). These demographics are representative of the patient population of Vanderbilt's Center for Medical Weight Loss.

Mean REE

Mean REE are listed in Appendix C: Table 8. The mean for the MREE using the KORR ReeVue indirect calorimeter was 1845 (±354) for females [95% confidence interval (CI); 1137, 2553] and 2385 (±488) kcal/day for males [95% CI; 1409, 3361]. On average, the estimated REE for females using each prediction equation was MSJ: 1752 (±273) kcal/day [95% CI; 1206, 2298], HB: 1808 (±250) kcal/day [95% CI; 1308, 2308], Owen: 1586 (±174) kcal/day [95% CI; 1238, 1934], ACCP 21: 2314 (±509) kcal/day [95% CI; 1296, 3332], ACCP 25: 2755 (±606) kcal/day [95% CI; 1543, 3967], WHO/FAO/UNU (using weight only): 1843 (±295) kcal/day [95% CI; 1253, 2433], and WHO/FAO/UNU (using both weight and height): 1826 (±275) kcal/day [95% CI; 1276, 2101]. On average, the estimated REE for males using each prediction equation was MSJ: 2224 (±360) kcal/day [95% CI; 1504, 2944], HB: 2480 (±482) kcal/day [95% CI; 1516, 3444], Owen: 2239 (±316) kcal/day [95% CI; 1607, 2871], ACCP 21: 2800 (±651) kcal/day [95% CI; 1498, 4102], ACCP 25: 3333 (±775) kcal/day [95% CI; 1783, 4883], WHO/FAO/UNU (using weight only): 2442 (±446) kcal/day [95% CI; 1550, 3334] and WHO/FAO/UNU (using both weight and height): 2423 (±463) kcal/day [95% CI; 1497, 3349].

Bland-Altman Plots of Mean REE Difference

Bland-Altman plots were performed to estimate agreement between the mean estimated REE from each prediction equation and the mean MREE from the KORR ReeVue indirect calorimeter. The confidence limit for clinical agreement was pre-specified at ±150 kcal/day.

Appendix C: Figure 2 displays the Bland-Altman plots of the difference between mean estimated REE from the prediction equations and mean MREE from the KORR ReeVue indirect calorimeter. The mean estimated REE for four prediction equations, MSJ, HB, WHO/FAO/UNU (using weight only), and WHO/FAO/UNU (using both weight and height), were within agreement of the mean MREE according to the pre-specified confidence limit. The mean REE difference was MSJ: -104 (±271) kcal/day [95% CI; -635.9, 427.7], HB: -15 (±278) kcal/day [95% CI; -560.2, 531.0], WHO/FAO/UNU (using weight only): +8 (±294) kcal/day [95% CI; -568.5, 585.3], and WHO/FAO/UNU (using both weight and height): -9 (±287) kcal/day [95% CI; -570.9, 553.2]. The mean estimated REE for the remaining prediction equations were not in agreement of the mean MREE according to the pre-specified confidence limit. Owen underestimated REE compared to MREE by a mean of -240 (±289) kcal/day [95% CI; -806.0, 326.4]. ACCP 21 overestimated REE compared to MREE by a mean of 461 (±399) kcal/day [95% CI; -360.6, 1241.8]. ACCP 25 overestimated REE compared to MREE by a mean of 917 (±476) kcal/day [95% CI; -15.4, 1848.9].

Relationship between Estimated REE from the Prediction Equations and MREE from the KORR ReeVue Indirect Calorimeter

Linear regression was used to assess the relationship between the mean estimated REE for each prediction equation and the mean MREE of the KORR ReeVue indirect calorimeter (see Appendix C: Figure 3). When using Spearman rho correlation coefficients, values >0.7 indicated a strong correlation, values 0.5-0.7 indicated a good correlation, values 0.3-0.5 indicated a fair/moderate correlation, and values <0.3 indicated a poor correlation [69]. Sixty percent of the variance in the MSJ prediction equation was explained by the MREE, with a strong correlation of Spearman r=0.72 ($p<0.0001$). Sixty percent of the variance in the HB prediction equation was explained by the MREE, with a strong correlation of Spearman r=0.71 (p<0.0001). Fifty-five percent of the variance in the Owen prediction equation was explained by the MREE, with a good correlation of Spearman r=0.68 (p<0.0001). Fifty percent of the variance in the ACCP 21 prediction equation was explained by the MREE, with a good correlation of Spearman r=0.67 (p<0.0001). Fifty percent of the variance in the ACCP 25 prediction equation was explained by the MREE, with a good correlation of Spearman r=0.67 (p<0.0001). Fifty-six percent of the variance in the WHO/FAO/UNU (using weight only) prediction equation was explained by the MREE, with a good correlation of Spearman r=0.69 (p<0.0001). Fifty-seven percent of the variance in the WHO/FAO/UNU (using both weight and height) prediction equation was explained by the MREE, with a good correlation of Spearman r=0.70 (p<0.0001).

Influence of Variables (Age, Sex, Race, and Obesity Grade)

Residual scatter and box plots were performed to confirm the statistical analysis should be completed using linear regression. Wald Chi-Squared tests were used to determine the significance of the explanatory variables of age, sex, race, and obesity grade (see Appendix C: Figures 4-10). Partial R-squared (R^2) was used to determine the percentage of variance explained by each significant explanatory variable to the overall model R^2.

Mifflin St. Jeor

Appendix C: Figure 4 illustrates the Wald Chi-Squared dot plot for MSJ equation. Race (p=<0.0001) and sex (p=0.0424) were important variables and significantly influenced the estimation of MREE when using the MSJ equation. Four percent of the variance was explained by race (R^2=0.0398, p=<0.0001) and 0.3% of the variance was explained by sex (R^2=0.0030, p=0.0424). Age (p=0.1206) and BMI (p=0.7079) did not significantly influence the estimation of MREE.

Harris Benedict

Appendix C: Figure 5 illustrates the Wald Chi-Squared dot plot for HB equation. Race (p=<0.0001) was the only important variable that significantly influenced the estimation of MREE when using the HB equation. Four percent of the variance was explained by race (R^2=0.0412, p=<0.0001). Sex (p=0.1808), age (p=0.1450) and BMI (p=0.4865) did not significantly influence the estimation of MREE.

Owen

Appendix C: Figure 6 illustrates the Wald Chi-Squared dot plot for Owen equation. Race (p=<0.0001), sex (p=<0.0001), and age (p=<0.0001) were all important variables and significantly influenced the estimation of MREE when using the Owen equation. Four percent of the variance was explained by race (R^2=0.0408, p=<0.0001), 2% of the variance was explained by sex (R^2=0.0166, p=<0.0001), and 5% of the variance was explained by age (R^2=0.0478, p=<0.0001). BMI (p=0.1431) did not significantly influence the estimation of MREE.

ACCP 21 and ACCP 25

Appendix C: Figures 7 and 8 illustrate the Wald Chi-Squared dot plots for ACCP 21 and ACCP 25 equations. All explanatory variables – race (p=<0.0001), sex (p=<0.0001), age (p=<0.0001), and BMI (p=0.0006) – were important and significantly influenced the estimation of MREE when using the ACCP 21 and ACCP 25 equations. Four percent of the variance was explained by race (R^2=0.0383, p=<0.0001), 4% of the variance was explained by sex (R^2=0.0383, p=<0.0001), 5% of the variance was explained by age (R^2=0.0460, p=<0.0001), and 1% of the variance was explained by BMI (R^2=0.0108, p=0.0006).

WHO/FAO/UNU (using weight only and both weight and height)

Appendix C: Figures 9 and 10 illustrate the Wald Chi-Squared dot plots for WHO/FAO/UNU equations using weight only and both weight and height. All explanatory variables – race (*p*=<0.0001), sex (*p*=0.0046 and *p*=0.0138), age (*p*=<0.0001), and BMI (*p*=0.0154 and *p*=0.0134) – were important and significantly influenced the estimation of MREE when using the WHO/FAO/UNU equations using weight only and both weight and height, respectively. In the WHO/FAO/UNU (using weight only) prediction equation, 4% of the variance was explained by race (R^2=0.0426, *p*=<0.0001), 0.7% of the variance was explained by sex (R^2=0.0067, *p*=0.0046), 3% of the variance was explained by age (R^2=0.0337, *p*=<0.0001), and 0.7% of the variance was explained by BMI (R^2=0.0067, *p*=0.0154). In the WHO/FAO/UNU (using both weight and height) prediction equation, 4% of the variance was explained by race (R^2=0.0407, *p*=<0.0001), 0.5% of the variance was explained by sex (R^2=0.0048, *p*=0.0138), 2% of the variance was explained by age (R^2=0.0211, *p*=<0.0001), and 0.7% of the variance was explained by BMI (R^2=0.0068, *p*=0.0134).

Chapter 5: Discussion

Sample

The sample of subjects in this study, predominantly female and white/non-Hispanic/Latino ethnicity, was similar to previous research on REE prediction equations. Few studies have investigated the effect of age, sex, race, or obesity grade on the agreement between estimated REE using prediction equations and MREE using the KORR ReeVue indirect calorimeter. Future research with a higher percentage of minority groups would be beneficial to gain further insight regarding the prediction accuracy of each prediction equation compared to MREE in those specific populations.

Mean REE

Obesity results from an energy imbalance, therefore determining accurate energy expenditure for obese adults is imperative in order to develop personalized nutrition recommendations to promote weight loss and reduce obesity-related disease risk. Due to the large variability of the data set, the confidence intervals for each mean REE were very wide and did not indicate any significant differences.

Mean REE Difference

As far as we are aware, this is the first study to use a confidence limit of ±150 kcal/day as the definition for clinical agreement. Previous studies [13, 37, 43, 70] used ±10% of MREE as agreement, but this percentage allows a larger difference between the estimated REE and MREE as REE increases. The researchers pre-specified a particular caloric number instead of a percentage for the confidence limit to provide a stricter definition of clinical agreement at any REE. Based on the results of this study, if clinical institutions or community settings did not have access to an indirect calorimeter, the prediction equations in agreement with MREE – MSJ, HB, WHO/FAO/UNU (using weight only) and WHO/FAO/UNU (using both weight and height) – would provide an accurate calorie recommendation for obese individuals hoping to lose weight and serve as the most appropriate formulas for clinical practice.

Mifflin St. Jeor (MSJ)

The estimated REE using the MSJ equation was in agreement with the MREE in this study, therefore MSJ provides an accurate estimation of energy expenditure. This is consistent with previous research comparing MSJ to MREE in overweight and obese adults [13, 37, 43, 51, 60, 71-74].

Harris Benedict (HB)

The estimated REE using the HB equation was in agreement with the MREE in this study. This is consistent with previous research comparing HB to MREE. The HB prediction equation is the oldest prediction equation still used today in clinical practice. This study confirmed it still provides an accurate estimation of energy expenditure when using actual body weight [13, 37, 43, 51, 60, 70-77].

Owen

The estimated REE using the Owen equation was not in agreement with the MREE in this study, as it underestimated MREE by almost -250 kcal/day for the entire sample [43, 51]. This differs from the literature, as most previous studies found the estimated REE using Owen fell within ±10% of MREE or overestimated MREE [71-74]. Only one study [13] found 43% of its obese subjects had an estimated REE using the Owen prediction equation that fell below the range of agreement.

ACCP 21 and ACCP 25

The estimated REE using both the ACCP 21 and ACCP 25 equations overestimated the MREE in both females and males. This is inconsistent with previous research [37, 67]. However, past research [67] that compared the estimated REE from the ACCP prediction equations used a confidence interval of 80-110% of MREE as clinical agreement, a very wide range that encompassed a large percentage of subjects. This study used a stricter confidence limit of ±150 kcal/day, therefore less subjects fell within agreement.

WHO/FAO/UNU (using weight only and weight and height)

The estimated REE using both WHO/FAO/UNU equations (using weight only and both weight and height) was in agreement with the MREE in this study, therefore WHO/FAO/UNU provides an accurate estimation of energy expenditure. This is consistent with previous research [43, 60, 73-75] comparing WHO/FAO/UNU prediction equations to measured REE, as majority of subjects in past studies fell within ±10% of MREE.

Influence of Variables (Age, Sex, Race, and Obesity Grade)

Wald Chi-Squared tests were used to determine *if* the explanatory variables of age, sex, race, and obesity grade significantly influenced the estimation of MREE when using the prediction equations, and partial R^2 was used to determine *how much* variance was explained by each significant explanatory variable. Overall, the R^2 values for each variable were rather low compared to the overall R^2 for the model, which could be due to the large variability in the data set.

Age

Age influenced the estimation of MREE in the prediction equations of Owen, ACCP 21, ACCP 25, WHO/FAO/UNU (using weight only) and WHO/FAO/UNU (using both weight and height). It did not influence MSJ or HB prediction equations. This outcome was expected, as both MSJ and HB prediction equations use age as a variable in their equation. The prediction equations of Owen, ACCP 21, and ACCP 25 do not use age as a variable in their equation, while WHO/FAO/UNU (using weight only) and WHO/FAO/UNU (using both weight and height) use a broad age range of 18-30 years, 31-60 years, or older than 60 years to specify which equation to use.

Sex

Sex influenced the estimation of MREE in the prediction equations of MSJ, Owen, ACCP 21, ACCP 25, WHO/FAO/UNU (using weight only) and WHO/FAO/UNU (using both weight and height). It did not influence the HB prediction equation. All prediction equations use sex as a variable in their equations, with the exception of ACCP 21 and ACCP 25, so this outcome was not expected. The influence of sex on the estimation of MREE when using prediction equations could be attributed to both genetic and environmental variations in individuals of both sexes [78].

Race

Overall, race was the only explanatory variable to significantly influence the agreement between estimated REE and MREE in all seven prediction equations. This outcome was expected as none of the prediction equations use race as a variable in their equations. In addition, the prediction equations were validated in primarily Caucasian populations. Although this study was comprised of 64% Caucasian individuals, there was some variability in racial/ethnic backgrounds with 29% black, 4% Hispanic/Latino, and 7% other.

Obesity Grade

BMI influenced the estimation of MREE in the prediction equations of ACCP 21, ACCP 25, WHO/FAO/UNU (using weight only) and WHO/FAO/UNU (using both weight and height). It did not influence the MSJ, HB, or Owen prediction equations. BMI is calculated using weight and height, which are both included as variables in the prediction equations of MSJ, HB, and WHO/FAO/UNU (using both weight and height). It is possible obesity grade still influenced the WHO/FAO/UNU (using both weight and height) prediction equation due to variance in fat-free mass, which has a strong influence on REE [79] but was not investigated in this study.

Limitations

There are limitations of this study. One limitation of this study was the variability in the indirect calorimetry measurements. Confounding factors such as consumption of food, alcohol, stimulants, and tobacco were controlled for by excluding patients who had consumed one or more within 12 hours of completing the test. However, physical activity is known to affect metabolic rate and no information was collected on participants' activity level, although subjects were advised to refrain from physical activity on the day of the test. Second, patient records were potentially incomplete when using existing clinical records. If a disease/symptom was absent from a patient's chart, it was assumed the patient did not possess that disease/symptom. Medical conditions such as hypothyroidism, hyperthyroidism, and cancer, as well as medication usage, can impact metabolic rate [9, 57, 58]. Two medical assistants conducted the REE tests to reduce risk of environmental/operator error. The KORR ReeVue indirect calorimeter had a minimum test duration of ten minutes, but may continue the test until a steady state was reached or until a maximum duration of thirty minutes was reached [20]. If the REE test continued past the ten-minute mark, the medical assistants manually ended the tests prematurely between minutes ten and eleven. Due to the manual conclusion of the test after its minimum duration yet prior to reaching a steady state, results with a test duration greater than 10.1 minutes were excluded from the study.

Implications for Future Studies

Future research should further validate the KORR ReeVue indirect calorimeter against a gold standard method of measuring REE. The previous studies validating this particular indirect calorimeter are of poor quality due to small sample size and failure to publish in a peer-reviewed journal [14, 39]. MREE from the KORR ReeVue indirect calorimeter was used as the benchmark for comparison of all prediction equations in this study, but cannot be classified as a gold standard until further validation is completed.

In addition, future research should investigate the accuracy of each prediction equation at various age groups, sex, races, and obesity grades to provide guidance regarding which prediction equation should be used in each of the specific populations. This study determined if age, sex, race, or obesity grade significantly influenced each prediction equation, but did not determine the accuracy of each prediction equation at specific age groups, sex, races, or at various grades of obesity.

Chapter 6: Conclusion

An increasing number of institutions and community settings are investing in the KORR ReeVue indirect calorimeter to determine MREE and provide recommendations to patients. This study investigated if the investment is worth the cost or if prediction equations are just as sufficient by evaluating agreement between the two methods. The study found the prediction equations of MSJ, HB, WHO/FAO/UNU (using weight only), and WHO/FAO/UNU (using both weight and height) accurately estimated REE in obese adults within ±150 kcal/day of MREE. Of these four equations, HB had the least amount of contributing variables that influenced the estimation of MREE (only race contributed) and MSJ had the second least amount (race and sex contributed). This could be because both HB and MSJ use age, sex, height, and weight as variables within the equation, but not race. In conclusion, the use of these prediction equations yielded similar data as the MREE from the KORR ReeVue indirect calorimeter and would be sufficient for use by institutions or community settings who may not have access to an indirect calorimeter. The prediction equations of Owen and American College of Chest Physicians, however, under- and overestimated MREE, respectively, and were influenced by almost all explanatory variables so their use should be avoided in clinical practice.

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Appendix A – Data Collection and Analysis Instruments

- Data Collection
    - KORR ReeVue Indirect Calorimeter
        - http://korr.com/products/medical-metabolic-rate-analysis-system/
- Data Analysis
    - R (Version 3.3.0)

Appendix B – Prediction Equation Tables

Table 1: Prediction Equations for Resting Energy Expenditure (REE)		
Reference	Equation	Prediction Variables
Mifflin St. Jeor (MSJ) [21]	**Men**: REE = (9.99 X weight) + (6.25 X height) – (4.92 X age) + 5 **Women**: REE = (9.99 X weight) + (6.25 X height) – (4.92 X age) – 161	Weight (actual): kilograms (kg) Height: centimeters (cm)
Harris Benedict (HB) [22]	**Men**: REE = 66.47 + 13.75(weight) + 5(height) – 6.76(age) **Women**: REE = 655.1 + 9.56 (weight) + 1.7 (height) – 4.7 (age)	Weight (actual): kilograms (kg) Height: centimeters (cm) Age: years
Owen [23, 24]	**Men**: REE = 879 + 10.2 X weight **Women**: REE = 795 + 7.18 X weight	Weight (actual): kilograms (kg)
American College of Chest Physicians (ACCP) 21 and 25 [25, 37]	ACCP 21: REE = 21 kcal x weight ACCP 25: REE = 25 kcal x weight	Weight (actual): kilograms (kg)
World Health Organization/Food and Agriculture Organization/United Nations University (WHO/FAO/UNU) [26]	<u>Weight only</u> **Men**: 18-30 years: REE = 15.3 X weight + 679 31-60 years: REE = 11.6 X weight + 879 Older than 60 years: REE = 13.5 X weight + 487 **Women**: 18-30 years: REE = 14.7 X weight + 496 31-60 years: REE = 8.7 X weight + 829 Older than 60 years: REE = 10.5 X weight + 596 <u>Weight and height</u> **Men**: 18-30 years: REE = 15.4 X weight – 27 X height + 717 31-60 years: REE = 11.3 X weight + 16 X height + 901 Older than 60 years REE = 8.8 X weight + 1128 X height – 1071 **Women**: 18-30 years: REE = 13.3 X weight + 334 X height + 35 31-60 years: REE = 8.7 X weight – 25 X height + 865 Older than 60 years: REE = 9.2 X weight + 637 X height – 302	Weight (actual): kilograms (kg) Height: meters (m) Age: years

Table 2: Validation Studies used to Evaluate the Mifflin-St. Jeor (MSJ) Prediction Equation			
Reference	Subjects	BMI Level	Findings
Anderegg et al. [37]	36 men and women (ages 32-62 years)	Obese	19.4% of subjects fell within ±10% of MREE with limits of agreement 215.8±470.7 and r=0.41 (*p*=0.0135)
DeLorenzo et al. [51]	320 men and women (ages 18-59 years)	Normal, Overweight, Obese	**Men:** Mean difference of -422±656 kcal/day between measured and predicted REE (95% confidence interval) **Women:** Mean difference of -435±585 kcal/day between measured and predicted REE (95% confidence interval)
Frankenfield et al. [13]	130 men and women (ages 20-78 years)	Normal, Overweight, Obese	**Normal/Overweight BMI:** Predicted values fell within ±10% of MREE in 82% of subjects. 10% of subjects had a predicted REE above the range of agreement (±10% of MREE) & 8% had a predicted REE below the range of agreement. **Obese BMI:** Predicted values fell within ±10% of MREE in 70% of obese subjects. 9% of obese subjects had a predicted REE above the range of agreement and 21% had a predicted REE below the range of agreement.
Heshka et al. [71]	127 men and women (ages 27-50 years)	Normal, Overweight, Obese	**Men:** Regression coefficient of 249±205, R^2=0.60, Mean Error of -132 (*p*<0.01) **Women:** Regression coefficient of 310±128, R^2=0.60, Mean Error of -23
Karlsson et al. [60]	22 men (age >82 years)	Normal, Overweight, Obese	Mean difference of 37±133 kcal/day between measured and predicted REE; Correlation (r) = 0.79 (*p*<0.0001)
Liu et al. [72]	223 men and women (ages 20-78 years)	Normal	Mean difference of 158±111 kcal/day between measured and predicted REE; Correlation coefficient (r) = 0.84 (*p*=0.0001)
Marra et al. [43]	1851 men and women (18-65 years)	Obese	**Men:** Mean difference of -342±321 kcal/day between measured and predicted REE; Bias of -11.9%; Root mean square error (RMSE) of 377 kcal/day **Women:** Mean difference of -257±254 kcal/day between measured and predicted REE; Bias of -11.3%; Root mean square error (RMSE) of 289 kcal/day
Siervo et al.	157 women	Normal,	**Normal BMI:** Bias -132.71±-38.94 (95%

[73]	(ages 18-35 years)	Overweight, Obese	confidence interval) **Overweight BMI:** Bias -112.61±-40.8 (95% confidence interval) **Obese BMI:** Bias -97.65±-7.63 (95% confidence interval)
Taafe et al. [74]	116 women (ages 60-82 years)	Normal, Overweight, Obese	Difference of -57 kcal/day between measured and predicted REE; Root mean squared prediction error (RMSPE) = 131 kcal/day

Table 3: Validation Studies used to Evaluate the Harris Benedict (HB) Prediction Equation			
Reference	Subjects	BMI Level	Findings
Anderegg et al. [37]	36 men and women (ages 32-62 years)	Obese	REE calculated using **actual** weight: 38.9% of subjects fell within ±10% of MREE with limits of agreement 110.1±478.3 and r=0.41 (*p*=0.0133) REE calculated using **adjusted** body weight: 11.1% of subjects fell within ±10% of MREE with limits of agreement 480.8±423.4 and r=0.54 (*p*=0.0006)
Case et al. [75]	36 women (ages 19-52 years)	Normal, Overweight	Mean difference of 110.6±15.5 kcal/day (*p*<0.001)
DeLorenzo et al. [51]	320 men and women (ages 18-59 years)	Normal, Overweight, Obese	**Men & Women:** There was no significant difference between measured and predicted REE (*p*<0.001)
Feurer et al. [76]	112 men and women (ages 27-50 years)	Obese	REE calculated using **current** weight: **Men:** MREE was 88.4±15.0% of predicted **Women:** MREE was 89.5±16.9% of predicted REE calculated using **ideal** body weight: **Men:** MREE was 120.0±39.9% of predicted **Women:** MREE was 138.6±22.39% of predicted
Frankenfield et al. [13]	130 men and women (ages 20-78 years)	Normal, Overweight, Obese	**BMI≥30:** Predicted values with adjusted body weight fell within ±10% of MREE in 26% of subjects. 2% of subjects had a predicted REE above the range of agreement (±10% of MREE) & 72% had a predicted REE below the range of agreement. **BMI≥40:** Predicted REE with adjusted body weight underestimated MREE in 100% of subjects (n=27)
Heshka et al. [71]	127 men and women (ages 27-50 years)	Normal, Overweight, Obese	**Men:** Regression coefficient of 563±172, R^2=0.60, Mean Error of -408 (*p*<0.01) **Women:** Regression coefficient of 97±147, R^2=0.60, Mean Error of -81 (*p*<0.01)
Karlsson et al. [60]	22 men (age >82 years)	Normal, Overweight, Obese	Mean difference of 105±155 kcal/day between measured and predicted REE; Correlation (r) = 0.67 (*p*<0.005)

Liu et al. [72]	223 men and women (ages 20-78 years)	Normal	Mean difference of 92±97 kcal/day between measured and predicted REE; Correlation coefficient (r) = 0.88 (*p*=0.0001)
Marra et al. [43]	1851 men and women (18-65 years)	Obese	**Men:** Mean difference of -76±317 kcal/day between measured and predicted REE; Bias of -1.7%; Root mean square error (RMSE) of 257 kcal/day **Women:** Mean difference of -181±258 kcal/day between measured and predicted REE; Bias of -7.2%; Root mean square error (RMSE) of 243 kcal/day
Pavlou et al. [70]	31 men (ages 30-60 years)	Normal, Overweight, Obese	REE calculated using **current** weight: MREE was 92±10% of the predicted REE; 64% of subjects had an REE within ±10% of expected REE REE calculated using **ideal** body weight: MREE was 119±12% of the predicted REE; 26% of subjects had an REE within ±10% of expected REE
Siervo et al. [73]	157 women (ages 18-35 years)	Normal, Overweight, Obese	**Normal BMI:** Bias -225.96±-133.13 (95% confidence interval) **Overweight BMI:** Bias -198.74±-126.81 (95% confidence interval) **Obese BMI:** Bias -174.4±-85.52 (95% confidence interval)
Taafe et al. [74]	116 women (ages 60-82 years)	Normal, Overweight, Obese	Difference of 30 kcal/day between measured and predicted REE; Root mean squared prediction error (RMSPE) = 114 kcal/day
van der Ploeg et al. [77]	41 men (ages 30-60 years)	Normal, Overweight, Obese	R^2=0.753 with a standard error of estimate 432 kcal/day

Table 4: Validation Studies used to Evaluate the Owen Prediction Equation			
Reference	Subjects	BMI Level	Findings
DeLorenzo et al. [51]	320 men and women (ages 18-59 years)	Normal, Overweight, Obese	**Men:** Mean difference of -736±727 kcal/day between measured and predicted REE (95% confidence interval) **Women:** Mean difference of -644±669 kcal/day between measured and predicted REE (95% confidence interval)
Frankenfield et al. [13]	130 men and women (ages 20-78 years)	Normal, Overweight, Obese	**Normal/Overweight BMI:** Predicted values fell within ±10% of MREE in 73% of subjects 6% of subjects had a predicted REE above the range of agreement (±10% of MREE) & 21% had a predicted REE below the range of agreement. **Obese BMI:** Predicted values fell within ±10% of MREE in 51% of subjects. 6% of obese subjects had a predicted REE above the range of agreement & 43% had a predicted REE below the range of agreement.
Heshka et al. [71]	127 men and women (ages 27-50 years)	Normal, Overweight, Obese	**Men:** Regression coefficient of 194±245, R^2=0.53, Mean Error of -132 (P<0.01) **Women:** Regression coefficient of -249±198, R^2=0.57, Mean Error of 137 (p<0.01)
Liu et al. [72]	223 men and women (ages 20-78 years)	Normal	Mean difference of 137±114 kcal/day between measured and predicted REE; Correlation coefficient (r) = 0.84 (p=0.0001)
Marra et al. [43]	1851 men and women (18-65 years)	Obese	**Men:** Mean difference of -352±324 kcal/day between measured and predicted REE; Bias of -12.1%; Root mean square error (RMSE) of 261 kcal/day **Women:** Mean difference of -439±282 kcal/day between predicted and measured REE; Bias of -20%; Root mean square error (RMSE) of 445 kcal/day
Siervo et al. [73]	157 women (ages 18-35 years)	Normal, Overweight, Obese	**Normal BMI:** Bias -35.93±-55.45 (95% confidence interval) **Overweight BMI:** Bias 13.2±88.41 (95% confidence interval) **Obese BMI:** Bias 93.43±183.6 (95% confidence interval)

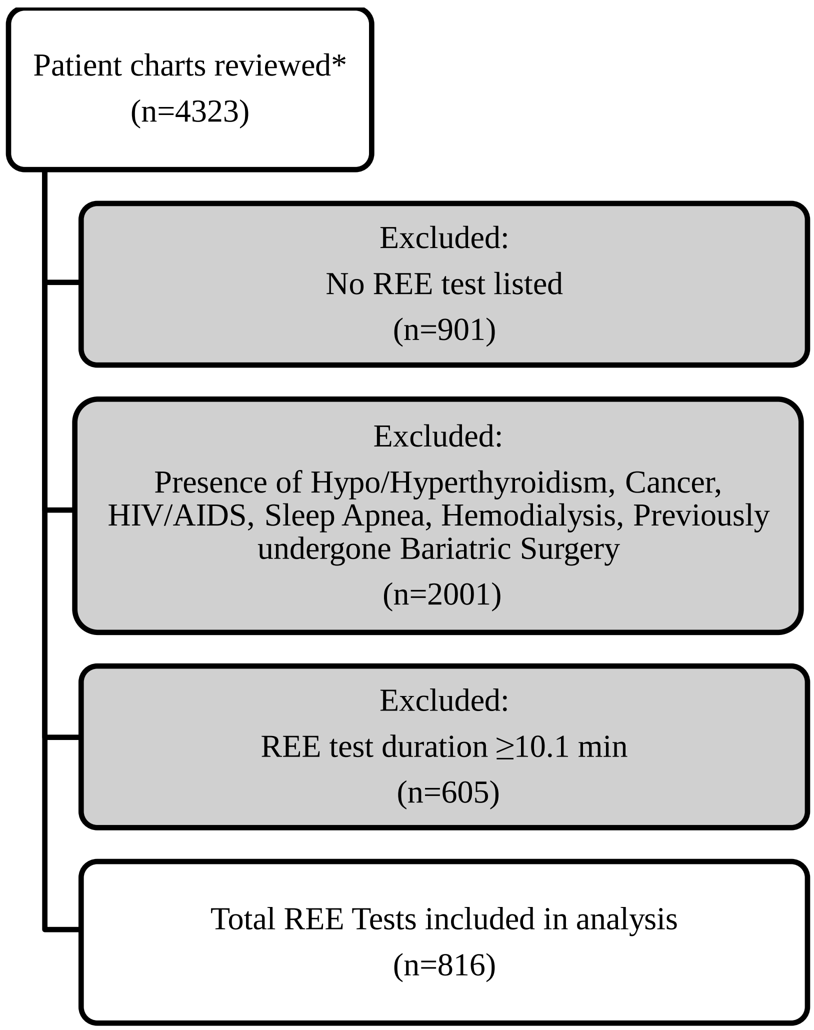
Taafe et al. [74]	116 women (ages 60-82 years)	Normal, Overweight, Obese	Difference of 16 kcal/day between measured and predicted REE; Root mean squared prediction error (RMSPE) = 115 kcal/day

Table 5: Validation Studies used to Evaluate the American College of Chest Physician (ACCP) Prediction Equations			
Reference	Subjects	BMI Level	Findings
Anderegg et al. [37]	36 men and women (ages 32-62 years)	Obese	**21** kcal per kg using **actual** body weight: 41.7% of subjects fell within ±10% of measured REE with limits of agreement -271±641.7 and r=0.18 (*p*=0.3004) **25** kcal per kg using **adjusted** body weight: 38.9% of subjects fell within ±10% of measured REE with limits of agreement 135.5±456.2 and r=0.46 (*p*=0.0048) **25** kcal per kg using **actual** body weight: 19.4% of subjects fell within ±10% of measured REE with limits of agreement -713.7±707.3 and r=0.18 (*p*=0.2974)
Reid [67]	27 men and women (ages 41-73 years)	Normal, Overweight	**25** kcal per kg using **adjusted** body weight: Bias of 219±27.7 kcal/day (95% confidence interval) with limits of agreement -533 to 971 and r=0.510 (*p*<0.0001) **25** kcal per kg using **actual** body weight: Bias of 183±26.5 kcal/day (95% confidence interval) with limits of agreement -535 to 902 and r=0.592 (*p*<0.0001)

Table 6: Validation Studies used to Evaluate the World Health Organization/Food and Agriculture Organization/United Nations University (WHO/FAO/UNU) Prediction Equations			
Reference	Subjects	BMI Level	Findings
Case et al. [75]	36 women (ages 19-52 years)	Normal, Overweight	Mean difference of 95.9±11.8 kcal/day ($p<0.01$)
Karlsson et al. [60]	22 men (age >82 years)	Normal, Overweight, Obese	Mean difference of 142±165 kcal/day between measured and predicted REE; Correlation (r) = 0.62 ($p<0.005$)
Marra et al. [43]	1851 men and women (18-65 years)	Obese	**Men:** Mean difference of -52±343 kcal/day between measured and predicted REE; Bias of -0.7%; Root mean square error (RMSE) of 273 kcal/day **Women:** Mean difference of -106±290 kcal/day between measured and predicted REE; Bias of -3.6%; Root mean square error (RMSE) of 239 kcal/day
Siervo et al. [73]	157 women (ages 18-35 years)	Normal, Overweight, Obese	**Normal BMI:** Bias -169.61±-77.1 (95% confidence interval) **Overweight BMI:** Bias -182.45±-106.86 (95% confidence interval) **Obese BMI:** Bias -213.87±-115.85 (95% confidence interval)
Taafe et al. [74]	116 women (ages 60-82 years)	Normal, Overweight, Obese	Difference of 101 kcal/day between measured and predicted REE; Root mean squared prediction error (RMSPE) = 154 kcal/day

Appendix C – Results Tables and Figures

Figure 1. Subjects



REE: Resting Energy Expenditure

*Individuals with the following characteristics were excluded prior to establishing care at the Center for Medical Weight Loss: BMI <30 kg/m^2, age <18 years, pregnant, lack of health insurance, or current treatment of chemotherapy/radiation. Individuals who completed any of the following were prohibited from completing an REE test: Consumption of caffeine, tobacco, stimulant medications, inhalers, herbal supplements or nasal sprays within 12 hours of REE test, consumption of food or beverages (besides water) within 12 hours of REE test, or exercise on the day of REE test.

Table 7: Descriptive statistics by sex and obesity grade.

	Total Sample		Class I Obesity (BMI: 30 - 34.9)		Class II Obesity (BMI: 35 - 39.9)		Class III Obesity (BMI: >40)	
	F	M	F	M	F	M	F	M
N	681 (83%)	135 (17%)	159 (19%)	25 (3%)	173 (21%)	48 (6%)	326 (40%)	60 (7%)
Age (years)	43.2 ± 12.7	46.1 ± 14.9	44.3 ± 12.1	47.4 ± 14.7	44.8 ± 12.5	49.9 ± 14.9	42.2 ± 12.8	42.1 ± 15.0
Weight (kg)	110.2 ± 24.2	133.3 ± 31.0	89.5 ± 7.5	106.2 ± 9.1	100.3 ± 8.9	119.7 ± 11.0	128.1 ± 22.7	157.3 ± 30.1
Height (cm)	163.9 ± 6.4	178.3 ± 7.6	164.6 ± 6.3	179.5 ± 7.7	163.5 ± 6.6	177.5 ± 7.1	163.8 ± 6.3	178.7 ± 7.5
BMI	41.0 ± 8.6	41.9 ± 9.0	33.0 ± 1.3	32.9 ± 1.1	37.4 ± 1.5	37.9 ± 1.4	47.7 ± 7.8	49.2 ± 8.6
Race								
B	215 (26%)	24 (3%)	39 (5%)	3 (0.4%)	51 (6%)	7 (0.9%)	123 (15%)	14 (2%)
W	420 (51%)	101 (12%)	106 (13%)	18 (2%)	108 (13%)	37 (5%)	188 (23%)	44 (5%)
O	46 (6%)	10 (1%)	14 (2%)	4 (0.5%)	14 (2%)	4 (0.5%)	15 (2%)	2 (0.2%)
Ethnicity								
HL	25 (3%)	5 (1%)	10 (1%)	2 (0.2%)	7 (0.9%)	1 (0.1%)	7 (0.8%)	2 (0.2%)
NH	656 (80%)	130 (16%)	149 (18%)	23 (3%)	166 (20%)	47 (6%)	319 (39%)	58 (7%)

BMI: Body Mass Index; F: Female; M: Male; Class I Obesity: BMI 30-34.9 kg/m^2; Class II Obesity: BMI 35-39.9 kg/m^2; Class III Obesity: BMI >40 kg/m^2; B: Black; W: White; O: Other; HL: Hispanic/Latino; NH: Not Hispanic/Latino

Data are expressed as mean ± s.d.; Categorical variables are expressed as N (percent).

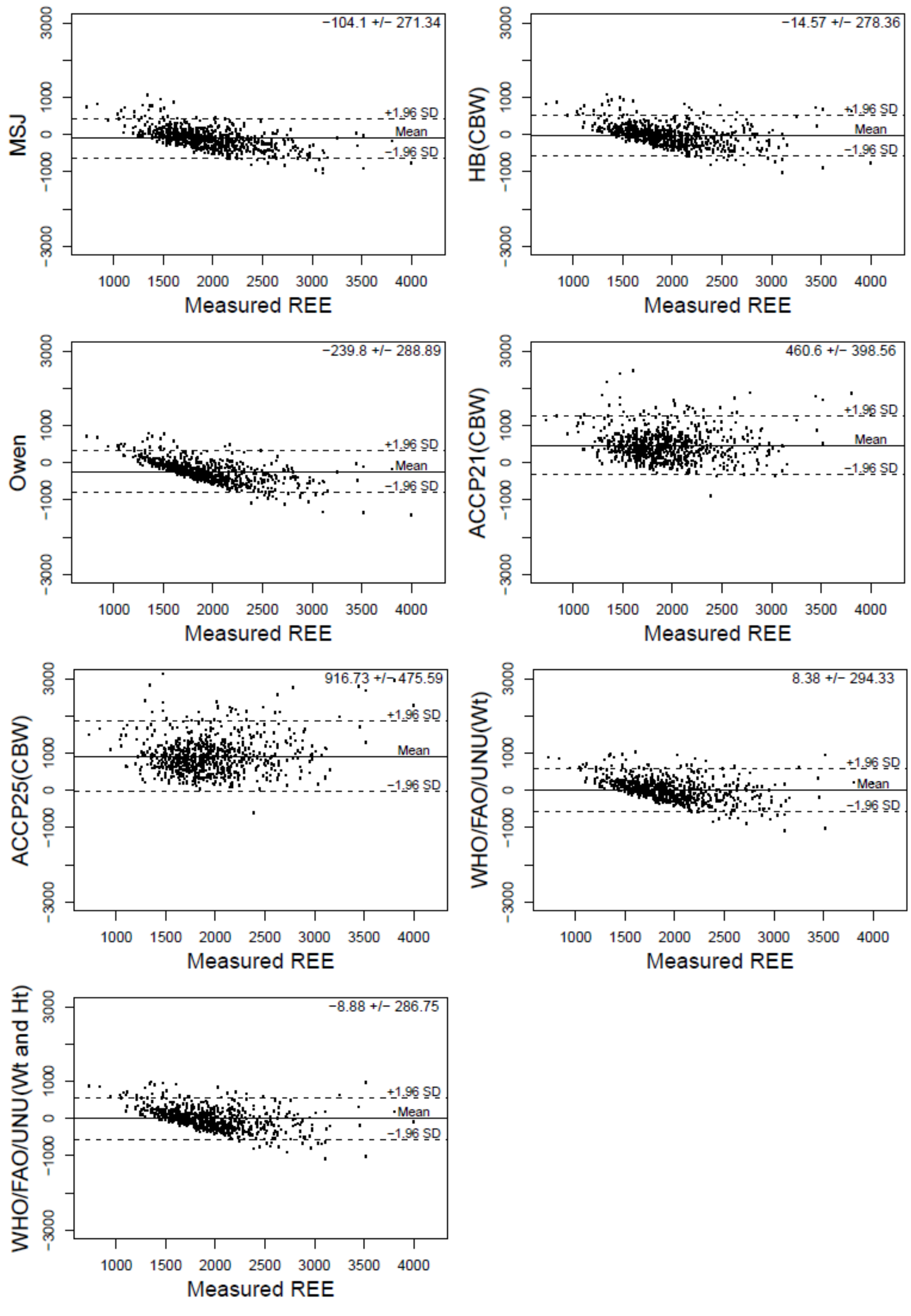
Table 8: Mean resting energy expenditure (REE) by sex and obesity grade.

	Total Sample		Class I Obesity (BMI: 30 - 34.9)		Class II Obesity (BMI: 35 - 39.9)		Class III Obesity (BMI: >40)	
	F	M	F	M	F	M	F	M
MREE (kcal/day)	1845 ± 354	2385 ± 488	1703 ± 273	1949 ± 295	1730 ± 288	2254 ± 365	1998 ± 360	2693 ± 462
MSJ	1752 ± 273	2224 ± 360	1545 ± 124	1955 ± 156	1642 ± 159	2064 ± 192	1935 ± 265	2486 ± 355
HB (CBW)	1808 ± 250	2480 ± 482	1607 ± 97	2104 ± 193	1705 ± 128	2263 ± 241	1985 ± 240	2839 ± 474
Owen	1586 ± 174	2239 ± 316	1438 ± 54	1962 ± 93	1515 ± 64	2100 ± 112	1715 ± 163	2483 ± 307
ACCP 21 (CBW)	2314 ± 509	2800 ± 651	1880 ± 157	2230 ± 191	2105 ± 188	2513 ± 230	2691 ± 477	3303 ± 632
ACCP 25 (CBW)	2755 ± 606	3333 ± 775	2238 ± 187	2655 ± 228	2507 ± 223	2992 ± 274	3204 ± 567	3932 ± 753
WHO/FAO/UNU (Wt)	1843 ± 295	2442 ± 446	1635 ± 103	2088 ± 157	1739 ± 156	2237 ± 213	2025 ± 298	2779 ± 441
WHO/FAO/UNU (Wt & Ht)	1826 ± 275	2423 ± 463	1626 ± 96	2097 ± 170	1726 ± 146	2200 ± 267	2001 ± 275	2762 ± 467

BMI: Body Mass Index; F: Female; M: Male; Class I Obesity: BMI 30-34.9 kg/m^2; Class II Obesity: BMI 35-39.9 kg/m^2; Class III Obesity: BMI >40 kg/m^2; MSJ: Mifflin St. Jeor; HB: Harris Benedict; ACCP: American College of Chest Physicians; WHO/FAO/UNU: World Health Organization/Food and Agriculture Organization/United Nations University; CBW: Current body weight; Wt: Weight; Ht: Height

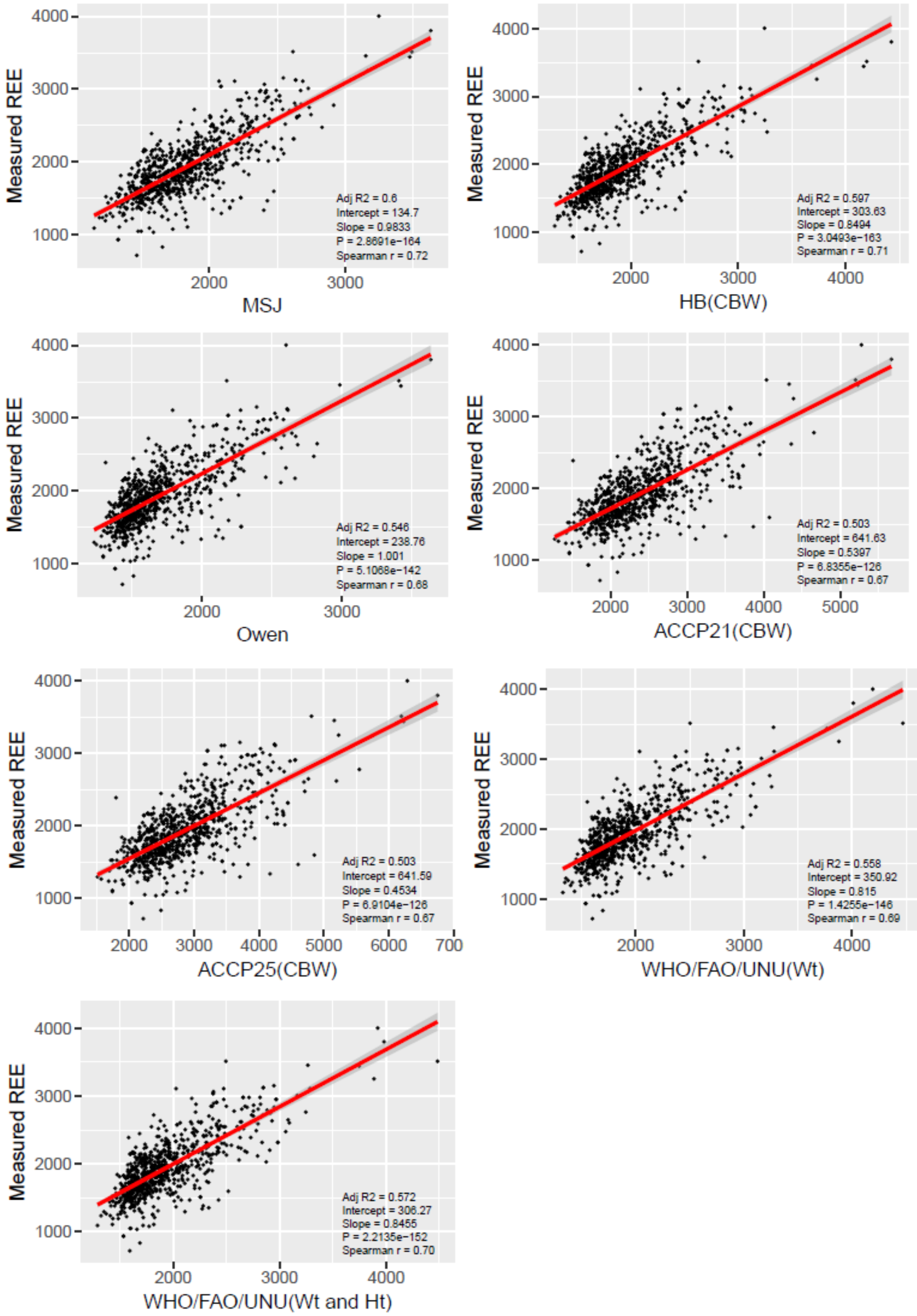
Data are expressed as mean ± s.d.

Figure 2: Bland-Altman plots of the difference between estimated resting energy expenditure (REE) of each prediction equation and measured resting energy expenditure (MREE). Confidence limit for clinical agreement: ±150 kcal/day.



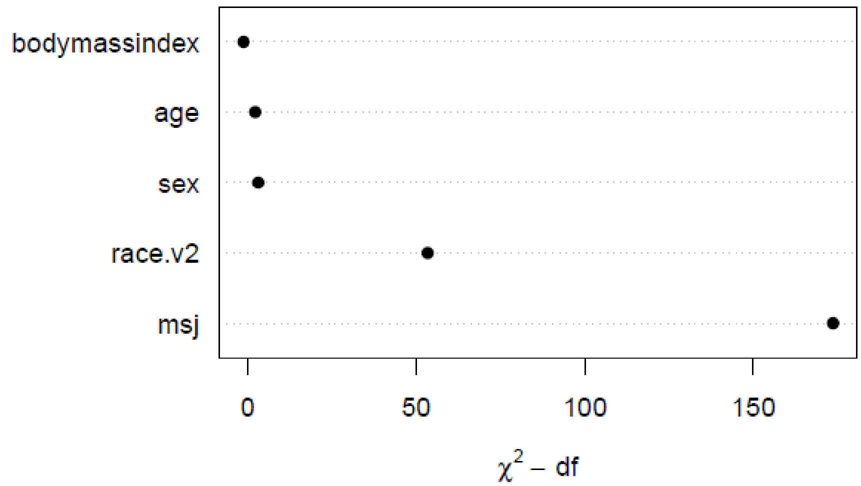
MSJ: Mifflin St. Jeor; HB: Harris Benedict; ACCP: American College of Chest Physicians; WHO/FAO/UNU: World Health Organization/Food and Agriculture Organization/United Nations University; CBW: Current body weight; Wt: Weight; Ht: Height

Figure 3: Relationship between the estimated resting energy expenditure (REE) for each prediction equation compared to measured resting energy expenditure (MREE) in obese adults.



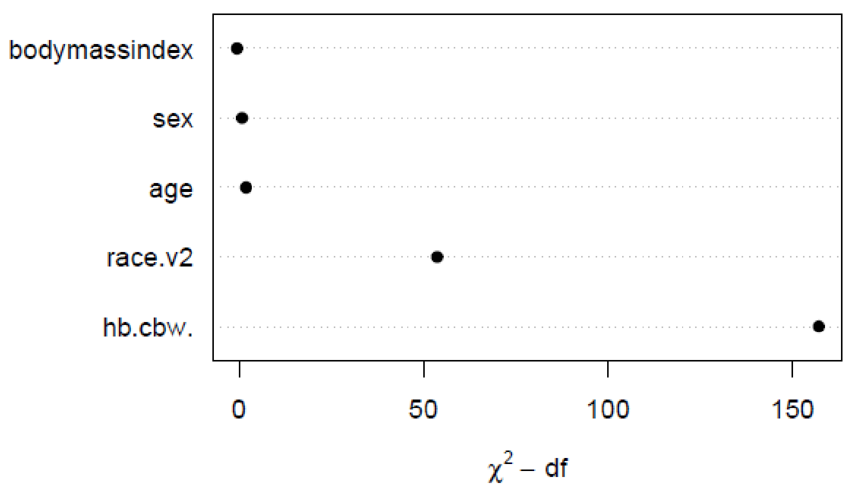
MSJ: Mifflin St. Jeor; HB: Harris Benedict; ACCP: American College of Chest Physicians; WHO/FAO/UNU: World Health Organization/Food and Agriculture Organization/United Nations University; CBW: Current body weight; Wt: Weight; Ht: Height

Figure 4: Wald Chi-Squared Dot Plot depicting influence of explanatory variables (age, sex, race, and body mass index) for Mifflin St. Jeor (MSJ) equation.



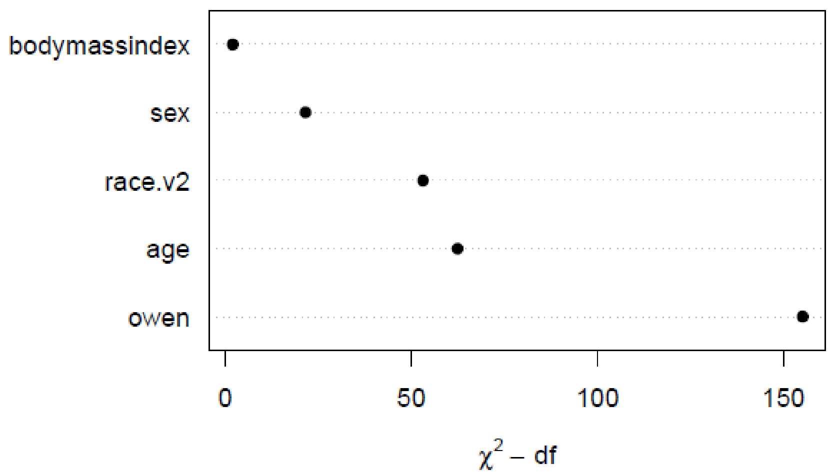
χ^2	*P*	R^2
0.69	0.7079	0.0005
4.23	0.1206	0.0030
4.12	0.0424	0.0030
55.37	<0.0001	0.0398
174.66	<0.0001	0.1257

Figure 5: Wald Chi-Squared Dot Plot depicting influence of explanatory variables (age, sex, race, and body mass index) for Harris Benedict (HB) equation.



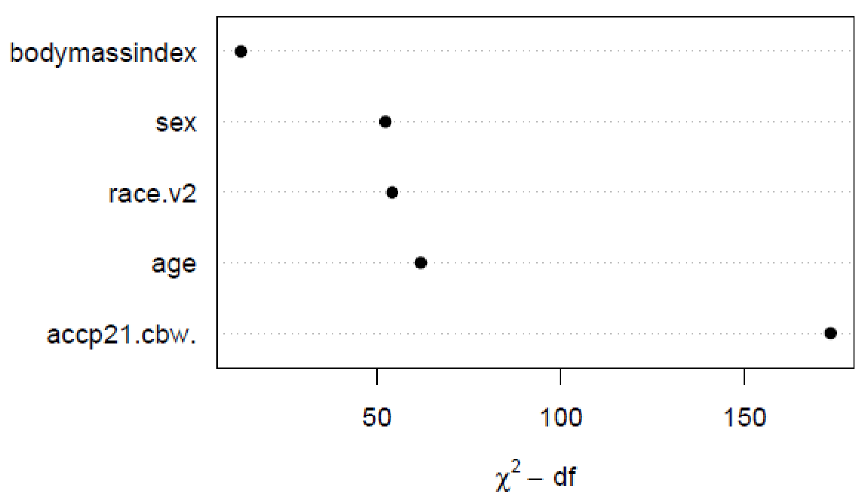
χ^2	*P*	R^2
1.44	0.4865	0.0011
1.79	0.1808	0.0013
3.86	0.1450	0.0029
55.70	<0.0001	0.0412
158.18	<0.0001	0.1169

Figure 6: Wald Chi-Squared Dot Plot depicting influence of explanatory variables (age, sex, race, and body mass index) for Owen equation.



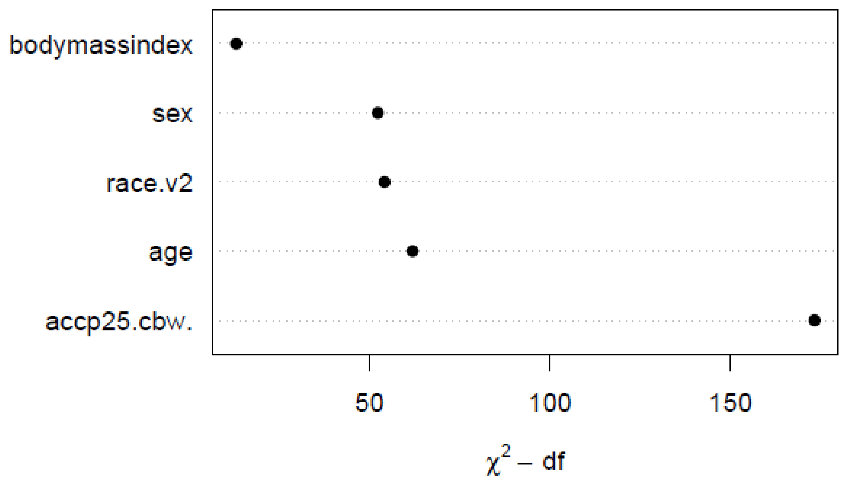
χ^2	*P*	R^2
3.89	0.1431	0.0029
22.44	<0.0001	0.0166
55.07	<0.0001	0.0408
64.39	<0.0001	0.0478
156.15	<0.0001	0.1158

Figure 7: Wald Chi-Squared Dot Plot depicting influence of explanatory variables (age, sex, race, and body mass index) for American College of Chest Physicians (ACCP) 21 equation.



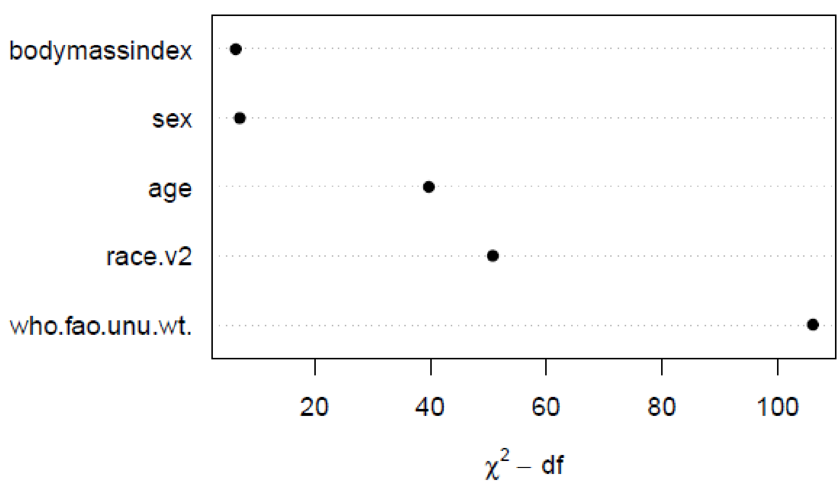
χ^2	*P*	R^2
14.97	0.0006	0.0108
53.22	<0.0001	0.0383
56.10	<0.0001	0.0404
63.85	<0.0001	0.0460
174.37	<0.0001	0.1255

Figure 8: Wald Chi-Squared Dot Plot depicting influence of explanatory variables (age, sex, race, and body mass index) for American College of Chest Physicians (ACCP) 25 equation.



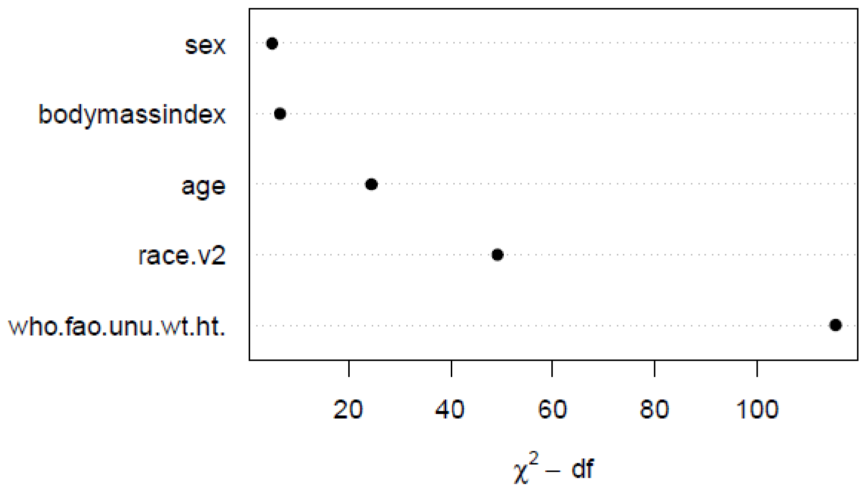
	χ^2	*P*	R^2
bodymassindex	14.96	0.0006	0.0108
sex	53.26	<0.0001	0.0383
race.v2	56.12	<0.0001	0.0404
age	63.85	<0.0001	0.0460
accp25.cbw.	174.36	<0.0001	0.1255

Figure 9: Wald Chi-Squared Dot Plot depicting influence of explanatory variables (age, sex, race, and body mass index) for World Health Organization/Food and Agriculture Organization/United Nations University (WHO/FAO/UNU) (weight only) equation.



	χ^2	*P*	R^2
bodymassindex	8.34	0.0154	0.0067
sex	8.03	0.0046	0.0065
age	41.73	<0.0001	0.0337
race.v2	52.79	<0.0001	0.0426
who.fao.unu.wt.	107.13	<0.0001	0.0865

Figure 10: Wald Chi-Squared Dot Plot depicting influence of explanatory variables (age, sex, race, and body mass index) for World Health Organization/Food and Agriculture Organization/United Nations University (WHO/FAO/UNU) (using both weight and height) equation.



χ^2	*P*	R^2
6.07	0.0138	0.0048
8.63	0.0134	0.0068
26.54	<0.0001	0.0211
51.20	<0.0001	0.0407
116.38	<0.0001	0.0924