Weight-Gain and Energy Balance

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WEIGHT-GAIN AND ENERGY BALANCE

by

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ABSTRACT

Energy balance is the result of a dynamic relationship between energy intake (EI), energy expenditure (EE) and energy storage (ES). These three components of energy balance have extremely complicated associations, and all three major components are consistently influenced by physiologic, psychological, and sociologic factors. Concerted changes between EE and EI result in alterations of the ES. Most often in clinical and research settings, bodyweight is used as marker of body composition (i.e., ES) changes. Traditional measurements of bodyweight do not give an accurate portrayal of ES change or the role it has in energy balance. This dissertation supplies new methods of monitoring ES that better estimate an individual’s true change in ES over time. These new methods were then applied and used to categorize weight gain, loss and maintenance. Further, the association between these categorizations and EE was investigated. Thus this dissertation begins with an investigative analysis of one component of energy balance and then progresses to the association between two components and the overall influence of the association on energy balance. The three papers of this dissertation examine 1) the overall bodyweight changes that occur over a year period in healthy adults 2) the overall body composition changes that occur over a year period in healthy adults; and 3) the associations of bodyweight and composition changes with average energy expenditures over a year period. This dissertation used clinical measurements of bodyweight, composition and objectively measured EE values, which were collected as a part of the
first year of the Energy Balance Study (a comprehensive study designed to determine the associations of caloric intake and EE on changes in bodyweight and composition in a population of healthy men and women). The aims of the current dissertation are crucial to providing insight and results for the primary aim of the Energy Balance Study.

The first study revealed that the participants of the Energy Balance Study are on average gaining roughly a kilogram (kg) of bodyweight over a year period, which is similar to estimates that have been made for the United States (US) population. However, while 43% of the participants were found to be gaining weight, a greater majority (46%) were maintaining bodyweight over the year period. The participants gaining and losing the most weight were substantially heavier than those who maintained bodyweight. Lastly, when the traditional measurements of monitoring bodyweight were compared to linear mixed model estimations of bodyweight change they were found to largely over or underestimate changes in the individual.

Study two showed that the average bodyweight the participants from the Energy Balance Study gained (roughly 1kg) was predominantly due to increases in fat mass (FM). Subsequently, on average the group gained slightly less than 1 kg of FM in a year period. Similar to the trends seen in bodyweight changes, the greatest majority of participants were considered to be maintaining fat mass. While overall the fat-free mass (FFM) of the participants did not change substantially it was negatively correlated with FM.

In the last study overall total daily EE was shown to be substantially elevated in the participants considered as weight gainers and participants considered as fat-gainers.
However, the elevated total daily EE was most likely due to the substantially heavier starting bodyweight of these two groups. When the total daily EE was analyzed on a per kg of bodyweight basis, the trend was reversed and the weight maintenance group had the highest values of EE. However, this was most likely due to the differences between groups body surface area relative to bodyweight ratio. Lastly, the bodyweight and composition maintenance groups had a lower percentage of total EE coming from sedentary activities relative to the substantial bodyweight and composition gainers.
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LIST OF SYMBOLS

N   Sample size
β   Regression slope
SE_β Standard Error of the regression slope
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<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>AEE</td>
<td>Activity energy expenditure</td>
</tr>
<tr>
<td>AHA</td>
<td>American Heart Association</td>
</tr>
<tr>
<td>AMA</td>
<td>American Medical Association</td>
</tr>
<tr>
<td>BMI</td>
<td>Body mass index</td>
</tr>
<tr>
<td>CAD</td>
<td>Coronary artery disease</td>
</tr>
<tr>
<td>CDC</td>
<td>Center for disease control</td>
</tr>
<tr>
<td>DLW</td>
<td>Doubly labeled water technique</td>
</tr>
<tr>
<td>DXA</td>
<td>Dual x-ray absorptiometry</td>
</tr>
<tr>
<td>EB</td>
<td>Energy balance</td>
</tr>
<tr>
<td>EE</td>
<td>Energy expenditure</td>
</tr>
<tr>
<td>EI</td>
<td>Energy intake</td>
</tr>
<tr>
<td>ES</td>
<td>Energy storage</td>
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<tr>
<td>FG</td>
<td>Fat Gain</td>
</tr>
<tr>
<td>FL</td>
<td>Fat loss</td>
</tr>
<tr>
<td>FM</td>
<td>Fat mass</td>
</tr>
<tr>
<td>FFM</td>
<td>Fat-free mass</td>
</tr>
<tr>
<td>GI</td>
<td>Gastrointestinal</td>
</tr>
<tr>
<td>LMM</td>
<td>Linear Mixed Model</td>
</tr>
<tr>
<td>MET</td>
<td>Metabolic equivalent of task</td>
</tr>
<tr>
<td>MLIC</td>
<td>Metropolitan life insurance Company</td>
</tr>
</tbody>
</table>
NEAT ............................................................... Non-exercise activity thermogenesis
NIH ............................................................... National Institute Health
NHANES ...................................................... National Health and Nutrition Examination Survey
NHES ............................................................. National Examination Survey
RMR ............................................................... Resting metabolic rate
SD ............................................................... Standard deviation
SFG ............................................................... Substantial fat gain
SFL ............................................................... Substantial fat loss
SWG ............................................................... Substantial weight gain
SWL ............................................................... Substantial weight loss
TD2 ............................................................... Type 2 diabetes
TEF ............................................................... Thermogenic effect of food
US ............................................................... United States
USDA ............................................................. United States Department of Agriculture
WG ............................................................... Weight gain
WHO ............................................................. World Health Organization
WL ............................................................... Weight loss
WM ............................................................... Weight maintenance
CHAPTER 1
OVERALL INTRODUCTION

Over the past 20 years obesity has come to the forefront of public health concern. During this short period, prevalence rates of overweight or obese individuals have exploded. In 1991 the estimated obesity prevalence in the United States (US) was 12.0%, the value has now ballooned to 35.7%. And if current trends continue, an estimated 51% of the population will be obese by 2030 (1;2). The rising obesity prevalence rates are associated with a staggering rise in medical costs. Some investigators have estimated obesity in the U.S. to be associated with 114 billion dollars per year in direct costs, although it should be noted that these numbers have not been adjusted for the positive effects of physical activity and exercise (3). Because of these widespread health and economic costs associated with the disorder, researchers, specifically in the past two decades have made a concerted effort to better understand it.

In medicine, obesity is known as a state of increased bodyweight, referring explicitly to adipose tissue in large enough surplus to produce adverse health consequences (4). These excessive amounts of adipose tissue are created when there are alterations in the energy balance (EB) equation. The fundamental variables of EB are energy intake (EI), energy expenditure (EE) and energy storage (ES) (5). EI is the total amount of calories consumed by an individual including the total consumption of three the major macronutrients, and to a lesser extent alcohol. The net absorption of these nutrients varies depending on the individual, the type of food, how the food was prepared...

1
and intestinal enzymatic activity (6). Depending on the aforementioned factors, 2-10% of energy consumed is not absorbed and lost during excretion. The energy that is absorbed by the gastrointestinal tract (GI) is known as metabolizable energy, this is what most researchers consider true EI. While the absorbed calories are considered true EI, most investigators calculate EI by the amount of calories that are consumed because of the difficulty measuring the total amount absorbed (6). The calories taken up by the GI are either stored by the body or used immediately for biological processes throughout the day and lifespan of an individual. Every cell in the body is constantly in need of ATP to conduct biological processes, therefore there is always a need for EI.

Collectively the energetic costs of all biological processes are the total EE. The largest component of total EE takes place in the resting phase known as resting metabolic rate RMR. This component typically comprises roughly two thirds of total daily EE. RMR varies widely between individuals, mainly due to size, and body composition (7). Typically, increases in lean mass cause substantial increases in RMR (8). Along with RMR the thermogenic effect of food (TEF) also contributes to total EE. TEF is the EE associated with the digestion and absorption of food, contributing roughly 10% of total EE. The largest influential factor affecting TEF appears to be varying levels of macronutrients; an example being the level of alcohol consumption. Increasing alcohol consumption increases total EE, but also increases the amount of fat stored in the body (9;10). Lastly, representing 15-30% of total EE is the active energy expenditure (AEE), which represents all the energy consumed in activities requiring more than resting energy level. AEE is typically segmented into exercising activity and non-exercising activity (NEAT) (6).
Chronic imbalances between EE and EI result in alterations of the ES. The predominant mode of ES in the body is the use of triglycerides. The average human stores tens of thousands of calories in the form of triglycerides, while an obese individual may store up to a million calories (11). Additional energy is stored in the form of glycogen and protein, but while these two storage deposits have specific purposes, triglycerides are able to store almost double the amount of calories in one gram.

The three major components of EB (i.e., EE, EI and ES) are constantly in flux, as a result the values of EE and EI are almost never equal on a day-to-day basis. When bodyweight is lost, the total EI is routinely less than the total EE for an extended period of time, meaning ES must be used to match the EE. When bodyweight is gained the total EI is routinely greater than total EE for an extended period of time, the additional energy absorbed is stored. Changes in ES are stressful for the body and can lead to problems others than those simply associated with obesity (12).

Changes in ES are typically measured by changes in overall weight. For the general public and clinicians, bodyweight affords a method for ES trajectory. However, measurements of bodyweight can be misleading for making assumptions on changes in ES. Fluctuations in bodyweight can be attributed to other factors aside from changes in ES such as, additional clothing, food and water consumption, measurement error, fluid retention, and electrolyte imbalances (13). Some researchers have seen diurnal variations in bodyweight of roughly 5lbs, this is with a consistent measurement protocol and without a concerted effort from the participant to change weight during the measurement period (13). Individuals making a concerted effort to change their weight can have much more dramatic fluctuations. An investigation using high school wrestlers found that in a
12hr period (from weigh-in for the competition until the actual competition) the competitors gained an average of 2.2±1.7% of their bodyweight, with the biggest gain being 7.2% of their original bodyweight (14). These massive fluctuations in bodyweight are mainly due to changes in body water. The average human is comprised of 60% water, with gender, age and ethnicity causing variations (15). In normal healthy adults water volume can fluctuate up to ±5% daily. This means that an adult male weighing 200lbs can fluctuate up to 6lbs with typical changes in water. These substantial variations in bodyweight can lead to incorrect assumptions regarding changes in ES (primarily regarding body fat).

The actual ES changes that lead to obesity are hypothesized to be small but substantial increases over an extended period of time. Hill et al. proposed that the obesity pandemic has arisen from small differences between EE and EI (i.e., <100 kcals) (16). This small gap between EE and EI requires several months of consistency to result in a substantial change in ES. Thus average increases in bodyweight for the US over an entire year are small estimated at about 1-3lbs (16). These small changes can be masked behind the previously mentioned fluctuations in water levels, electrolytes and other physiologic changes, making predictions of true weight-gain and true weight-loss very difficult (6).

More accurate estimations of changes in energy storage can be made by measuring body composition. As previously mentioned triglycerides are the main form of stored energy in the body, unlike fat-free mass, triglycerides have very low water content (roughly 15% of water). Measurements of fat-mass and fat-free mass give a more accurate depiction of what the trend of ES, better predicting the risk for obesity and associated health-risks. While measurement of body composition shows ES change, there
are still measurement errors depending on which method is utilized. In addition, the measurement of fat-free mass still holds the possibility of inaccuracies due to diet, hydration level and electrolyte level.

The measurement errors and physiologic fluctuations of body composition and bodyweight create low precision and misinterpretation of cross-sectional measurements. To understand a rate of change in ES, multiple measurements such as in a longitudinal study can be used in a linear mixed model (LMM) to estimate the rate of change in either body composition or weight. Over multiple time points, LMM is capable of producing a more accurate estimation of weight change of a period of time than cross-sectional measurements.

As previously mentioned, ES is heavily influenced by EI and EE. When EI is greater than EE, energy is stored. When EE is greater than EI, ES is used. The creation and use of ES has been shown to be heavily influenced by other metabolic and physiologic factors. Varying the protein and carbohydrate content of meals can greatly impact whether excess energy is stored as fat mass or fat-free mass. A recent study by Bray et al. measured the effects of varying the amount of protein in participants diets (17). The investigation revealed that no matter what the variation of macronutrients a range of 50-90% of all calories were stored as fat, and all of the groups gained similar amounts of total fat. However, the groups that were fed a high-protein diet gained a substantially greater amount of fat-free mass than the low protein group. In addition, a recent meta-analysis by Peterson et al. found that the weighted pooled estimate of mean lean body mass change was 1.1kg, and that higher volumes of training were associated with larger increases in lean mass (18). While there have been several studies that have
investigated various environmental influences on ES, no study has measured the specific effect of varying levels of EE on ES.

There have been several studies that have explored the topics of EE and EI in varying populations, but there are no large-scale studies that have closely followed EE and EI over an extended period time to investigate the relationships between EE, EI, ES, weight-gain and obesity. More investigations are required for the proper investigation on bodyweight and composition change, and the development of obesity. Specifically, there is a need to clinically measure the amount of weight-gain over an extended period of time to truly understand how individuals are gaining weight and the relevance of this weight-gain. In addition, there is a need to clinically measure the amount of body composition change over an extended period of time to understand how individuals are changing their body composition along with changing weight. Lastly, the average EE associated with changes in ES are not fully understood, and need to be further elucidated. This dissertation will attempt to clarify questions regarding energy balance and the affects of its components on weight balance, weight gain and obesity

**Statement of Problem**

The positive EB associated with storing ES, and gaining excess body fat to the point of obesity is not well understood. The amount and rate of unhealthy weight-gain relative to healthy weight-gain and health outcomes of both are unclear. Further, the long-term patterns of average total daily EE and their effect on weight maintenance and body composition is not clear. The overall goal of this dissertation is to first better understand how bodyweight and composition change in healthy adults, and how these
changes are associated with EE. This will be determined through the following specific aims. [1] To determine the overall bodyweight changes that occurs over a year period in a group of 344 healthy adults. [2] To determine the overall body composition changes that occurs over a year period to a group of 344 healthy adults. [3] To determine how average total daily EE is associated with changes in bodyweight and composition of a year period.

**Hypothesis**

The following hypotheses are intended to test the given specific aims

**Specific Aim 1**

To determine the overall weight changes that occurs over a year period in a group of 344 healthy adults.

1a. To determine the overall change in bodyweight of 344 healthy adults over a period of 12 months by measuring bodyweight at five time points (baseline, 3 month, 6 month, 9 month and 12 month).

1.1 The overall average weight-change of the 344 participants will be similar to estimations of yearly weight gain of Americans, roughly 1-2kg.

1b. To estimate the weight-change of 344 healthy adults by using five bodyweight measurements over a 12-month period in a LMM.

1.2 The LMM will give a precise prediction of each participant’s weight-change as compared to the difference of two cross-sectional measurements (i.e., 12 month minus baseline). The use of several measurements as opposed to two
measurements will better account for variations between measurements and other varying factors yielding a better depiction of weight-change over time.

1c. To define weight-change by grouping the trajectories (produced by the LMM) into five specific groups: participants that are gaining substantial amounts of bodyweight, those who are gaining bodyweight, those maintaining bodyweight, those losing bodyweight and those who are losing substantial amounts of bodyweight. The groups will be based off each participant’s measure variation by comparing the LMM calculated bodyweight and the overall slope standard error.

1.3 The group of weight-gainers will contain the largest number of participants, while the weight-maintenance group will have the least amount of participants.

Specific Aim 2

To determine the overall body composition changes that occurs during a year period to a group of 344 healthy adults.

2a. To determine the overall change in body composition from 344 healthy adults over a period of 12 months by using dual X-ray absorptiometry (DXA) estimates of body composition at five time points (baseline, 3 month, 6 month, 9 month and 12 month) over a year period.
2.1 The overall average body composition changes of the 344 participants will predominantly be due to changes in body fat. Subsequently, the weight-change experienced by participants will be primarily due to changes in body fat.

2b. To estimate the weight-change of 344 healthy adults by using five bodyweight measurements over a 12-month period in a linear mixed model (LMM).

2.2 The LMM will give precise predictions of body composition. The LMM will take into account several measurements, which will adjust body composition predictions based on measure-to-measure variation in each participant.

2c. To define body composition change by grouping the trajectories (produced by the LMM) into ten (2 non-independent groups of 5 based on fat-change and fat-free mass change) groups: participants who are gaining substantial amounts of body fat, those who are gaining body fat, those maintaining body fat, those losing body fat, those who are losing substantial amounts of body fat, those who are gaining substantial amounts of fat-free mass, those who are gaining fat-free mass, those who are maintaining fat-free mass, those who are losing fat-free mass and those who are losing substantial amounts of fat-free mass.

2.3 The groups gaining body fat will have the most participants while the groups maintaining fat will have the least number of participants. Lastly, the values for the fat-gainer groups and the fat-stable groups will be highly correlated with the weight-gainers and the weight-stable groups.
Specific Aim 3

To access the association between changes in ES and average EE values during the time period of ES change.

3a. To determine whether participants categorized as gaining substantial weight or fat have different associated total daily EE (with a SenseWear Mini Armband worn over a 10-day period at quarter-annual intervals) relative to the participants classified as weight or fat stable.

3.1 The participants who maintain bodyweight over the year period will have the higher relative total daily EE.

3b. To determine whether participants categorized as gaining substantial fat mass have different total daily EE (with a SenseWear Mini Armband worn over a 10-day period at quarter-annual intervals) relative to those who are maintaining fat-mass.

3.2 The participants who maintain body fat over the year period will have the higher total daily EE.

3c. To determine whether participants categorized as gaining substantial bodyweight derive a higher percentage of their total daily EE (recorded with a SenseWear Mini Armband worn over a 10-day period at quarter-annual intervals) from sedentary activities relative to participants classified as weight-stable.

3.3 The participants gaining substantial bodyweight will derive a higher percentage of their total daily EE from sedentary behavior.
Scope

The current investigation is limited to describing the estimated rate weight-change, body composition changes and the influence varying levels of activity EE has in a group of 344 random 21-35 yr old healthy adults over the course of 12 months time. Extrapolation of these results to the general population, other age groups, or individuals with specific disorders should be made with caution.

Literature Review

In the past century obesity has ascended from a relatively unknown disorder with prevalence rates so low that no records were kept, to a prevalence of over 500 million people worldwide (19). The World Health Organization (WHO) has recognized obesity as being the 5th highest cause of death in the world, with over 2.8 million lives being lost a year. Obesity is not just a problem of carrying excess adipose tissue; obesity is also linked to an extensive list of chronic diseases and disorders. Diseases such as type 2 diabetes (TD2), heart disease, stroke, osteoarthritis, dementia, Alzheimer’s, colon and breast cancer and many others are associated with obesity (20;20-25). Obesity also comes with an enormous economic cost as well. When the yearly medical costs of an average sized adult are compared to that of an obese adult, on average the medical costs for the obese individual is 30% greater than that of the regular-sized adult (26). Further, by 2030 the total additional healthcare costs of obesity for the U.S. are estimated at 48-66 billion (Both references failed to adjust these values for the beneficial effects of exercise) (19).
The economic and health related numbers reveal obesity as the true public health threat that it has become.

While many of the problems associated with obesity are clearly established, the etiology of obesity is less than clear. How did a disorder with such a low prevalence for thousands of years suddenly erupt in the past twenty years, rising to one of the biggest public health problems of the century? The etiology of obesity is extremely complex, with interactions occurring between environment, behaviors, genetics, epigenetics, changing physiological conditions and several other factors. Changing environmental factors such as declining rates of physical activity, declining rates of total daily EE, increasing energy density of foods, increasing total daily EI, the presence of toxins in our drinking water, changes in macronutrient composition of diets, even the proposed existence of an obesity virus may also play central roles for the rise in obesity (27-32).

While the causes of obesity are still being sifted out, the measurement and monitoring of ES are still misunderstood as well. Proper measurement and examination of ES change is essential for understanding obesity and future prevention of the disorder. The remainder of this review is dedicated to giving an extensive look into the maintenance and measurement of bodyweight and composition. Additionally, this review focuses on the measurement of EE and the potential association between EE and ES.

**Bodyweight**

Bodyweight is the most commonly used marker of ES change. The maintenance of bodyweight is a crucial aspect of survival in most mammals including humans. In addition, weight management is stressed by most organizations in order to avoid obesity.
While bodyweight changes can indicate an energy storage change, the two are not interchangeable. Acute changes in bodyweight can occur strictly because of inter and extra-cellular water changes which have no effect on the total amount of body energy. Researchers have seen diurnal variations in bodyweight due strictly to body water changes of roughly 5lbs, this is without a concerted effort from the participant to change weight during the measurement period (13). Individuals making a concerted effort to change their weight can have much more dramatic fluctuations. A investigation using high school wrestlers found that in a 12hr period (from weigh-in for the competition until the actual competition) the competitors gained an average of 2.2±1.7% of their bodyweight, with the biggest gain being 7.2% of their original bodyweight (14). These acute fluctuations in body water can confound changes that appear to be due to energy storage alteration. However, sustained changes in bodyweight do typically mean changes in energy storage.

The importance of bodyweight in relation to obesity can be seen with organizations such as the WHO, Center for Disease Control (CDC), and the Obesity Society and how they categorize obesity. These organizations and subsequently most of the world use BMI, which is directly dependent on bodyweight to classify obese and non-obese individuals.

In 1980 the United States Department of Agriculture (USDA) and the U.S. department of Health and Human Services worked together to create the U.S. dietary guidelines. The new guidelines used a formula known as BMI to determine whether an individual was overweight or not. BMI was originally created in the 1830’s by Belgian Adolph Quetelet for purposes not related to obesity. Quetelet wanted to define the
‘normal man’ in every way possible including the average overall size; as a result he came up with the BMI scale. While quest to find the average man was extremely important to Quetelet, the information was largely useless to most researchers, and because Charles Darwin had not yet released his fundamental text *The Origin of Species* and his ideas on evolution, the research was only pertinent to individuals of that time period. Therefore the BMI scale was largely overlooked for the majority of 1800’s and 1900’s. Mainly the method was ignored because as previously mentioned during the 1800’s and early 1900’s there was no tremendous need for a method of defining obesity. However, by 1972 obesity was slowly moving to the forefront of public health in the developed world, requiring a method for defining the disorder. That year the previously mentioned Ancel Keys, who was already renowned in the scientific-community for his association of saturated fats, coronary artery disease (CAD), and cholesterol, released a investigation promoting BMI as the best indication of an individual’s body fat and subsequently their future risk for certain chronic diseases (18). In this investigation Keys et al. states explicitly that BMI to explain an individual’s relative body fat only works for population studies, on the individual level there is too much variation and BMI becomes inaccurate. The idea that BMI could evaluate obesity on a population scale was embraced and the previously mentioned 1980’s Dietary Guidelines had markers for what ideal body fat based on BMI, anything under 25-26kg/m² was considered ideal for males. The BMI values for ideal, overweight and obese have been changed a redefined by several associations over the past 34 years (103). Typically there are two values that organizations can base cut-offs for obesity and overweight, one is criterion standards and the other is reference values. Reference values are typically based on observed population
distributions of measured weights. In contrast, criterion standards are based on the relation of weight to morbidity or mortality outcomes. While there is a benefit of using BMI for population estimations of obesity, BMI is unable to clinically diagnose an individual with obesity, even though most physicians use BMI as a clinical diagnostic tool. Obviously, since BMI only takes into account height and weight, there is no actual measure of body fat. Rothman et al. considers there to be three major issues to consider when using BMI, [1] errors stemming from the fact that BMI is an indirect measure of obesity, [2] errors in self-reported data and [3] the poor sensitivity and specificity of BMI. There are several instances in the regular population where misclassifications can occur with BMI, with aging body fat is typically gained and muscle is typically lost (104). There is a strong relationship between BMI and body fat, but that relationship is not linear. Once BMI passes a certain level body fat no longer increases with BMI (105). While BMI values are usually correlated with body fat values on a population level, body fat is more important marker of obesity on the individual level.

If current markers of obesity are used on old measurements of weight and height, the values of obesity look different. Some of the first reliable height and weight measurements came from population estimations at the beginning of the 1960’s through the used off the National Examination Survey (NHES). From 1959-1962 the NHES conducted surveys on body measurements and other predictors of chronic disease. The survey revealed that the average BMI for a male in the early 1960’s was 25.14±3.87, while the average BMI for a female was 25.14±3.87. The obesity in the time frame of 1959-1962 was estimated to be 16% for females and 10% for males (102;106). These measurements would estimate that the average U.S. citizen was overweight by the current
BMI cut-points. A similar study very similar to the NHES was begun in 1971 called the National Health and Nutrition Examination Survey (NHANES). Like the NHES before, the NHANES data looked at risk factors, medical, dental and physiological measurements. However unlike the NHES the NHANES combined the interviews with physical examinations. By the first recorded measurements of the NHANES in 1971 the BMI for women had gone up to 25.05±5.54 and the BMI for men had risen to 25.56±4.14. The rates of obesity in 1971 also increased for 17% in women and 12% for men. By 1988 when the third round of NHANES statistics was being collected the mean BMI for females was 26.17±6.09 and the average BMI for males was 26.36±4.85 with an estimated 23% of women being obese and 18% of men. Throughout the 1990’s obesity exploded, the average BMI for females was 28.34±7.13 and the average BMI for males was 27.75±5.57. Obesity prevalence in 1999 was estimated at 34% for females and 27% for males. Over an 8 year period from 1991 to 1999 the obesity rate increased an average of 10% for the American population.

According to the behavioral risk factor surveillance system the estimated average obesity rate for both males and females was 11% in 1990 and by 2000 it was hovering around 30%. The current estimates for obesity in America hover at roughly 35%. Despite having slowed down over the past 15 years the prevalence of obesity is still expected to increase dramatically over the next 20 years. Finkelstein et al. estimates that over the next 20 years there will be a 33% increase in the total prevalence obesity, meaning that nearly half the population will be considered obese (2). An even more staggering estimation was performed by Wang et al. who estimate that by 2030 over 90% of the country will be overweight and 51% will be considered obese (107).
Numerous studies have investigated the overall weight change of adults. On average, bodyweight increases have been documented in humans well into the seventh decade of life (36). The practice of closely monitoring bodyweight and its relation to mortality and morbidity are attributed to insurance companies over 70 years ago (36). These records of weight-change show increases in bodyweight in the average adult throughout the adult life. Steady weight-gain throughout adult life has been viewed as physiologically normal (37). Most weight-change studies in America have used cross-sectional measurements overtime to look at average change in the population. These original research papers show small yearly weight-changes of roughly 1-2 kg (16;38).

While many researchers have assumed these changes to be normal and attributed them to a slowing metabolic rate, others attribute these changes as a primary reason for obesity pandemic and point to a low energy flux as the reason for the slow weight-gain (5). Better assumptions and predictions regarding ES change can be made when body composition is measured.

**Body Composition**

While obesity is classified by the WHO using BMI (height and weight measurements), they define obesity as abnormal or excessive fat accumulation that may impair health. As previously mentioned, the use of BMI for the classification of obesity was first promoted by the Ancel Keys. Organizations like the WHO, Center for Disease Control (CDC), Obesity Society, American Heart Association (AHA), and the American Obesity Association (AOA) all define obesity as an excess amount of adipose tissue, yet classify it based off of height and weight (BMI) (39). Because of their high-cost and
sometimes impractical nature, no actual methods of body composition measurement have
been used in large-scale epidemiological studies or for regular obesity-related clinical use
(40). Nonetheless, measurement of body composition and its changes over time are just
as critical in understanding the true etiology of obesity and disturbances in EB.

Obesity has been viewed as a severe health risk for thousands of years (41), but
more recently the reasons for the connection between obesity and health have emerged.
Researchers have shown that both the total amount of body fat and the level of physical
fitness are independent health risk factors associated with obesity. There is a clear
association between obesity and physical inactivity and a large body of evidence
indicates that the level of physical fitness is the most crucial aspect in determining all-
cause mortality and morbidity independent of bodyweight or composition (42-45).
However, some researchers have shown that the total amount of body fat may influence
all-cause mortality and morbidity independent of the level of physical activity (40;46-48).
The relationship of total body fat and health risk is less clear than the relationship of
physical fitness and health risk.

Attempts to accurately measure body composition began several hundred years
ago, but accurate non-invasive measurements have only been available for the last few
decades (49). Currently, body composition is looked at on a five-level system with each
level increasing in complexity. When viewing body composition in this system, the five
levels are: whole-body, tissue-organ, cellular, molecular, and atomic. Thanks to the
advances in technology and understanding of body composition, the human body can be
examined at all five levels with varying degree of accuracy today. However, this was not
the case 70 years ago when the monitoring of body composition first began. Human body
composition actually began with attempts to accurately measure the body composition of fish. Researchers investigating a way of determining the oil content of fish created a ‘two-compartment’ model to describe the characteristics of the body composition of the fish (49). Albert Behnke (often considered the father of modern body composition measurement) developed an underwater weighing system (hydrodensitometry) that included adjustment for residual air trapped in the lungs for humans based off the ‘two-compartment’ model that divided the body into fat-free mass (FFM) and fat mass (FM) (50). Behnke’s development was essential for understanding body composition. Several years later in 1953, Keys and Brozek discovered that the FFM, unlike the FM was not heterogeneous, FFM contained water, protein, minerals and carbohydrates (51;52). Even though the composition of FFM was considered heterogeneous the density of FFM was considered to be stable and consistent from person-to-person. Much later due to better technology, researchers were able to discern that the FM was divided into fats and nonfat lipids and determine that FFM density was not the same (53). However before these discoveries Siri determined the density of FM as roughly 0.9 g/cm³ and the density of FFM as 1.1g/cm³. The determination of these densities led to the accurate estimation body composition based off of density and the foundation of all two compartment body composition estimations.

In the late 1950’s Siri determined that body composition could be more accurate than just a two compartment model, he divided the model into a three compartment model by separating the FFM into lean mass and non-lean mass (54). Later a four compartment model was constructed separating FFM into water, bone, bone mineral and non-bone (55). Currently, in order to gain the most accurate measurements of body
composition researches estimate the densities of a six compartment model including: fat mass, water, bone mineral, lean mass, soft-tissue minerals and glycogen (56). Ultimately multi-component models were created to provide estimates on various components of FFM and the more components that are included the more accurate the models become.

While the multi-compartment techniques are very accurate, for the majority of clinical purposes the use of simple two compartment model is more cost effective and is typically favored. The two-compartment model has remained relevant in research predominantly because of the pandemic of obesity and the overarching health problems associated with excess adipose tissue. The accuracy of the multi-compartment models is lost in the two compartment model because the assumption must be made that FFM has a consistent density. Nonetheless, some of these two-compartment techniques still give very accurate estimations of FFM and FM. The measurement of FM remains difficult for most measuring tools; on the contrary FFM is easier to measure. Subsequently, most methods estimate FFM and then subtract the FFM from total mass to estimate the FM (55). Total body water, hydrostatic weighing, urinary creatinine excretion, total body potassium and skinfold measurements all use the two-compartment model to estimate FM and FFM.

As previously mentioned hydrodensitometry is the oldest technique which utilizes the two-compartment model. Because it the oldest technique for estimating body density it is often viewed as the gold-standard even though other techniques are more accurate. The practice of underwater weighing requires the subject to be completely submerged in water. The volume of water displaced once the subject is underwater is then used to calculate the overall body density. Because of the already mentioned variations in FFM
density several assumptions must be made based off of ethnicity, growth, sexual maturation, physical activity and disease (57;58).

At roughly the same time hydrodensitometry was being developed and implemented the techniques for total body potassium measurement were also being made. The analysis of total body potassium (TBK) was not possible until the practice of nuclear weapons and facilities required workers to be monitored for radioactivity. To facilitate this need of monitoring radioactivity in workers, whole body counters were created. Soon after the monitors were created it was noted that a constant peak of radiation was being emitted from all workers independent of exposure levels, this peak was due to $^{40}\text{K}$. Researchers soon connected the potassium isotope with levels of lean mass, and made the assumption that potassium levels were constant throughout lean mass. However, like many assumptions in body composition the idea that potassium levels were constant throughout lean mass was also disproven (59;60). When using potassium as a predictor of lean mass the researcher is truly looking at the working body cell and estimating the amount of FFM (55) The benefit of TBK is the overall precision of measurement. TBK has the highest precision of the two-compartment techniques, but the drawback is the accuracy has been shown as less than stellar (61;62).

In a fashion similar to TBK, total body water (TBW) has also been used to estimate FFM. The water compartment of the body makes up roughly 73% of FFM and 60% of the total body weight, so the use of TBW to estimate total FFM and total body composition affords usable values (63). However, the amount of water in FFM and the total body is not consistent with age, race, muscle mass and several other factors. In addition the inter-individual variation of TBW is extremely high due to hydration status,
food choice and medication status. However, while TBW varies from day to day in an individual the hydration ration (TBW/FFM) remains relatively constant. Typically TBW is measured by using the dilution principle using a tracer dose of labeled water and the collection of blood, urine or saliva. The radioisotopes (tritium, deuterium, or oxygen-18) are very expensive, and like TBK their use does not afford the greatest accuracy. Typically, there is a standard error of roughly 10% associated with absolute fat mass measurement using TBW (55).

Another technique using the two-compartment model is skin fold-measurements. Like the previously discussed techniques, skin fold measurement estimations of body composition are made with numerous underlying assumptions. The previously mentioned researchers Brozek and Keys were the first to use skinfold calipers for body composition estimation in 1951 (64). Like TBK and TBW, this method makes an assumption. Skin fold measurements assume that subcutaneous fat is directly correlated with total body fat. Like the assumptions made for TBK and TBW the correlation assumption for skin folds has been disproven as well.

The multi-compartment models are used more often in clinical settings relative to the two compartment techniques. The most recognized of these techniques include DXA, computerized tomography (CT) scan, and magnetic resonance imaging (MRI). Out of the three multi-compartment models the DXA is the most widely used. Most DXA scans provide estimates of soft, lean, bone and fat tissue. The DXA scans are very accurate, but they are also expensive and expose the participant to very small amounts of radiation (65). The CT scan actually is more accurate in estimating body composition because the scans have the ability to delineate organ size, calculate fat and muscle distribution and
bone size. However, the CT equipment is more expensive than DXA equipment and the participant is exposed to more radiation. The MRI is arguably the most accurate of the three mentioned multi-compartment models. The associated downside of the MRI is that they are expensive and take longer than the other two scans. Along with the CT scan they share the distinction of being able to accurately estimate visceral fat because they take a three-dimensional scan. Visceral fat has recently been independently linked to many chronic diseases and disorders (66), so the ability to differentiate between visceral and subcutaneous fat is extremely vital to health. More recently DXA scans have acquired the ability to quantify visceral fat, but are assumed by most to be less accurate because the DXA scan only scans in a 2-dimensional field unlike the MRI and CT scans (67).

The association between body composition and energy expenditure

Collectively the energetic costs of all biological processes are the total EE. The largest component of total EE takes place in the resting phase known as resting metabolic rate (RMR). This component typically comprises roughly two thirds of total daily EE. RER varies widely between individuals, mainly due to size, and body composition (7). Typically, increases in lean mass cause substantial increases in RMR (8). Along with RMR the thermogenic effect of food (TEF) also contributes to total EE. TEF is the EE associated with the digestion and absorption of food, contributing roughly 10% of total EE. The largest influential factor affecting TEF appears to be varying levels of macronutrients; an example being the level of alcohol consumption. Increasing alcohol consumption increases total EE, but also increases the amount of fat stored in the body (9;10). Lastly, representing 20-30% of total EE is the active energy expenditure (AEE),
which represents all the energy consumed in activities requiring more than resting energy level. AEE is typically segmented into exercising activity and non-exercising activity (6).

The techniques for measuring EE began nearly 400 years ago. Robert Boyle took mice and sealed them in glass jars, not surprisingly the mice died. Along with mice Boyle placed a candle and noted that the lives of the mice vanished at the same time as the flame of the candle. From this experiment Boyle arrived at two conclusions, first, that human life is combustible like a candle flame, and second that human life requires air (113). The work of Boyle was quickly followed by the work of John Mayrow, who performed a similar experiment to that of Boyle. Mayrow placed mice in sealed jars, but recorded the changes in air in the jars, and found that mice died once they had consumed roughly one fourteenth of the air in the jar. Mayrow, correct in his deductive reasoning concluded that the air must consist of different parts. The work of Mayrow eventually led to the first respirometer which quantified the consumed portion of air (114;115).

The elementary yet vital experiments Mayrow were followed by the experiments of Lavoisier and Seguin nearly a century later (116). Lavoisier was a chemist enamored with the process of combustion. Lavoisier and his admiration of combustion eventually proved the phlogiston theory to be obsolete (117). The phlogistion theory was founded in alchemy and hypothesized a fire-starting element was present inside of all combustible entities and when combustion took place the phlogiston was released. Lavoisier was intent on finding the true process of combustion in humans. Through countless studies Lavoisier found that heat was produced between the steps of inhaling and exhaling and that gas was exchanged. Eventually, Lavoisier was the first to describe a resting metabolic rate (RMR), a resting VO2, and differences in these values between individuals.
of varying physiological attributes. Perhaps the most important attribute of the investigations made by Lavoisier was the founding of methodology for indirect calorimetry and the measuring of EE in humans (114). Indirect calorimetry was continually improved upon throughout the 18th and 19th century where Wilbur Olin Atwater, a research chemist at Wesleyan University started using the methodology of indirect calorimetry. Dr. Atwater unlike Lavoisier and Boyle before him was extremely interested in human nutrition and composition of EI. While investigating EI, Dr. Atwater inadvertently started studying EE as well using indirect calorimetry. With a 4 x 8 foot container that measured oxygen consumption and carbon dioxide production, and energy expenditure of humans. More importantly Dr. Atwater was one of the first scientists to truly measure the interplay between EE and EI. While many of his advancements on indirect calorimetry and EE still stand today, most of his beliefs on nutrition have been proven false (118).

Predominantly, the measurement of oxygen consumption that was used in the 18th and 19th century is still used today. While the instruments have become more sophisticated and open-flow systems are used in place of closed systems, the concepts and general principles remain. The measures of EE were advanced upon by A.V. Hill and the measurement of oxygen consumption and EE during different levels of athletic performance (119). Interestingly, in the late 1920’s there was an increased EE following exercise and found that EE rate was steady during exercise as long as the intensity was below metabolic threshold. While Hill’s research discoveries further elucidated the mysteries of human EE, indirect calorimetry fell short when trying to truly measure total daily EE. Being restrained to a small container or strapped to Douglas bags for the
purpose of measuring oxygen consumption limited the capacity of testing EE. However, around the time of Hill’s discoveries the use of direct observation began to be used to measure the EE of physical activity.

Direct observation of physical activity is a very labor intensive job requiring several skilled observers to record the activity being monitored. These methods of accessing activity have mostly been used when evaluating the activities of either team sports or of industrial workers who have highly repetitive movements. Many of the early studies were initiated to improve work efficiency to improve profits. Frank Gilbreth and Frederick Winslow Taylor performed many of these original investigations with the primary motive of improving work efficiency (120). The goal was not to solely track the amount of energy expended, but to track the movements that were unnecessary. The skilled observer would also carry a stopwatch to find the minimum time in which the skill could be performed, then work out notes on how the worker could possibly reach that minimum time. Frederick Winslow Taylor was so consumed with this concept of making tasks faster that he was known to constantly have a stopwatch around his neck. While these studies were the foundation for time-and-motion studies, none of the experiments were focused on the EE of the employees.

In 1931, William Giaque and Herrick Johnston isolated two different isotopes of oxygen, followed in the same year by the discovery of deuterium (hydrogen isotope) by Harold Urey (121). These isotopes were not well understood at the time, primarily because the neutron had yet to be discovered. Nonetheless these isotopes were extremely important; primarily because of their heavier mass they could be tracked and followed through biological processes. Even though they were discovered in the early 30’s they
were relatively unused in humans until the beginning of the 1950’s because of their price and lack of availability. Coincidentally the Second World War and the development of atomic weapons solved most of these problems. In 1949 Lifson et al. injected mice with stable isotopes of oxygen and forced them to breathe air enriched with heavy oxygen. The end result of these experiments was there was a dose of oxygen isotope introduced into the body is removed by the rates of water flow, inspired oxygen and carbon dioxide (122). This result was the foundation of what would become the doubly labeled water technique (DLW). Introducing both an isotopic labeled oxygen and isotopic hydrogen into the body the labeled oxygen would be eliminated by the production of both carbon dioxide and water. However, the isotopic label of hydrogen would only be eliminated by water; therefore the difference of the elimination rate of the two isotopic labels would be able to measure carbon dioxide production and indirectly EE. Six years after the seminal research paper a working DLW methods paper was performed measuring carbon dioxide production by the standard respirometry and the DLW technique (123). Through the results of this research showed the DLW technique extremely correlated with standard respirometry. However, the true significance was that EE could now be accurately measured without being restrained to the confines of a respiratory chamber.

Even though the methodology was available after the initial Lifson et al. study in 1949, the first DLW study to measure animal metabolism was not performed until 1965. Further the method was only used by researchers from Lifson’s research group until 1970 (115). Without a doubt the DLW technique is one of the most, if not the most, accurate method for estimating EE. However, even though the method was extremely accurate, the
method was only cited sparingly throughout the 70’s and 80’s in scientific literature (115). The reason this method was so rarely used is the enormous price tag it carries.

Regardless of measurement methods, EE is a process of energy production from energy substrates (carbohydrates, lipids, proteins, and alcohol) combustion, in which there is oxygen consumption and carbon dioxide production. This results in part of the energy being lost as heat, and the remaining energy being stored in the high-energy bonds of the ATP. The total energy required for an organism to function can be divided into three components, RMR, TEF and AEE. The RMR is the minimal energy required for body vital function maintenance. In an average-sized human the RMR represents roughly 60-70% of EE for those who are sedentary and roughly 50% for those who are physically active. As previously mentioned the original RMR measurements were performed by Lavoisier with indirect calorimetry. However early in the 20th century several intricate and advanced(for their time) investigations were coordinated by Francis G. Benedict in the Nutrition Laboratory of the Carnegie Institution of Washington (124). The purpose of these studies was to develop a database which could be used to establish normal standards for RMR and be the basis for RMR prediction equations (125). Amazingly, while other prediction equations have been generated since the creation of the Harris-Benedict studies (126), the original equations are still heavily used today to estimate RMR. With some specific populations the Harris-Benedict prediction equations have been shown to not accurately predict RMR (127). Nonetheless, these studies revealed the impact of RMR on total EE, showing that over 60% of calories are dedicated to resting maintenance of the body. In addition, the Harris-Benedict studies found that RMR varied heavily with several factors including ethnicity, weight, lean body mass, age, smoking
habits, physical activity levels, diet, and environmental temperatures have all been shown to affect an RMR.

While RMR has been shown by many investigations to be influenced by ethnicity (128), the extent to which it influences RMR is open to speculation. Some investigators reason that when other factors that influence RMR are accounted for except for ethnicity, what are left are phenotypes not genotypes. Although ethnicity is a social way in which humans recognize visual characteristics, they are not all genetically homogenous (129). Unlike ethnicity, bodyweight and overall size have been repeatedly shown to substantially influence RMR (130;131). Generally, a higher bodyweight results in a higher absolute RMR. However, when looking at RMR per kg of bodyweight the RMR does not have as strong a relationship with bodyweight. The most influential factor regarding RMR is the amount of lean mass on an individual (8). The more lean muscle mass an individual carries the higher the RMR. Even at rest muscle is substantially more metabolically active than adipose tissue which causes these dramatic rises in RMR. Some researchers postulated that the major differences in seen in fat-free mass are due to different sizes in the very metabolically active tissues like the kidneys and the heart (132). However, multiple investigations have shown that when these metabolically active tissues are accounted for the prediction equations for resting energy expenditure are no better than the equations created with simply fat-free mass not accounting for the metabolically active organs.

The TEF is also known as diet-induced thermogenesis and is defined as the increase in RMR following consumption of a meal (133). The previously mentioned Seguin and Lavoisier were the first to show that oxygen consumption was increased
following a meal (134). More studies followed Lavoisier, showing that meals high in protein caused greater increases in TEF than meals high in carbohydrates and fats. Wang et al., was the first to question whether TEF played a role in obesity(135). The research group eventually concluded that TEF played an insubstantial role in the development of obesity. The responses of TEF are based on the activation of the sympathetic nervous system, and there are known differences between obese and non-obese individuals in the activation of the sympathetic nervous system (136). The TEF is thought to represent a total of 3-10% of total EE, while this seems like a relatively small amount of calories there are researchers that think TEF plays a substantial role in the development of obesity (137). Many factors have been shown to affect TEF, one of the most substantial variables is the size of the meal being ingested. D’Alessio et al. found that when a 1000-kcal meal in consumed the fasting values accounts for roughly 10% of the total EI and this percentage increases with an increasing caloric value (138). As previously mentioned the macronutrient composition of a meal has also been investigated as far as the influence on TEF. Proteins have the largest effect on TEF, while carbohydrates increase the value less. Interestingly, it appears that fat has very little effect on the TEF (139-141). In addition to the size, caloric and macronutrient content of a meal the meals of the day preceding measurement appear to make a noticeable difference. Some researchers also hypothesize that the amount of carbohydrate currently stored in the form of glycogen will dictate how much TEF increases. This shows that the conversion of glucose to lipid instead of glucose being converted to glycogen before being oxidized requires a greater amount of energy (142). Body fat also influences TEF and has negative correlation that appears to
be independent of insulin resistance, however, insulin resistance combined with a high body fat have shown extremely reduced values of TEF.

The last component of total daily EE is AEE, which on average comprises roughly two-thirds of total daily EE. Typically AEE is further subdivided into exercise EE and NEAT. For the vast majority of the world exercise EE has been negligible for centuries, and NEAT has been the predominant component of AEE (143). Even in modern society including the most passionate athletic exercisers, NEAT still includes the majority of calories included in AEE. NEAT includes every aspect of being an animated human including all activities in daily life except for planned programmed exercise. Because this obviously includes an extreme wide-variety of activities often times it is difficult to define the parameters and how influential NEAT is to total daily EE. In addition, NEAT is the most variable component of EE both within individual measurement and between individual measurements. Interestingly, humans and animals seem to vary enormously in the amount of spontaneous physical activity they accumulate. Further, NEAT unlike exercise, may not require regulation from the higher cortex for the brain, but instead from more autonomic brain sites such as the hypothalamus. Some researchers believe that unconscious and volitional movement are under homeostatic regulation and may be switched on or off in response to under or overnutrition (144). While the theory that the brain regulates all NEAT in response to fluctuations in eating there is relatively no testing supporting or negating this idea. Another interesting theory is that NEAT is an intrinsic trait set by genes, and inherited at a different level for each individual. However these levels of NEAT interact and fluctuate with the environment (145). Those individuals who fidget more or spend more time
standing are more resistant to gaining weight than others (146;147). Intriguingly, both theories have been supported by research. Regardless of the complete validation of either theory it appears that there is a large neural component contributing to the control of NEAT.

EE and ES are two of the three critical variables of the EB equation. Typically the EB equation is viewed as ΔES=ΔEI-ΔEE, meaning that with concerted efforts to change EI or EE a direct change in ES will be made. The regulation of the three variables of the energy balance equation is heavily controlled by the endocrine system, the gut biota of the gastrointestinal (GI) tract and the higher functioning centers of the central nervous system (CNS). However, this is beyond the scope of the current review, for more information on the regulation of the EB equation the reader should refer to the listed references (4;68-71). There is an inherent efficiency to this regulation, and many researchers believe that energy balance is best regulated for weight maintenance at a high energy flux. Energy balance was left largely uninvestigated until the 1950’s. Jean Mayer, Ph.D., D.SC, was one of the first to investigate energy balance and the etiology of obesity. Mayer recognized that while an inflated EE realized through increased physical activity generally results in an equivalent spike in EI, this does not always occur. His previous animal studies show when rats are exercised on treadmills for incremental predetermined volumes, EI varies linearly with exercise only within certain limits of activity (108). Low enough activity levels termed the “sedentary” range do not evoke a subsequent decrease in food intake, instead caused a substantial increase. Further, the energy imbalance within the sedentary range resulted in an increase in both weight and fat content of the rats. While intriguing, these experimental results had not been
explicated in humans; leaving the possibility that this was purely a rat phenomenon and had no translation.

In the 1956 manuscript *Relation between Caloric Intake, Bodyweight and Physical Work: Studies in an Industrial Male Population in West Bengal*, Mayer et al. investigated the energy balance of 213 male workers of the Ludlow Jute Co., Ltd., at Chengail, West Bengal (109). The workers of the West Bengal factory had an extreme range of physical activity demands within the confines of their jobs allowing Mayer et al. to attempt to correlate physical activity with food intakes and bodyweight. The workers were divided into five roughly even-sized groups (Sedentary, light work, medium work, heavy work and very heavy work) based upon their general daily physical activity. The EI of all five groups were obtained through dietary interviews. Additionally, their diets were analyzed for the amounts of animal protein, vegetable protein, total protein, fat, carbohydrate, calories, thiamine, riboflavin, niacin, and vitamin C. Along with activity level and EI other information was obtained including height, weight and various socio-economic parameters.

Bodyweights of the Indian workers recorded as a function of physical activity displayed an exponential decline with increasing physical activity, showing an asymptote in bodyweight starting at the light group workers. The discrepancy between the sedentary group and the activity workers is also seen in their BMI. The four working groups hold BMIs of approximately 20, while the sedentary group hovers around a 25. The caloric intake as a function of physical activity results mirrored those of the previous animal studies. Between groups there were two established zones, the normal activity zone and the sedentary zone. The normal activity zone containing the light work, medium work,
heavy work and very heavy work groups revealed a linear relationship among physical activity and EI. The lightest workers in the normal activity zone have the lowest calories consumed per day and the heaviest workers have the highest amount of calories consumed per day. However, once the workers level of physical activity dips into the sedentary zone the level of EI increases drastically, to a point approximately equal to that of the heavy workers. This research importantly highlighted the evidence that potentially there is an unregulated energy balance zone. Once the EE dipped into this sedentary zone the regulatory factors of the endocrine and CNS was unable to control EI. While the exemplary work of Mayer et al. helped reveal some of the associations between EE and ES, the relationship is still not completely understood. The association between changes in ES and levels of EE need to be explored.
CHAPTER II:  
METHODS

Overall Methods:

The Energy Balance Study

The current dissertation will analyze data that was collected as a part of The Energy Balance Study in an effort to elucidate the previously mentioned aims. The primary outcome of The Energy Balance Study was to clinically monitor changes in bodyweight and composition among young healthy adults. In addition, try to measure the extent to which total daily energy expenditure (EE) and total daily energy intake (EI) contribute to the measured bodyweight and composition changes. The aims of this dissertation closely follow the overall aims of The Energy Balance Study, mainly how is the bodyweight and composition changing over a year. The steep rise in obesity prevalence over the past two decades has revealed that Americans are gaining weight consistently. However, the exact amount of weight-gain and the rate at which the weight is gained is unknown. Energy storage (ES) change is nearly impossible to predict with only two bodyweight measurements. Dramatic daily fluctuations in total bodyweight are caused by other factors aside from changes in ES, mainly water. With up to 65% of the body being comprised of water; changes in hydration level greatly affect overall bodyweight. These rapid changes in body water conceal the true trajectories of ES
Several questions remain regarding weight-gain and obesity. These questions remain because there have been almost no studies with precise repeated measures of bodyweight and composition in a clinical environment arranged in a longitudinal study design. The Energy Balance Study is a clinical longitudinal study attempting to measure the potential variables of weight gain and energy balance more accurately than ever before.

Sample Population

The study recruited 430 healthy young adults (344 participants will be used in the analysis of the three aims), age 21-35 years, with a body mass index (BMI) of 20-35 kg/m². The recruited participants who completed their baseline had an average age of 27.7±3.8 yrs. The gender distribution of the participants was 212 males and 218 females, while the racial distribution was 66.5% were Caucasian, 12.6% were African American, 10.7% were Asian, 3.0% Hispanic and the remaining 7.2% were reported as other or mixed. Educationally, the sample population was comprised of 83.7% college graduates. Lastly, the majority of participants (85.1%) did not have children and were not married (52.1%).

The inclusion and exclusion criteria were generated in attempts to recruit participants who would be healthy enough and available to participate for at least one year of clinical measurements. The final exclusion criteria incorporated into the study design were the following: medications used for weight-loss, started or stopped smoking within 6 months of beginning the study, any type of weight-loss surgery, moving from
the area within the next 15 months, hypertensive (150mmHg systolic and/or 90mmHg diastolic), currently diagnosed or taking medications for a major chronic health conditions, history of depression, taking selective serotonin reuptake inhibitors, ambulatory blood glucose levels $\geq 145$ mg/dl, giving birth within the 12 months, planning to start or stop birth control in the next 12 months while participating in the first year of the study. The Energy Balance study protocols were approved by the University of South Carolina Institutional Review Board.

For the current set of studies, the analyses will include all participants who completed the measurements for bodyweight and composition, and wore an armband activity monitor for each of the measured time points (baseline, 3m, 6m, 9m and 12m). Lastly, outliers will be removed on per aim basis depending on the measurements being used.

Study timeline

After baseline measurements, participants will be measured roughly every three months over a year period. This dissertation will include data collected through the 12 month assessment. Table 2.1 includes all of the measurements that will be taken and Table 2.2 includes all of the questionnaires that will be administered. The following are detailed descriptions of all measurements to be used in the analyses for the current dissertation.
Anthropometric Measurements:

All anthropometric measurements for the five primary visits (baseline, 3, 6, 9, and 12 month) were performed with the participant dressed in a pair of surgical scrubs and bare feet. For all visits the BMI (kg/m²) was calculated from the average of three height and weight measurements using a traditional stadiometer and electronic scale. The values for both bodyweight and height were recorded to the nearest 0.1 centimeter and 0.1kg. Body composition was measured using a Lunar fan-beam dual X-ray absorptiometry (DXA) scanner (GE Healthcare model 8743, Waukesha, WI). The scans recorded total fat mass (FM) and fat-free mass (FFM), as well as torso, arm and leg composition. In addition, the scans recorded bone mineral density and content. For the baseline, 6 and 12 month visits the waist and hip circumference of each participant was measured. The waist and hip circumferences were measured using a calibrated spring-loaded tape measure. Waist circumference was determined at the point midway between the costal margin and iliac crest in the mid-axillary line approximately 2 inches above the umbilicus. Hip circumference was measured at the widest point around the greater trochanter. Circumferences recorded were the average of three measurements and were rounded to the nearest 0.1cm.

Energy Expenditure:

The Energy Balance study used three measurement methods for the estimation of energy expenditure (EE). The three methods included the SenseWear Mini Armband (BodyMedia Inc. Pittsburgh, PA), the ActivPal (small inclinometer), and doubly labeled
water (DLW). Because the Activpal does not give a true estimation of EE and DLW was only given to half of the participants, the SenseWear Mini Armband (BodyMedia Inc. Pittsburgh, PA) was used as the primary measure of EE. The portable, multi-sensor device is worn on the upper-left arm with the sensor itself resting over the triceps muscle. EE is measured using a combination of a tri-axial accelerometer with biological sensors measuring heat flux, galvanic skin response, near-body ambient temperature, and skin temperature. The various measures are then entered into an algorithm using a Naïve Bayes classifier for superior pattern recognition of estimating the context of an activity. The combination of sensors gives the Mini Armband an enhanced ability to detect a wider variety of activities (72). The detection ability of the Mini Armband has gone through laboratory, free-living conditions (against DLW), and been compared to other previously validated accelerometers. In a recent investigation by Johannsen et al. the SenseWear Mini Armband was compared to the EE values generated by the use of free-living DLW. The Mini Armband was exceptionally valid showing an average of 22 kcal/day difference in total daily EE, with error rates as low as 8.3±6.5%. The precise results culminated in a regression analysis showing an $R^2=0.71$ and intraclass correlations of 0.85. The intraclass correlations suggested that only 15% of the variance was due to the difference in DLW and armband methods, while the other 85% was due to differences among individuals (72).

At each measurement period the participants were instructed to wear the monitor for 10 consecutive days constantly for 24 hours except during water activities (i.e., swimming, bathing, showering, or water aerobics). When the participant did remove the monitor the participants recorded these periods in an activity log. Each participant was
instructed to record any time the armband was removed in as much detail as possible including the exact time the armband was removed and put back on. The non-wear activities were then incorporated into the estimations of EE based on corresponding MET values according to the 2011 Compendium of Physical Activities (73). The MET values were then multiplied by the participant’s own measured resting metabolic rate (RMR). The participant was considered to be compliant if they had seven days of (including 5 week days and 2 weekend days) at least 23 hours of verifiable time (either logged non-wear time or armband worn).

Specific Aim 1

To determine the overall weight changes that occurs over a year period in a group of 344 healthy adults.

Overview: 344 healthy men and women aged 21 to 35 years old with a BMI of 20-35kg/m² from the Energy Balance Study will be used. The participants were monitored for 12 months for weight changes and anthropometric changes. Each participant had laboratory measurements performed at five different time points including a baseline, 3-month, 6-month, 9-month and 12-month. The same clinical measurement protocols were followed for each measurement period to ensure consistency among measurements. For a full list and description of the measurements refer to Table 2 and the overall methods section. The 12-month data for participants who performed all measurement periods will be used for analysis. Once the 12-months of data are completed, the weight measurement at each quarterly measurement period including baseline will be used to construct a linear
mixed-model (LMM) for weight change. The model will use bodyweight as a dependent variable so that the interdependence of each measurement is taken into account. The LMM will calculate an overall average slope indicating the rate of weight-change for the entire population. The overall average slope will take into account the sum of the fixed slopes for the entire group. In addition, the individual’s slope will be calculated as well using the sum of the fixed (average) slope. The individual (total) slope, will be the sum of the fixed and random slope estimates, and will represent the rate of change in weight for each participant. Once the slopes are calculated the standard error (SE) of each individual slope will be computed as the square root of the sum of the variances for each estimate. The SE of the random slope estimate for each participant will be computed using the *predict* command’s *reses* option in STATA 13 (Stata Corp., College Station, TX).

Following the creation of the SE values, the participants will then be grouped based these values into five groups including substantial weight gainers, weight gainers, weight maintenance, weight losers, and substantial weight losers. The groups will be determined by comparing the participants projected bodyweight change, as calculated by the LMM relative to the SE. The participant’s weight-change will be categorized into five categories including: substantial weight-loss (SWL), weight-loss (WL), weight-maintenance (WM), weight-gain (WG) and substantial weight-gain (SWG).

*Research Design*

The Energy Balance Study was an observational longitudinal study consisting of 430 healthy men and women aged 21 to 35 years old with a BMI of 20-35kg/m². The group was followed for 12-months having measurements taken roughly every three months at
the time periods baseline, 3m, 6m, 9m, 12m. The participants will all measurements during the 12 months of data will be used for analysis. The weight will be gathered from the electronic scale measurements and the data will be used for a LMM which will provide rate of change trajectories for weight-change.

**Hypothesis**

1.1 The overall average weight-change of the 344 participants will be similar to estimates for the yearly weight gain of Americans, roughly 1-3lb.

1.2 The LMM will give predictions with less intra-subject variability and therefore a more precise rate of bodyweight change. The use of several measurements as opposed to two measurements will better account for intra-subject variation.

1.3 The overall amount of weight gainers will be greater than the other two groups. The weight-stable group will have the least amount of participants.

**Anticipated Outcomes**

The trajectories produced by the LMM will show that the total EB group has a greater amount of weight-gainers than when compared to weight-change using cross-sectional analysis of 12-month weight minus the baseline measurement.

The trajectories of weight gain will be similar across gender as well as the entire age range of the group (21-35yr).
Specific Methods

Anthropometric Measurements:

All anthropometric measurements for the five primary visits (baseline, 3, 6, 9, and 12 month) were performed with the participant dressed in a pair of surgical scrubs and bare feet. For all visits the BMI (kg/m^2) was calculated from the average of three height and weight measurements using a traditional stadiometer and electronic scale. The values for both weight and height were recorded to the nearest 0.1 centimeter and 0.1kg.

Linear Mixed Model Analysis for Weight-change Trajectory

A LMM will be used to analyze the estimated weight-change of the 344 participants over 12 months using 5 (Baseline 2, 3, 6, 9, and 12 month) of the time point weight measurements. However prior to solidifying the permanent mixed-effect regression model the measurements and assumptions made will be checked to ensure the residuals and estimates of the random intercepts are normally distributed. An iterative influence diagnostics performed on SAS 9.3 in order to identify any outliers or abnormal measurements. Because of the large volume of participants in the study the dates between follow-up measurements will be on slightly different days meaning the observations will be uneven. The mixed effect regression model accounts for these differences in measurement time making it a premier tool for analysis of longitudinal data. In addition, weight measurements vary depending on fluid retention, electrolyte balance, menstruation and other acute factors. These vary factors can cause deviations in the weight measurement that do not reflect a true increases or decreases in energy storage,
the mixed effect regression model accounts for these variations. The random-effects model will allow individual participants to have their own intercepts and slopes which allow for the precise changes that are needed to monitor weight over extended periods of time.

Grouping of weight-change

Once the trajectories from the LMM are created the participants will be divided based on gender and the amount of weight-change that was experienced during the 12-month period. There will be 5 specific groups of weight-change for each gender including: Substantial weight-gain, weight gain, weight maintenance, weight-loss and substantial weight-loss. The calculation of each participants slope and associated standard error (SE) will be used to categorize annual weight change into 5 categories: substantial weight gain (SWG) if positive and 95% CI excluded 0; weight gain (WG) if positive and 68% CI excluded 0; weight maintenance (WM) if 68% CI contained 0; weight loss (WL) if negative and 68% CI excludes 0; and substantial weight loss (SWL) if negative and 95% CI excludes 0.

Specific Aim 2

To determine the overall body composition changes that occurs over a year period to a group of 344 healthy adults.

Overview: 344 healthy men and women aged 21 to 35 years old with a BMI of 20-35kg/m² from the Energy Balance Study will be used. The participants were monitored for 24 months (however for this aim 12-months of data will be used) for weight-changes
and anthropometric changes. Each participant had laboratory measurements performed at 7 different time points including a baseline 1, baseline 2, baseline 3, 3-month, 6-month, 9-month and 12-month. The same clinical measurement protocols were followed for each measurement period to ensure consistency among measurements. For a full list and description of the measurements refer to table 2 and the overall methods section. The 12-month data for participants who performed all measurement periods will be used for analysis. Once the 12-months of data are completed, the body composition measurements at each quarterly measurement period including baseline will be used to construct a LMM for body composition. The model will use FM and FFM as two correlated dependent variables in a single multivariate model, so that a covariance matrix is formed for the residuals allowing FFM and FM to be correlated within person at each time point. The individual slopes for FM and FFM will be used to create ten (2 non-independent groups of 5 based on fat-change and fat-free mass change) groups: participants who are gaining substantial amounts of FM, those who are gaining FM, those maintaining FM, those losing FM, those who are losing substantial amounts of FM, those who are gaining substantial amounts of FFM, those who are gaining FFM, those who are maintaining FFM, those who are losing FFM, and those who are losing substantial amounts of FFM.

**Research Design**

The Energy Balance Study was an observational longitudinal study consisting of 430 healthy men and women aged 21 to 35 years old with a BMI of 20-35kg/m². The group was followed for 12-months having measurements taken roughly every three months at the time periods baseline, 3m, 6m, 9m, 12m. The participants will all measurements
during the 12 months of data will be used for analysis. The body composition will be gathered from the DXA measurements and the data will be used for a LMM which will provide rate of change trajectories for fat-free and FM.

**Hypothesis**

2.1 The overall average body composition changes of the 344 participants will exhibit changes in body fat similar to the changes seen in overall bodyweight. Primarily the weight gained by participants will be due to additional body fat.

2.2 The LMM will give a better representation of each participant’s true body composition changes as compared to a traditional simple cross-sectional measurement. The linear mixed model will include several measurements. The use of several measurements as opposed to two measurements will better account for random fluctuations and give a true determination of body composition changes over a year.

2.3 The three groups of fat gainers will have a greater amount of participants than the other 6 groups. The fat-stable groups will have the least amount of participants. The values for the fat-gainer group and the fat-stable groups will be highly correlated with the weight-gainers and the weight-stable groups.
**Anticipated Outcomes**

The trajectories produced by the linear mixed-effects model will show that the total EB group has a greater amount of fat-gainers than when compared to fat change using cross-sectional measurements of 12-month weight minus the baseline measurement.

The trajectories of fat and fat-free change will be similar across gender as well as the entire age range of the group (21-35yr).

**Specific Methods**

*Anthropometric Measurements:*

All anthropometric measurements for the 5 primary visits (baseline, 3, 6, 9, and 12 month) were performed with the participant dressed in a pair of surgical scrubs and bare feet. For all visits the BMI (kg/m$^2$) was calculated from the average of three height and weight measurements using a traditional stadiometer and electronic scale. The values for both weight and height were recorded to the nearest 0.1 centimeter and 0.1kg. Body composition was measured using a Lunar fan-beam dual X-ray absorptiometry (DXA) scanner (GE Healthcare model 8743, Waukesha, WI). The scans recorded total fat and FFM, as well as torso, arm and leg composition. In addition, the scans recorded bone mineral density and content. For the baseline, 6 and 12 month visits the waist and hip circumference of each participant was measured. The waist and hip circumferences were measured using a calibrated spring-loaded tap measure. Waist circumference was determined at the point midway between the costal margin and iliac crest in the mid-
axillary line approximately 2 inches above the umbilicus. Hip circumference was measured at the widest point around the greater trochanter. Circumferences recorded were the average of three measurements and were rounded to the nearest 0.1 cm.

Linear Mixed Model Analysis for Weight-change Trajectory

A LMM will be used to analyze the estimated body composition changes of the 344 participants over 12 months using 5 (Baseline 2, 3, 6, 9, and 12 month) body composition measurements. However prior to solidifying the permanent mixed-effect regression model the measurements and assumptions made will be checked to ensure the residuals and estimates of the random intercepts are normally distributed. An iterative influence diagnostics performed on SAS 9.3 in order to identify any outliers or abnormal measurements. Because of the large volume of participants in the study the dates between follow-up measurements will be on slightly different days meaning the observations will be uneven. The LMM accounts for these differences in measurement time making it a premier tool for analysis of longitudinal data. The model will use FM and FFM as two correlated dependent variables in a single multivariate model, so that a covariance matrix is formed for the residuals allowing FFM and FM to be correlated within person at each time point. The multivariate model will create two fixed intercepts, two fixed slopes, 2 random intercepts and 2 random slopes; essentially there will be 2 univariate equations into a single equation. The correlated residuals for each of the equations will allow FFM and FM to be correlated within the person at each time point.
**Grouping of body composition change**

The ten categories will be generated once the trajectories from the LMM are created for FFM and FM. There will be 10 non-exclusive groups of fat change and fat-mass change including: Substantial fat-gain (SFG), fat gain (FG), fat maintenance (FMM), fat loss (FL), substantial fat loss (SFL), substantial fat-free gain (SFFG), fat-free gain (FFG), fat-free maintenance (FFMM), fat-free loss (FFL), substantial fat-free loss (SFFL). The calculation of each participants slope and associated standard error (SE) will be used to categorize annual FM and FFM change into ten categories: substantial fat gain or fat-free gain (SFG or SFFG) if positive and 95% CI excluded 0; fat or fat-free gain (FG or FFG) if positive and 68% CI excluded 0; fat or fat-free maintenance (FMM or FFMM) if 68% CI contained 0; fat or fat-free loss (FL or FFL) if negative and 68% CI excludes 0; and substantial fat or fat-free loss (SFL or SFFL) if negative and 95% CI excludes 0.

**Specific Aim 3**

To determine the effect of total average daily activity EE on body composition independent of changes in EE due to changes in bodyweight.

**Overview:** 344 healthy men and women aged 21 to 35 years old with a BMI of 20-35kg/m\(^2\) from the Energy Balance Study will be used. The participants were monitored for 24 months (however for this aim 12-months of data will be used) for weight-changes and anthropometric changes. Each participant had laboratory measurements performed at five different time points including a baseline, 3-month, 6-month, 9-month and 12-month. The same clinical measurement protocols were followed for each measurement period to
ensure consistency among measurements. For a full list and description of the measurements refer to table 2 and the overall methods section. Once the 12-months of data are completed, the 5 EE measurement periods, consisting of 10-days of constant wear-time for each participant will be averaged to generate overall-mean EE for each participant. The overall average EE for all of the participants will then be compared based on the groups of bodyweight and composition change from aims 1 and 2. The overall EE, EE per kg of bodyweight, percentage of EE from sedentary activity and physical activity EE will be compared between the groups of bodyweight and composition change. The four measurements of EE will tested amongst the bodyweight and composition groups with a single ANOVA.

**Research Design**

The Energy Balance Study was an observational longitudinal study consisting of 430 healthy men and women aged 21 to 35 years old with a BMI of 20-35kg/m$^2$. The group was followed for 12-months having measurements taken roughly every three months at the time periods baseline, 3m, 6m, 9m, 12m. The complete 12 months of data will be used for analysis. The EE measurements will come from the use of the SenseWear Mini Armband measurements. The bodyweight and composition rate of values produced in aim 1 and 2 will be used for each participant.

**Hypothesis**

3.1 The participants who maintain bodyweight over the year period will have the higher relative total daily EE.
3.2 The participants who maintain body fat over the year period will have the higher total daily EE.

3.3 The participants gaining substantial bodyweight will derive a higher percentage of their total daily EE from sedentary behavior

**Anticipated Outcomes**

Participants who are gaining weight but have a high EE will experience a greater amount of FFM than relative to those participants gaining weight with a low EE.

Participants who are losing weight but have a high EE will lose a higher percentage of FM as opposed to FFM relative to those participants losing weight that have a low EE.

The largest majority of participants will be weight-gainers and have a low EE. These participants will gain more fat-mass relative to the other groups of participants.

**Specific Methods**

*Anthropometric Measurements*

All anthropometric measurements for the 5 primary visits (baseline, 3, 6, 9, and 12 month) were performed with the participant dressed in a pair of surgical scrubs and bare feet. For all visits the BMI (kg/m²) was calculated from the average of three height and weight measurements using a traditional stadiometer and electronic scale. The values for both weight and height were recorded to the nearest 0.1 centimeter and 0.1kg. Body
composition was measured using a Lunar fan-beam dual X-ray absorptiometry (DXA) scanner (GE Healthcare model 8743, Waukesha, WI). The scans recorded total fat and FFM, as well as torso, arm and leg composition. In addition, the scans recorded bone mineral density and content. For the baseline, 6 and 12 month visits the waist and hip circumference of each participant was measured. The waist and hip circumferences were measured using a calibrated spring-loaded tap measure. Waist circumference was determined at the point midway between the costal margin and iliac crest in the mid-axillary line approximately 2 inches above the umbilicus. Hip circumference was measured at the widest point around the greater trochanter. Circumferences recorded were the average of three measurements and were rounded to the nearest 0.1cm.

*Energy Expenditure*

The Energy Balance study used three types of measurement for estimation of energy expenditure. The three types included the SenseWear Mini Armband (BodyMedia Inc. Pittsburgh, PA), the ActivPal (small inclinometer), and DLW. Because the Activpal does not give a true estimation of EE and DLW was only given to half of the participants, the SenseWear Mini Armband (BodyMedia Inc. Pittsburgh, PA) is used as the primary measure of energy expenditure. The portable, multi-sensor device is worn on the upper-left arm with the sensor itself resting over the triceps muscle. Energy expenditure and activity are measured using a combination of a tri-axial accelerometer with biological sensors measuring heat flux, galvanic skin response, near-body ambient temperature, and skin temperature. The various measures are then entered into an algorithm using a Naïve
Bayes classifier for superior pattern recognition of estimating the context of an activity. The combination of sensors gives the Mini Armband an enhanced ability to detect a wider variety of activities (72). In addition, the Mini Armband has gone through both laboratory and free-living conditions (against DLW) and other previously validated accelerometers. In a recent investigation by Johannsen et al., the SenseWear Mini Armband was compared to the EE values generated by the use of free-living DLW. The Mini Armband was exceptionally valid showing an average of 22 kcal/day difference in total daily EE, with error rates as low as 8.3±6.5%. The precise results culminated in a regression analysis showing an $R^2 =0.71$ and intraclass correlations of 0.85. The intraclass correlations suggested that only 15% of the variance was due to the difference in DLW and armband methods, while the other 85% was due to differences among individuals (72).

At each measurement period of The Energy Balance Study the participants were instructed to wear the monitor for 10 consecutive days, for 24 hours a day, except during water activities (i.e., swimming, bathing, showering, or water aerobics). If the monitor was removed the participants recorded the type and duration of activity that was performed while the armband was removed in an activity log. The non-wear activities were then incorporated into the estimations of EE based on corresponding MET values according to the 2011 Compendium of Physical Activities (73). The MET values were then multiplied by the participant’s own measured resting metabolic rate (measured during the baseline, 6-month and 12-month visits). The participant was considered to be compliant if they had 7 days of (including 5 week days and 2 weekend days) at least 23 hours of verifiable time (either logged non-wear time or armband worn).
**Linear Mixed Model Analysis for Weight-change Trajectory**

The LMMs created in aim 1 and 2 to analyze the estimated rate of bodyweight and composition change of the 344 participants over 12 months using 5 (Baseline 2, 3, 6, 9, and 12 month) will be used in aim 3 to compare relative to the participants energy expenditure.

**Statistical Analysis**

Data will be analyzed with commercial software (Sigma Stat, SPSS, Chicago, IL). Statistical analysis will consist of one-way ANOVA’s to test for differences in the four measures of EE across the groups of bodyweight and composition change created in aims 1 and 2. Post-hoc power calculations will be done. Statistical significance will be set with an alpha value of p<0.05. Data will be presented as means ± SEM in figures and means ±SD in tables.
Table 2.1: Measurements Taken for the Energy Balance Study

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>3M</th>
<th>6M</th>
<th>9M</th>
<th>12M</th>
<th>15M</th>
<th>18M</th>
<th>21M</th>
<th>24M</th>
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Table 2.2: List of Questionnaires Administered in the Energy Balance Study

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CHAPTER III

RATES OF WEIGHT-CHANGE IN THE ENERGY BALANCE STUDY OVER A ONE YEAR PERIOD

Abstract:

Introduction: The current research literature lacks detailed evidence on how bodyweight changes throughout adult life. Tracking bodyweight measurements from measurement to measurement tends to increase intra-person variability because of body water flux. A better method for monitoring bodyweight-change over time is needed to better understand weight maintenance and weight-gain.

Objective: The purpose of this study was to measure bodyweight changes in young healthy adults for a year period. Then, develop a linear mixed model (LMM) to predict bodyweight changes in the adults participating in the study.

Methods: 339 healthy young adults completed a year-long longitudinal study, which included five clinical measurement sessions where bodyweight was measured. The recorded bodyweight measurements were used to create an LMM, which calculated the rate of bodyweight-change. Based on the predicted LMM measurements the participants were categorized into one of five groups (substantial weight loss (SWL), weight loss (WL), weight maintenance (WM), weight gain (WG), or substantial weight gain (SWG).
Results: The male participants who completed the study had a calculated yearly weight-change of 1.34±2.28, and female participants who completed the study had a calculated yearly weight change of 0.79±2.08. Once the male participants were grouped, roughly 93% (154 participants) were considered to either be maintaining or gaining weight. Only approximately 7% (12 participants) were considered as losing weight over the year period. For females a similar trend was recorded with 86% (148 participants) being considered maintaining or gaining, while only 14% (25 participants) were considered to be losing weight. Lastly, for both males and the females the SWG and SWL groups had a substantially heavier bodyweight at baseline relative to the WM group.

Conclusion: The calculated weight-change for males and females by the LMM was very similar to measured weight-change over 12 months. However, when both values are viewed for each individual in the study, the LMM predicted change and the measured change are significantly different. Assessing bodyweight from measurement to measurement may lead to a misinterpretation of how bodyweight is truly changing over time.

Keywords: Bodyweight, Linear mixed model, weight-change, weight-gain

Introduction

Obesity is a public health concern in the United States, (US), with over a third of the population being affected by the disorder. As evidenced by the dramatic increases in obesity prevalence, Americans are rapidly gaining weight. While there is clear understanding that Americans are gaining weight, little is actually known regarding the
pattern and rate of weight-gain. What percentage of the population is gaining weight? What percentage of the population is maintaining weight? Is the percentage of the population who are gaining weight equal across genders? What is the difference between substantial weight gain and inconsequential weight gain?

Weight-change is often thought of as the result of an energy storage change, which is not always the case. Typically body composition is viewed in a two compartment model divided into fat mass (FM) and fat-free mass (FFM) (15). These two components have drastically different energy densities, and fluid levels. FFM is comprised of a much higher percentage of water than FM; roughly 80% of FFM is water. The water composition of fat tissue is much less, but can range from 7 to 43% (74).

Considering that the amount of FFM is typically much higher than fat-mass, the total water content of the body may be as high as 75% of the total mass. Relatively moderate changes in this large volume of water can account for dramatic acute changes in weight. The body typically loses 2-3 liters of water a day with the amount of water being lost fluctuating dramatically depending on the amount of physical activity performed and environmental stressors. This water is gained back through hydration in food and drink and hydration levels in an individual can vary greatly day-to-day. These large fluctuations in water cause changes in weight not due to a true change in energy storage in the tissue, since water has no energy value.

Traditionally studies measuring weight-change, take a starting measurement relative to an ending measurement to describe weight-change over a certain period of time. There are several inadequacies in this form of measuring weight-change. The difference between two cross-sectional bodyweight measurements cannot account for
changes due to fluctuations in water, i.e., inter-measurement variability. The simple difference method assumes that the starting measurement is what the individual weighed at the time of measurement, whereas the LMM gives a prediction of their starting weight based on all of the measurements taken. Multiple measurements may be used when longitudinal data is employed to monitor weight-change. Factoring in multiple measurements and the precision of these measurements an LMM is able to predict a rate of change.

The following study predicts rates of weight-change using clinical bodyweight measurements in a linear mixed model (LMM) over a 12-month period with healthy participants ages 21-35yr at baseline. This investigation affords precise estimates of overall weight-change and rates of weight-change in healthy young Americans.

**Methods**

**Study Population**

The current study uses data that were collected from June 2011 to January 2014 as part of The Energy Balance Study. The complete methods and overall study design have been described (75). The current study uses a subset of The Energy Balance population including 344 healthy young adults (339 were used for final analysis after exclusion of outliers) ages 21-35 years old, with a body mass index (BMI) of 20-35 kg/m². Exclusion criteria included planned weight-loss surgery, hypertension (150- mmHg systolic and/or 90 mmHg diastolic), taking selective serotonin reuptake inhibitors, giving birth within the past 12 months, planning to start or stop birth control in the next 12 months while participating in the first year of the study, history of depression, currently diagnosed or taking medications for a major chronic health condition, using medications to lose
weight, started or stopped smoking within the last 6 months and ambulatory blood glucose levels ≥ 145 mg/dL. All study protocols were approved by the University of South Carolina Institutional Review Board. Participants who completed all measurements in the first year of visits (baseline, 3, 6, 9 and 12 month) were included in the current analysis.

The weight measurements were taken with other anthropometric measurements. Anthropometric measurements for the five visits over the 12-month period (baseline, 3, 6, 9, and 12 month) were performed with the participant dressed in a pair of surgical scrubs and bare feet. For all visits the BMI (kg/m2) was calculated from the average of three height and weight measurements using a traditional stadiometer and electronic scale. The values for both weight and height were recorded to the nearest 0.1 centimeter and 0.1kg.

Statistical Analysis

In previous studies that have evaluated rate of weight-change the participants have been categorized based on ages. However, the previous studies showed relatively similar weight-change throughout the used age category of 21-35, so in the current study no age divisions were made (76;77). All statistical analyses were performed separately by gender. A LMM for each gender was created to predict the weight-change over the 12 months of data collection for the 339 participants included in analysis. The LMM treated the amount of time within the study (Days) as the predictor of weight-change:

\[ Weight_{ij} = \beta_0 + \beta_1 Days_{ij} + \delta_{0j} + \delta_j Days_{ij} + e_{ij} \]

Within the current model \( i=1 \) to \( m \) Days from baseline and \( j=1 \) to \( n \) subjects. \( \beta_0 \) represents the fixed intercept across all \( i \) and \( j \) displaying the sample mean value of Weight at \( Days=0 \), and \( \beta_1 \) is the fixed slope for Days (across all \( i \) and \( j \)) representing the average
linear trend (rate of change) across $Days$. $\delta_{0j}$ calculates the random intercept for each $j$ representing the deviation of each person’s intercept from $\beta_0$ (at $Days=0$), and $\delta_{1j}$ is the random slope for $Days$ for each $j$ representing the deviation of each person’s slope from $\beta_1$. The individual (total) slope, which is the sum of fixed and random slope estimates, $\beta_1 + \delta_{1j}$, represents the rate of change in weight for subject $j$. The SE of this individual slope was computed as the square root of the sum of the variances for each estimate. The SE of the random slope estimate for each individual was computed using the `predict` command’s `reses` option in STATA 13 (Stata Corp., College Station, TX). Iterative influence diagnostics including Cook’s Distance were performed using SAS 9.3 software in order to identify any outliers or abnormal measurements. The LMM was fit so that the intercept estimate was set on the baseline day of the study allowing for weight prediction of the initial measurement and for the last measurement.

Once the model was fitted each participant’s were divided based on gender and the amount of weight-change that was experienced during the 12-month period. Five specific groups of weight-change for each gender including: Substantial weight-gain, weight gain, weight maintenance, weight-loss and substantial weight-loss. The calculation of each participants slope and associated standard error (SE) were used to categorize the weight change into the five categories: substantial weight gain (SWG) if positive and 95% CI excluded 0; weight gain (WG) if positive and 68% CI excluded 0; weight maintenance (WM) if 68% CI contained 0; weight loss (WL) if negative and 68% CI excludes 0; and substantial weight loss (SWL) if negative and 95% CI excludes 0.
For comparison between groups the weight-change groups paired t-test were used and a p-value <0.05 was used to determine significance. For comparison between gender a paired t-test was used and a p-value<0.05 was used to determine significance.

**Results**

The average yearly weight-change for males was calculated by the LMM to be 1.34±2.28 kg (1.64±2.77%), while females were calculated to have a change of 0.78±2.07kg (1.09±2.81%) per year. The average weight-change trajectory for each gender can be seen in Figure 3.1. When the average yearly weight-change was calculated for males using the simple difference method measurement (i.e., subtracting the baseline from the 12-month measurement), the result was 1.28±3.47kg. For females the simple difference method yielded a result of 0.76±2.93kg. For both genders the simple difference method of measurement and LMM appear very similar, yielding roughly equivalent averages for the year. However, the difference between absolute values of the simple difference measurement and the calculated weights accrued from the LMM was 1.02±0.91kg for males and 0.82±0.71kg for females, showing that there were substantial differences between the two methods on the individual participant level.

Out of the 166 male participants, 154 were considered as either maintaining or gaining weight. For the 173 female participants, 148 participants were considered as either maintaining or gaining weight. When viewing the weight-change groups, the SWG group had the highest average calculated weight-change for males and females (4.20±1.10kg for males and 3.83±1.15kg for females). The weight trajectories for both
genders can be seen in Figure 3.2. The simple difference method yielded a weight-change of 4.72±1.86kg for males and an almost identical 4.72±1.92kg for females, which was not considered substantially different than the calculated LMM values. The absolute difference between the simple difference measurement and the LMM calculated measurement for the SWG group was the second highest difference amongst the five weight-change groups for both genders as seen in Figures 3.4 and 3.5. The greatest difference between the two weight-change values was a difference of 5.28kg; the participant had a measured weight-change of 9.20kg and the LMM calculated weight-gain of 4.39kg.

Males in the WG group gained an average of 2.19±0.40kg and females gained an average of 1.88±0.40kg. The simple difference method revealed a weight-gain of 2.62±0.84kg for males and 2.16±0.91kg. The weight trajectories for both genders can be seen in Figure 3.2. Interestingly the calculated weight-change values for males were considered substantially different (p=.003) than the simple difference method values. However, this did not hold true for the females (p=.117). However, the greatest difference for either gender between the two weight-change values was a difference of 2.25kg; the participant had a measured weight-change of 4.70kg and the LMM calculated weight-gain of 2.45kg.

Both genders for the WM group had a very modest weight-change. For males the weight-change was 0.10±0.85kg and for females the weight-change was calculated as 0.19±0.67kg. The weight-change over the year period can be seen in Figure 3.3. Interestingly, the simple difference method measured the both males and females in the WM group as losing bodyweight over the 12-months. For men the simple difference
method recorded a weight-change of -0.43±1.57kg and for women the simple difference method recorded a weight-change of -0.07±1.14. This difference was only significantly different for males \((p=0.12)\). The absolute difference for both genders between the simple difference measurement and the calculated estimates were actually larger than either measurements of weight-change at 0.76±0.60kg for males and 0.46±0.60kg for females. The greatest difference between the two weight-change values was a difference of 2.76kg; the participant had a measured weight-change of -3.75kg and the LMM calculated weight-change of -0.99kg.

The changes for both genders in the SWL and WL can be seen in Figure 3.4. For males in the SWL group the simple difference method revealed an average weight-loss of -7.78±1.77kg which was substantially different \((p<0.001)\) from the calculated LMM measurements. For females in the SWL group the average weight loss was -5.24±1.78kg which was not significantly different than the calculated LMM measurements. In addition, the SWL group had the largest absolute difference for males between the simple difference measurements and the calculated estimates of the LMM with a difference of 2.10±1.52kg. The greatest difference between the two weight-change values was a difference of 3.92kg; the participant had a measured weight-change of -9.19kg and the LMM calculated weight-loss of 5.63kg. For the WL group the difference between the LMM calculated weight-change and the simple difference measured weight-change was considered to be substantial \((p<0.001)\) and resulted in an absolute difference between means of 1.29±1.04 for males and 0.90±0.50kg. The greatest difference between the two weight-change values was a difference of 3.03kg; the participant had a measured weight-change of -5.02kg and the LMM calculated weight-loss of 2.0kg. Full descriptions of the
calculated bodyweight-changes divided by gender using the LMM over the 12-months are listed in Table 3.1.

Once the outliers were removed from the final number of participants there were a total of 166 men and 173 females. Males and females had a similar number of participants in each weight-change group. However, the WL group for females contained 17 participants whereas for males the WL group only contained six participants. When viewing the absolute weight-change difference between the simple difference method and the LMM values it seems that males have larger differences between the two methods. However, when these differences are measured as a percentage of their starting baseline weight they are no longer significant. In addition, there were substantial differences within gender among baseline measurements of weight and BMI, as seen in Table 3.2. The WM group had an average weight of 79.08±12.17kg and was substantially lighter than the SWL and SWG groups which had average starting weights of 89.12±12.33kg ($p<.001$) and 86.07±14.09kg ($p=0.038$). The substantial differences in weight subsequently caused substantial differences in BMI as well ($p<0.001$). The trends for starting bodyweight and starting BMI were also seen for females as seen in Table 3.3. The starting weight for women in the WM group was 64.09±9.96, while the starting weight for the SWL group was 75.19±10.23 and for the SWG group it was 74.99±15.32. These starting weights were substantially different ($p<0.001$) and subsequently made the BMI values substantially different as well ($p<0.001$).

**Discussion**

The current study is distinct from many longitudinal weight-change studies in the consistency of clinical measurement protocols and the use of a LMM. While a few
research groups have used an LMM to monitor bodyweight, to our knowledge this is the first study to use each individual participant’s own slope and variability in measurements to define their bodyweight change. Each participant’s measurements for the current study were taken on the same calibrated scale with the same clothing at approximately the same time of day for each participant. The measurement period tracked 339 participants over a period of roughly one year (a minimum of 299 days and a maximum of 512 days), with measurements being taken at roughly three month intervals. High variability between the total amounts of days for each participant makes it harder to measure rate of change using the simple difference method. The use of an LMM provided predictions of rate of weight-change over the year period that could be used to predict a 12-month change value. In addition further analysis of the estimated individual rate of weight-change afforded the categorizations of the changes. The SE of each participant was used to group the overall predicted weight-change. This allowed for more variability between measurements to be accounted. The overall male and female weight change shown in Figure 3.1 reveals a linear change based off the 5 measurements, indicating that the linear approach as opposed to a curvilinear or quadratic approach seems appropriate for modeling steady state weight-change.

The average LMM predicted yearly weight gain from the current study was 1.34±2.28kg for males and 0.79±2.08kg for females, which is comparable to average weight gain that have been estimated for the American population, roughly 1-2 lbs (5). Most previous estimations of weight-change over time have used two measurements taking the starting weight and simply subtracting the ending weight, with the resulting difference being the weight-change. In this population when the simple difference
method is applied, the average weight-change is 1.19±3.24kg for males and 0.71±2.76kg. When the averages of the calculated and measured weight-changes are compared there is only a slight difference of .05kg, indicating that for population estimates there is little different between the two methods.

The major difference between the simple difference method and LMM estimations surfaced on the individual level of analysis. The difference between the absolute values of the simple difference method and the LMM estimations is 0.92±0.82kg, which is nearly the same size as the weight-change experienced by participants. However, the absolute difference is not realized in the overall averages because relative to the LMM estimations the simple difference measurement overestimated and underestimated participant values. Looking at the difference between the two methods shows that the simple difference method is a flawed indicator of the rate of change over the time span. Out of the 339 total participants only 67 (20%) had calculated LMM values that were greater than those measured with the simple difference method. All of the simple difference measurements for the participants who experienced weight-loss (n=39) were overestimated, while only 17% of the weight-gainers (n=146) were underestimated. The most weight-change values which were underestimated by the simple difference method were in the WM group where 27% of the total 156 participants had a higher predicted yearly weight-change relative to the simple difference method. However, the largest underestimated discrepancy between the simple difference measurement and the LMM estimations was 1.64kg. The simple difference measurement recorded a weight-gain of 0.55kg while the LMM calculated a weight-gain of 2.19kg.
The differences seen between the two measurement methods did not appear to be influenced by gender in any of the five groups (SWL, WL, WM, WG, and SWG). In all groups males had a larger discrepancy between the two predictions and in all groups the largest discrepancy was a male participant except for the SWG. The female participant in the SWG group had the largest difference between the two methods of bodyweight measurement with an absolute difference of 4.87kg.

Once the LMM estimations were available, the categorization of weight-change (SWG, WG, WM, WL, and SWL) gave insight to which individuals were gaining and losing weight. As previously mentioned only 10% of the total population had a negative weight trajectory. This is not too surprising considering most adults go through four periods dieting in a year (78-80). Most of these periods of dieting are unsuccessful and the individual rebounds in weight which results in very few individuals who actually lose weight over a year period. Conversely, there were 146 participants who were considered to be gaining bodyweight and the increases seen were due more too random variability in measurements. Interestingly, there are 239 participants who had a positive predicted yearly weight gain. When all participants who have a positive weight-change are considered, it includes 70% of the total population which is roughly the same percentage of Americans who are currently considered obese or overweight (81).

The weight-change groups also had substantially different starting weights, with the weight maintenance group having a substantially lower starting weight than the SWL and SWG groups. The differences in baseline weights reveal that on average the individuals who are gaining substantial amounts of weight are significantly heavier than
those individuals maintaining their weight. Additionally, those individuals losing substantial weight are significantly heavier than those maintaining their bodyweight.

Using the LMM calculated weight-changes enabled the variation between measurements to be factored in to the yearly calculated weight; this limited the influence of rapid bodyweight fluctuations due to water retention or dehydration.

Conclusion

The average calculated LMM weight-change for the males and females in the entire Energy Balance population was very similar to the weight-change measured by taking the 12-month measurement and subtracting the baseline measurement. In addition, both values were close to estimated bodyweight-changes by the U.S. population in current literature (5). However, while the simple difference measurement average and the LMM prediction average were close, they were very different on a person-to-person basis. Using the LMM enabled the variation between measurements to be factored into the yearly calculated weights; this limited the influence of rapid bodyweight fluctuations due to water retention or dehydration. Because of the elimination of random variation between measurements the LMM method gives a more accurate estimation of weight-gain and more accurately depicts weight maintenance, and weight-loss as well.

The Energy Balance sample population was made up of predominantly weight-maintenance participants (n-156). However, nearly the same number of participants was considered as weight-gainers (n-146). Also interesting to note were that the two heaviest groups at baseline were the SWG and SWL groups, while the WM group had a baseline weight that was substantially less than SWG and SWL. More research needs to be
performed to better understand the reason why the WM group was able to maintain a consistent bodyweight over the year period.

**Funding:** This study was supported by an unrestricted grant from The Coca-Cola Company.

**Acknowledgement:** We thank the Energy Balance Staff for the collection and management of the data used in this study and the participants for the dedication to completing the measurements. We also thank our International Advisory Board for help and guidance throughout the study.
Table 3.1: Weight-Change Distribution of the Total Energy Balance Population

<table>
<thead>
<tr>
<th>Population</th>
<th>Total Participants (n)</th>
<th>Calculated Yearly Wt. Change (kg)</th>
<th>Female Participants (n)</th>
<th>Calculated Yearly Wt. Change (kg)</th>
<th>Male Participants (n)</th>
<th>Calculated Yearly Wt. Change (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SWL</td>
<td>14</td>
<td>-4.18±1.17</td>
<td>8</td>
<td>-3.77±1.34</td>
<td>6</td>
<td>-4.72±0.73</td>
</tr>
<tr>
<td>WL</td>
<td>23</td>
<td>-1.91±0.36</td>
<td>17</td>
<td>-1.81±0.34</td>
<td>6</td>
<td>-2.18±0.31</td>
</tr>
<tr>
<td>WM</td>
<td>156</td>
<td>0.15±0.76</td>
<td>84</td>
<td>0.18±0.68</td>
<td>72</td>
<td>0.11±0.86</td>
</tr>
<tr>
<td>WG</td>
<td>77</td>
<td>2.06±0.42</td>
<td>33</td>
<td>1.88±0.40</td>
<td>44</td>
<td>2.18±0.40 *</td>
</tr>
<tr>
<td>SWG</td>
<td>69</td>
<td>4.03±1.13</td>
<td>31</td>
<td>3.83±1.16</td>
<td>38</td>
<td>4.20±1.10</td>
</tr>
</tbody>
</table>
Table 3.2: Characteristics of Male Participants in the Five Weight-Change Groups

<table>
<thead>
<tr>
<th>Males</th>
<th>Age (yrs)</th>
<th>BMI (kg/m(^2))</th>
<th>Baseline Weight (kg)</th>
<th>Baseline Height (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SWL</td>
<td>27.07±3.50</td>
<td>27.48±3.12</td>
<td>89.12±12.33</td>
<td>179.86±2.82</td>
</tr>
<tr>
<td>WL</td>
<td>28.86±3.18</td>
<td>25.95±2.59</td>
<td>82±5.54</td>
<td>178.13±8.39</td>
</tr>
<tr>
<td>WM</td>
<td>27.82±3.81</td>
<td>24.87±2.95</td>
<td>78.45±10.89</td>
<td>177.51±6.92</td>
</tr>
<tr>
<td>WG</td>
<td>26.98±3.88</td>
<td>25.06±3.17</td>
<td>79.08±12.17</td>
<td>177.47±6.39</td>
</tr>
<tr>
<td>SWG</td>
<td>28.27±3.80</td>
<td>26.84±3.66</td>
<td>86.07±14.09</td>
<td>178.94±8.62</td>
</tr>
</tbody>
</table>
Table 3.3: Characteristics of Female Participants in the Five Weight-Change Groups

<table>
<thead>
<tr>
<th>Females</th>
<th>Age (yrs)</th>
<th>BMI Baseline Weight (kg)</th>
<th>BMI Baseline Height (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SWL</td>
<td>28.00±4.52</td>
<td>27.13±4.25</td>
<td>75.19±10.23</td>
</tr>
<tr>
<td>WL</td>
<td>27.68±4.27</td>
<td>27.03±4.78</td>
<td>75.79±16.51</td>
</tr>
<tr>
<td>WM</td>
<td>28.27±3.66</td>
<td>24.09±3.87</td>
<td>64.09±9.96</td>
</tr>
<tr>
<td>WG</td>
<td>26.96±3.18</td>
<td>26.42±4.73</td>
<td>72.85±12.73</td>
</tr>
<tr>
<td>SWG</td>
<td>27.38±3.55</td>
<td>26.91±4.26</td>
<td>74.99±15.32</td>
</tr>
</tbody>
</table>
Figure 3.1 Average Measured Weights with Linear Model Trajectories for All Participants
Figure 3.2 Average Measured Weights with Linear Model Trajectory for Weight Gain and Substantial Weight Gain Group
Figure 3.3 Average Measured Weights with Linear Model Trajectory for Weight Maintenance Group
Figure 3.4 Average Measured Weights with Linear Model Trajectory for Weight-Loss and Substantial Weight-Loss Group
Figure 3.5 Differences Between Measured Yearly Weight Change and Linear Mixed Model Calculated Yearly Weight Change
CHAPTER IV

YEARLY RATES OF BODY COMPOSITION CHANGE IN THE ENERGY BALANCE STUDY

Abstract:

Introduction: The rate of body composition (fat mass (FM) and fat-free mass (FFM)) change is extremely important in the risk for obesity and in monitoring overall health. The amounts of FM and FFM changes that occur in young adults over time have not been studied on a large-scale or with great accuracy. Simple difference methods of measuring body composition changes under and overestimate the actual changes that occur, specifically in fat-free mass. There is a need to fully define the rate of body composition change in healthy adults in order to better understand the fluctuation of body composition over a year period.

Objective: The purpose of this study was to measure body composition changes in young healthy adults for a year period. Then, develop a multivariate linear mixed model (LMM) to accurately predict FM and FFM changes in the adults participating in the study.

Methods: 337 healthy, young adults completed a year-long longitudinal study including 5 clinical measurement sessions where body composition was measured using Dual-energy X-ray absorptiometry (DXA). The five body composition measurements were
then used to create a linear mixed model (LMM) that estimates the rate of body composition change. The body composition changes were then categorized into 5 groups based off of changes in FM (substantial fat loss (SFL), fat loss (FL), fat mass maintenance (FMM), fat gain (FG), substantial fat gain (SFG)).

**Results:** After accounting for outliers the entire group of 337 participants had a calculated yearly FM change of 0.91±2.03kg (Range: -6.79 – 8.00kg). FFM did not substantially change over the course of a year in the participants of the Energy Balance Study. The LMM created for body composition had no random slope for FFM, which meant no overall change in FFM. Once the participants were grouped based on their fat-change, 45% (153 participants) were considered to maintain fat mass over the year period. Additionally, about the same amount (144 participants) was considered to be gaining fat-mass.

**Conclusion:**

Body composition changes seen in the sample population were almost due entirely to changes in FM. On average the FFM did not change substantially. The LMM average calculated fat-gain for the entire Energy Balance population was very similar to the measured fat-change. However, the values were substantially different on the individual level. Estimates of FM over time such as the estimates gathered in this study may give more accurate risk assessments of obesity and excessive fat gain.
Introduction

Obesity affects the lives of approximately 100 million Americans. The disorder is associated with many chronic diseases, early death, and disability (83). The health and economic burdens of obesity are well established (26). Clinically, as recognized by most organizations, obesity is categorized by body mass index (BMI). Originally known as the Quetelet index, BMI divides an individual’s body mass by their height squared (84). Keys et al. originally revealed BMI as having high correlations with body density and skinfold measurements on the population level (85). The NIH Consensus Development Conference on the Health Implications of Obesity convened 13 years later and was the first to define obesity by BMI (86). Most organizations use BMI to define obesity because BMI correlates with body FM (87). Even though there are well established associations between BMI and health, increased adiposity is an important component of obesity, and an independent risk factor for cardiovascular disease, all-cause mortality and other obesity related risk (46;88;89).

Many health organizations include excess adiposity in their definitions of obesity, yet do not include values for what is considered excessive fat-gain. Accurate estimates of body composition change over time could be used to estimate risks and discrepancies between different demographic groups and better describe obesity and metabolic syndrome. Relatively few studies have investigated body composition change over time with accurate clinical measurements (38;90). Presently no studies have used a method as accurate as dual-energy X-ray absorptiometry (DXA) to estimate change in body composition over time. Previous studies measuring body composition change have used two measurements and simply used the difference in measurements as body composition
change over time. There are several inadequacies in this form of measuring body composition change. The simple difference measurement style is fairly accurate when looking at body composition change for an entire population, but when evaluating changes in the individual, accuracy is lost. Longitudinal data analysis of accurate measurements such as DXA results will result in more reliable changes in body composition. In addition the results will allow for a better categorization for what is truly considered substantial FM and FFM changes relative to FM and FFM maintenance.

The following study estimates rates of body composition change using DXA measurements in a LMM over a 12-month period with healthy participants who were ages 21-35yr at baseline. This investigation affords precise estimates of overall body composition and categorizes these changes for healthy young Americans.

Methods
Sample Population
The current study uses data that was collected as part of The Energy Balance Study; the data was collected from June 2011 to January 2014. The complete methods and overall study design have already been described in detail in previous publications (75). The sample data for the current study includes 342 healthy young adults ages 21-35 years old, with a body mass index (BMI) of 20-35 kg/m², who completed all body composition measurements of the first year of the Energy Balance Study. Exclusion criteria for the study included planned weight-loss surgery, hypertensive (150- mmHg systolic and/or 90 mmHg diastolic), taking selective serotonin reuptake inhibitors, giving birth within the past 12 months, planning to start or stop birth control in the next 12 months while participating in the first year of the study, history of depression, currently
diagnosed or taking medications for a major chronic health condition, using medications to lose weight, started or stopped smoking within the last 6 months and ambulatory blood glucose levels ≥ 145 mg/dL. All study protocols were approved by the University of South Carolina Institutional Review Board.

*Body Composition and Anthropometric Measurements*

The body composition measurements were taken with all other anthropometric measurements. All clinical measurements for the 5 primary visits (baseline, 3, 6, 9, and 12 month) were performed with the participant dressed in a pair of surgical scrubs and bare feet. For all visits the BMI (kg/m²) was calculated from the average of three height and weight measurements using a traditional stadiometer and electronic scale. The values for both weight and height were recorded to the nearest 0.1 centimeter and 0.1 kg. Body composition was measured using a Lunar fan-beam dual X-ray absorptiometry (DXA) scanner (GE Healthcare model 8743, Waukesha, WI). The scans recorded total fat and fat-free mass, as well as torso, arm and leg composition. In addition, the scans recorded bone mineral density and content. For the baseline, 6 and 12 month visits the waist and hip circumference of each participant was measured. The waist and hip circumferences were measured using a calibrated spring-loaded tap measure. Waist circumference was determined at the point midway between the costal margin and iliac crest in the mid-axillary line approximately 2 inches above the umbilicus. Hip circumference was measured at the widest point around the greater trochanter. Circumferences recorded were the average of three measurements and were rounded to the nearest 0.1 cm.
**Statistical Analysis**

A multivariate LMM was created for both genders to predict the body composition change over a year period for the 342 participants included in analysis. The LMM treated the amount of time within the study as the predictor of body composition using FFM and FM as dependent variables. Within the LMM that was created, \( i=1 \) to \( m \) Days and \( j=1 \) to \( n \) subjects. \( B_0 \) represents the fixed intercept regardless across all \( i \) and \( j \) displaying the value of Weight at \( Days=0 \), and \( \beta_i \) is the fixed slope for \( Days \) (across all \( i \) and \( j \)) representing the average linear trend across \( Days \). \( \Delta_{0j} \) calculates the random intercept for each \( j \) representing the deviation of each person’s intercept from \( \beta_0 \) (at Days=0), and \( \delta_{ij} \) is the random slope for \( Days \) for each \( j \) representing the deviation of each person’s slope from \( \beta_i \). After the LMM was created but before final analyses, model assumptions were checked to ensure the residuals and estimates of the random intercepts were normally distributed. An iterative influence diagnostics program on SAS 9.3 software was used in order to identify any outliers or abnormal measurements. 5 outliers were identified out of the original 342. One participant was trying to activity gain-weight and put on muscle mass over the year period, another participant was injured and unable to walk for several months. Another participant limited EI to extreme proportions drastically cutting bodyweight and therefore adjusting their body composition. The last outlier consistently increased energy expenditure every measurement period and reportedly reduced EI every measurement period. These 5 outliers were removed, leaving 337 participants for final analysis. For the final analysis descriptive characteristics of participants in each fat-mass change category were summarized using means and
standard deviations. T-tests analyzed differences between groups and genders for body composition.

*Fat-Mass Change Categories*

Once the model was created the fat-mass change calculated by the LMM was categorized into five groups including: substantial fat-loss (SFL), fat-loss (FL), fat mass-maintenance (FMM), fat-gain (FG) and substantial fat-gain (SFG). The five categories were generated by using each participant’s overall standard error of the slope generated from the LMM. If the calculated FM change was greater than 2 SE above 0 then the participant was considered to be in the SFG group. Next, if the calculated fat change was between one SE and two SE above 0 the participant was considered to be in the FG group. In fat-loss, if the calculated FM change was between one SE and two SE below 0 then the participant was considered to be in the FL group. If the calculated body composition change was greater than two SE below 0 then the participant was considered as part of the SFL group. Lastly, if the calculated FM change was neither 1 SE above 0, nor 1 SE below 0, than the participant was considered in FMM.

*Results*

The LMM created for FFM and FM yielded no random slope for the FFM variable meaning for the Energy Balance population FFM on average did not vary from measurement to measurement, nor did it change substantially over time. The overall fixed average slope created for FFM was not substantially different from 0, meaning that on average the change in bodyweight was predominantly due to FM. Overall the FFM in the sample population was extremely stable, but FM changed substantially over the year
period. While FFM had no substantial increase, and no variability, it was found to be negatively correlated with FM within the individual over time (i.e., small decreases in FFM were consistently associated with increases in FM.). Because no significance was found in variability or change of FFM, the remainder of the results will be dedicated to describing the changes that were seen in FM.

The average yearly FM change for the total 337 participants as calculated by the LMM was $0.91 \pm 2.03\text{kg} (1.41 \pm 2.58\%)$. The average FM trajectory for all participants carried a slope of $0.0025\text{kg per day}$, seen in Figure 4.1. When the average yearly FM is calculated by the traditional measurement, which is simply the baseline measurement subtracted from the 12-month measurement, the resulting value is $0.98 \pm 2.70\text{kg}$. Similar to bodyweight, the change in FM on a population level appeared similar between the traditional method and the changes calculated by the LMM. However, the average absolute difference between the traditional measurement and the calculated FM accrued from the LMM was $0.84 \pm 0.73\text{kg}$, showing that there were substantial differences between the two methods of FM quantification on the individual participant level.

Out of the 337 total participants 297 were considered as either maintaining or gaining FM. Only 40 participants, slightly more than 10% of the entire group was considered as losing FM. When viewing the total population as divided into FM yearly-change groups, the SFG group had the highest average calculated FM change of $3.61 \pm 1.11\text{kg} (4.42 \pm 1.36\%)$ with a daily average fat change of $0.010\text{kg per day}$ as seen in Figure 4.2. The traditional method revealed a FM change of $4.02 \pm 1.84\text{kg}$, which was not considered substantially different than the calculated LMM values ($p=0.116$). However, the absolute difference between the traditional measurement and the LMM calculated
measurement for the SFG group was over a kilogram different at 1.00±0.88kg. The greatest difference between the traditional measurement and the LMM prediction was a difference of 3.77kg; the participant had a measured FM increase of 10.92kg and the LMM calculated a fat increase of 7.14kg.

As expected, the FG group gained substantially more fat than the FMM group and substantially less fat than the SWG group with an average yearly fat-gain of 1.90±0.42kg (2.47±0.59%), while the traditional method revealed a fat-gain of 2.37±1.03.

Subsequently, as seen in Figure 4.2, the slope (fat-gain per day) is substantially less for the FG group as well. Unlike the SFG group, the FG calculated fat-change values were considered substantially different (p<0.001) than the fat change values gathered by the traditional method. The absolute difference between the traditional measurement and calculated estimate was lower than the SFG group at 0.79±0.61kg. Nonetheless, the greatest difference between the calculated and measured values was a difference of 3.65kg; the participant had a measured fat change of 5.39kg and the LMM calculated fat change of 1.74kg.

As expected, the FMM group had a small fat change of 0.15±0.66kg (0.21±0.94%) as calculated by the LMM. As seen in Figure 4.3 the small gain left the daily fat-gain at nearly 0 (0.0004kg per day). The traditional method measured the FMM group an even smaller gain of 0.10±1.22kg of fat mass over the 12-months, which was not considered substantially different (p=0.665) from the measures calculated by the LMM. The absolute difference between the traditional measurement and the calculated estimates was larger than either measurement at 0.59±0.52kg. The greatest difference
between the measurement and LMM estimate was a difference of 2.33 kg; the participant had a measured fat-change of 3.3 kg and the LMM calculated fat-change of 0.97 kg.

The SFL group lost substantially more fat than the FL group with respective losses of -3.96 ± 1.40 kg (-5.09 ± 1.72%) and -1.73 ± 0.31 kg (-2.37 ± 0.57%). As seen in Figure 4.4, the SFL group had the second greatest fat-change (second to the SFG group) per day of -0.011 kg per day. Measured with the traditional method the SFL group had an average weight-loss of -5.61 ± 2.52 kg which was substantially different (p < 0.001) from the calculated LMM measurements. In addition, the SFL group had the largest absolute differences between the traditional measurements and the calculated estimates of the LMM with a difference of 1.66 ± 1.45 kg. The greatest difference between the measured and calculated values was a difference of 4.12 kg; the participant had a measured fat change of -10.22 kg and the LMM estimated fat-loss of 6.10 kg.

The FL group was found to have a yearly fat-loss of -2.01 ± 1.13 when measured by the traditional method. The difference between the LLM estimated fat-change and the traditional method of measuring fat-change was considered to be substantial (p < 0.001). In addition, the absolute difference between means was 0.77 ± 0.54. The greatest difference between the measured value and calculated value was a difference of 2.1 kg; the participant had a measured fat-change of -4.1 kg and the LMM calculated weight-loss of 2.0 kg. Full descriptions of the calculated fat changes separated by gender using the LMM over the year measurement are listed in Table 3.1.

Once the outliers were removed from the final number of participants there were a total of 164 men and 173 females. The five fat-change groups were mostly even between genders. However, the WL group did have the most disparity between genders and was
predominantly female (17/25 or 68%). When viewing the absolute fat-change between genders in each of the fat-change groups there appear to be substantial gender differences. However, if percent body fat is used instead of overall mass, there is no substantial difference between the fat-change in genders. While there was no significance in fat-change between genders, there were substantial differences within gender among baseline measurements of weight and BMI, as seen in Table 4.2. The FMM group had an average baseline weight of 72.49±12.59kg and was substantially lighter than the SFL and SFG groups which had average starting weights of 84.96±14.73kg (p<0.001) and 86.13±14.26kg (p<0.001). The substantial differences in weight subsequently caused substantial differences in BMI as well (p<0.001). The trends for starting bodyweight and starting BMI were also seen for females as seen in Table 4.3. The starting weight for women in the FMM group was 64.90±10.57, while the starting weight for the SFL group was 78.18±13.44 and for the SWG group it was 74.23±14.42. These starting weights were substantially different (p<0.001) and subsequently made the BMI values substantially different as well (p<0.001).

Discussion

A surprising outcome of using the LMM with two dependent variables was that FFM did not substantially change over the course of a year in the participants of the Energy Balance Study. The LMM created for body composition had no random slope for FFM, which meant no overall change in FFM. Further, there was no variance from measurement to measurement for the average participant, nor did the measurements change substantially over time. The overall fixed average slope created for FFM was not substantially different from 0, meaning that on average the change in bodyweight was
predominantly due to FM. Overall the FFM in the sample population was extremely stable. A stable FFM is understandable in this population. One reason for a stable FFM is the age of the population; the average age of the population is roughly 28 years old. The average age for the participant is one in which there are no expected increases in FFM due to growth and no expected substantial decreases due to aging. In spite of the age of the population there are ways in which the participants could have increased their FFM. For example, certain types of resistance training can cause dramatic increases in FFM. While certain lifestyle adaptations can dramatically increase FFM very few of these were used by the participants Energy Balance Study. As a result the majority of body composition changes that were seen in the study’s participants were due to FM changes.

Considering there was no change in FFM, most of the changes in bodyweight were similar to the changes in FM. The categorizations of fat-mass change were crucial to truly understanding whether a participant in the study was gaining, maintaining or losing fat-mass. SE of each participant was used to group the overall calculated fat-change. This allowed for more accurate assessments because of true fat-change versus large variability between measurements. Originally the study was planned to group both FM and FFM change for the 337 participants. But, because the LMM revealed no changes in FFM only FM was grouped. Since only FM changed substantially it was hypothesized that the bodyweight-changes and groups that were made in a previous paper would be similar. However, there were several members of the sample population that were not categorized into the same relative groups for bodyweight and composition. Three participants were considered SFL, but not SWL and 2 participants were considered SWL, but not SFL. Eight participants were considered WL, but not FL and 10 were
considered FL, but not WL. Forty-seven participants were considered WM, but not FMM, and 46 were considered FMM, but not WM. 16 participants were considered WG, but not FG, while 17 were considered FG, but not WG. Lastly, 6 participants were considered SWG, but not SFG and 5 were considered SFG, but not SWG. So, despite there being similarities between bodyweight-change and fat-change, there are also substantial differences between groups.

Like the LMM created for bodyweight, eliminates some of the within participant variation between measurements. FM, unlike FFM has a very low water percentage. Because of the low water content it would be expected to fluctuate less rapidly. Nonetheless there were still large differences between the LMM calculated values and the traditional measured values. The average absolute difference between the two values almost eclipsed the overall fat-change of the group. The total average fat-change of the population was 0.91±2.03kg, while the absolute difference between the two values was 0.79±0.74kg. Since, the measurements were at least 70 days apart it allowed participants to diverge from their typical fat-gain trajectory.

Once categorized the composition of the body composition groups was similar to that of the bodyweight groups with the majority of participants being characterized as fat-stable (n-153) they had a calculated fat-change of 0.15±0.06kg (0.21±0.94%). Nearly as many participants were considered fat-gainers (n-144). Further, there were very few people roughly 11% that were considered as fat-losers. Interesting to note, the SFL group had the largest absolute difference between the measured values and the calculated values of the LMM. This is especially apparent in the males where the absolute difference between the two values was 2.39±1.58kg. The discrepancy between the LMM and the
actual measured values can be seen in Figure 4.3. The difference between the average FM value of the 6 month visit and 3 month visit is 0.18kg, whereas the difference between the average FM value of the 6 month and 9 month visit is 3.53kg. These dramatic differences between rates of fat-loss caused the overall trajectory line to be much different from the measurements.

Conclusion

The calculated fat-change by the LMM averaged for the entire Energy Balance population was very similar to the weight-change calculated by the LMM created for bodyweight-change. This would be expected considering the population had no substantial changes in FFM. Using the Energy Balance Study population as a sample population for young healthy adults in America would indicate that the majority of young American’s are gaining a relatively small (<1kg) of body fat per year that is heavily contributing to a yearly bodyweight gain of roughly 1-2kg. More studies are needed to understand the best ways of preventing this small fat gain to minimize the risk of obesity. However, when viewed on an individual basis the values for each participant are substantially different. Traditional measurements of bodyweight are inaccurate for accessing bodyweight-change.

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Acknowledgement: We thank the Energy Balance Staff for the collection and management of the data used in this study and the participants for the dedication to completing the measurements. We also thank our International Advisory Board for help and guidance throughout the study.
Table 4.1: Fat Mass Change Distribution

<table>
<thead>
<tr>
<th></th>
<th>Total Participants (n)</th>
<th>Calculated Yearly Fat. Change (kg)</th>
<th>Calculated Yearly Percentage of Fat Change (%)</th>
<th>Female Participants (n)</th>
<th>Calculated Yearly Fat Change (kg)</th>
<th>Calculated Yearly Percentage of Fat Change (%)</th>
<th>Male Participants (n)</th>
<th>Calculated Yearly Wt. Change (kg)</th>
<th>Calculated Yearly Percentage of Fat Change (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SFL</td>
<td>15</td>
<td>-3.96±1.40 0</td>
<td>-5.09±1.72</td>
<td>8</td>
<td>-3.55±1.44</td>
<td>-4.62±1.84</td>
<td>7</td>
<td>-4.67±1.17</td>
<td>-5.81±1.38</td>
</tr>
<tr>
<td>FL</td>
<td>25</td>
<td>-1.74±0.3 01</td>
<td>-2.37±0.57</td>
<td>17</td>
<td>-1.74±0.33</td>
<td>-2.45±0.64</td>
<td>8</td>
<td>-1.71±0.26</td>
<td>-2.19±0.32</td>
</tr>
<tr>
<td>FM</td>
<td>153</td>
<td>0.15±0.6 06</td>
<td>0.21±0.94</td>
<td>85</td>
<td>0.13±0.59</td>
<td>0.84±0.53</td>
<td>68</td>
<td>0.17±0.74</td>
<td>-0.08±0.94</td>
</tr>
<tr>
<td>FG</td>
<td>76</td>
<td>1.90±0.4 02</td>
<td>2.47±0.59</td>
<td>32</td>
<td>1.69±0.35</td>
<td>2.34±0.60</td>
<td>44</td>
<td>2.05±0.40</td>
<td>2.57±0.57</td>
</tr>
<tr>
<td>SFG</td>
<td>68</td>
<td>3.61±1.1 01</td>
<td>5.01±2.39</td>
<td>31</td>
<td>3.45±1.11</td>
<td>5.49±2.57</td>
<td>37</td>
<td>3.73±1.11</td>
<td>4.61±2.18</td>
</tr>
</tbody>
</table>
Table 4.2: Characteristics of Male Fat-change Groups

<table>
<thead>
<tr>
<th>Males</th>
<th>Age (yrs)</th>
<th>BMI (kg/m$^2$)</th>
<th>Baseline Weight (kg)</th>
<th>Baseline Height (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Substantial fat-loss (SFL)</td>
<td>26.89±3.47</td>
<td>27.13±3.74</td>
<td>84.96±14.73</td>
<td>176.68±7.26</td>
</tr>
<tr>
<td>Fat-loss (FL)</td>
<td>30.07±4.31</td>
<td>26.25±2.49</td>
<td>80.80±8.29</td>
<td>175.44±5.29</td>
</tr>
<tr>
<td>Fat maintenance (FM)</td>
<td>27.71±3.62</td>
<td>24.25±3.04</td>
<td>72.49±12.59</td>
<td>172.54±9.70</td>
</tr>
<tr>
<td>Fat-gain (FG)</td>
<td>27.41±4.07</td>
<td>25.28±2.85</td>
<td>79.48±10.83</td>
<td>177.20±6.12</td>
</tr>
<tr>
<td>Substantial fat-gain (SFG)</td>
<td>27.75±3.62</td>
<td>26.71±4.01</td>
<td>86.13±14.26</td>
<td>179.47±8.23</td>
</tr>
</tbody>
</table>
Table 4.3: Characteristics of Female Fat-change Groups

<table>
<thead>
<tr>
<th>Females</th>
<th>Age (yrs)</th>
<th>BMI</th>
<th>Baseline Weight (kg)</th>
<th>Baseline Height (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Substantial weight loss (SWL)</td>
<td>27.72±4.77</td>
<td>28.20±4.14</td>
<td>81.28±14.06</td>
<td>169.55±8.27</td>
</tr>
<tr>
<td>Weight-loss (WL)</td>
<td>28.03±4.25</td>
<td>27.21±4.75</td>
<td>74.76±14.69</td>
<td>165.58±6.93</td>
</tr>
<tr>
<td>Weight-maintenance (WM)</td>
<td>27.89±3.41</td>
<td>24.17±4.10</td>
<td>64.90±10.57</td>
<td>164.06±6.75</td>
</tr>
<tr>
<td>Weight-gain (WG)</td>
<td>27.91±3.82</td>
<td>26.70±4.73</td>
<td>72.98±12.52</td>
<td>165.53±5.98</td>
</tr>
<tr>
<td>Substantial weight-gain (SWG)</td>
<td>27.14±3.60</td>
<td>26.57±4.28</td>
<td>74.23±14.43</td>
<td>166.87±6.18</td>
</tr>
</tbody>
</table>
Figure 4.1 Average Measured Fat Mass with Linear Model Trajectory for Fat Gain Group
Figure 4.2 Average Measured Fat Mass with Linear Model Trajectory for Fat Maintenance Group
Figure 4.3 Average Measured Fat Mass with Linear Model Trajectory for Fat Loss Group
Figure 4.4 Differences Between Measured Yearly Fat Change and Linear Mixed Model Calculated Yearly Weight Change
CHAPTER V
THE ASSOCIATION BETWEEN CHANGES IN BODYWEIGHT AND COMPOSITION WITH TOTAL DAILY ENERGY EXPENDITURE

Abstract

Introduction: Energy expenditure (EE) and energy storage (ES) are two crucial components of energy balance. With the increases in the prevalence of obesity, investigations focusing on energy balance are necessary for a better understanding of how to prevent and categorize risk for this serious disorder. On average the adult American increases bodyweight and composition throughout adulthood. Although increased EE through higher levels of physical activity (PA) have been heavily promoted by public health officials, the association between EE and changes in bodyweight is not clearly understood in America today.

Objective: The purpose of this study was to better define the association between changes in bodyweight and composition with averages of EE over a year period.

Methods: 337 healthy, young adults completed a year-long longitudinal study including 5 clinical measurement sessions, where body composition was calculated using Dual-energy X-ray absorptiometry (DXA) and bodyweight was measured. The bodyweight and composition measurements were then used to create two linear mixed models (LMM)
that calculated the rate of bodyweight and composition change. The participants were then
categorized into groups of bodyweight and composition change. The EE of these groups,
including total daily EE, total daily EE per kg of bodyweight, RER and percentage of EE
from sedentary activities were compared.

**Results:** The average total daily EE was substantially greater for the participants
categorized as substantially gaining weight (SWG) and substantially gaining fat (SFG)
relative to the eight other categories of weight and fat change (substantial weight-loss
(SWL), weight-loss (WL), weight maintenance, (WM), weight-gain (WG), substantial
fat-loss (SFL), fat-loss (FL), fat-maintenance (FM) and fat-gain (FG)). A similar result
was seen in body composition, a substantially higher average total daily EE was found in
those participants gaining substantial body fat. However, when viewing total daily EE on
a per kilogram basis the trends seen with total daily EE are reversed; the weight and fat
maintenance groups expend the most energy on a per kilogram basis.

**Discussion:** Multiple influential factors are associated with bodyweight and composition
change. However along with energy intake (EI), EE make up the primary components
causing ES changes. Because of the greater body mass, heavier people require more
energy to do the same activity as a lighter individual with less body mass. So there was
an association between the substantial weight-change groups and increased energy
expenditure. However, when EE is compared on a per kilogram basis the weight
maintenance group had substantially greater EE values due to the ratio of body surface
area relative to weight.
**Conclusion:**

There were substantial differences observed in total daily EE, total daily EE per kg of bodyweight, and percentage of EE from sedentary activities amongst groups of bodyweight and composition. The SWG and SFG groups were significantly different from the maintenance groups in the previously mentioned variables. The SWG and SFG groups had a higher total daily EE due to their substantially higher starting bodyweight, while the maintenance groups had a higher EE per kg. Lastly the maintenance groups spent less percentage of their total EE in sedentary activities, suggesting a higher level of activity to maintain weight.

**Introduction**

The maintenance of bodyweight and composition are critically linked to overall health. Previous cross-sectional and longitudinal data from the United States (US) have shown that healthy adults gain an average of 1-2kg of bodyweight per year, with subsequent changes in body composition (90). With younger adults the changes in body composition are primarily due to increases in FM. Excess increases in FM lead to obesity and are associated with a myriad of chronic diseases (83). The overall preservation of healthy levels of FM and FFM are essential for health. While a basic understanding of FFM and FM changes associated with normal adults has been established, the changes in obese individuals are less understood. Nearly one third of the US population is obese (92). A better understanding of how excessive body composition changes over time are associated with factors such as energy expenditure (EE) is needed.
While there have been some studies that have investigated the longitudinal changes in bodyweight-change (38;77;93), only a select few investigations have investigated the longitudinal changes in body composition (90;94). In addition, these studies did not categorize the bodyweight or composition change, highlighting the difference between weight-maintenance and substantial weight-gains. Moreover, the factors that influence bodyweight and composition, specifically EE, were not fully explored. Physical activity and total daily EE have been promoted as methods of weight maintenance and healthy bodyweight over the adult lifespan (95;96). The associated total daily EE for adults increasing bodyweight relative to those maintaining bodyweight are not well understood.

The purpose of the current study was to establish a better understanding of how changes in bodyweight and composition in a group of young (ages 21-35) healthy adults is associated with total daily EE.

Methods

The current study uses data that was collected as part of The Energy Balance Study; data was collected from June 2011 to January 2014. The complete methods and overall study design have already been described in detail in previous publications (75). The current study uses a subset of The Energy Balance population including 344 healthy young adults (339 were used for final analysis after exclusion of outliers) ages 21-35 years old, with a body mass index (BMI) of 20-35 kg/m². Exclusion criteria included planned weight-loss surgery, hypertensive (150- mmHg systolic and/or 90 mmHg diastolic), taking selective serotonin reuptake inhibitors, giving birth within the past 12 months, planning to start or stop birth control in the next 12 months while participating in
the first year of the study, history of depression, currently diagnosed or taking medications for a major chronic health condition, using medications to lose weight, started or stopped smoking within the last 6 months and ambulatory blood glucose levels \( \geq 145 \text{ mg/dL} \). All study protocols were approved by the University of South Carolina Institutional Review Board. Participants who completed all measurements in the first year of visits (baseline, 3, 6, 9 and 12 month) were included in the current analysis.

The body composition measurements were taken with other anthropometric measurements. Anthropometric measurements for the 5 visits over the 12-month period (baseline, 3, 6, 9, and 12 month) were performed with the participant dressed in a pair of surgical scrubs and bare feet. For all visits the BMI (kg/m²) was calculated from the average of three height and weight measurements using a traditional stadiometer and electronic scale. The values for both weight and height were recorded to the nearest 0.1 centimeter and 0.1kg. Body composition was measured using a Lunar fan-beam dual X-ray absorptiometry (DXA) scanner (GE Healthcare model 8743, Waukesha, WI). The scans recorded total fat and fat-free mass, as well as torso, arm and leg composition. For the baseline, 6 and 12 month visits the waist and hip circumference of each participant was measured. The waist and hip circumferences were measured using a calibrated spring-loaded tap measure. Waist circumference was determined at the point midway between the costal margin and iliac crest in the mid-axillary line approximately 2 inches above the umbilicus. Hip circumference was measured at the widest point around the level of the greater trochanter. Circumferences recorded were the average of three measurements and were rounded to the nearest 0.1cm.
Total Daily Energy Expenditure Values

The EE values were measured using a SenseWear Mini Armband (BodyMedia Inc. Pittsburgh, PA). The portable, multi-sensor device is worn on the upper-left arm with the sensor itself resting over the triceps muscle. EE and activity are estimated using a combination of a tri-axial accelerometer with biological sensors measuring heat flux, galvanic skin response, near-body ambient temperature, and skin temperature. The Mini Armband has gone through validation with both laboratory and free-living conditions (against DLW) and other previously validated accelerometers. In a recent investigation by Johannsen *et al.* The SenseWear Mini Armband was compared to the EE values generated by the use of free-living DLW (72). At each measurement period of The Energy Balance Study the participants were instructed to wear the monitor for 10 consecutive days constantly for 24 hours except during water activities (i.e., swimming, bathing, showering, or water aerobics). When the participant did remove the monitor the participants recorded these periods in an activity log. Each participant was instructed to record any time the armband was removed in as much detail as possible including the exact time the armband was removed and put back on. The non-wear activities were then incorporated into the estimations of EE based on corresponding MET values according to the 2011 Compendium of Physical Activities (73). The MET values were then multiplied by the participant’s own measured resting metabolic rate. The participant was considered to be compliant if they had 7 days of (including 5 week days and 2 weekend days) at least 23 hours of verifiable time (either logged non-wear time or armband worn).
**Groupings for Analysis**

The Energy Balance Study population was divided into two categorization groupings based off of bodyweight and composition changes experienced over a 12-month period. The two grouping systems of bodyweight and composition were not exclusive. The calculation of each participant's slope and associated standard error (SE) were used to categorize both bodyweight and composition into the categories: substantial weight gain (SWG) if positive and 95% CI excluded 0; weight gain (WG) if positive and 68% CI excluded 0; weight maintenance (WM) if 68% CI contained 0; weight loss (WL) if negative and 68% CI excludes 0; and substantial weight loss (SWL) if negative and 95% CI excludes 0. For the fat categories: substantial fat gain (SFG) if positive and 95% CI excluded 0; fat gain (FG) if positive and 68% CI excluded 0; fat maintenance (FMM) if 68% CI contained 0; fat loss (FL) if negative and 68% CI excludes 0; and substantial fat loss (SFL) if negative and 95% CI excludes 0.

Once the categorizations for bodyweight and composition change of the year period were created the 10 groups were compared based on the average EE values that were created from the SenseWear Mini Armband data.

**Results**

The Energy Balance Study population was divided into two categorization groupings based off of bodyweight and composition. The 10 groups of bodyweight and composition were not equal in total participant number or gender. The number and gender of participants in each weight and composition class can be seen in Table 5.1. In
total 339 participants were used in the categorizations of bodyweight and 337 participants were categorized for body composition. Both bodyweight and composition analysis started with 344 participants, but 5 were excluded as outliers from the bodyweight analysis, as well as 7 from the body composition analysis. Considering there was no change in FFM and most change in bodyweight was due to increases in body fat there are strong similarities between groups. However, there are several participants who do not fall in the same category of weight-change as their fat-change and as well as the converse. 3 participants were considered SFL, but not SWL and 2 participants were considered SWL, but not SFL. 8 participants were considered WL, but not FL and 10 were considered FL, but not WL. 47 participants were considered WM, but not FMM, and 46 were considered FMM, but not WM. 16 participants were considered WG, but not FG, while 17 were considered FG, but not WG. Lastly, 6 participants were considered SWG, but not SFG and 5 were considered SFG, but not SWG. So, despite there being similarities between bodyweight-change and fat-change, there are also substantial differences between groups.

**Bodyweight Results**

When total daily EE was averaged for all 5 groups, the SWG group had a substantially higher value than the WM group when looking at genders combined. The other three groups were not substantially different as seen in Table 5.2. The significance continued when looking at genders separately, with the SWG having a substantially higher average total daily EE than WM for both male and female, refer to Figure 5.1. When gender was combined the SWG group expended over 200 more calories per day relative to the WM group. As seen in Table 5.1, the groups the WM group held a higher
percentage of females and the SWG held a higher percentage of males, thus exacerbating the already substantial difference seen in the separate gender values to a greater extent in the combined gender value.

The trends that are seen in total daily EE values are reversed when the EE is expressed on a per kilogram of bodyweight basis. The WM group has an average of 37.44±4.65, while the SWG group has an average of 34.61±4.83, making the difference substantially different ($p<0.001$). While the WM group did have a higher average than the SWL group the difference was not substantial ($p=0.092$), as seen in Figure 5.3. With EE per day of roughly 38 kcal/(kg day), the males in all groups except for the SWG had very similar values. The differences seen in the values for the combined gender groups are mainly due to the differences seen in the female participants. The difference between SWG and WM in women is substantial ($p<0.001$), and while the $p$ value for the difference between the SWL group and the WM is smaller it still is not substantial ($p=0.081$).

When viewing the measured calories per day required for RER, the SWG burned substantially more calories per day in RER relative to the WM ($p<0.001$). No other differences were seen between groups in the measured RER. While there were no substantial differences between groups in calories expended in physical activity (PA) the WM group have the highest absolute value. All of the values for total daily EE, total daily EE per kg of bodyweight, RER and PA EE can be seen in Table 5.2. Lastly, the percentage of calories from sedentary activities was analyzed for each bodyweight group. The SWG group derived substantially more of their total calories from sedentary...
activities relative to the WM group ($p=0.034$). All averages of EE from sedentary activities can be seen in Table 5.3.

**Body Composition Results**

The results seen for the body composition groups were similar to those seen with bodyweight, but there were some differences. Total daily EE was averaged for all 5 groups of body composition; the SFG group was substantially higher value than the WM group when looking at genders combined ($p<0.001$). The other three groups were not substantially different as seen in Table 5.2. A similar trend was seen when viewing genders separately, with the SFG having a substantially higher average total daily EE than FMM for both genders. When gender was combined the SFG group expended over 250 more calories per day relative to the FMM group, refer to Figure 5.2. Similar to the bodyweight groups, the FMM group held a higher percentage of females and the SFG held a higher percentage of males, which made the difference between FMM and SFG greater in the combined gender totals.

The trends seen for bodyweight groups were similar to those seen in the body composition groups. The total daily EE value trends were reversed when the EE was expressed on a per kilogram of bodyweight basis. The FMM group was substantially higher than SFG ($p<0.001$). The FMM group was not substantially different from the SFL group ($p=0.261$), as seen in Figure 5.4. Unlike the bodyweight groups, the males in the FL group had the highest level of EE per kg of bodyweight with the FMM group very close. In general there was more difference between all of the male groups than there was
in the bodyweight groups. Therefore the differences seen in the values for the combined gender groups are due to differences seen in both genders.

When viewing the measured calories per day required for RER, the SFG burned substantially more calories per day in RER relative to the FMM \((p<0.001)\). No other differences were seen between groups in the measured RER. While there were no substantial differences between groups in calories expended in physical activity (PA) the FMM group have the highest absolute value. All of the values for total daily EE, total daily EE per kg of bodyweight, RER and PA EE for the body composition groups can be seen in Table 5.2. Like the bodyweight groups, the percentage of calories from sedentary activities was also analyzed for each body composition group. The SFG group derived substantially more of their total calories from sedentary activities relative to the FMM group \((p=0.019)\). All averages of EE from sedentary activities can be seen in Table 5.4.

**Discussion**

When analyzed, the EE of the bodyweight and composition groups had substantial differences within groups. As previously mentioned the LMM that was created for body composition included FFM as a dependent variable. If FFM did not change significantly over time than it may be deduced that the majority of bodyweight-changes that occurred over the year would be due to FM alone. Since this was the scenario it would seem that categorizing the population based on yearly FM change and yearly bodyweight-change would yield very similar results. While there were some definite similarities between the FM and bodyweight groups there were also some apparent differences. These differences are echoed in the values seen for EE.
For total daily EE the group with highest value was the SFG, but there was a mere 6 kcal difference between SFG and SWG. Both SFG and SWG were substantially higher than the respective FMM and WM groups. The differences seen in overall total daily EE are not surprising considering the respective starting weights of both the SFG and SWG groups. These two groups have baseline weights that are roughly 10kg higher than the two maintenance groups. The larger mass requires a substantial more amount of energy to sustain which lead to the substantially higher total daily EE. While the differences in total daily EE for females are slightly less exaggerated, most likely this is due to smaller amount of total calories burned. Since the SWG and SFG groups are adding a tremendous amount of ES over the relatively short amount of time (a year), an expected reason would be a reduced EE. Looking at the values of total daily EE there seems to be the opposite trend, the groups gaining the most mass are on average expending the most calories. However keeping in mind the previously mentioned baseline weights the differences in EE are understandable.

Viewing EE on a per kg basis the values are rearranged and the two maintenance groups of WM and FMM become the highest calorie expending groups. Once again because of the substantial differences in starting weight the differences in EE per kg are to be expected. But even though EE per kg is higher for the maintenance groups does not necessarily mean these groups are expending substantially more calories when factoring in the differences of weight. While EE is affected by bodyweight and composition it is also affected by body surface area (BSA). A greater BSA relative to bodyweight creates a higher basal metabolic rate, which is the reason for a taller thinner individual’s having a
higher metabolic rate (97). Factoring in bodyweight and BSA would afford a more
accurate way of looking at the EE of each of the participants.

Another way to analyze the EE of the participants was through the analysis of the
measured RER. Following the same trend as overall total daily EE, the RER was
substantially increased for the SFG and SWG groups. When the values of RER are
divided by the total daily EE a percentage of calories derived from purely sedentary
activities can be calculated. Looking at the percentage of calories coming from sedentary
activities shows that the SWG and SFG groups derive a substantially larger percentage of
their EE from sedentary activities. Conversely the weight and fat maintenance groups
derived a substantially less percentage of expended calories from sedentary activities. In
addition to the SFG and SWG groups expending substantially less calories in non-
sedentary activities relative to the WM and FMM groups, the SWL and SFL groups did
as well. Even though the participants of the SWL and SFL were losing a large percentage
of ES over a year period they had a lower EE per kg of bodyweight and were deriving
proportionately more expended calories from sedentary activities relative to the
maintenance groups. This supports the idea that the members of the SWL and SFL
groups reduced their total and fat mass through reductions in EI rather than substantial
increases in EE. In addition the SWG and SFG groups appear to have gained significant
amounts of ES through a decreased EE per kg.

Conclusion

There were substantial differences among weight and fat mass change groups in
all of the observed EE variables that were measured including, total daily EE, total daily
EE per kg of bodyweight, RER and percentage of EE from sedentary activities. The SWG
and SFG groups were substantially different from the maintenance groups in total daily EE, expending a substantially more amount of calories. However, the increased calorie expenditure was due to a significantly higher starting bodyweight that by the end of the year period was on average 4kg greater. While the bodyweight did increase significantly over the year period there was no subsequent increase in EE of the five measurements. This would be more likely in the SFG and SWG groups considering the 4kg increase in bodyweight. The WM and FMM groups had substantially higher EE when analyzed on a per kg basis relative to the SWG and SFG groups. In addition, the WM and FMM groups had substantially less percentage of their total EE derived from sedentary activities, which suggests a higher activity level relative to the SWL, SFL, SFG and SWG groups. More research is needed to incorporate the fluctuations in EI to fully understand the energy balance in relation to weight gain and weight maintenance.

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**Acknowledgement:** We thank the Energy Balance Staff for the collection and management of the data used in this study and the participants for the dedication to completing the measurements. We also thank our International Advisory Board for help and guidance throughout the study.
<table>
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<tr>
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<th>Total Participants (n)</th>
<th>Female Participants (n)</th>
<th>Male Participants (n)</th>
<th>Female BMI</th>
<th>Female Baseline Weight (kg)</th>
<th>Female Baseline Height (cm)</th>
<th>Male BMI (kg/m²)</th>
<th>Male Baseline Weight (kg)</th>
<th>Male Baseline Height (cm)</th>
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<td>7</td>
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<td>84.96±14.73</td>
<td>176.68±7.26</td>
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<tr>
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<td>25</td>
<td>17</td>
<td>8</td>
<td>27.21±4.75</td>
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<tr>
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<td>82±5.54</td>
<td>178.13±8.39</td>
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<tr>
<td>SWG</td>
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<td>38</td>
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<td>74.99±15.32</td>
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Table 5.2: Total EE for Bodyweight and Composition Groups

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<th></th>
<th>Total Daily EE (kcal/day)</th>
<th>Total Daily EE/kg (kcal/kg/day)</th>
<th>Measured RER (kcal/day)</th>
<th>Physical Activity EE (kcal/day)</th>
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<td>F:1431.0±187.20</td>
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<td>M:33.35±5.94</td>
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<td>M: n-44</td>
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<td>T=Total Energy Balance Population, M=Male Participants, F=Female Participants</td>
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Table 5.3: Percentage of Calories from Sedentary Activities for Body Composition Groups

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<th>FM</th>
<th>FG</th>
<th>SFG</th>
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<td>%Sedentary</td>
<td>T:56.59±8.88</td>
<td>T:53.72±7.25</td>
<td>T:53.06±7.71</td>
<td>T:55.19±9.28%</td>
<td>T:55.67±6.94%</td>
</tr>
<tr>
<td></td>
<td>M:54.08±6.34</td>
<td>M:49.34±4.93</td>
<td>M:52.92±7.97</td>
<td>M:54.37±9.24%</td>
<td>M:55.66±7.07%</td>
</tr>
<tr>
<td></td>
<td>F:59.08±9.97</td>
<td>F:55.79±7.36</td>
<td>F:53.06±7.54</td>
<td>F:56.32±9.35%</td>
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<td>SWL</td>
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<td>WM</td>
<td>WG</td>
<td>SWG</td>
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<td>--------------------------</td>
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<tr>
<td>%Sedentary</td>
<td>T:56.03±9.35%</td>
<td>T:53.57±6.64%</td>
<td>T:53.29±7.47%</td>
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<td>M:52.65±5.57%</td>
<td>M:51.96±7.31%</td>
<td>M:53.33±7.04%</td>
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Table 5.4: Percentage of Calories from Sedentary Activities for Bodyweight Groups
Figure 5.1: Total Daily Energy Expenditure for Weight-Change Groups
Figure 5.2: Total Daily Energy Expenditure for Fat-Change Groups
Figure 5.3: Total Daily Energy Expenditure per Kilogram of Bodyweight for Weight-Change Groups
Figure 5.4: Total Daily Energy Expenditure per Kilogram of Bodyweight for Weight-Change Groups
CHAPTER VI

OVERALL SUMMARY AND CONCLUSIONS

The balancing of energy in the human body throughout adult life is an extremely intricate process that affects weight-change, risk of obesity and overall health. The current dissertation has served to investigate several areas of energy balance to better understand how energy balance and weight-change are viewed by the public.

The major purpose of this dissertation was to characterize bodyweight and composition change in terms of steady state rate of change. Lastly, see how EE is associated with the various categorizations of bodyweight and composition change. Specifically, the purpose of the current dissertation was to:

1) To determine the overall weight-changes that occurs over a year period in a large group of healthy adults.

2) To determine the overall body composition changes that occurs over a year period to a group of 344 healthy adults.

3) To determine the association between changes in bodyweight and composition and EE.

The three investigations of this dissertation were collected as a part of the first year of the Energy Balance Study (a comprehensive study designed to determine the
associations of caloric intake and energy expenditure on changes in bodyweight and composition in a population of healthy men and women). The investigations of the current dissertation are crucial to providing insight and results to the primary aim of this study.

The three studies of this dissertation used the quarter-annual clinical measurements that were collected over the first year of the Energy Balance study. The first two studies utilized linear mixed models (LMM) to examine the effects of bodyweight and composition. The use of an LMM accounted for between participant changes, and for inter-measurement variation for each participant. The LMM provided a distinctive perspective on both bodyweight and composition changes, which is not typically seen in the current research literature. The primary aim of the Energy Balance study was to observe the changes of bodyweight and composition over an initial timeframe of 12-months. To truly observe rates of change and account between measurement variations, a LMM is necessary. The first and second aim gave deeper insight into the question of how energy storage changes over extended periods of time, which is crucial to better understand energy balance. The third aim took the data regarding ES that was gained in aims 1 and 2 and associated this with the EE of each participant.

The primary results from these three studies include:

1. The calculated weight-change by the LMM averaged for the entire Energy Balance population was very similar to the weight-change measured by taking the 12-month measurement and subtracting the baseline measurement. However,
when viewed on an individual basis the values for each participant are substantially different. Traditional measurements of bodyweight are inaccurate for accessing bodyweight-change.

2. There were substantial differences observed in total daily EE, total daily EE per kg of bodyweight, RER and percentage of EE from sedentary activities amongst groups of bodyweight and composition. The SWG and SFG groups were substantially different from the maintenance groups in the previously mentioned variables. The SWG and SWF groups had a higher total daily EE due to their substantially higher starting bodyweight, while the maintenance groups had a higher EE per kg. Lastly the maintenance groups spent less percentage of their total EE in sedentary activities, suggesting a higher level of activity to maintain weight.

3. There were substantial differences observed in total daily EE, total daily EE per kg of bodyweight, RER and percentage of EE from sedentary activities amongst groups of bodyweight and composition. The SWG and SWF groups were substantially different from the maintenance groups in the previously mentioned variables. The SWG and SWF groups had a higher total daily EE due to their substantially higher starting bodyweight, while the maintenance groups had a higher EE per kg. Lastly the maintenance groups spent less percentage of their total EE in sedentary activities, suggesting a higher level of activity to maintain weight.

The results from the current dissertation provided crucial information for better understanding energy balance. The chief novelties of these studies are the
examination of bodyweight and composition with LMM, which allow for more understanding of how ES changes in the individual over time. In addition, the last study shows that there is a link between EE and maintaining bodyweight and composition. The participants who were considered in weight maintenance weighed substantially less than the participants gaining substantial amounts of mass. This suggests that the behaviors and tendencies that have driven EE and EI in the participants gaining mass during the length of the study, have most likely been driving their EE and EI for several years before the study. The first two papers suggest that anyone with a positive trajectory of weight is at risk for weight to increase above a healthy level. Regardless of fluctuations in water, the yearly trend shows gains in weight. The first two papers also show that while there were many participants in the Energy Balance study who were trying to lose weight, very few succeeded in having a negative trajectory of weight for the entire year. The third paper added associations of EE with the novel groupings of weight-change and fat-change that were created in papers 1 and 2. Paper 3 suggests that the individual’s maintaining their weight and fat-mass are deriving substantially less of their calories from sedentary activities. The studies of this dissertation are the first to look at changes of bodyweight and composition of the same sample population using a LMM to more accurately predict the changes. Further studies should include how the EI of an individual varies over time so that a more accurate assessment of the full energy balance equation may be depicted.

In summary, the use of an LMM depicting changes in mass and weight were more accurate than traditional methods for projecting mass and weight gain over extended
periods of time. The LMM eliminated much of the between measurement extraneous fluctuation that is due to water flux and other factors. The two models for bodyweight and composition were compared and in this population of young healthy adults it was realized that the predominant amount of bodyweight-change was due to fat change. Lastly, connections between ES and EE were made in the last paper showing an association between a substantially decreased percentage of total daily EE coming from sedentary activities and the maintenance of bodyweight and composition. Therefore, these three papers stress the importance of proper monitoring of bodyweight and composition and the importance of non-sedentary EE
REFERENCES


