THESIS

EFFECTS OF OBESITY ON THE ENERGETICS OF GRADIENT WALKING

Submitted by

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ABSTRACT

EFFECTS OF OBESITY ON THE ENERGETICS OF GRADIENT WALKING

Walking is a popular and convenient form of physical activity and can play an important role in the treatment and prevention of obesity. During level walking, obese adults are reported to have a greater net metabolic rate (W/kg) but a similar metabolic cost (J/kg/m) compared to non-obese adults. Individuals routinely walk up or down grades, but the metabolic response to gradient walking in obese individuals is not well understood. **PURPOSE:** To quantify metabolic rate and metabolic cost during level and gradient walking in obese and non-obese adults. A secondary purpose was to determine metabolic prediction equations' ability to estimate energy expenditure in obese adults. **METHODS:** Thirty-two obese (18 female, mass = 103.2 (15.8) kg, BMI = 35.0 (4.5) kg/m^2, mean (SD)) and nineteen non-obese (10 female, mass = 64.9 (10.6) kg, BMI = 21.6 (2.0) kg/m^2) volunteers participated in this study. We measured oxygen consumption while subjects stood and walked on a dual-belt force measuring treadmill at eleven speed/grade combinations ranging from 0.50 m/s to 1.75 m/s and -3° to 9°. We calculated gross and net (gross-stand) metabolic rate and metabolic cost for each condition. A two-factor repeated measures ANOVA determined how group (obese vs. non-obese) and speed/grade affected metabolic rate/cost. Bland-Altman plots and linear regression was used to determine the accuracy of prediction equations compared to measured oxygen consumption. **RESULTS:** Net metabolic rate increased with walking

peed and grade, ranging from 1.91 (0.06) W/kg at 1.25 m/s, -3° to 5.91 (0.13) W/kg at 1.50 m/s, 3°, (mean (SE)). Obese individuals walked with a smaller gross metabolic rate ($p<0.001$), net metabolic rate ($p=0.013$), gross metabolic cost ($p<0.001$) and net metabolic cost ($p=0.006$) compared to non-obese adults. Body fat percentage, VO_2 peak, and step width did not explain the variance in metabolic rate. Positive joint work was related to net metabolic rate during level walking, but not during uphill walking. ACSM and Pandolf prediction equations did not accurately predict metabolic rate/energy expenditure at all speed/grade combinations. Thus, we developed a new prediction equation for obese adults that is more accurate in predicting the energetics of walking.

CONCLUSIONS: The smaller metabolic rate in obese adults suggests these individuals have better economy when walking on level or uphill/downhill grades. The mechanism by which economy is improved in obese adults has yet to be discovered.

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CHAPTER I

INTRODUCTION

Obesity prevalence and the associated risks for chronic disease are a major health concern in many parts of the world [1]. Obesity is associated with heart disease, diabetes, and certain cancers and is one of the main preventable risk factors for osteoarthritis [2, 3]. Obesity is typically caused by a chronic energy imbalance, where energy intake exceeds expenditure [4]. As a result, individuals interested in weight management are advised to modify diet and engage in at least 30-60 minutes of moderate-vigorous (40-60% VO_2max) physical activity (MVPA) most days of the week [5].

Walking is the most popular form of physical activity (PA) for weight management because it is easy, accessible, relatively safe (i.e. small risk of musculoskeletal injury) and requires considerable metabolic energy [6]. In order for weight management to be successful, individuals must know how much energy is expended during PA. While it has been well established that obese individuals expend more metabolic energy (gross metabolic rate, W) during level walking compared to non-obese [7-10], the energy expended by obese adults during gradient walking (i.e. uphill and downhill) is not well understood. Given the frequency with which individuals encounter grades during walking (either by necessity or choice), an understanding of the physiological responses to changes in gradient is needed to develop comprehensive guidelines for walking as a form of PA.

Gross metabolic rates ($E_{gross,}$ W) are greater in obese vs. non-obese individuals during level walking across a range of walking speeds [7-10]. These differences in metabolic rate between obese and non-obese adults are reduced when metabolic rate is normalized by total body mass ($W \cdot kg^{-1}$), although the mass-specific metabolic rates are still greater in obese adults [7, 8]. This suggests that body mass is a key determinant of the metabolic rate during level walking, but that other factors affect metabolic rate. Net metabolic rate (gross-standing, E_{net}) has been reported as a quantity that reflects the economy of the walking movement [11]. Given the smaller mass-specific resting (E_{rest})/standing (E_{stand}) metabolic rates of obese individuals [12], E_{net} ($W \cdot kg^{-1}$) during level walking are greater in obese vs. non-obese adults [8, 13-16]. This suggests that obesity reduces level walking economy.

The greater E_{net} and lower economy of obese compared to non-obese adults has been linked to anthropometric and biomechanical characteristics including body composition/distribution [17, 18] and step width [19, 20]. Obese individuals have heavier limbs that must be accelerated/decelerated during swing and walk with wider steps [20], both of which have been shown to increase walking metabolic rate in non-obese adults [21, 22]. In addition, the mechanical work ($J \cdot kg^{-1}$) performed by the lower extremity joints is a determinant of metabolic rate during level walking in non-obese adults [10]. The mechanical joint work in obese adults has been shown to be greater than non-obese adults [23], suggesting a potential explanation for an increased metabolic rate in this population.

Importantly, the E_{gross} of walking in weight-reduced obese adults is reduced by more than would be expected based on changes in body mass (i.e. walking economy

improves with weight loss), suggesting that obese adults may alter their gait to improve economy [9]. It has also recently been reported that walking economy is inversely associated with mass-specific peak oxygen uptake ($mlO_2 \cdot kg^{-1} \cdot min^{-1}$) in non-obese adults [24]. As obese individuals typically have much lower mass-specific peak oxygen uptakes compared to non-obese individuals [8, 11, 16, 25], this would suggest walking economy may be improved with obesity.

Walking on inclines increases E_{net} in non-obese adults compared to level walking at the same speed, while decline walking reduces E_{net} [26, 27]. However, there have been few studies that have investigated the energetics of gradient walking in obese adults. A recent study by Lafortuna et al. reported that absolute E_{net} (W) in class III obese women ($BMI > 40\ kg \cdot m^{-2}$) was greater during incline treadmill walking compared to non-obese women [26]. However, differences in mass-specific E_{net} ($W \cdot kg^{-1}$) was dependent upon treadmill speed as E_{net} was similar in non-obese and obese at 1.0 m/s and 4% incline but greater in obese when the treadmill speed was 1.3 m/s and the incline was 4% [26]. These results suggest that differences in E_{net} and economy due to adiposity may only be observed at greater workloads (i.e. faster speeds/greater inclines).

Further insights into how obesity may affect the energetics of gradient walking may be gained by results from load-carrying studies. Research has shown that mass-specific gross oxygen consumption (ml/kg/min, gross VO_2) increases with load carriage during uphill walking [27]. However, these increases in gross VO_2 are quite modest when comparing unloaded and loaded gradient walking in non-obese adults (21.4 vs. 24.4 ml/kg/min with 10 kg load (12% of body mass), and 21.4 vs. 27.4 ml/kg/min with 20 kg load (25% of body mass)) [27]. When normalized to total mass (body and load), rates of

oxygen consumption were similar, ~21.4, 21.7, and 22.0 ml/kg/min, for the unloaded, 10kg and 20kg load conditions, respectively, despite the loads being carried in the hands [27]. Sagiv et al. demonstrated that changes in the gradient of walking contributed more to the increased metabolic response than faster walking speeds, regardless of the amount of load carried on the back [28]. Similar to other studies, this study also reported that metabolic rate normalized to total mass was smaller compared to unloaded walking [28]. These results suggest that walking with loads may improve economy. Research has also shown that metabolic rate during loaded walking does not always increase linearly as a function of the carried weight [29, 31], suggesting chronic exposure to walking with loads might mitigate some of the expected increase in metabolic rate due to the load [29].

Individuals interested in weight management require accurate estimates of physical activity energy expenditure (EE). Typically, individuals and equipment (e.g. treadmill) manufacturers use published prediction equations to estimate VO_2, metabolic rate or EE during specific tasks, with the ACSM [30] and Pandolf [31] equations being the most common for walking. However, these equations may not be accurate for obese individuals, particularly given the differences reported in the metabolic rate of walking in obese vs. non-obese adults. Surprisingly, few studies have examined the accuracy of these common prediction equations across a range of walking speeds and grades in obese adults, with much inconsistency between predicted and measured EE [30-33]. If existing prediction equations are inaccurate across speed/grade combinations, new equations for obese individuals need to be developed.

Statement of Problem

The primary purpose of this study was to compare the metabolic rate and cost of level and gradient walking for class I and class II obese vs. non-obese men and women. A secondary purpose was to compare the accuracy of common energy expenditure prediction equations to a new prediction equation based on the current study.

Hypotheses

We hypothesized the following: 1) Net metabolic rate would be greater for obese compared to non-obese adults across a range of speed/grade combinations that elicit moderate-vigorous intensities. 2) Net metabolic rate would be positively correlated with adiposity, step width and positive joint work in obese vs. non-obese adults and will explain the increase in net metabolic rate in obese adults. 3) Gross and net metabolic cost would be greater for obese compared to non-obese adults across the same speed/grade combinations. 4) ACSM and Pandolf metabolic rate prediction equations would be inaccurate for obese adults at some speed/grade combinations.

CHAPTER II

LITERATURE REVIEW

Obesity Pandemic

Obesity adversely affects the health and quality of life in an increasing number of people and is recognized as one of the leading health concerns in many parts of the world [34]. The prevalence of overweight adults exceeds 34% in the United States, with an additional 32.2% percent of adults considered obese [34]. Obesity is defined as having a Body Mass Index (BMI) > 30 kg/m^2 and significantly increases the risk for many chronic diseases including hypertension, stroke, respiratory disease, type 2 diabetes, osteoarthritis and certain cancers [35, 36]. Heart disease is the number one cause of death in United States, with over 700,000 deaths per year [37]. Importantly, 20-30% of mortality associated with cardiovascular disease is attributed to excess body weight [38].

Type 2 diabetes and obesity also have a very strong association, in both genders, and across all ethnic groups [2]. Women with a BMI $\geq$ 31 kg/m^2 are 40 times more likely to get diabetes compared to women with a BMI $\leq$ 22 kg/m^2 [39]. Similarly, research has shown men with a BMI $\geq$ 35 kg/m^2 are nearly 42 times more likely to get diabetes compared to men with a BMI $\leq$ 23 kg/m^2 [40]. Additionally, weight gain seems to precede the development of diabetes. In longitudinal research on the Pima Indians, an increase in body weight preceded the development of diabetes [41]. However, weight

reduction is beneficial in reducing the risk for these conditions and is therefore considered an integral part of treating chronic morbidities, such as diabetes and cardiovascular disease [2].

There are many factors that are thought to play a role in the development of obesity including genetic, metabolic, environmental and behavioral influences. Due to the rapid increase in prevalence, behavioral and environmental influences have been suggested to predominate, with genetic changes having less influence. It is thought that the most important element responsible for excessive weight and body fat mass gain is the chronic imbalance between energy intake and energy expenditure [42]. It is not surprising that diet and PA trends have changed over time; however, the relative contribution of these factors is still being debated. Many studies support the notion that energy intake has increased, mostly attributed to an increased percentage of food consumed outside the home, greater consumption of soft drinks, and larger portion sizes [43]. However, there have been inconsistent results in quantifying changes in energy consumption, suggesting that changes in energy expenditure may also play a significant role. There are multiple ways energy expenditure has been reduced: decrease in activity required for work and living [44], increased sedentary time, and a reduced amount of time spent participating in moderate-to-vigorous physical activity (MVPA) [45].

Physical Activity and Obesity

There is a strong relationship between decreased levels of PA and obesity rates. Obese children spend less time than their non-obese counterparts doing moderately

intense PA such as walking and more time in sedentary activities [42]. Furthermore, rates of obesity are significantly higher in sedentary adult males (27%) compared to moderately active (17%) and active males (20%) [46]. The same holds true for sedentary adult women (27%) and moderately active women (21%), compared to active women (14%) [46]. Fulton et al. reported that moderate to vigorous levels of PA had a negative correlation with both BMI and fat mass [47]. Low physical fitness and PA are independent predictors for all-cause mortality, CVD mortality and cardiovascular events [2], thereby increasing the risk even more, because obese adults tend to be less active.

Dietary intervention combined with exercise is likely the most effective method in combating the obesity epidemic [48]. Walking is the most popular and convenient form of exercise and is an important component of weight management [49-51], as it is responsible for expending more metabolic energy than any other daily physical activity [52]. It is typically a low-impact and familiar form of PA, and is often prescribed to previously sedentary adults. Furthermore, research has reported weight loss in overweight and obese persons during either long or short bouts of brisk walking [51]. Richardson et al., in a Meta-Analysis of the literature, report that the mean weight loss during a pedometer based walking program (independent of diet) was approximately 1 kg [53]. The duration of the intervention ranged from four weeks to one year, with a mean weight loss of 0.05 kg per week [53]. Although this is a modest weight loss, it provides evidence that weight loss can be accomplished with moderate levels of walking PA. Apart from weight loss, brisk walking for five or more hours per week has also been associated with a 40% reduction in the risk of developing obesity related diseases [54]. Additionally, walking PA is associated with other health benefits such as reduced risk of

cardiovascular events, lower blood pressure, and improved glucose tolerance in individuals with either impaired glucose or type 2 diabetes [55, 56].

In 1995, as a result of research demonstrating the positive health benefits of PA, the Centers for Disease Control and Prevention (CDC) and the American College of Sports Medicine (ACSM) recommended that every "US adult should accumulate 30 minutes or more of moderate-intensity (40-60% of VO_2max) PA on most, preferably all, days of the week." ACSM updated their PA recommendations in 2007 to include participating in moderate intensity activity for 30 minutes, 5 days per week, or vigorous intensity activity for 20 minutes, 3 days per week [5]. The recommendations also allow for combinations of both moderate and vigorous activities which can be completed in increments of 10 minutes. Importantly, these recommendation are based merely on preventative effects of cardiovascular disease (CVD) and other chronic diseases, while not considering their potential effect on musculoskeletal health or weight loss [5]. Research has also shown that greater levels of PA may be necessary for weight loss and management [57, 58]. As a result, US Dietary Guidelines suggest 60 minutes per day of moderate intensity PA to prevent weight gain [59], while more recent data report ~150-300 minutes per week for moderate weight loss (<3% of initial body weight) [58, 60]. ACSM recommends 60 to 90 minutes a day for weight loss and weight maintenance [5].

Despite the known positive benefits in cardiovascular, metabolic, musculoskeletal health and weight management, a significant majority of American adults do not achieve the minimum PA guidelines set forth by ACSM [61]. It is suggested that the low levels of PA in obese adults is partly due to difficulty in performing activities that require a greater effort to raise/lower their body mass against gravity (e.g. walking) [62]. For

example, obese adults require a greater percentage of their maximal oxygen uptake as well as greater metabolic EE at a given walking speed compared to non-obese individuals [63, 64].

In addition, research shows that slight increases in weight bearing activities such as walking, can induce musculoskeletal discomfort and pain in obese persons, possibly leading to injury [16]. It has been suggested that the increased risk of musculoskeletal injury is due to the relative lack of muscle mass and excess adiposity of obese persons [65], or relatively large loads on the musculoskeletal system due to mass. This reduced muscle mass to fat mass ratio may be due to physical inactivity or obesity itself. Hence, individuals with low levels of PA would be more likely to develop such injuries during activity. Hootman and colleagues have reported an association between physical activity and musculoskeletal injury in both active and sedentary adults, with over 80% of the total all-cause musculoskeletal injuries in men and women related to PA (run/walk/jog or sports program) [6]. More importantly, more than 75% of men and 65% of women, reported injuries that stopped them from participating in their exercise program temporarily, with ~25% of those adults reporting injuries that stopped them from participating in their exercise program permanently [6].

Energetics of Walking

Walking is a complex process with interactions between muscular and inertial forces that result in smooth progression of the body through space while minimizing mechanical and physiological energy [66-69]. Walking consumes a significant amount of

metabolic energy and is the most common form of PA performed by individuals. Therefore, understanding the energetics of walking in obese vs. non-obese individuals is essential. The energetics of walking can be quantified by recording oxygen consumption and carbon dioxide production via indirect calorimetry. Typically, the energetics of walking is described by reporting the oxygen consumption (VO_2, L/min), metabolic rate (E, W), or rate of energy expenditure (EE, kcal/min). These rate variables can be used to provide insights into walking economy. The energetics of walking can also be described as the metabolic cost necessary to walk a certain distance (C_w, J/m), which can provide insights into preferred walking speed.

Metabolic rate and walking economy

Metabolic rate during level walking is dependent upon several factors including walking speed and body mass. In general the metabolic rate (W) vs. walking speed relationship is J-shaped, with faster walking speeds requiring disproportionately greater metabolic rates [70]. Relatively few studies have examined the energetics of level walking across a range of walking speeds in obese adults. These studies suggest that obese adults walk with a greater VO_2 (L/min) [14, 16], E_{gross} (W) [8, 11] and EE (kcal/min) [9] compared to non-obese adults. When $_{gross}$ is normalized by body mass, the differences between obese and non-obese adults are reduced or eliminated, suggesting that body mass is a primary determinant of the metabolic rate of walking [8, 13, 15, 16].

E_{net} (gross-standing) may provide a better measure of the metabolic energy required for the walking movement as it removes standing metabolic rate. E_{stand} (W/kg)

is significantly smaller in obese adults compared to non-obese adults. Browning and Kram reported an 11% difference in mass-specific E_{net} in obese vs. non-obese adults across six different level walking speeds [8]. Additionally, this study found that obese women had the greatest E_{net}: 10% greater than obese men and non-obese women, and 20% greater than non-obese men [8]. This suggests that sex also affects the metabolic rate during level walking in obese adults. In obese adolescents, E_{net} is ~25% greater when compared to non-obese across a range of level walking speeds [42]. These findings have been supported by a recent study which predicts a 10% greater E_{net} of walking in obese vs. non-obese adults while walking at 1.4 m/s [15]. Using E_{net} as an indicator of economy, this suggests that obese adults are less economical than their non-obese counterparts. Because obese persons have heavier legs and walk with a greater step width and leg swing circumduction, one might expect that the metabolic rate would be substantially greater in obese vs. normal weight adults [19, 20]. However, this is not always the case and Browning and Kram have hypothesized that as a person becomes obese, "they learn to walk in a way that reduces the mechanical work required to lift, lower, accelerate, and decelerate their center of mass" [71].

The energetics of uphill walking in the non-obese population has been thoroughly investigated. Some of the first work was done by Margaria in 1938. He found that as grade increased from -20% to +20%, metabolic rate also increased [72]. Ardigo et al. reported an increase in metabolic rate while walking up moderate inclines (<10°), compared to level walking at the same speed [73]. Others have reported a significant increase in mass-specific VO_2 when walking up gradients of 10 and 15% compared to level, however no differences were seen between level and 5% inclines [74]. There were

no significant gender differences at 0 and 5% inclines, however, at 10 and 15% inclines, non-obese women had a significantly increased VO_2 compared to their non-obese male counterparts [74].

There is much less research regarding the effects of obesity on the energetics of gradient walking. Lafortuna reported a 6-13% greater E_{net} (W/kg) in obese vs. non-obese individuals when walking up moderate inclines of 4% [26]. Importantly, these young obese women walked at 75% of their estimated maximal capacity, at 1.3 m/s and 4% incline, suggesting that this task could not be sustained by untrained individuals [26]. Freyschuss and Melcher reported ~33% greater VO_2 (ml/kg/min) in Class III (BMI>40 kg/m^2) obese adults, walking at 1.0 m/s across a range of inclines (1-7%) [14].

Further insights into the energetics of gradient walking in obese vs. non-obese adults are provided by non-obese individuals walking uphill with loads. Laursen et al. reports VO_2 increased 70% while subjects walked uphill carrying 10 kg loads, and VO_2 doubled when the load was 20 kg [9]. However, these increases in gross VO_2 are quite modest when comparing unloaded and loaded gradient walking in non-obese adults (21.4 vs. 24.4 and 27.4 ml/kg/min with 10 kg load (12% of body mass), and 20 kg load (25% of body mass), respectively) and when normalized to total mass (body and load), rates of oxygen consumption were similar, ~21.4, 21.7, and 22.0 ml/kg/min, for the unloaded, 10kg and 20kg load conditions, respectively [27]. However, these loads were carried in the hands of the participants, and may not represent the effects of excess weight carried in obese adults. Work done by Sagiv et al. suggests that changes in the gradient of walking were a more important contributor to an increased metabolic response than faster speeds, regardless of load [28]. For example, while walking at a 5% gradient, oxygen uptake was

19.2 ml/kg/min with a 25kg load, with only a modest increase in VO_2 to 21.9 ml/kg/min with a 35kg load [28]. However, when the metabolic rate is divided by the total mass carried (mass of the person plus the mass of the load) the metabolic rate is reduced compared to the unloaded condition [28]. Thus, if normalized by the total mass, a person carrying a load uphill is more economical compared to walking without a load. Another example of this can be shown using the Pandolf prediction equation. If a person weighs 74kg and walks up a 5% incline at 1.6m/s, the Pandolf equation predicts gross metabolic power of 8.14 W/kg. If this same person carries a 25kg load during the same walking condition, they can either be more or less economical depending on the normalization method. If normalized by body mass, Pandolf predicts a metabolic power of 10.69 W/kg. However, if we assume that obesity is merely added mass and treat the load as such, the metabolic power predicted is 7.99 W/kg when normalized to total mass.

Previous research suggests that degree of obesity plays a role in metabolic rate and economy, as metabolic EE increases with increasing BMI [15]. However, Browning and colleagues reported similar E_{net} (W/kg) in a small sample of class III compared to class II obese individuals during level walking [11]. The similarity between these two groups may be because the slope of the percent body fat vs. BMI relationship decreases above the class II obesity standard [75]. Browning et al. speculated that their class II and class III individuals may have had similar body fat percentages, regardless of differing BMIs, although body composition was not directly measured [11]. Further evidence of this is the similar E_{stand} (W/kg) in class III compared to class II obese, despite a 50% greater body mass [11].

Weight loss has also been associated with a decrease in standing and walking metabolic rate. Research has shown that the reduction in metabolic rate after weight loss is greater than expected based on the reduced body mass [9, 76, 77]. With a 20% reduction in body mass, Foster et al. reported a ~30% decrease in energy cost of walking [9]. Hence, weight-reduced adults may save metabolic energy by not only reducing the body mass carried with each stride, but by also potentially decreasing the EE associated with overcoming friction (thighs and arms) [78] and performing body clearance maneuvers, such as an increased step width and leg circumduction [78, 79]. Weigle and Brunzell reported a 9% reduction in non-resting EE after replacement of full exogenous weight (21%) [80]. This is typically due to short-term reductions in resting EE that are greater than the changes in body weight itself [9]. Over the long-term, once body mass and energy intake stabilize, reductions in resting EE are equivalent with reductions in body weight and fat-free mass [9]. dePeuter et al. reported no differences in energy expenditure between non-obese and weight-reduced women (at least 6 months post weight loss), while sitting, standing and walking at 3 different speeds [81]. The metabolic rate was normalized to fat free mass, however, there were no significant differences in fat free mass between groups [81]. This finding suggests that energy expenditure, whether at rest or during activity, is not smaller in weight-reduced women over the long-term, thus the increased economy in weight-reduced adults is temporary.

Normalization

There is much discussion regarding the appropriate normalization method to use when measuring and reporting energetics, especially in heterogeneous populations that vary in age or size. One of the most common and widely used variables is body mass as a ratio standard, in which $VO_{2,gross}$ or metabolic rate is divided by body mass. Importantly, this suggests that the relationship between $VO_{2,gross}$ or metabolic rate and mass is in direct proportion. However, research dating back to 1949 suggests such a relationship does not exist [82]. When expressed per kilogram of body mass, the energy required to walk a fixed distance or at a given speed (metabolic cost) can be two to three times greater in smaller vs. larger individuals (e.g. children vs. adults) [83]. Weyand et al. have reported an inverse relationship between stature and mass-specific C_w (J/kg/m). They suggest that mass-specific metabolic costs associated with level walking are set by the length of a person's body, and only minimally affected by body mass variations at any given stature [83]. However, obese and non-obese adults with similar statures have been reported to walk with similar mechanics [11, 84], and very similar metabolic costs (mass-specific) [7, 11, 84].

Other methods have been determined more successful at removing confounders in groups with much variance in energetics. One such method is *allometric scaling*. This relationship is described by: $Y = aX^b$, with *a* and *b* determined empirically [82]. This method provides excellent results when comparing species whose mass varies widely because the confidence with which *b* can be determined is dependent upon the number of orders of magnitude over which the anthropometric data varies [82]. A more recent method, *nondimensionalization,* extracts parameters independent of the original units of

measure. This method is chosen for its simplified set of governing equations, reduced number of independent variables and an increased ability to predict the behavior of complex systems [82]. For example, a nondimensional normalization technique proposed by Schwartz and colleagues effectively normalized net cost and consumption results, independent of height, weight and mass [82]. However, body mass is the primary determinant of metabolic rate in obese adults, accounting for ~40-90% of the variance [9, 11, 26]. Thus, in homogenous populations (e.g. moderately obese adults), body mass appears to be an effective method for normalization and removing body mass as a confounding factor.

Metabolic cost and preferred walking speed

The metabolic cost of walking (C_w) is defined as the metabolic energy required to travel a distance (J/kg/m). After subtracting the E_{stand}, $C_{w,net}$ has been reported to be ~10% greater in obese adults compared to their age-matched counterparts [8]. $C_{w,gross}$ in obese adolescents has been shown to be 25% greater than their non-obese counterparts [63]. However, Peyrot et al. reported a 25% greater $C_{w,net}$ in obese adolescents compared to non-obese adolescents across a range of speeds [42], although age may contribute to this difference.

C_w is a U-shaped curve when plotted vs. walking speed [85], with slower or faster walking speeds requiring a greater metabolic cost [86]. Thus, a single speed exists that minimizes the EE required to walk a certain distance on level ground, which typically coincides with preferred walking speed [8]. Studies have shown obese adults

prefer to walk at slower speeds than non-obese adults (~1.1-1.2 vs. 1.4m/s) [8]. Mattsson et al. reported preferred walking speed of 1.18 m/s for moderately obese women [16]; Melanson et al. reported a similar speed in moderately obese adults at 1.19m/s [15]. Spyropoulos et al. measured a preferred speed in Class III obese men of 1.09 m/s [20], with other research showing a preferred speed of merely 0.75 m/s in Class III obese women [76]. However, Browning and Kram reported no significant differences in preferred walking speed between moderately obese (Class II) and non-obese men and women [8]. The differences in measured preferred speed could be linked to the mode of testing, in that Browning and Kram measured preferred walking speed outdoors, while the other studies used indoor walkways or treadmills. After surgery-induced weight loss, obese adults preferred to walk faster and had lower ratings of perceived exertion associated with those faster walking speeds [76]. Importantly, most studies have measured preferred speed over relatively short distances (15-50 meters), and because of limited functional capacities, obese adults may reduce walking speed during a longer walking task.

Additionally, the relative effort (%VO_{2max}/kg) at preferred walking speed is greater in obese individuals, suggesting their preferred speed might be mildly taxing to sustain [8]. Mattsson et al. report obese adults preferred walking speed required 56% of their VO_{2max} (per kg), compared to 36% in non-obese adults [16]. More importantly, one-fourth of the obese patients in Mattson's study required 64-98% of their VO_{2max} to walk at their self-selected speed.

Determinants of Metabolic Rate

Research shows that the variance in body mass can explain 82-92% of the variance in metabolic rate under different walking conditions [26]. Other biomechanical, physiological and anthropometric characteristics such as an increased body fat percentage [11], step width [19, 20], greater leg circumduction [87], VO2 peak [24, 88] and joint work [71, 89] and have also been suggested as factors that are associated with the metabolic rate during level walking. Browning et al. has shown E_{net} (W/kg) to be positively associated with percent body fat, partly due to a lower mass-specific standing metabolic rate with greater total body fat mass. They report body fat percentage explaining 45% of the variance in E_{net} of walking [11]. This would suggest that body fat percentage isn't the only determinant of metabolic rate, but may be an important contributor, accounting for a significant portion of the variance.

In 1990, Donelan et al. reported that humans prefer a step width that minimizes metabolic cost [21]. Their research showed that step-widths greater than foot width caused an increase in step-to-step transition external work and metabolic rate, and narrow step widths resulted in increased metabolic rate presumably associated with increasing lateral limb swing [21]. A greater step width in obese adults has been reported in the literature due to an excessive amount of adipose tissue in the thigh region, thus a larger thigh circumference [22]. This greater step width is typically also associated with a greater leg swing circumduction [87] which has also been shown to increase $C_{w,net}$ (J/kg/m) due to heavier legs swinging more laterally [22]. Furthermore, when non-obese adults doubled their step width, their C_w increased by 25% [21]. This is important because obese persons walk with twice the step width of non-obese [20]. Obese adults

also exhibit a 47% increase in mid-swing hip abduction angle compared to non-obese adults [20]. In non-obese adults, increasing leg circumduction has accounted for increases up to 30% in the C_w [22]. Collectively, these increases in metabolic rate are much greater than the difference between obese and non-obese reported in the literature, suggesting obese individuals may walk such to minimize the metabolic penalty of an increased step width and leg circumduction.

In sedentary women, an inverse association between VO_2max and walking economy at 3.0 mph has been reported [90]. Sawyer et al. reports a greater VO_2 throughout a range of walking speeds in individuals with greater VO_2 peak [24]. Hunter et al. ascribes this to a positive correlation between VO_2 and type IIa muscle fiber percentage of the gastrocnemius muscle [88]. It was suggested that individuals with high concentrations of energetically inefficient type IIa muscle fibers will be less economical with a greater oxidative capacity, with this greater capacity being a consequence of a higher O2 demand from the inefficient type IIa fibers [88].

Mechanical work

Mechanical work, which measures the change in energy of a system (e.g. center of mass or leg) is an important quantity when analyzing human movement. In biomechanics, mechanical work is typically classified into three categories: external, internal or joint work. External work is defined as the mechanical work done on the body's center of mass during locomotion [91]. This work represents changes in energy of the center of mass and reportedly accounts for ~50% of the metabolic rate (W/kg) of

walking [89]. External work is typically measured from the integration of force plate data or differentiation of kinematic data to derive center of mass position and velocity estimates [66]. The determination of external work requires calculation of instantaneous total mechanical energy of the center of mass (E_{CM}):

$$E_{CM} = mgh + \frac{1}{2} mV^2_{ap} + \frac{1}{2} mV^2_{v} + \frac{1}{2} mV^2_{ml}$$

Where m is body mass, *g* is gravitational acceleration (9.81 m/s), *h* is height of the center of mass and V_{ap} and V_v are the antero-posterior and vertical components of the linear velocities of the center of mass (Mian, 2006). External work is then computed by summing the positive increments in E_{CM} over the gait cycle.

Research in non-obese adults has shown external work to be one of the primary determinants of the C_w [71] but no significant differences in this measure have been reported between obese and non-obese individuals during level walking. Browning et al. report similar external work values in their obese (0.29 J/step/kg) and non-obese (0.31 J/step/kg) groups [71], as did Malatesta et al. [92]. This suggests that obese adults do not adjust their gait to reduce the external work done on their center of mass. Therefore, the increased metabolic rate during walking is not likely to be due to obese adults having to perform more external mechanical work [71].

Internal work is the work needed to move the body segments relative to the body's center of mass [93]. It is relevant because performing reciprocal limb movements (e.g. leg swing) can result in no movement of the center of mass, and not be measured as external work. Internal work is computed as the sum of the absolute changes in body segment kinetic and potential energy [93, 94] relative to the center of mass. In order to

determine internal work, the instantaneous kinetic energy of each segment relative to the center of mass must be calculated (KE_r):

$$KE_r = ½\ mv2ap,r + ½\ mv2v,r + ½\ mv2ml,r + ½\ mK^2\omega^2$$

Where *m* is the mass of the segment, V_{ap} and V_v are the antero-posterior and vertical components of the linear velocities of the center of mass velocities, K is segment radius of gyration and ω is angular velocity of the segment [95]. KE_r of each segment within the same limb is then summed to give the kinetic energies of the left and right upper and lower limbs, and the head-trunk. The positive increments in the kinetic energy of each limb and the head-truck segments are then summed separately over a number of strides to determine the internal work of each limb and the head-trunk. Internal work for each limb and the head-trunk are then summed together to get total internal work [95]. This method assumes energy transfers take place between the segments of the same limb but not between limbs (Mien, 2006).

Importantly, only some of the work can be measured: work done to accelerate the body segments relative to the body's center of mass, and the work done during the double support phase of walking generated by the trailing leg and absorbed by the leading leg [96]. Work that cannot be directly measured includes the work done to stretch the series elastic components of the muscles during isometric contractions, work done to overcome antagonistic co-contractions, and work done to overcome viscosity and friction [96]. However, some have shown the greater energy cost indicated in obese gait has been attributed to increased internal work resulting from a larger moment of inertia, due to disproportionately heavier limbs [97].

Joint work is thought to best represent musculotendon work (compared to internal and external work) during level walking [98] and as a result is a predictor of metabolic rate during level walking [10]. It is computed as the time integral of net joint power, with joint power being the product of the net muscle moment (Nm) and joint angular velocity (rad/s) [66].

When co-contraction is present, joint work is limited in its ability to account for individual muscle contributions to mechanical work [98]. Thus, some researchers argue that joint work doesn't estimate metabolic rate very well [Neptune, [98], as walking requires substantial co-contraction across the knee and ankle joints [99, 100] and elastic energy storage and return in the calcaneus tendon [101, 102]. Both of those parameters are difficult to account for using joint work calculations [98]. However, co-contraction across the knee and ankle joint is minimal during level walking. In addition, joint work has been shown to be greater in obese vs. non-obese adults, suggesting a possible mechanism to explain the increase metabolic rate in obese adults [23].

There may be a few gait characteristics that effectively reduce metabolic rate in obese individuals. It has been reported that these individuals walk with straighter legs and a more erect posture, which may require smaller muscle forces [103], thereby reducing the cost of supporting body weight [23]. However, this altered gait has not been consistently reported and thus it remains unclear whether obesity results in an altered gait pattern. Obese adults may also use the body more effectively as an inverted pendulum, reducing the work performed on the center of mass [11]. This is characterized by an improved recovery of mechanical energy (transfer of kinetic/potential) during the stance phase of walking [104]. However, Malatesta and colleagues reported obese adults do not

alter their gait to more effectively recover mechanical energy while walking at preferred speeds [92].

As previously mentioned, research has proposed that estimating metabolic cost from mechanical work measures such as external, internal and joint-based measures, may have significant limitations [98]. Thus, muscle-driven forward dynamics simulations of walking (musculoskeletal models) provide an ideal framework because every source of mechanical work, including biarticular muscles, tendon and passive joint work, and co-contraction can all be estimated [98]. In the future, musculoskeletal model studies need to be done to determine the muscle contributions during level and gradient walking. This will help give a better understanding of the influence of excess body mass and will help quantify if obese adults adopt a walking pattern that conserves metabolic energy.

Prediction Equations

Weight loss and weight maintenance programs require an accurate estimate of EE. This can be measured through various methods including indirect calorimetry. However, these methods are typically expensive and are only measured in research settings. Consequently, prediction equations have been developed in which anthropometric characteristics such as weight and height, and other important factors such as speed and grade of walking are used to help estimate metabolic rate and EE. These are especially important to health professionals when appropriate exercise intensities need to be prescribed, to avoid inappropriately-selected intensities that might discourage overweight or obese individuals from participating in exercise. Some prediction equations

commonly reported in the literature used to estimate EE during walking include: ACSM prediction equation [105], van der Walt prediction equation [106], and Pandolf prediction equations [31]. Ideally, prediction equations should be formulated to encompass a comprehensive range of walking speeds and grades. Unfortunately, several prediction equations exist but have not been thoroughly compared to actual measures. Of equal importance, most of these equations have been developed to predict EE in non-obese adults, possibly reducing their ability to estimate EE for children and elderly, as well as adults who are overweight or obese.

ACSM prediction equation

The ACSM prediction equation was developed for steady state exercise and is often used in clinical settings [105].

ACSM Equation: VO_2 (mL/kg/min) = 0.1 (m/s) + 1.8 (m/s)(fractional grade (%))+ 3.5
This equation assumes 1) direct relationship between $VO_{2,gross}$ and walking speed, 2) resting (3.5 ml/kg/min) and $VO_{2,net}$ per meter distance traveled (0.1 ml/kg/m) are constants [105]. It can be used to predict EE during walking or running, however, it is limited in that it does not consider the potential differences during overground vs. treadmill locomotion. Significant differences between measured values VO_2 and predicted values with the ACSM equation have been reported in the literature, creating potential problems when prescribing exercise for weight loss. Hall et al. report a 3.8% (14.4 kJ) underestimation of walking VO_2 in recreationally active 18-30 year olds [32], but Agiovlasitis reported no significant differences in estimated and measured $VO_{2,gross}$

in a group of young , healthy adults [107]. However, due to the linear relationship between $VO_{2,gross}$ and speed, this formula may not apply to individuals with conditions that alter gait, effectively increasing or decreasing metabolic rate [107].

Van der Walt prediction equation

The Van der Walt equation was developed for a wide range of speeds and body weight using data from six untrained men.

Van der Walt Equation: VO_2 (L/min) = 0.00599 (M) + 0.000366 (M) $(V)^2$

Where M = body mass (kg) and V = velocity (m/s). This equation is based on the idea that at any given speed, metabolic rate is proportional to walking velocity squared, which accounts for the curvilinear metabolic rate vs. speed relationship. [108]. Unfortunately, only one known study has quantified estimated vs. measured VO_2; Hall et al. reported an over-estimation of walking by 19.7% or ~67kJ [32].

Pandolf prediction equation

The Pandolf prediction equation is commonly used to estimate metabolic power, and uses body weight, external load carried, walking speed and grade, and terrain in its calculation [31].

Pandolf Equation: Gross metabolic rate (W) = 1.5M + 2.0 (M+L) $(L/M)^2$ + n(W+L) [$1.5V^2$ +0.35VG]

Where w = subject's weight (kg), L = external load (kg), V = speed of walking (m/s), G = grade (slope, %), and n = terrain coefficient (n = 1 for treadmill). This equation has been shown to have slight differences when compared to measured metabolic power, however these differences are quite modest with a 2.8% overestimation of walking in young adults [32]. Browning et al. also reported that the Pandolf equation overestimated EE by ~7.4% (14.5 vs. 13.5 ml/kg/min) [11].

Importantly, even a small positive energy balance has been shown to be a risk factor for the development of obesity [48], so slight inaccuracies in prediction equations are important to consider. Furthermore, if the equations we are using to prescribe exercise for weight loss and weight maintenance are inaccurate in obese adults, a new prediction equation should be considered to more effectively estimate EE in this population.

CHAPTER III

METHODS AND PROCEDURES

Subjects

Eighty (80) individuals were recruited and screened and 32 obese (18 female) and 19 non-obese (10 female) participants met the inclusion criteria and were included in this study. Subjects were in good health (no known acute/chronic disease or PA limitations, [5]), sedentary to lightly active (< 4 hours of PA per week), not taking any medications known to alter metabolism and body mass stable (< 2.5 kg net change during the previous 3 months). All non-obese subjects had a BMI's of less than 25 kg/m^2, while obese subjects had a BMI between 30-50 kg/m^2. Subjects gave written informed consent that followed the guidelines and was approved by the Colorado State University Human Research Institutional Review Board (IRB).

Experimental Protocol

Each subject completed three experimental sessions. During the first visit, which followed a 12-hour fast, subjects underwent a physical examination, body composition was measured and we recorded anthropometric characteristics required to determine lower body segment parameters [109]. Finally, subjects completed a standard graded exercise stress test to determine maximal oxygen uptake (VO_2max). During the second

and third session, each followed by a 4-hour fast, we collected data as subjects stood and walked (with shoes) at 16 speed/grade combinations (8 per session). Treadmill speeds ranged from 0.50 – 1.75m/s in increments of 0.25 m/s (six total) and grades were -3°, 0°, 3°, 6° and 9°. We collected metabolic and biomechanics data during 11 trials (see Table 1). Trials were 6 minutes in duration and subjects were allowed 5 minutes of rest between trials. The 11 speed-grade trials were selected to elicit similar metabolic responses. The trials included in this study are represented by "B+M" in Table 1. Subjects were also given an acclimatization period prior to data collection by walking at a comfortable pace on the treadmill for up to ten minutes.

Table 1. Speed/Grade Trials. B+M: biomechanics and metabolic data collected

	Speed (m/s)					
Grade	**0.5 m/s**	**0.75**	**1.00**	**1.25**	**1.50**	**1.75**
-3°				B + M		
0°				B + M	B + M	B + M
3°			B + M	B + M	B + M	
6°		B + M	B + M			
9°	B + M	B + M				

Assessments

Physical Health and Activity

During the first visit, each subject completed a health history form and was interviewed and assessed by a physician. Blood was drawn to test for normal metabolic function. Resting levels of thyroid-stimulating hormone and blood cell count were measured and confirmed to be within normal ranges. PA levels were assessed via a

questionnaire and only individuals with < 4 hours of moderate-vigorous PA per week were invited to participate.

Body Composition

We measured each subject's body composition using dual X-ray absorptiometry (DEXA; Hologic Discovery, Bedford, MA). We determined percent body fat and percent lean mass for the entire body and 3 regions of interest: thigh, shank and foot. Regions of interest were manually identified using the DEXA software. The thigh segment proximal end was defined as a line between the superior border of the iliac crest and the inferior border of the coccyx, excluding the pelvis. The thigh segment distal end and shank proximal end was a line between the femoral condyles and the tibial plateau. The shank segment distal end was a line between the inferior aspects of the medial and lateral malleolus. The foot segment was the remainder of the leg below the distal end of the shank.

Maximal Oxygen Uptake

We used a modified Balke treadmill protocol to determine each subject's maximal oxygen uptake (VO_2max). Subjects were familiarized with the treadmill and the Borg Rating of Perceived Exertion scale (6-20) [110]. A 12-lead electrocardiogram was used to monitor heart function. Each subject's resting heart rate and blood pressure was measured in the supine, sitting, and standing position to test for orthostatic intolerance.

Subjects warmed up for ~5 minutes after which we slowly increased the speed of the treadmill until subjects reported a rating of perceived exertion (RPE) indicative of moderate intensity exercise (~11). Treadmill speed was then held constant and the grade was increased by 1% every minute. The subjects were encouraged to continue to exhaustion. During the test, physiological responses to exercise were measured by recording heart rate, blood pressure, and RPE every 3 minutes. Heart function was examined by a physician. We determined oxygen consumption (VO_2) via open circuit respirometry (Oxycon Mobile, Yorba Linda, CA) with expired gas data averaged every 30 seconds. The Oxycon Mobile has been shown to provide valid measures of oxygen consumption across a range of exercise intensities [111].

Energetic Measurements

Energetic measurements were collected during sessions two and three while subjects walked on a treadmill over a range of speeds and grades. To determine metabolic rate during standing and walking, we measured the rates of oxygen consumption (VO_2) and carbon dioxide production (VCO_2) using a portable open circuit respirometry system (Oxycon Mobile, Yorba Linda, CA). Before the experimental trials, we calibrated the system and measured $_{stand}$ for 6 minutes. For each trial, we allowed 4 minutes for subjects to reach steady state (no significant increase in VO_2 during the final 2 minutes and a respiratory exchange ratio <1.0) and calculated the average VO_2 and VCO_2 (ml/sec) for the final 2 minutes of each trial. We calculated $_{gross}$ (W) from VO2 and VCO2 using a standard equation [112]. From E_{gross}, we calculated absolute and

mass-specific E_{net} (gross-stand) and $C_{w,gross}$ and $C_{w,net}$ (metabolic rate/speed) for each speed/grade combination. We also derived the speeds at which the C_w was a minimum in both groups during the level and 3° walking trials by fitting the data to a second order polynomial, setting the equation equal to zero and differentiating.

Biomechanics Measurements

To record biomechanics data we used a 7-camera three-dimensional motion capture system (Nexus, Vicon, Centennial, CO) and a dual-belt, inclinable, force-measuring treadmill (Bertec, Columbus, OH). We placed lightweight retro-reflective spheres in accordance with the modified Helen Hayes marker set to identify anatomical landmarks and delineate lower extremity segments [113]. Markers were placed on the sacrum (S1), and anterior superior iliac spine (anterior to the actual ASIS, on the soft tissue), sternum, clavicle, 10^{th} thoracic vertebrae (T10), 7^{th} cervical vertebrae (C7), mid-thigh, femoral epicondyle, mid-shank, lateral malleolus, second metatarsal head, and calcaneous of each leg. Marker trajectories were recorded at 100 Hz using optoelectronic cameras. Ground reaction forces (GRF) and moments were recorded at 1000 Hz by force platforms embedded under each treadmill belt. Kinematic and kinetic systems were synchronized through the motion capture system. Data was collected for 30 seconds during the final minute of each trial.

Raw coordinate and kinetic data was smoothed using a fourth-order, zero lag digital Butterworth filter with a cutoff frequency of 5 Hz and 12 Hz respectively. After exporting the data, we used vertical GRF data and a threshold of 15N (based on the

standard deviation of the vertical GRF signal during swing [114]) to determine heel strike and toe off for each leg and computed temporal characteristics of each trial using motion capture analysis software (Visual 3D, C Motion, Germantown, MD). Step width was determined as the distance between the mid-stance center of pressure of the right and left leg during consecutive steps. To determine the thigh and shank body segment parameters, we used the DEXA data to estimate thigh and shank mass and used the regression equations provided by Durkin and Dowling to determine radius of gyration [115]. Segment mass and radius of gyration were used to calculate frontal plane moment of inertia. We used frontal plane values to represent sagittal plane moment of inertia of the thigh and shank [116]. Foot segment parameters were estimated using Visual 3D software (Visual 3D, C Motion, Germantown, MD). Three-dimensional lower extremity kinematic and kinetic variables (joint angles and NMM) were also computed using Visual 3D software which uses the anthropometric data, estimated joint centers, segment velocities and accelerations and the GRFs in a full inverse dynamics model.

Ankle and knee joint centers were calculated by taking half of the measured width at the medial and lateral malleoli, and the width between the lateral and medial epicondyles. The hip joint center (HJC) was determined as follows: We measured pelvic width via the DEXA image. A pelvic depth to pelvic width ratio of 83.7% for females and 74.3% for males was used to estimate pelvic depth [117]. Two virtual ASIS markers were then placed forward (anterior) from the sacrum marker a distance equivalent to the pelvic depth and laterally ½ of the measured pelvic width. We then used the Bell method to estimate HJC from the new ASIS location [118]. All kinematic and kinetic variables were normalized to represent a percentage of stance. Positive and negative work at each

joint was determined by numerically integrating the instantaneous positive and negative joint power (product of joint NMM and joint angular velocity) over the stance phase from using a custom Matlab program (Matlab v12.0, Mathworls, 2007). We calculated the mean of each variable of interest of the right leg over 10-25 strides at each speed/grade combination for each subject and the mean across subjects and groups for each speed/grade combination. The biomechanics trials used in this study include 1.25 and 1.50 m/s at 0°, 1.25 m/s at 3°, 0.75 m/s at 6° and 0.50 m/s at 9°.

Prediction Equation Accuracy

VO_2 was estimated using the ACSM prediction equation (equation 1) for each speed and grade combination [30] and this was converted to EE (kcal/min) assuming a energy equivalent of 4.8 kcal/LO_2 (standard mixed diet) [30].

We also determined gross metabolic power (W) using the Pandolf prediction equation (equation 2) for each speed/grade combination [31]. EE was calculated from estimated gross metabolic power using a standard conversion of $2.388x10^{-4}$ kcal/J. EE from the ACSM and Pandolf prediction equations were compared to the measured EE after converting metabolic power to EE.

Equation 1, ACSM: VO_2 (ml/kg/min) = 0.1 (v_1) + 1.8 (v_1)(G) + 3.5

Equation 2, Pandolf: Gross metabolic rate (W) = 1.5m + 2.0 (m+L) (L/m)2 + n (m+L) [$1.5v_2^2$ +0.35v_2G]

Where m = subject's mass (kg), L = external load (kg), v_1 = speed of walking (m/min), v_2 = speed of walking (m/s), G = grade (slope, %), and n = terrain coefficient (n = 1 for treadmill).

Statistical Analysis

Statistical analysis was done using SAS version 9.2. A separate mixed model was fit for each response variable (gross VO_2, E_{gross}, E_{net}, $C_{w,gross}$, $C_{w,net}$) using proc mixed. The models included fixed effects corresponding to obesity status, gender, speed/grade and all interactions of these terms. The model also included a random subject effect. Linear contrasts were used to test for a difference in mean performance comparing obese vs. non-obese participants at each speed grade. The p-values corresponding to these tests were adjusted using Bonferroni multiple testing adjustment. Residual diagnostics plots were examined. Some of the variables showed evidence that assumptions of equality of variance and normality may not be met. However, the departures were not severe. We considered using a log (natural log) transformation which did help satisfy assumptions, but did not change the main conclusions. Hence, for simplicity we present the results of the analysis on the original scale.

Second order polynomial regressions were used to determine the minimum cost of walking associated with level and 3° walking trials. We used linear regression analyses to determine the relationship between metabolic rate and the determinants of metabolic rate. We developed a new metabolic energy expenditure prediction equation using body mass, treadmill speed and grade as predictor variables of energy expenditure in a multiple linear regression model. We used a paired t-test to compare measured vs.

ACSM/Pandolf/New predicted EE across all speed/grades. We evaluated the accuracy of the prediction equations using modified Bland-Altman plots [119]. We defined accurate as predicting EE to within 4% of measured values. This level of precision equates to ~0.3 kcal/min. Given that daily walking physical activity EE is ~300 kcal [120], this equates precision to ~12kcal or approximately one-third of the "energy gap" associated with weight gain [121].

CHAPTER IV

RESULTS

The subject characteristics are shown in Table 2. There were significant differences in body fat percentage between sexes in both non-obese men and women (18.3% vs. 30.4%, $p<0.001$) and obese men and women (33.9% vs. 44.2%, $p<0.001$). Non-obese and obese females had greater body fat percentages ($p<0.001$) and smaller VO_2 peak values than their male non-obese and obese counterparts ($p<0.001$, $p=0.010$, respectively). E_{stand} (W/kg) was greater in the non-obese compared to the obese participants ($p<0.001$) but was not different between the sexes within the non-obese or obese group ($p=0.554$, $p=0.180$, respectively).

Table 2. Physical characteristics of participants

	Obese		Non-Obese	
Subject Characteristics	*M (n=14)*	*F (n=18)*	*M (n=9)*	*F (n=10)*
Age (years)	29.5 (2.0)	27.2 (1.8)	22.9 (0.8)	22.7 (1.4)
Height (m)	1.81 (0.02)	1.70 (0.01)*	1.81 (0.02)	1.65 (0.02)*
Body Mass (kg)	110.7 (4.5)	95.6 (3.0)*	71.4 (3.2)	58.1 (2.2)*
BMI (kg/m^2)	33.6 (1.1)	34.2 (0.8)	22.0 (0.6)	21.2 (0.7)
Percent body fat (%)	33.9 (1.6)	44.2 (0.9)*	18.3 (1.5)	30.4 (1.3)*
Lean body mass (kg)	70.2 (3.1)	51.2 (1.7)*	54.4 (2.1)	37.5 (1.3)*
VO_2 Peak (ml/kg/min)	33.8 (1.8)	25.8 (1.0)*	43.0 (1.4)	37.9 (1.2)*
$_{stand}$ (W/kg)	1.19 (0.04)	1.12 (0.03)	1.57 (0.08)	1.51 (0.05)
M = Male, F = Female, Values are mean (SD), *Significant difference between sexes				

Metabolic Rate

There were no significant differences in metabolic rate between sexes in either the obese or non-obese group (p=0.11, p=0.98 for obese and non-obese, respectively), therefore the data from both sexes was combined into obese and non-obese adults. VO_2, E_{gross} and E_{net} increased with walking speed and grade in both obese and non-obese adults (Figure 1). Mean VO_2 ranged from 0.70 (0.03) L/min at 1.25 m/s, -3° to 1.98 (0.05) L/min at 1.50 m/s, 3° and E_{gross} ranged from 235.8 (11.2) W at 1.25 m/s, -3° to 684.9 (18.8) W at 1.50 m/s, 3° (mean (SE)). Obese adults had significantly greater VO_2 and E_{gross} compared to non-obese adults (P<0.001). Mean mass-specific E_{gross} ranged from 3.06 (0.07) W/kg at 1.25 m/s, -3° to 7.50 (0.13) W/kg at 1.50 m/s, 3° and E_{net} ranged from 1.91 (0.06) W/kg at 1.25 m/s, -3° to 5.91 (0.13) W/kg at 1.50 m/s, 3° (Table 3, Figure 1c, 1d). Obese individuals walked with a significantly smaller mass-specific E_{gross} (p<0.001) and mass-specific E_{net} (p=0.013) compared to non-obese individuals, across the speed/grades tested.

Table 3. Gross and net metabolic rate.

	E_{gross} (W/kg)		E_{net} (W/kg)	
Speed/Grade	*Obese*	*Non-Obese*	*Obese*	*Non-Obese*
1.25 m/s, -3°	3.06 (0.07)	3.68 (0.12)*	1.91 (0.06)	2.15 (0.11)*
1.25 m/s, 0°	3.92 (0.07)	4.46 (0.09)*	2.74 (0.07)	2.92 (0.09)
1.50 m/s, 0°	4.88 (0.10)	5.29 (0.10)*	3.73 (0.09)	3.78 (0.10)
1.75 m/s, 0°	6.23 (0.12)	6.70 (0.17)*	5.04 (0.12)	5.16 (0.16)
1.00 m/s, 3°	4.60 (0.07)	5.33 (0.12)*	3.45 (0.06)	3.81 (0.13)*
1.25 m/s, 3°	5.51 (0.07)	6.20 (0.11)*	4.36 (0.06)	4.67 (0.11)*
1.50 m/s, 3°	6.80 (0.10)	7.45 (0.13)*	5.65 (0.10)	5.91 (0.13)*
0.75 m/s, 6°	5.06 (0.06)	5.67 (0.09)*	3.91 (0.06)	4.13 (0.08)
1.00 m/s, 6°	6.30 (0.09)	7.07 (0.10)*	5.17 (0.09)	5.54 (0.11)*
0.50 m/s, 9°	4.86 (0.06)	5.46 (0.11)*	3.70 (0.06)	3.91 (0.09)
0.75 m/s, 9°	6.47 (0.09)	7.08 (0.12)*	5.32 (0.08)	5.55 (0.12)
Mean (SE), Significant main effect of obesity, *Significant difference OBG vs. NBG				

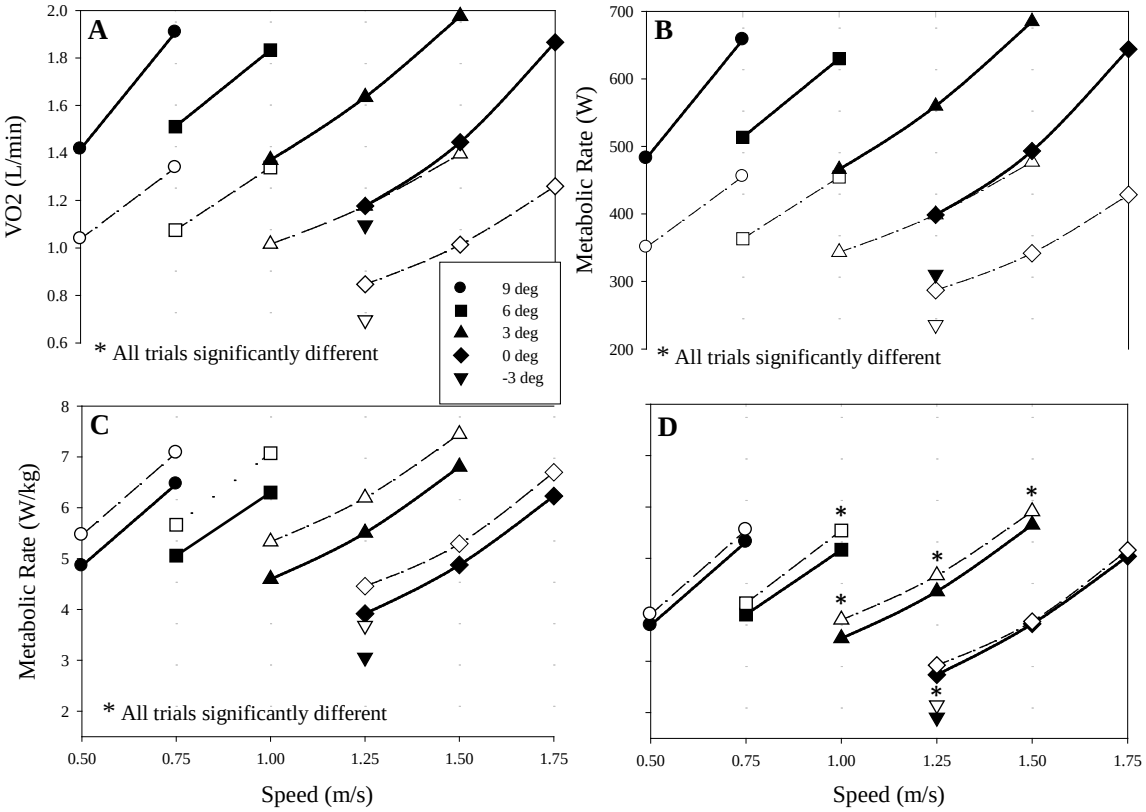

Figure 1. E_{gross} and E_{net} during treadmill walking in non-obese (open shapes) and obese adults (filled shapes). The average $VO_{2,gross}$ (A), E_{gross} (B), mass-specific E_{gross} (C), and mass-specific E_{net} (D) plotted as a function of walking velocity. *Significant difference between obese and non-obese groups.

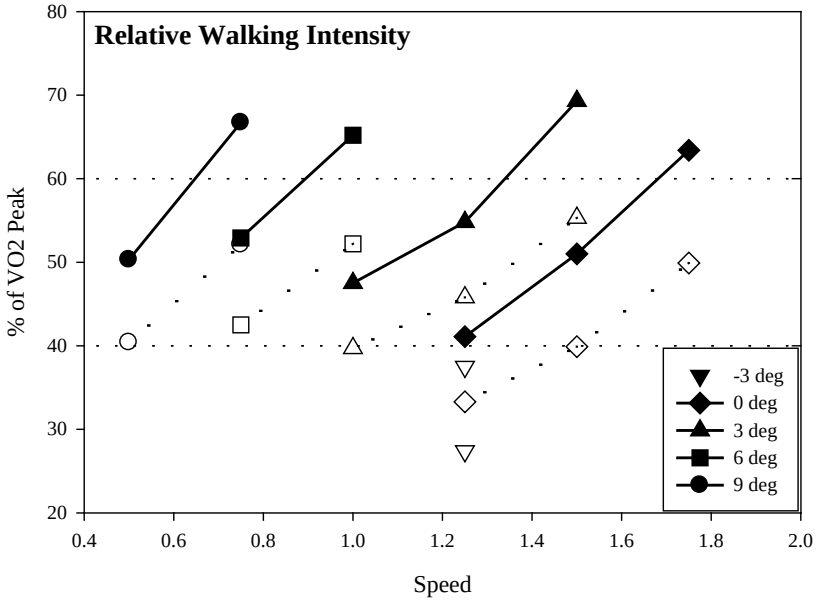

Figure 2. Relative walking intensity (% VO_2 peak) in non-obese (open shapes) and obese adults (filled shapes) for each speed/grade walking condition. The dashed horizontal lines represent 40-60% of VO2 Peak, defined as moderate-intensity exercise.

Metabolic Cost

Obese individuals had significantly smaller $C_{w,gross}$ and $C_{w,net}$ (J/kg/m) of walking compared to their non-obese counterparts ($p<0.001$, $p=0.006$, respectively, Figure 2). The speed associated with the minimum $C_{w,gross}$ was slower in obese adults than non-obese adults at both 0° and 3°. $C_{w,gross}$ was minimized at a slower speed in non-obese adults when walking at 3° compared to 0° (1.37m/s vs. 1.44m/s), while the opposite was true in obese adults (1.27m/s vs. 1.22 m/s at 3° and 0°, respectively). $C_{w,net}$ was a minimum at ~1.08 m/s and 0.84 m/s when obese adults walked up the 3° incline and level walking, respectively. As was the case with $C_{w,gross}$, non-obese adults' $C_{w,net}$ was minimized at a slower speed during the 3° incline compared to level walking (1.19m/s vs. 1.35m/s, respectively).

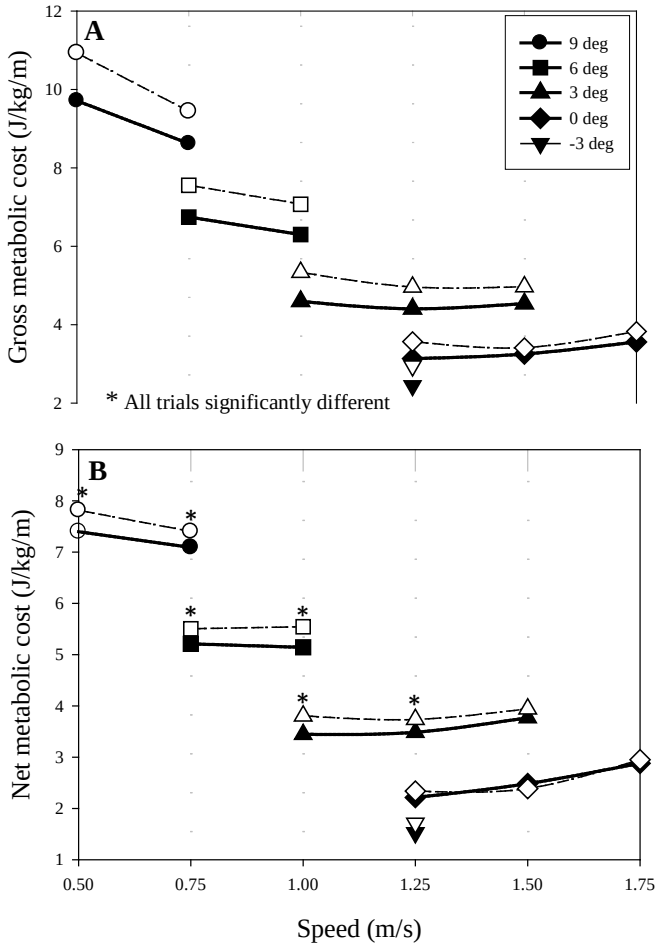

Figure 3. $C_{w,gross}$ (A) and $C_{w,net}$ (B) in non-obese (open shapes) and obese (filled shapes) adults. Significant main effect of obesity on $C_{w,gross}$ and $C_{w,net}$. *Significant difference between obese and non-obese groups.

Determinants of metabolic rate

Regression analysis showed no relationship between body fat percentage and E_{net} (W/kg, Figure 3). There were no significant relationships between E_{net} and VO2 peak or E_{net} and step width during the level or uphill trials. Positive joint work was related to E_{net} at the level walking trials ($p<0.001$, $r^2= 0.38$) but not during the uphill trials.

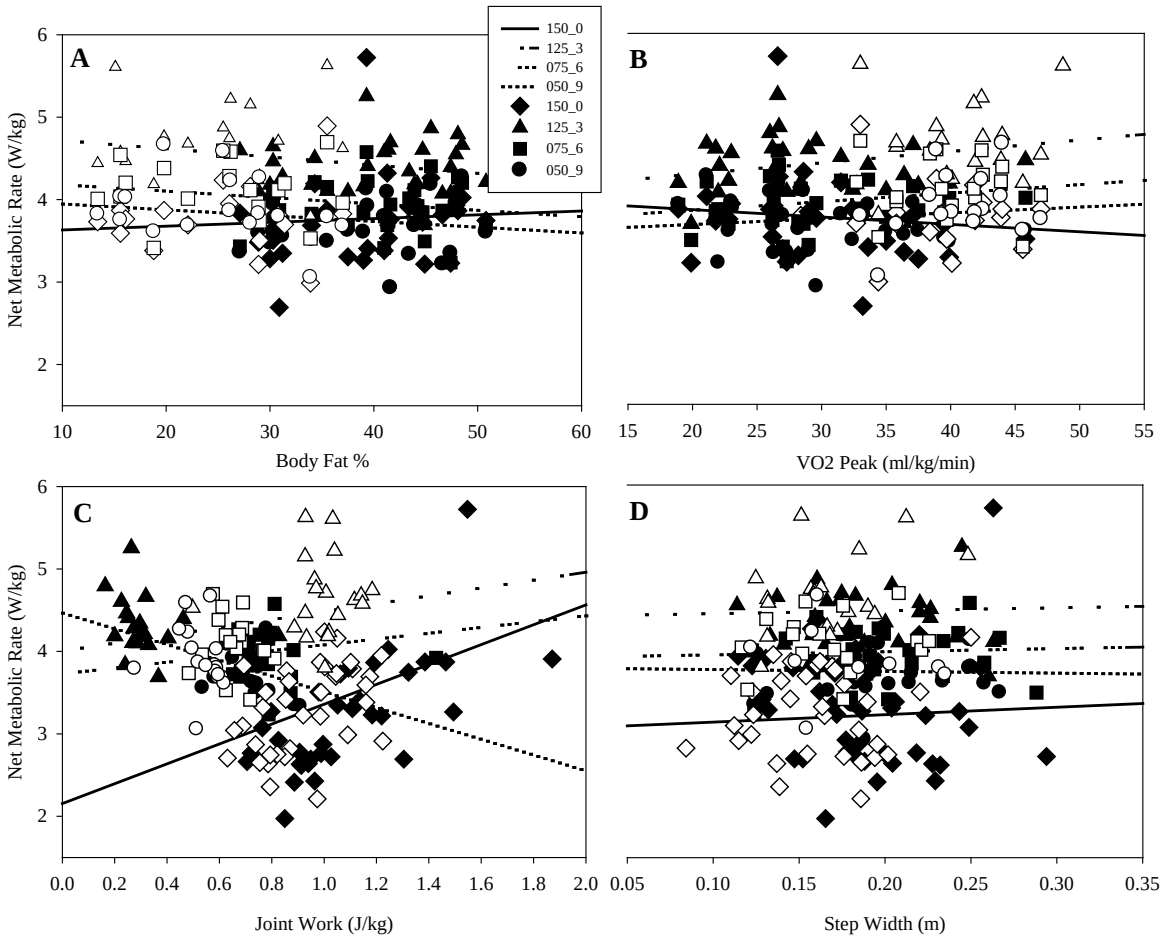

Figure 4. Determinants of metabolic rate in obese (filled shapes) and non-obese (open shapes) adults. E_{net} is plotted as a function of body fat % (A), VO2 peak (B), positive joint work (C), and step width (D). The solid line and diamond shape in figures C and D represent a combination of level trials (125_0 and 150_0). No significant relationship between E_{net} and body fat %, VO_2 peak or step width was observed. There was a significant relationship between E_{net} and joint work during level walking ($p<0.001$).

Prediction Equations

While the mean ACSM predicted EE for the obese subjects was not significantly different than measured values (8.04 vs. 7.73 kcal/min, p=0.052, Table 3), the ACSM equation underestimated fast level walking EE and overestimated EE during the 6 and 9 degree walking trials (Figure 4a). The Pandolf equation significantly overestimated EE in

the obese adults (8.34 vs. 7.73 kcal/min, p=0.04, Table 3). We developed a new prediction equation for EE (kcal/min) for obese adults that estimated EE more accurately (7.732 vs. 7.733 kcal/min, p=0.99), based on speed, grade and body mass:

$$\underline{\text{EE (kcal/min)}} = -9.027 + (0.0656 * m) + (6.407 * v) + (0.746 * G)$$

Where m=body mass (kg), v=velocity (m/s) and G=grade (degrees). The accuracy of the predicted values are shown in figure 4; the new prediction equation explained more of the variance in the difference between measured and predicted (r^2=0.832, Figure 4c), followed by Pandolf (r^2=0.785, Figure 4b) and ACSM (r^2=0.665, Figure 4a) prediction equations.

Table 4. Mean predicted and measured values.

	Predicted	Measured	P value
ACSM (kcal/min)	8.04	7.73	**0.052**
Pandolf (kcal/min)	8.34	7.73	**0.004***
New (kcal/min)	7.73	7.73	**0.994**

*Significant differences between measured and predicted values.

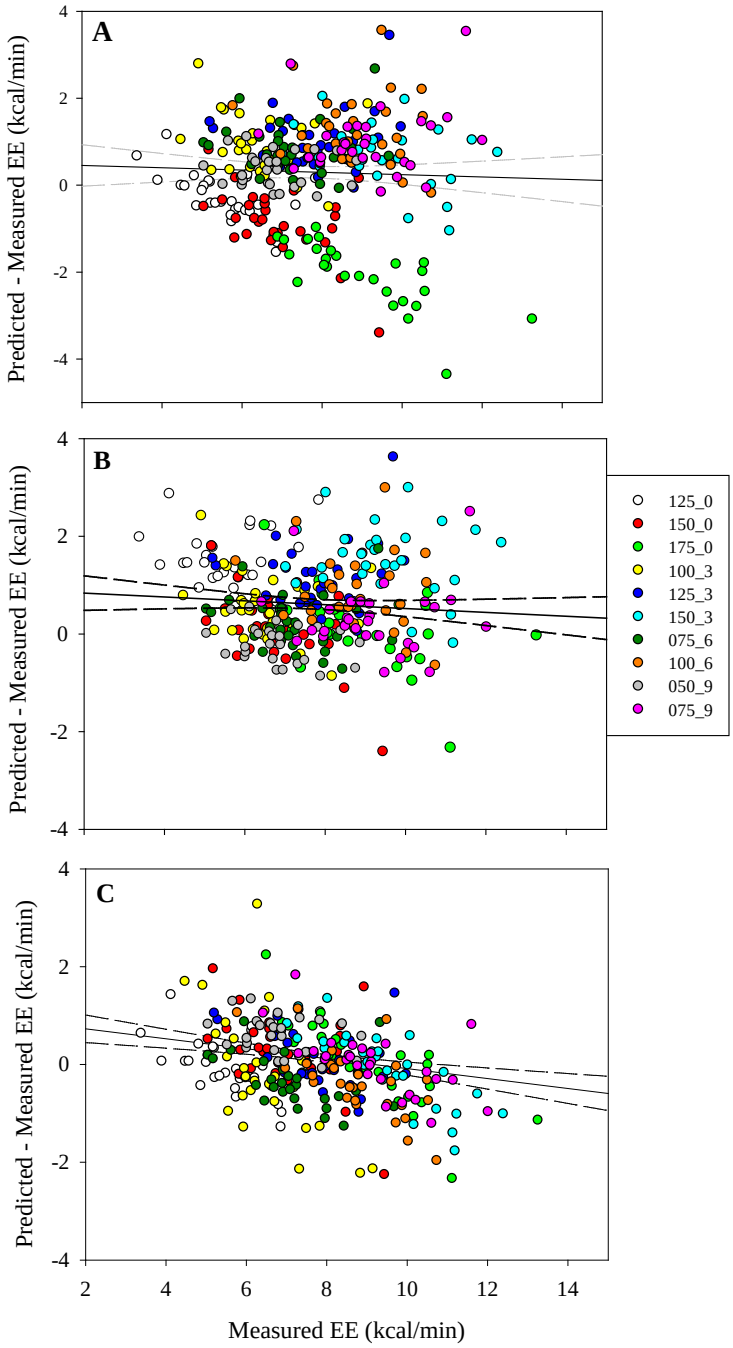

Figure 5. Modified Bland-Altman plot of prediction equations for obese adults: ACSM (A), Pandolf (B), and the new prediction equation (C)

CHAPTER V

DISCUSSION

We reject our hypothesis that mass-specific E_{net} would be greater for obese adults compared to non-obese adults across the range of speeds and grades used in this experiment. Mass-specific E_{gross} and E_{net} were significantly less in obese adults compared to their non-obese counterparts, especially when walking up inclines. The better economy of obese adults was not explained by adiposity, aerobic capacity, joint work or step width. We also accept our hypothesis that the ACSM and Pandolf prediction equations would be less accurate for obese adults, and we have developed a new equation for obese adults that provides more accurate estimates of EE during walking.

This study provides additional insight into how speed and grade influence the energetics of walking and suggests that obese adults can walk uphill more economically than their non-obese counterparts. Although the mechanism by which obesity is related to improved economy remains elusive, our results suggest that obese individuals alter their gait in some way to reduce the energetic demands of walking uphill. These results can be used to guide exercise prescription as they demonstrate that a range of walking speeds/grades can be used to elicit an appropriate cardiovascular stimulus. Given the differences in metabolic rate between obese and non-obese, it is not surprising that existing prediction equations inaccurately predict energy expenditure in obese adults and

we propose a new equation that can be used to estimate energy expenditure in obese individuals.

Energetics of Walking

As expected, metabolic rate increased with walking speed and was greater when walking up inclines. As has been reported by others, obese adults had a much greater absolute metabolic rate compared to non-obese adults [11, 26, 42]. We found that E_{gross} (W) was 35-50% greater in obese vs. non-obese participants. When metabolic rate was normalized by body mass, E_{gross} (W/kg) was smaller in the obese compared to the non-obese adults. These results suggest that obese individuals are more economical than non-obese adults, at least across the range of speeds and grades used in this study. Our level walking metabolic rate results are consistent with those reported by our previous study using moderately obese adults [8, 11, 26] In that study, we reported E_{gross} of ~4.7W/kg when moderately obese adults walked on a level treadmill at 1.5m/s, which is similar to the 4.9W/kg reported here [11]. Contrary to our findings, others have reported that obese have greater mass-specific E_{gross} across a range of walking speeds [13, 14]. A potential reason for this difference is the subject population. Previous studies included individuals with greater BMI's (>45 kg/m^2) and metabolic rate has been shown to increase with increasing BMI [15]. In addition, our mass-specific E_{gross} for the non-obese individuals are greater than those reported by others [26]. However, Lafortuna et al. had a small sample (N=6) of females who had smaller BMI's and body fat percentages than the non-obese subjects of our study [26]. As previously mentioned, metabolic rate has been

shown to increase with increasing BMI, so it is not surprising that our subjects had a greater metabolic rate. Browning and Kram also report smaller E_{gross} values for their non-obese adults while walking at 1.25 and 1.50m/s (~3.8 and 4.7 W/kg, respectively) [8]. On the other hand, Burdett et al. report similar $_{gross}$ values of ~5.15 W/kg for non-obese adults walking at 1.50 m/s compared to the 5.29 W/kg reported here [10].

The obese individuals in this study had smaller mass-specific E_{net} (W/kg) compared to the non-obese individuals. While this difference was typically small (~5%), it was significant, particularly during uphill walking. Several studies have reported that E_{net} is greater in obese vs. non-obese during level walking. Browning et al., Mattsson et al., and Melanson et al. reported a ~10% greater E_{net} in obese adults compared to non-obese adults [11, 15, 16]. In addition, Bloom and Foster et al. have shown larger differences (25-45%) between the metabolic rates of obese vs. non-obese adults [9, 13]. However, that study included a relatively small number of participants that were morbidly obese while walking uphill. Not only would the greater BMI in this population contribute to the increased metabolic response, but walking uphill might also play a role, unfortunately very few studies have quantified the energetics of uphill walking in morbidly obese adults. A recent study by Lafortuna et al. reported that mass-specific E_{net} was significantly greater in obese females when walking at 1.3 m/s up a 4% grade, but there with no differences between groups when walking at 1.0 m/s at 0 and 4% grades [26].

The differences in E_{gross} and E_{net} between obese and non-obese reported here and other studies may be due, in part, to variations in locomotor and standing metabolic rate. Wergel Kolmert & Wohlfart report a ~5% within-subject day-day variation in walking

energy expenditure [122]. Previous studies have also shown within-subject and day-to-day coefficients of variation in resting metabolic rate of 2-10% of [123-125]. It seems reasonable to assume that variability in E_{stand} would be similar. Our obese subjects had similar E_{stand} values compared to those reported in the literature; however E_{stand} of the non-obese subjects were different than those reported by others. Browning et al. and Browning and Kram report values less than the ones reported here (~1.3 W/kg vs. ~1.5 W/kg) [8, 11] while Peyrot et al. and Lafortuna et al. report greater E_{stand} (~2 W/kg) [26, 42]. However, Peyrot et al. studied adolescents, which have been shown to have a greater $E_{stand,}$ thus influencing net metabolic rate [126, 127]. On the other hand, Burdett et al. report resting values nearly identical to the ones presented here [10]. A greater E_{stand} in non-obese adults would reduce net metabolic rate, potentially making E_{net} of non-obese adults less than that of obese adults. The sensitivity of E_{net} to variations in E_{stand} suggests that, as with measurement of resting metabolic rate, a standardized procedure for quantifying E_{stand} should be used. In addition, given that the differences in E_{net} between obese and non-obese are typically small, caution must be used when interpreting E_{net} data.

Studies that have quantified the energetics of load-carrying during incline walking provide support for better uphill walking economy in obese vs. non-obese adults. Sagiv et al. reported greater oxygen consumption values for non-obese individuals carrying 25 and 35 kg loads (34% and 48% of mean body mass, respectively) compared to unloaded walking at 0, 5 and 10% gradients [28]. However, when the oxygen consumption is normalized to total mass (body mass plus load), metabolic rate during load carrying is smaller compared to walking without a load. Thus, if obesity is considered analogous to

walking with added mass (adipose tissue), one would expect that obese adults would be more economical than their non-obese counterparts during uphill walking.

Metabolic rate has been shown to be related to several anthropometric and biomechanical factors, including adiposity, mass distribution [17, 128], mass-specific VO_2 peak [24], leg mass and step width [21, 22, 42], and joint work [10]. Surprisingly, our results suggest that, with the exception of joint work during level walking, the other factors did not explain the variance in mass-specific E_{net}. Browning et al., reported that body fat percentage explained 45% of the variance in E_{net} during level walking at 1.50 m/s [11]. This is not surprising in that increasing body fat decreases the standing metabolic rate but does not appear to change the mass-specific E_{gross} during walking [129]. Our results suggest adiposity did not explain the variation in E_{net}, despite a 63.1% increase in body fat percentage in obese vs. non-obese adults. The fact that we didn't find a relationship between E_{net} and body fat percentage during level or uphill walking may be due to the greater E_{net} reported for non-obese adults. There have been surprisingly few studies that that have reported the relationship between body fat percentage and E_{net}, thus more research is needed to determine how metabolic rate is affected by adiposity.

It has been suggested that maximum oxygen uptake (VO_2 peak) has an inverse relationship with economy during walking [24, 88]. However, the relationship between walking economy and VO_2 peak is modest, with correlation coefficients ranging from 0.11 - 0.30 at 2 - 4 MPH, respectively [24, 88]. We found no such relationship in our population. Our subjects were relatively sedentary men and women, with body fat percentages ranging from 13 to 49%, while those in Sawyer et al. were moderately

trained (VO_2 peak of 42.5 mL/kg/min) and did not include obese individuals [24]. Thus, it may be that training status affects this relationship. It is also possible that improvements in economy due to relatively poor aerobic capacity are offset by a reduced percentage of type I muscle fibers in obese individuals [130]. If the obese individuals in this study had to rely on less efficient type II muscle fibers, economy would be reduced. However, data on fiber type distribution in obese individuals is scarce and it could be that the primary locomotor muscles have similar fiber type distributions.

Obese individuals have an increased step width compared to non-obese individuals [19, 20]. This increased step width has been associated with metabolic cost (C_w [87]) and increased leg circumduction which has been reported to be metabolically expensive [22]. The step-width values reported here are slightly greater than those reported by Spyropoulos et al. (0.19m at 1.25m/s vs. 0.16m at 1.0m/s, respectively), while the relationship between step width and metabolic rate was not significant [20]. However, step width did not change with increasing grade in either group. Step width is also associated with medio-lateral center of mass (M-L COM) displacement, which is greater in obese adults [42]. However, Peyrot et al. suggested this M-L COM displacement may be relatively metabolically inexpensive, because it did not induce an increase in external work in obese compared to non-obese adults [42]. Thus, even though obese adults walk with a greater step width and a larger M-L COM displacement, our results suggest that obese adults may adopt a different gait, especially walking uphill, to minimize the metabolic penalty associated with these characteristics.

Walking requires muscles to perform work to support and move the center of mass, as well as swing the legs [131]. We were not able to quantify individual muscle

work, but joint work has been used as a proxy measure [132]. In agreement with the literature, joint work was predictive of E_{net} during level walking [132], however, there was no relationship with joint work and E_{net} when walking on inclines. This may be because joint work is unable to account for the co-activation across the lower extremity joints during this type of locomotion [98]. There is a need for muscle activation (EMG) and musculoskeletal modeling studies that are able to estimate distinct muscle contributions to metabolic rate in obese and non-obese individuals.

Obese adults had a significantly smaller $C_{w,\ gross}$ and $C_{w,net}$ (J/kg/m) compared to non-obese adults, particularly during uphill walking. There were no differences during level walking between groups, and only small differences in $C_{w,net}$ at 3°. This is in agreement Lafortuna et al., in which non-obese and obese women had similar $C_{w,net}$ (J/kg/m) at 1.0 m/s on 0% and 4% inclines, despite a greater degree of obesity (mean BMI = ~41kg/m^2) than our participants [26]. Peyrot et al. reported a 25% greater $C_{w,net}$ (J/kg/m) in obese adolescents compared to their non-obese counterparts, consistent with their E_{net} data [42] but, as mentioned above, this may have been due to the age of their participants. Minimum $C_{w,gross}$ has been associated with preferred walking speed in obese and non-obese adults. Our level walking results are consistent with research reporting that preferred walking speeds are slower in obese compared to non-obese adults [8, 11]. However, our results for incline walking suggest that individuals do not walk at a speed that would minimize C_w, particularly at the steeper gradients. For example, the slope of C_w vs. speed when walking up a 6° incline, would suggest that the minimum C_w is at a much faster speed than individuals, particularly obese, could walk. While our data does not permit what might influence preferred uphill walking speed, it may be that

individuals choose a speed that elicits a certain relative aerobic effort (%VO2peak) or walk at a speed that minimizes muscle mechanical work. Future studies that investigate the energetics and biomechanics of preferred uphill walking speeds are needed to improve our understanding of gradient walking energetics.

The range of metabolic rates and costs across the speed/grade trials in this study are potentially important for exercise prescription. While E_{net} ranged from ~2.5-5 W/kg, the range of C_w was much greater, ~3-10 J/kg/m, implying that obese adults could walk slowly uphill and expend much more metabolic energy for a given distance compared to walking on level ground. For example, C_w during walking up a 9° incline at 0.5m/s is ~3x greater than walking on a level treadmill at 1.50m/s. Thus, slow, incline walking may potentially be an avenue for exercise prescription in obese individuals.

Prediction Equations

The difference in metabolic rate between obese and non-obese adults suggests that energy expenditure prediction equations need to be based on a specific population. Both the ACSM and Pandolf equations were derived using non-obese participants, therefore it is not surprising that these equations were limited in their ability to predict energy expenditure for obese adults. Furthermore, the ACSM equation assumes that resting metabolic rate is a constant [105], but there are significant differences in resting metabolic rate between obese and non-obese individuals. The new prediction equation developed using obese individuals estimates EE more accurately using the same input variables used by the ACSM equation, especially at workloads that would typically be

used for exercise prescription. The slight over or underestimations in EE observed with both common prediction equations could be critical given the relatively small positive energy balance associated with weight gain. For example, walking at a moderate workload of 1.0 m/s at 3°, ACSM predicts an EE of ~7.4 kcal/min vs. ~6.3 kcal/min using the new equation while actual EE is ~6.5 kcal/min. Although there is a slight underestimation, prediction equations that underestimate EE may be more applicable to weight loss than those that over-estimate EE.

Limitations

Our protocol required that participants walk for 45-60 minutes at light-vigorous intensities. We acknowledge that the protocol may have caused mild fatigue in some participants (e.g. obese individuals). However, the inclusion of regular rest periods, randomization and relatively short duration of trials and submaximal intensity likely minimized the fatigue experienced by participants. In addition, no participants indicated that the protocol was fatiguing and we did not observe a change in ratings of perceived exertion as the protocol progressed. If participants did experience fatigue, we would anticipate that metabolic rate would have increased during the most strenuous trials, making obese less economical during these speed/grade combinations. Given that our data for fast, level walking is consistent with previous literature, we do not think fatigue was a significant limitation of this study.

Some have challenged the method of normalizing by body mass as metabolic rate may not be directly proportional to body mass. While we acknowledge this might be

true, we normalized our metabolic data using a non-dimensional method [82], and obtained similar results, with obese adults having a significantly smaller mass-specific E_{net} ($p = 0.033$). Height has been reported to play a role in the mass-specific C_w across a relatively wide range of heights (children vs. adults) [83]. However, there were no significant differences in height between our groups in this study ($p = 0.78$), thus we do not believe differences in metabolic rate were due to height. The data was also normalized to lean mass, with no significant differences in E_{net} between groups ($p = 0.20$). This is not surprising in that obese adults typically have a greater absolute amount of lean mass [133, 134].

Net muscle moment (NMM) data allowed us to determine joint work at the ankle, knee and hip during stance. However, NMM do not reflect individual muscle contributions, but are a resultant moment necessary to satisfy the Newtonian equations of motion for that joint. Thus, a limitation of this approach is an inability to account for co-contractions that occur, especially during uphill walking. Furthermore, net muscle moments are highly dependent upon correct marker placement, and with excess adiposity in obese adults, this is a definite challenge. Thus, joint work measures are highly dependent upon the accuracy of net muscle moment calculations.

Conclusions

The metabolic rate of walking increases with speed and grade, with similar increases in obese vs. non-obese adults. Obese adults walk with a smaller mass-specific E_{net} and $C_{w,net}$, suggesting these individuals are more economical than their non-obese

counterparts, especially when walking uphill. Variables that have been shown to be related to metabolic rate during level walking (e.g. body composition) did not explain the variance in metabolic rate in our population. As a result, the mechanisms by which obese adults walk more economically remain unclear and more energetics/biomechanics research is needed. Our metabolic cost results suggest that while individuals prefer a speed that minimizes metabolic cost during level walking, preferred speed is not likely set by minimizing metabolic cost during uphill walking. Finally, because the metabolic response to walking is different in obese and non-obese adults, traditional prediction equations are not accurate for obese and our new prediction equation may be more effective in prescribing/quantifying exercise in this population.

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APPENDIX A

INFORMED CONSENT

Consent to Participate in a Research Study
Colorado State University

TITLE OF STUDY: Biomechanics and Energetics of Gradient Walking in Adults

PRINCIPAL INVESTIGATOR: Ray Browning, PhD. 970-491-5868

WHY AM I BEING INVITED TO TAKE PART IN THIS RESEARCH? You are a sedentary or moderately physically active man or woman between the ages of 18-45 years and you do not have any major health problems and are not pregnant. Our research study is designed to determine the effects of level, uphill and downhill walking on how many calories your burn and the loads on your leg joints.

WHERE IS THE STUDY GOING TO TAKE PLACE AND HOW LONG WILL IT LAST? The study will be performed in the Physical Activity (PA) laboratory on Colorado State University's campus. This study will require you to visit the lab three times and each visit will take approximately 60-90 minutes of your time. The total amount of time required for this study will be approximately 3-4.5 hours.

WHAT WILL I BE ASKED TO DO? If you agree to participate in this study, you will be asked to schedule 1 visit to the HPCRL and 2 visits to the PA lab. Each visit will take about 1-1.5 hours of your time. We will try to make your testing appointments as convenient as possible for you.

Visit 1: Pre-study screening and maximal exercise test

- You will be asked about the medical history of you and your family and your level of physical activity.
- You will undergo a standard health and physical exam by a physician.
- We will draw a small amount of your blood from a vein in your arm.
- We will measure your body composition using a DXA machine. This machine is like a large X-ray machine. You will lay on the surface of the machine while a beam passes over your body. This procedure takes a few minutes.
- We will measure your resting EKG (heart function) and blood pressure.
- You will also complete a maximal exercise test (VO_2max test). You will be asked to walk on a motorized treadmill and we will increase the degree of incline every few minutes until you reach exhaustion. We will measure the rate at which you consume oxygen by analyzing the air that you breathe out. This will involve wearing a mask that covers your nose and mouth.

Visit 2 and 3: Treadmill walking

- The second and third visit will be very similar. You will be asked to walk at eight different speed/grade combinations for either 2 or 6 minutes.
- During each 2 minute trial, we will measure the forces you exert against the treadmill belt and your leg movements. We will attach reflective markers to your

skin to record your leg movements. We will also measure the electrical activity of your muscles by attaching small adhesive (sticky) electrodes to your skin. Prior to attaching the electrodes, we will use rubbing alcohol and a fine grain abrasive cloth to clean your skin.

- During each 6 minute trial, we will measure the rate at which you consume oxygen by analyzing the air that you breathe out. This will involve wearing a mask that covers your nose and mouth.
- After each trial, you will be given the option of a 5 minute rest.

ARE THERE REASONS WHY I SHOULD NOT TAKE PART IN THIS STUDY?

If you are not 18-45 years of age, are pregnant, are a regular smoker, use illicit drugs (cocaine or methamphetamine), have a condition that limits your ability to walk or run (e.g. knee pain during walking), or have any diseases that would affect our measurements, we will not be able to include you in the research.

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

The potential risks associated with this study are similar to those involved in recreational athletics. None of the procedures should cause discomfort. However, if you do experience any discomfort, you may terminate the experiments at any time. There is a risk of falling from the treadmill and injuring yourself. To minimize this risk, you will be instructed in proper safety procedures before the treadmill is turned on. It is very important is to always grab the handrails when the treadmill is starting or stopping. You may feel some mild muscle discomfort or fatigue in your legs for a few days after participating in this study. Other specific risks include:

- Maximal Exercise Testing- There is a very slight chance of an irregular heartbeat during exercise (< 1% of all subjects). Other rare risks of a stress test are heart attack (< 5 in 10,000) and even death (<2 in 10,000). There is a small risk of fainting and fatigue. Finally, exercise can cause fatigue and minor discomfort.
- Body Composition - There is a small amount of radiation exposure associated with the DXA, which is less than 1/20 of a typical chest x-ray. The more radiation one receives over the course of one's life, the more risk of having cancerous tumors or of inducing changes in genes. The changes in genes possibly could cause abnormalities or disease in a subject's offspring. The radiation in this study is not expected to greatly increase these risks, but the exact increase in such risks is unclear.
- Treadmill Testing - You could injure yourself by falling while walking on a motorized treadmill. However, you will be instructed in proper safety procedures before the treadmill is turned on. The most important instruction is to always hold the handrails when the treadmill is starting or stopping. Dr. Browning has six years of experience conducting these sorts of experiments and has never had a subject experience a serious injury. If you sustain an injury that requires immediate medical attention, we will make sure you receive it.
- Instrumentation - the devices used to measure energy expenditure, biomechanics (i.e. forces and leg movements), and muscle activity are non-invasive and pose no known risk.

- It is not possible to identify all potential risks in research procedures, but the researcher(s) have taken reasonable safeguards to minimize any known and potential, but unknown, risks.

RETENTION OF BLOOD SAMPLES

You should understand that we plan to keep any extra blood samples that are not used in the analysis for this study. In other words, if we have any "extra" blood we will keep them in a freezer in our lab. It is very possible that we will use all of the blood obtained in this study and will have none left, but in the event that we do, we would like your permission to keep the samples in the event that they can be used for further research. We will use these samples in the future solely for additional research on obesity and metabolism; specifically, all future research will simply be an extension of what we hope to accomplish with the current study. We may simply analyze your blood for the presence of other hormones or metabolites. Your stored samples will be coded in such a way that your confidentiality will be maintained. Only the Principal Investigator (Professor Browning) will have access to the coding system for your samples. There is a possibility that your samples may be shipped to other departments on the CSU campus, or to colleagues at other Universities for assistance with analysis. Under such circumstances, the same coding system will be used, so researchers in other labs will not be able to identify you. We do not anticipate ANY commercial product development from your tissue, the samples will be used solely for research purposes. You should be advised that we do NOT have plans to re-contact you in the future regarding any additional analyses, but will seek full approval of the CSU Regulatory Compliance Office prior to initiating any further research on your samples.

By checking "Yes" below and signing on the accompanying line, you are agreeing to allow the investigators retain any blood samples obtained during this study. If you do not wish the investigators to retain any samples, please check the box marked "No" and also sign on the accompanying line.

The investigators may keep any blood samples obtained during the course of this study for future research on obesity and metabolism:

☐YES ☐NO

ARE THERE ANY BENEFITS FROM TAKING PART IN THIS STUDY? There are no direct benefits to you for participating in this study except knowing your level of fitness and how many calories you burn when walking at various speed/grade combinations.

DO I HAVE TO TAKE PART IN THE STUDY? Your participation in this research is voluntary. If you decide to participate in the study, you may withdraw your consent and stop participating at any time without penalty or loss of benefits to which you are otherwise entitled.

WHAT WILL IT COST ME TO PARTICIPATE? There is no cost to you for participating except that associated with your transportation to our testing location.

WHO WILL SEE THE INFORMATION THAT I GIVE?
We will keep private all research records that identify you, to the extent allowed by law.

Your information will be combined with information from other people taking part in the study. When we write about the study to share it with other researchers, we will write about the combined information we have gathered. You will not be identified in these written materials. We may publish the results of this study; however, we will keep you name and other identifying information private.

We will make every effort to prevent anyone who is not on the research team from knowing that you gave us information, or what that information is. For example, your name will be kept separate from your research records and these two things will be stored in different places under lock and key. You should know, however, that there are some circumstances in which we may have to show your information to other people. For example, the law may require us to show your information to a court.

CAN MY TAKING PART IN THE STUDY END EARLY? Your participation in the study could end in the rare event of an injury or if you become pregnant.

WILL I RECEIVE ANY COMPENSATION FOR TAKING PART IN THIS STUDY? You will receive $75 for completing this study. If you do not complete the study, we will compensate you for the parts that you do complete at a rate of $25 per visit.

WHAT HAPPENS IF I AM INJURED BECAUSE OF THE RESEARCH? The Colorado Governmental Immunity Act determines and may limit Colorado State University's legal responsibility if an injury happens because of this study. Claims against the University must be filed within 180 days of the injury.

WHAT IF I HAVE QUESTIONS?
Before you decide whether to accept this invitation to take part in the study, please ask any questions that might come to mind now. Later, if you have questions about the study, you can contact the investigator, Ray Browning at 970-491-5868. If you have any questions about your rights as a volunteer in this research, contact Janell Barker, Human Research Administrator at 970-491-1655. We will give you a copy of this consent form to take with you.

Your signature acknowledges that you have read the information stated and willingly sign this consent form. Your signature also acknowledges that you have received, on the date signed, a copy of this document containing 3 pages.

_____ _____

Signature of person agreeing to take part in the study Date

_____

Printed name of person agreeing to take part in the study

_____ _____

Name of person providing information to participant Date

_____

Signature of Research Staff