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DEVELOPMENT AND CROSS-VALIDATION OF A CADENCE-BASED METABOLIC EQUATION FOR WALKING

A Thesis Presented

by

CHRISTOPHER C. MOORE

Submitted to the Graduate School of the
University of Massachusetts Amherst in partial fulfillment
of the requirements for the degree of

MASTER OF SCIENCE

May 2019

Kinesiology

DEVELOPMENT AND CROSS-VALIDATION OF A CADENCE-BASED METABOLIC EQUATION FOR WALKING

A Thesis Presented

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CHRISTOPHER C. MOORE

Approved as to style and content by:

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Catrine Tudor-Locke, Chair

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John R. Sirard, Member

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Richard Van Emmerik, Member

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Jane Kent, Department Chair
Department of Kinesiology

DEDICATION

To my parents;

Anastasia and Robert

ACKNOWLEDGEMENTS

First, I cannot begin to express my gratitude to my advisor, Catrine Tudor-Locke, for the tremendous amount of time and care she devoted to my personal and professional development. I have grown immensely through the opportunities that you provided me over the past three years. As time goes by, I realize more and more how extraordinary you have been as a mentor and I am privileged to have studied with you.

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ABSTRACT

DEVELOPMENT AND CROSS-VALIDATION OF A CADENCE-BASED METABOLIC EQUATION FOR WALKING

MAY 2019

CHRISTOPHER C. MOORE, B.S, UNIVERSITY OF MASSACHUSETTS AMHERST

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The ACSM Metabolic Equation is a widely recognized equation for predicting metabolic intensity from walking speed. However, an equation that uses an observable metric (i.e., cadence [steps/min]), accounts for individual characteristics, and is validated across walking conditions may enable more accessible and accurate predictions of walking intensity. **PURPOSE:** To develop metabolic equations that predict metabolic intensity (oxygen consumption; mL/kg/min) from cadence using a large treadmill walking dataset (Study One) and cross-validate these equations during overground unconstrained and cadence-constrained walking conditions (Study Two). **METHODS:** In Study One, 193 adults (21-81 years) completed treadmill walking bouts while oxygen consumption was measured with indirect calorimetry (converted to metabolic equivalents [METs]; 1 MET=3.5 mL/kg/min=1 kcal/kg/min). Directly-observed step counts divided by bout duration produced cadence. The least squares regression of the cadence-intensity relationship produced a *simple* equation and a *full* equation was developed using best subsets regression (additional possible predictors of leg length, body mass, BMI, percent body fat, sex, and age). Predictive accuracy and bias of each cadence-based metabolic equation and the ACSM Metabolic Equation was evaluated through k-fold cross-validation. In Study Two, these three metabolic equations were applied to data collected from 20 young adults during overground walking at self-selected paces (unconstrained) and with foot-strikes entrained to music tempos (cadence-constrained). **RESULTS:** In Study One, the simple equation predicted walking intensity within 0.5 METs, on average, and approximately no bias (<0.01 METs). The full equation had only marginally (<0.1 MET) greater accuracy, despite including leg length, age, BMI, and sex as predictors. During both overground walking conditions (Study Two), the cadence-based metabolic equations exhibited similar predictive capacities to treadmill walking (≤0.1 MET differences in accuracy). The ACSM Metabolic Equation systematically underpredicted walking intensity by ~1 MET during treadmill walking and demonstrated 0.1-0.9 MET lower accuracy than the simple equation in each walking condition. **CONCLUSIONS:** The simple equation performed comparably to the full equation (which accounted for individual characteristics) and appreciably better than the ACSM Metabolic Equation. The simple cadence-based metabolic equation is an improved, user-friendly tool for predicting and prescribing walking intensity with reasonable accuracy (within ~0.5 METs; 45 kcals/hr for the average American).

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LIST OF ABBREVIATIONS

ACSM – American College of Sports Medicine

ANOVA – Analysis of Variance

BMI – Body Mass Index

DS – Down Syndrome

MAE – Mean Absolute Error

MAPE – Mean Absolute Percent Error

MET – Metabolic Equivalent

MS – Multiple Sclerosis

MVPA – Moderate-to-Vigorous Intensity Physical Activity

SEE – Standard Error of Estimation

PA – Physical Activity

RAC – Rhythmic Auditory Cue

RMSE – Root Mean Square Error

RMSPE – Root Mean Square Percent Error

VO_2 – Volume Rate of Oxygen Consumption

CHAPTER 1

INTRODUCTION

1.1 Background

Considerable research has demonstrated the beneficial effects of physical activity (PA) on health. These studies have provided strong evidence that PA can treat and prevent cardiometabolic diseases, reduce cancer risk, improve body weight management, attenuate age's effects on physical function, and enhance cognition and mental health.[1] *Metabolic intensity* of PA, defined as the rate at which energy is expended (e.g., kcal/hr, mLO_2/kg/min) when performing a given activity,[1] is an essential effect modifier of the relationship between PA and longevity.[2] A minimum level of PA metabolic intensity is also necessary to improve cardiorespiratory fitness[3] and several other physiological health outcomes.[4-6] That being said, there is an inverse relationship between metabolic intensity of PA and affect response (i.e., enjoyment).[7] Because affect response is a central driver of behavior and motivation,[8,9] inappropriately high intensity PA programs have resulted in decreased exercise program adherence.[10] Thus, metabolic intensity is an important component of PA to quantify and consider in exercise programming.

PA guidelines (e.g., in terms of frequency, intensity, duration, etc.) for achieving health benefits have been published by the U.S. Department of Health and Human Services[11] and American College of Sports Medicine (ACSM).[12] These guidelines operationally define metabolic intensity in several ways, including in terms of absolute amounts of oxygen consumed, relative to maximal heart rate, and according to perceived exertion.[13] Still, oxygen consumption is not a feasible metric for measuring and prescribing metabolic intensity of PA in public health. Similarly, heart rate recommendations are often based on percentages of a predicted maximum and may ultimately be too complicated and burdensome for individuals in the general population to calculate and implement. Because of the subjectivity of perceived exertion, this measure of an activity's metabolic intensity also has reduced accuracy and can be confounded by factors like motivation, individual temperament, type of exercise, biological sex, and the rating scale used.[14] Thus, there is a need for methods of measuring and prescribing PA metabolic intensities that are simpler and more practical as well as objective and evidence-based.

Walking is an accessible, easily performed,[15] and pleasurable mode of PA.[9] It is also reported as the most common form of PA in adults globally.[16] Numerous studies (discussed in more detail below) have attempted to develop equations for quantifying walking intensity using speed as the primary predictor. Arguably, the most widely recognized of these metabolic equations for walking is that published by the ACSM in 1980.[17] The ACSM Metabolic Equation attempts to use walking speed (*S*; m/min) and grade (*G*; decimal form) to predict oxygen consumption (VO_2; mL/kg/min) with the following linear equation:[18]

$$VO_2 = [0.1 \bullet S] + [1.8 \bullet S \bullet G] + 3.5 \qquad \text{Eq. 1}$$

The coefficient for the speed component of this equation [0.1•*S*] was derived from a 1965 study of repeated treadmill bouts at various speeds performed by three trained men, including two 23-year old participants and the author, 42 years of age.[19] The homogeneity and small size of this sample calls into question the generalizability and external validity of this equation. Additionally, a re-analysis of this study's data determined that the observed speed-VO_2 relationship was actually quadratic instead of linear.[20] Subsequent validation studies[21-23] of the ACSM metabolic equation have reported that it systematically and significantly under estimates walking intensity. One of these studies[21] evaluated the accuracy of the ACSM Metabolic Equation in predicting the average walking intensities of 25 participant groups aggregated from 10 studies (409 total participants), and reported it under estimated intensity with a standard error of estimation (SSE) of 4.5 mL/kg/min. Similarly, another study[22] including 459 adults from 20-54 years of age (divided into four-year age groups) reported that the ACSM Metabolic Equation under estimated the intensity of level treadmill walking at 81 m/min (3.0 mph) with SEE values of 4.2-5.8 mL/kg/min. The magnitudes of these predictive errors exceed 1 MET (3.5 mL/kg/min). Such underestimations could lead to walking intensity prescriptions that are higher than intended, which may reduce adherence to PA programs.[7-10]

The application of speed-based metabolic equations for walking, like the ACSM metabolic equation (Eq. 1), is further limited by the use of treadmill walking speeds in their development. Treadmills facilitate tight control and monitoring of walking speed but over-reliance on treadmill protocols impedes the use of such speed-based equations in many real-world settings where walking serves as a practical and enjoyable mode of PA.[9] Distance and time are both required to calculate speed. However, walking distance is challenging to ascertain if a previously established course has not been laid out. As such, monitoring overground walking beyond measured tracks and corridors is challenging. Global positioning system (GPS) technology can enable the quantification of walking speed, but remains expensive, inaccurate indoors, and not yet incorporated into many PA measurement devices.[24] Thus, there is also a need to consider a more accessible metric when developing a metabolic equation that may translate between treadmills and the overground walking conditions that are more common in daily living.

Step counting with wearable devices has been embraced in recent decades by researchers and the public as a simple and practical method for quantifying walking volume expressed as steps/day. Lay public users easily recall steps/day recommendations when implemented in public health campaigns[25] and PA counseling.[26] Still, step counting has been criticized for its inability to directly capture the metabolic intensity of walking, a central aspect of public health recommendations. To address this limitation, several studies have investigated the relationship between walking *cadence* (steps/minute) and intensity in adults.[27-43] Tudor-Locke & Rowe[42] analyzed the data from five published studies and reported a strong correlation (r = 0.93) between cadence and absolutely-defined intensity (metabolic equivalents; METs; where 1 MET = standardized resting metabolic rate of 3.5 mL O_2/kg/min[44]). This strong natural relationship supports using cadence as a simple and accessible proxy indicator for walking intensity. Prescribing and monitoring cadence may be a practical method for implementing intensity recommendations in PA programs. Additionally, the measurement of time-stamped patterns of step accumulation with modern accelerometry enables the quantification of cadence as a transparent and comprehensive method of measuring PA volume (steps/day) and intensity (cadence patterns).

The studies examining cadence and walking intensity in adults have typically used a “threshold approach.” That is, their primary aims were to identify the minimum cadence needed to reach an absolutely-defined moderate or vigorous intensity (3 and 6 METs, respectively). This approach is advantageous for a simple public health translation of PA guidelines and for deriving time spent at these intensities, but it only evaluates metabolic intensity of PA as a binary outcome (i.e., reaching or not reaching the threshold). A model with walking intensity as a continuous outcome would more accurately represent the continuous nature of metabolic intensity, allow for more precise and individualized estimations and prescriptions of walking intensity, and may better communicate that “more is better.” An additional gap in the existing cadence-intensity literature is the comparison and synthesis of results without consideration for the various walking conditions that different studies have implemented. For example, studies quantifying the relationship between cadence and intensity have examined both overground[28,30,31,36,43] and treadmill walking.[27,29,33,35,36,40] Those conducted during overground walking have also implemented constraints on either participants’ walking speeds[28,30,31,43] or cadences.[36] Further, cadence-based walking prescriptions may be implemented by constraining cadence to the tempo of a metronome or music. As walking at the same speed with different constraints has shown to result in differences in the kinematics[45,46] and metabolic cost[47,48] of walking, more studies are needed to confirm that the cadence-intensity relationship does not differ with various walking constraints, or on different walking surfaces (i.e., treadmill or overground). Finally, although several studies[39,41,42] have concluded that a cadence of 100 steps/min is a reasonable heuristic (i.e., evidence-based but practical and rounded) value indicative of absolutely-defined moderate intensity walking for public health applications, these same studies have also acknowledged considerable inter-individual variability in the cadence-intensity relationship. This variability has been attributed to additional factors such as height/leg length,[27,31,36] body mass,[39] body mass index (BMI),[31,33] biological sex,[27,33,40,43] and age.[35,39] More research is needed to determine if such anthropometric and demographic variables influence the cadence-intensity relationship, and to incorporate their effects into cadence-based recommendations to better individualize and enhance predictions of walking intensity.

1.2. Purpose of Thesis

The purpose of this thesis was to develop metabolic equations that predict metabolic intensity (oxygen consumption; mL/kg/min) from cadence using a large treadmill walking dataset (Study One) and cross-validate these equations during overground unconstrained and cadence-constrained walking conditions (Study Two). More specific objectives included to: 1) develop a metabolic equation that uses cadence as the only predictor (a *simple* equation), 2) develop a metabolic equation that uses cadence and possible additional predictors including height, leg length, body mass, BMI, percent body fat, sex and age (a *full* equation), and 3) cross-validate these cadence-based metabolic equations under different walking conditions (i.e., overground unconstrained walking and overground cadence-constrained walking) in an independent sample.

1.3. Aims & Hypotheses

Aim 1: Determine if a linear or curvilinear model more accurately describes the relationship between cadence and metabolic intensity of treadmill walking, using data previously collected from a large sample of men and women across the adult lifespan.

> ***H_1*:** A curvilinear (quadratic) model will fit the cadence-intensity relationship significantly better than a linear model.

Aim 2: To develop simple and full cadence-based metabolic equations by calibrating regression models that predict metabolic intensity of treadmill walking, using the data from this same large sample of men and women across the adult lifespan.

***H*$_{2.1}$:** Cadence alone will be a significant predictor of metabolic intensity in the simple equation, with root mean square error (RMSE) and mean absolute error (MAE) values ≤1 MET when cross-validated within the original sample.

H$_{2.2}$: The full equation will minimally include the additional predictor of leg length, which will result in increased predictive accuracy.

Aim 3: To cross-validate these cadence-based metabolic equations under different walking conditions (using previously collected unconstrained and cadence-constrained overground walking data) and compare their predictive accuracies to that of the ACSM metabolic equation.

***H*$_{3.1}$:** The cadence-based metabolic equations will remain valid for overground unconstrained walking with RMSE and MAE values ≤1 MET, but underpredict the metabolic intensity of overground cadence-constrained walking.

***H*$_{3.2}$:** The cadence-based metabolic equations will have greater predictive accuracies than the ACSM metabolic equation.

1.4. Summary

The dose-response relationships between metabolic intensity of PA and various health outcomes is well-documented, and thus minimum intensity recommendations are extolled in PA guidelines. However, prescribing activities with inappropriately high metabolic intensities may compromise PA program adherence. Current approaches to expressing intensity for PA prescription and estimation purposes are limited. The popularity and practicality of walking as a mode for achieving PA guidelines has supported the development of numerous equations for predicting intensity from walking speed. The most popular of these, the ACSM metabolic equation for walking (Eq. 1), has demonstrated limited generalizability and systematic bias. Such speed-based metabolic equations are also limited in their real-world application by the difficulties of measuring and prescribing walking speed.

Alternatively, step counting has been long embraced as a simple and intuitive method for quantifying volume of walking, and more recently, cadence has emerged as a reasonable metric for estimating walking intensity. With its simplicity, accessibility, and strong correlation with metabolic intensity, cadence is a sensible predictor to be included in a walking metabolic equation. A cadence-based metabolic equation would model walking intensity as a continuous outcome, in contrast to the “threshold approach” of previous studies. This approach may allow for more precise predictions of walking intensity and better represent the continuous dose-response relationship between PA and health (e.g., walking at a higher cadence even when not reaching the next threshold for moderate or vigorous intensity). Additionally, studies examining the cadence-intensity relationship have implemented overground speed-constrained, overground cadence-constrained, and treadmill walking, but have not examined the influence of these various walking conditions on the relationship. These studies have also reported substantial inter-individual variability in walking intensity that is not explained by cadence alone. The knowledge gaps collectively call for more research to determine whether or not considering anthropometric and demographic predictor variables can individualize and enhance the precision of predictions.

CHAPTER 2

LITERATURE REVIEW

2.1. Overview

Considerable research in the fields of exercise physiology and biomechanics has investigated the metabolic intensity of walking. The purposes of this literature review are to: 1) determine what is known about the effects of anthropometric and demographic variables and walking conditions on the metabolic intensity of walking, 2) review the methods and theoretical basis used to develop several existing speed-based metabolic equations for walking, and 3) summarize all previous studies examining the cadence-intensity relationship.

2.2. Metabolic Intensity of Walking

2.2.1. Walking Mechanics and Metabolic Intensity Determinants

Walking consists of a repetitive and predictable series of movements characterized as a *gait cycle*. This gait cycle consists of a single-limb support phase, where one foot is in contact with the ground while the other leg is in a swing phase, followed by a heel-strike of the swing phase foot to begin the double-limb support phase (i.e., both feet are momentarily in contact with the ground). The foot initially in stance phase then exerts a force against the ground (toe-off) to begin its own swing phase, and another phase of single-limb support.[49] The mechanics of this gait cycle aids in the conservation of energy; the stance leg behaves like an inverted pendulum moving about the stance foot and the swing leg behaves like a normal pendulum moving about the hip.[50] Despite its inverted pendulum-like motion, single-limb support is associated with the greatest *metabolic cost* (i.e., amount of energy expended [kcals, Joules, mLO_2])

because of the work done against the ground to raise the body's center of mass vertically (*external work*). At cadences lower than those self-selected during normal walking, step-to-step transitions during the double-limb support phase are associated with the second greatest metabolic cost, where the body's center of mass is redirected from a downward to an upward trajectory. At cadences higher than those that are self-selected, the second greatest metabolic cost is associated with leg and arm swing (*internal work*).[51]

Walking speed is the product of cadence and *step length*, defined as the anterior-posterior distance between the left and right foot from one single-limb support phase to the next.[49] Increasing cadence is the primary strategy used to increase to a preferred walking speed[49] and up to this walking pace, the relationship between speed and cadence is highly linear ($R^2 = 0.98$).[52] There is also strong evidence that the ratio of cadence to step length, known as the *walk ratio* (step length / cadence), remains constant during treadmill and unconstrained overground walking, at least at speeds of ~60-120 m/min (2.2-4.5 mph).[53,54] This walk ratio remains at ~7 mm/step/min for men and ~6 mm/step/min for women,[49] and results in a predictable change in step length with changes in cadence at these speeds.

During normal human walking, self-selected walking parameters (e.g., cadence, step length, and speed) are strongly influenced by an innate attempt to minimize metabolic intensity, termed *metabolic optimization*.[20,45,49,55-57] For example, different cadence and step length combinations may be selected to produce a single walking speed. Testing these combinations has illuminated a U-shaped relationship between metabolic intensity of walking and cadence (or step length) at a constant speed (e.g., on a treadmill). For any given speed, humans tend to self-select the cadence and step length combination located at the lowest point of this curve and thus optimize the metabolic intensity of walking at a given speed.[20,45,58] These self-selected cadences and step lengths result in the invariant walk ratio previously discussed, which is believed to be an innate motor strategy for minimizing the metabolic intensity of walking.[49,57,59] Several factors determine the metabolic intensity of a cadence-step length combination and are thus simultaneously and inherently considered for metabolic optimization. Notably, the metabolically optimal cadence-step length combination must minimize both the external work for accelerating the body's center of mass vertically (lowest with shorter step lengths and higher cadences) and the internal work for accelerating the body's limbs (lowest with longer step lengths and lower cadences).[55] Additionally, metabolic optimization of walking must maximize mechanical efficiency and power (highest at intermediate cadences; reportedly ~108 steps/min),[60] and account for the cadence at which the metabolic cost of leg swing is minimized because it is primarily driven by gravity, termed the *natural frequency of the leg*, which is inversely related to leg length.[49]

2.2.2. Predictor Variables for the Speed-Intensity Relationship of Walking

Many anthropometric and demographic variables, such as body mass, BMI, percent body fat, height, leg length, age, and biological sex, have been investigated when attempting to understand and model the metabolic intensity of walking, as primarily represented by the rate of oxygen consumption measured using indirect calorimetry. Including such predictors along with basic gait parameters like walking speed and cadence has resulted in models that have explained more than 90% of the variation in walking intensity.[61-65] A large majority of this literature modeling the intensity of walking, beginning as early as 1915,[66] has used walking speed as the primary predictor –

thus the sections that follow summarize the effects of these variables as reported in speed-based studies examining the metabolic intensity of walking. The influence of these predictor variables in cadence-based models of walking intensity will be subsequently discussed.

2.2.2.1. Body Mass, BMI, and Percent Body Fat

Body mass is a measure of the total amount of matter an individual's body is comprised of (kg), including muscle, fat, bone, water, and other tissues and substances. Body mass index (BMI) is a metric of body mass in proportion to height (kg/m^2) and is used as a population-level indicator of overfatness (i.e., to classify individuals as healthy weight, overweight, or obese). The utility of BMI for individual-level applications is limited because it does not actually measure the proportion of fat mass versus fat-free mass, and thus an individual with more muscle mass per unit height is considered more overfat. In contrast, direct measures of percent body fat discriminate the proportion of fat mass comprising an individual's overall body mass for a more accurate determination of overfatness. These three variables are related. A higher percent body fat signifies excess fat mass, increasing body mass and resulting in a higher BMI.

When metabolic intensity is expressed in units that are not normalized to body mass (e.g., L/min, kcal/hr, etc.), body mass alone can explain 40% of the variation in metabolic intensity at various speeds,[67] and 68-78% of the inter-individual variation in metabolic intensity at a single speed.[63] This correlation can be largely explained by the greater energy requirement for accelerating a larger body mass and for supplying energy to more metabolically-active tissue.[68] Body mass is thus an important determinant of metabolic cost per step[65] and an important variable to consider when predicting such non-normalized measures metabolic intensity of walking.

Metabolic intensity expressed in units standardized to body mass (*mass-specific metabolic intensity*; e.g. mL/kg/min, kcal/kg/hr, etc.) is more commonly used in public health and exercise testing and programming,[11,12,69] and is the form of metabolic intensity generally referred to herein unless otherwise indicated. When units of metabolic intensity are mass-specific, the effect of body mass on metabolic intensity of walking substantially weakens but may still persist. To investigate the influence of body mass on the relationship between mass-specific metabolic intensity of walking and speed, Foster et al.[61] recruited 11 obese subjects (mean body $mass_{pre}$ = 104.5 kg) to walk at the same three speeds before and after a dietary intervention. Following a 21% reduction in body mass (mean body $mass_{post}$ = 83.6 kg), a decrease in metabolic intensity of walking was observed even when expressed in mass-specific units (exact magnitude not reported, $p < 0.001$). Like body mass, BMI and percent body fat were also significantly reduced and associated with the reduction in mass-specific metabolic intensity of walking (mean $BMI_{pre} = 38.9$ kg/m^2 versus mean $BMI_{post} = 31.1$ kg/m^2; mean body fat_{pre} = 45.6% versus mean body fat_{post} = 33.6%). The authors hypothesized that the reductions in body mass, BMI, and percent body fat resulted in: 1) less work required to overcome friction between the arms and torso and the thighs, 2) less extraneously wide movements when swinging the arms and legs because of a smaller torso and thigh, 3) changes in the distribution of mass, and 4) improved efficiency in pulmonary function. Similarly, Browning et al.[70] reported a 10% greater mass-specific metabolic intensity of treadmill walking in 19 class II obese (BMI 35.0-39.9 kg/m^2) men and women, as compared to 20 normal-weight participants. Obese women experienced the highest metabolic intensity of walking and had the highest thigh mass-to-body mass ratio, leading the authors to hypothesize that the greater internal work required to swing relatively heavier legs at a wider angle contributed to this difference. Previous studies have further demonstrated that loads carried more distally (e.g., on the lower limbs) result in a higher metabolic intensity of walking than the same load carried closer to the body's center of mass.[71] The use of mass-specific units of metabolic intensity does not account for such differences in walking efficiency and body mass distribution that have been observed with more extreme levels of obesity, but considering body mass, BMI, or percent body fat may.

In individuals of more normal weight status, the evidence has indicated there is no influence of body mass, BMI, or percent body fat on the mass-specific metabolic intensity of walking. For example, BMI did not contribute significantly to models of mass-specific metabolic intensity of walking in two studies by Agiovlasitis and colleagues: one[72] included 25 individuals with multiple sclerosis (MS) who had a mean ± SD BMI of 26.8 ± 6.9 kg/m^2 while the other[73] had a sample comprised of 61 healthy participants and 54 individuals with Down Syndrome (DS), with BMIs of 24.6 ± 5.2 kg/m^2 and 29.8 ± 5.6 kg/m^2, respectively.

Further, the relationship between mass-specific metabolic intensity of walking and body mass can be confounded by the tendency for taller individuals to also have a greater body mass (i.e., collinearity of body mass and height; r = ~0.9).[74] Thus, an effect of height (further discussed below) could be the direct cause of a relationship between body mass and mass-specific metabolic intensity of walking. For example, Weyand et al.[75] measured the metabolic intensity of walking in a sample of participants varying in height by a factor of 1.5 and body mass by a factor of 6 (BMIs not provided). After dividing their sample into four subgroups with significantly different body masses, they demonstrated an inverse relationship between body mass and mass-specific metabolic intensity at each treadmill speed. As the body mass-stratified subgroups also had corresponding differences in height, the between-group differences in metabolic intensity were attenuated when the potential effects of height were mathematically controlled. In other words, all participants had a similar metabolic intensity of transporting 1 kg of their body mass a distance equal to their height.[75] Thus, individuals with a similar percent body fat may demonstrate a correlation between body mass and metabolic intensity of walking because of differences in height. Such a correlation would therefore not be a result of the obesity-related decreases in walking efficiency previously discussed (e.g. friction at the arms and thighs, wide arm and leg swings, etc.) and differences in body mass distribution.[61,70]

The use of BMI and percent body fat may more accurately represent these obesity-related influences on the metabolic intensity of walking; BMI inherently standardizes body mass by height and percent body fat is a direct measure of overfatness. Additionally, fat mass contributes very little to the metabolic rate at rest and substantially less than fat-free muscle and organs mass to the metabolic rate during PA.[76] Percent body fat therefore indicates the proportion of metabolically-inactive tissue in the body. When modeling the mass-specific metabolic intensity of walking in 42 men (19-66 years of age, BMI and percent body fat values not reported), Pearce et al.[77] determined a significant interaction between percent body fat and treadmill speed (magnitude and direction not reported), although this may have been confounded by a correlation between percent body fat and age. Another study conducted by Hall et al.[78] with 12 men and 12 women (18-30 years of age) demonstrated a moderately strong correlation between percent body fat and the mass-specific metabolic intensity of treadmill and overground walking at 84.6 m/min and running at 169.2 m/min (r = -0.71 to -0.83, all $p < 0.01$). This suggests that measuring metabolic intensity of walking with mass-specific units does not account for inter-individual differences in the proportion of metabolically-active muscles mass. Still, when metabolic intensity was standardized to fat-free mass, the model reportedly failed to account for the additional energy requirement for transporting excessive fat mass in individuals with a higher percent body fat.[78] Therefore, fat-free mass and fat mass may have unique effects on the metabolic intensity of walking and both need to be considered using measures like body mass, BMI and percent body fat.

2.2.2.2. Height and Leg Length

Height and leg length are strongly collinear (r = 0.90), making considerations of their effects in models of walking intensity nearly identical[31] both statistically and mechanistically. Both of these variables have consistently been shown to influence step length and thus the cadence an individual will select at a given speed (reported r-values ranging from -0.66 to -0.77).[65,75,79,80] This lower cadence selected by taller individuals at a given speed was cited by Kramer & Sarton-Miller[79] and Steudel-Numbers & Tilkens[63] to explain the inverse relationships they observed between height and walking intensity, and significant improvements they observed in their speed-based models of walking intensity with the inclusion of leg length (all $p < 0.01$). Workman & Armstrong[65] similarly reported a negative correlation between height and cadence at each speed of treadmill walking in eight men (r = -0.66), and included height in their speed-based metabolic equation to give taller individuals a lower metabolic intensity of walking (in LO_2/min) at a given speed. Specifically, their equation was comprised of a cadence and a metabolic cost per step component ([LO_2/min] = [steps/min] • [LO_2/step]) and thus included a negative effect of height (and positive effect of speed) to predict cadence. A later study additionally concluded that the metabolic equation by Workman & Armstrong[65] was more accurate and robust than others because of its inclusion of height.[81] In this model of walking intensity (metabolic intensity = cadence • metabolic cost per step),[65] an inverse height-intensity relationship was mediated by step length and cadence. As proposed, this assumes that metabolic cost per step stays relatively constant. This assumption was supported by Weyand et al.,[23] who divided participants with a broad range of heights (1.07-2.11 m) into four groups by stature and reported that they had similar metabolic costs per step, despite height-related differences in cadence (and thus step length) and intensity of walking at a given speed. These studies provide strong evidence for a lower metabolic intensity of walking at a given speed in taller individuals, mainly attributable to increases in step length and decreases in cadence with increasing height.[63,65,80,82]

Additionally, variations in leg length may result in differences in the metabolic cost of leg swing. For example, the mechanical energy required for leg swing is greater for a longer and heavier leg.[79] Leg length is also inversely related to the natural frequency of the leg (i.e., the cadence at which the metabolic cost of leg swing is minimized). Therefore, the same enacted cadence in individuals of different leg lengths will result in different deviations from their natural frequency, resulting in different metabolic costs of leg swing.[49] Another potential mechanism for an influence of height was suggested by Cotes & Meade[80] after they also observed an inverse relationship between metabolic intensity of walking at a given speed and height. They reported that shorter individuals would have a theoretically larger angle of excursion between their legs at a given step length and thus perform more external (i.e., vertical lift) work and have a higher metabolic intensity. These additional mechanisms may also result in an influence of height on the metabolic intensity of walking, although their net magnitude and direction of effect has not been quantified.

2.2.2.3. Age

Compared to young and middle-aged adults, older adults tend to have shorter step lengths, reduced control of their hips in the medial-lateral plane resulting in greater step widths and step width variability (indicators of instability), increased time between contralateral heel strikes (step time), decreases in the spatiotemporal coordination of their limbs on opposite sides during walking (*gait symmetry*), and greater activity in stabilizing muscles that oppose the direction of movement (*antagonist muscle contraction*) during walking.[54,83,84] Such changes in gait parameters with age may be compensatory motor strategies for preserving balance and are related to declines in coordination.[83]

Several publications have reported significant effects of age on metabolic intensity of walking. In a study comparing eight young (age <30 years) and ten older (age ≥65 years) adults, Dean, Alexander, and Kuo[85] found that the older group had a 26% greater metabolic intensity of walking at 66 m/min (2.5 mph), along with a 41% wider step width and significantly greater variability in the step width of each step. In a similar study of treadmill walking at 42-108 m/min (1.6-4.0 mph), Ortega & Farley[86] reported that older adults (age = 76 ± 4 years) had a 20% higher metabolic intensity than young adults (age = 25 ± 4 years) at each speed, despite performing 10% less external work on average (for accelerating the center of mass upwards) during single-limb support. Because this external work component of walking is normally associated with the greatest metabolic intensity[51] (see section 2.2.1.), mechanical work did not explain the observed differences in walking intensity with age. The authors instead attributed their findings to balance- and coordination-related factors such as the cost of stabilizing the body, antagonist muscle contraction, gait symmetry, and the efficiency of the muscular system. Still, apparent differences in step width were not significant (step widths: older adult = 15 ± 3 cm, younger adults = 12 ± 3 cm; $p = 0.14$). In addition, the significantly higher cadence selected by older adults at each speed ($p = 0.034$) indicates they performed more internal work, which could further elevate their metabolic intensity of walking. The influence of age was also investigated by Pearce et al.[77] when developing speed-based metabolic equations for walking. They found that age group (young [19-29 years of age] versus older [55-66 years of age] adults) interacted with speed when predicting VO_2 of treadmill walking. The speed-based metabolic equations they presented therefore predicted greater differences in walking intensity between age groups with increasing walking speed, with a 0.13-1.71 mL/kg/min greater metabolic intensity in older adults at each speed between 41-120 m/min (1.5-4.5 mph). Thus, there is substantial evidence that older adults (≥65 years of age) have an increased walking intensity at a given speed, as associated with motor strategies for preserving balance and stability (e.g., increases in antagonist muscle contraction, cadence, and step width) and declines in coordination (e.g., reduced gait symmetry and muscular efficiency).[54,83-86] These age-related changes may also have a larger effect on metabolic intensity of walking at faster walking speeds.[77]

Other studies including only young and middle-aged adults (18-64 years of age) have not reported an influence of age on the metabolic intensity of walking. For example, age was not a significant predictor of metabolic intensity of walking (expressed as L/min but controlling for body mass and speed) in a study conducted by Kramer & Sarton-Miller[79] with 72 participants ranging between 7-59 years of age, and in a later study also by Kramer[67] with 11 adults 22-52 years of age ($p = 0.66$). Similarly, metabolic intensity of walking at a given speed was not influenced by age in a secondary analysis including 32 studies and 391 total participants 13-65 years of age,[87] and in a sample of 48 participants 5-32 years of age (results controlled for height).[75] The latter of these articles[75] also included a secondary analysis of previously published data where adults ≥65 years of age were explicitly excluded from the sample. The authors justified this exclusion criteria by citing the study by Ortega & Farley[86] discussed previously, and stating that adult of this older age "may not walk in a dynamically similar manner." Perhaps the strongest evidence for an influence of age on walking intensity in older but not young and middle-aged adults is provided in the study by Grimby & Soderholm[88] which included 14 younger (22-30 years of age), 22 middle-aged (34-46 years of age), and 10 older (56-63 years of age) adults. During treadmill walking at 75-98 m/min (2.8-3.7 mph), there were significant differences in metabolic intensity of walking at a given speed between older versus younger and older versus middle-aged adults, but not between younger versus middle-aged adults. More specifically, at 75 m/min, the average VO_2 values of the younger, middle-aged, and older groups were 13.1, 12.7, and 14.6 mL/kg/min, respectively ($p < 0.05$). The evidence from these studies[67,75,79,87,88] suggests that middle-aged adults have not begun to suffer from the age-related declines in balance, stability, and coordination that reportedly increase the metabolic intensity of walking in older adults. Age is therefore likely not an important predictor to include in predictions of walking intensity in these younger populations.

2.2.2.4. Biological Sex

There are well-known differences in the average physiological and anthropometric characteristics of men versus women, which could contribute to differences in their speed-metabolic intensity relationships of walking. Compared to men, women have a wider pelvis[89] and walk with a greater range of motion and speed of rotation at their hip and knee joints.[90,91] A wider pelvis can also increase the activity and metabolic demand of the hip abductors during walking, in an effort to prevent the trunk from rotating away from the stance leg.[92] Additionally, women generally have a more distal distribution[71] and higher percent body fat,[70,93] as well as a shorter stature, and a lower body mass.[94] These factors can theoretically result in sex-based differences in metabolic intensity of walking that may be more directly related to anthropometric differences between men and women.

Four studies[78,87,95,96] reported a greater metabolic intensity of walking at a given speed in men compared with women. In the review and secondary analysis by McDonald,[87] five studies enrolling a total of 70 men and 44 women were included for examining sex-based differences in the relationship between walking speed and metabolic intensity. The author reported that the metabolic intensity of walking at 30-105 m/min (1.1-3.9 mph) was 12% (1.12 kcal/kg/min) greater in men when controlling for speed (p <0.001). A potential mechanism for these differences was not provided. Molen & Rozendal[96] also determined that the metabolic intensity of treadmill walking was greater in men versus women (magnitude not reported) at each speed tested (20-110 m/min [0.7-4.1 mph]). They attributed these differences in walking intensity to men having a higher *standing metabolic rate* (i.e., the metabolic rate at rest plus that for the balance and posture of standing), as opposed to a greater metabolic intensity of the walking movement itself. The authors did not provide any rationale for the elevated standing metabolic rate they observed in men, but because fat mass is known to contribute marginally to the metabolic rate at rest[76] (see section 2.2.2.1.), this difference may be a result of women having a higher average percent body fat.[93] This mechanism is further supported by Hall et al.,[78] who reported that the 17% higher metabolic intensity they observed in men versus women during treadmill and overground walking at 85 m/min (3.2 mph) was attenuated after controlling for fat-free mass (percent fat: men = 11.6 ± 1.9%, women = 23.7 ± 2.2%). In another study by Booyens et al.,[95] men demonstrated a 9% and a 13% higher average metabolic intensity when walking at 91 and 107 m/min (3.4 and 4.0 mph) respectively, compared to women walking at the same speeds (p <0.05). At these speeds of 91 and 107 m/min respectively, the men exhibited cadences that were 16% and 20% lower (p <0.001) and step length-to-leg length ratios that were 6% and 9% higher (p-value not reported) than the women. As discussed previously (see section 2.2.1.), a longer step length results in a greater vertical displacement of the body's center of mass and therefore greater external work.[66] The lower cadence and higher ratio of step length-to-leg length in the men at each speed indicates they took longer steps (even proportionate to their leg length) than the women, and the authors thus attributed the observed sex-based differences in metabolic intensity of walking to the greater external work performed.

In contrast, three other studies[70,97,98] provide evidence that the metabolic intensity of walking at a given speed is greater in women compared to men. Blessey et al.[98] reported that men and women had the same metabolic intensity when walking at cadences of 60 and 120 steps/min, as well as at their self-selected pace where both sexes selected an average cadence of 116 steps/min. In each of these conditions where cadences were equal, women had lower step lengths and thus significantly slower walking speeds than men (speed in self-selected condition: men = 89 ± 11 m/min, women = 74 ± 11 m/min; p <0.01) but walking intensities were similar (VO_2 in self-selected condition: men = 13.4 ± 2.3 mL/kg/min, women = 12.5 ± 2.5 mL/kg/min). The women exhibited a metabolic intensity equal to that of men when walking at significantly slower speeds, indicating a greater metabolic intensity than men at equivalent speeds. In another study comparing the metabolic intensity of treadmill walking in 10 obese men and 9 similarly obese women (BMI: men = 33.5 ± 2.1, women 33.5 ± 20.3 kg/m^2), Browning et al.[70] also reported that women had a greater metabolic intensity of walking (values not reported, p <0.01). The observed difference correlated with the women's higher thigh-to-body mass ratio and percent fat at the shank, indicating a more distal distribution of mass. Similar to the research cited earlier to demonstrate that more distally-carried loads (e.g., loads on the lower limb) result in a higher metabolic intensity of walking than the same loads carried more proximally,[71] the authors attributed their findings to the proportionally heavier and more distally weighted limbs that these women were required to swing. The effect of this mechanism would theoretically increase with increasing speed because internal work of walking (i.e., for limb swing) becomes larger at faster walking speeds (see section 2.2.1.).[51] Interestingly, Browning et al.[70] also found that the differences in walking intensity between men and women were greater at faster walking speeds (i.e., significant sex-speed interaction; $p = 0.02$), therefore providing further support for this mechanism. Finally, Howley & Glover[97] reported that women had a significantly higher mass-specific energy expenditure than men during one mile of treadmill walking at similar speeds (0.82 kcal/kg/mile for women, 0.79 kcal/kg/mile for men, $p < 0.01$). This difference was attenuated when metabolic intensity was expressed per unit of body surface area, and the authors therefore attributed this difference to a greater body surface area in men.

In contrast, men and women may not have significant differences in metabolic intensity of walking when anthropometric variables are controlled. Specifically, in the two studies conducted by Weyand & colleagues[23,75] to develop a speed-based metabolic equation for walking (discussed below), no significant sex differences in the metabolic intensity of walking were observed when controlling for height (sex-specific heights not reported). Their speed-based metabolic equation for walking therefore included height but not sex. As men tend to be taller, and height and leg length correlate with step length (r-values ranging from 0.55-0.74 depending on the speed),[27,36] controlling for height may explain the sex-related variability in metabolic intensity of walking that is mediated by step length at a given speed. In summary, these studies demonstrate the conflicting evidence regarding sex-related differences in the metabolic intensity of walking, and whether such differences exist after controlling for height.

2.2.3. Walking Conditions

Walking condition is defined herein as the constraints that are placed on walking parameters (e.g., speed, cadence, and step length) and the surface on which walking occurs (i.e., treadmill or overground). Studies examining the metabolic intensity of walking generally employ three different walking conditions: 1) *overground unconstrained walking*, where speed, cadence, and step length are self-selected, 2) overground *cadence-constrained walking*, where cadence is controlled by matching heel-strikes to a *rhythmic auditory cue* (RAC) such as a metronome or music but step length and speed are self-selected, and 3) treadmill walking, where speed is controlled but cadence and step length are self-selected. With each of these walking conditions, individuals may select different gait parameters, limb kinetics and kinematics, and coordination and motor control strategies. The walking condition employed may therefore be an important variable to consider when attempting to accurately model the metabolic intensity of walking.

In overground unconstrained walking, the cadence, step length, and speed that are self-selected are strongly influenced by metabolic optimization as discussed in detail previously (see section 2.2.1).[20,45,49,55-57] This predilection for metabolic optimization is evidenced by individuals selecting the cadence with the lowest metabolic intensity for walking at a given speed. [20,45,58] It is also characterized by an invariant walk ratio resulting from proportional increases in cadence and step length with increasing speed.[49,53,54] Additionally, a person's anthropometric and demographic characteristics can influence their gait features during overground unconstrained walking. For example, taller individuals commonly walk with greater step lengths,[65,75,79,80] and older adults tend to walk more slowly with greater step widths, shorter step lengths, and potentially greater cadences.[83] These walking parameters may also be influenced by instruction to walk at a slow, normal, or fast pace, particularly in controlled research settings.[99]

In overground walking where cadence is constrained through entrainment to an RAC, the resultant speed can still vary according to the selected step length. This allows for various possible combinations of cadence, step length, and speed during cadence-entrained walking. The relationships between these three walking parameters apparently differ from those discussed during overground unconstrained walking. Specifically, Laurent & Pailhous[46] demonstrated that when eight men walked overground with cadences entrained to four different RAC tempos set above and below their self-selected cadence, the observed increases in speed (percent change = 37%) were driven primarily by the increases in cadence (percent change = 27%); step length increased proportionally less or did not change at all (percent change = 8%). The walk ratio therefore did not remain constant as it does during overground unconstrained and treadmill walking,[49,53,54] but instead decreased with increases in walking speed. Laurent & Pailhous[46] suggested that a natural tendency for humans to remain at their normal walking speed may have prevented expected increases in step length. A study by Bertram & Ruina[45] later confirmed this finding. Further, they compared the gait parameters of six men and six women during treadmill (speed-constrained) walking, overground cadence-constrained walking, and *overground step length-constrained walking*, a walking condition less common and practical to implement where the foot placements of each step are set by a series of ground markers. Each of these three walking conditions were reported to demonstrate unique relationships between cadence, step length, and walking speed. In other words, the same participant walking with the same cadence selected a different speed in each walking condition. A new hypothesis was proposed by Bertram & Ruina[45] to explain these findings: a common optimization function (e.g., minimizing metabolic intensity per unit distance) drove the selection of gait parameters in each walking condition, but the optimal cadence, step length, and speed combinations with each constraint differed because of their unique coordination requirements and potential effects on gait and posture. This hypothesis, termed *constrained optimization*, was further tested by Bertram[47] by collecting metabolic data during 49 different cadence-speed combinations and predicting the metabolically optimal cadence at a given speed under each constraint, using the constrained optimization hypothesis as a predictive model. When participants then performed several bouts under each of the three constraints individually, the relationships observed between cadence, step length, and speed differed between walking conditions but matched those predicted to be metabolically optimal (largely within 5%). This provides strong empirical evidence that the combinations of cadence, stride length, and speed that are metabolically optimal and therefore naturally selected differs depending on the walking condition, because of the unique effects of each constraint on the motor control systems for walking and gait mechanics.[47] Such differences in gait parameters may influence the relationship between cadence and metabolic intensity, making it an important factor to consider when modeling the cadence-intensity relationship.

Even without differences in gait parameters, the specific motor control-related demands of unconstrained versus constrained walking can influence metabolic intensity of walking. This was demonstrated in a study by Wezenberg et al.[48] where participants walked on a treadmill under three conditions: 1) with only speed constrained, 2) at that same speed with a constant cadence and step length equal to the average of their first trial (i.e., no variability), and 3) at that same speed with a real-time copy of their first trial's cadence and step length (i.e. equal variability). Despite their average gait parameters being the same in all three conditions, the second and third conditions elicited metabolic intensities that were 8% and 13%, higher than the first condition, respectively. Greater variations in center of pressure trajectories measured during these latter two conditions lead the authors to attribute their findings to increases in muscle activation for maintaining balance after foot placement. They also suggested that the more constrained walking conditions would require greater preparatory and antagonistic muscle activation for ensuring proper foot placement. Thus, the influences of constraint-specific motor control strategies on metabolic intensity of walking may be important considerations when modeling the cadence-intensity relationship, even without differences in gait parameters.

Many studies have compared the gait patterns observed in treadmill versus overground walking. Some studies have reported changes in the gait kinematics of young adults during treadmill walking that indicate walking instability, including increases in cadence and step width and decreases in step length and double-limb support times.[77,100-106] Differences in an individual's ground reaction forces[107,108] and muscle activity[107,109] have also been demonstrated during treadmill and overground walking. However, minimal to no differences in these same gait variables during the two walking conditions have also been reported within these studies and others.[77,101,107,109,110] This conflicting evidence may reflect studies observing different magnitudes of natural (within-condition) variability in walking, and whether this intra-condition variability was too high to be exceeded by the differences between conditions.[104,110-112] Additionally, some initial changes in gait variables during treadmill walking may subside after a six- to ten-minute treadmill habituation period.[103,113] Differences between treadmill and overground gait variables are also reportedly greater in older compared to younger adults,[77] even with such habituation periods.[114]

In his seminal theoretical analysis theory, Van Ingen[115] concluded there should be no mechanical differences between treadmill and overground walking. Still, he noted that differences may exist if: 1) ambulatory speed is high enough for differences in air resistance to be significant (i.e. in sprinting), 2) the surface of the treadmill belt influences vertical forces by adhering to the shoe, 3) the treadmill motor cannot overcome the forces of heel-strike and the treadmill belt momentarily slows with each foot contact, or 4) the differences in visual feedback from the surrounding have significant effects on balance and posture. The latter two mechanisms proposed by Van Ingen[115] for differences in the gait of treadmill walking have been supported empirically: first, studies[110,116] have reported 3-6% momentary decreases in belt speed during each heel-strike of treadmill walking. Second, without actual forward movement (as occurs in overground walking), the visual feedback of treadmill walking does not include a *focus of expansion,* where the visual environment in the direction of walking expands towards the person from a central point. Walking in the direction of the focus of expansion is the predominant strategy for navigation during overground walking; treadmill walking instead primarily uses *egocentric direction control* as a visual control strategy, where the individual walks straight while keeping a target in the center of the visual field.[117] An additional influence on treadmill gait may stem from the lateral constraint on foot placement that is inherent for walking on a treadmill belt.[110] These variations in treadmill belt speed and differences in motor control strategies for treadmill walking may explain its possible kinematic, kinetic, and muscle activity discrepancies from overground walking.

There is mixed evidence as to whether these differences must be accounted for when modeling the metabolic intensity of walking. Three studies[77,118,119] conducted with young, healthy adults have demonstrated 8-9% lower oxygen consumptions during treadmill walking, as compared to overground walking at the same speeds (50-100 m/min [2.0-3.7 mph]). Although all three of these studies[77,118,119] stated that the rationale behind the lower intensity they observed during treadmill walking was unclear, they hypothesized it may be due to shorter step lengths resulting in decreased external work for vertical lift and differences in the walking terrain (treadmill versus asphalt). A study of similar design conducted with relatively older adults (age = 60.6 ± 7.4 years)[120] conversely reported a 6% greater metabolic intensity of treadmill walking at their self-selected normal walking speed (average of 69 m/min [2.6 mph]). Because older adults already may have an elevated metabolic intensity of walking because of age-related declines in balance and coordination (see section 2.2.2.),[54,83-86] walking on a treadmill may exaggerate these effects and thus give them a higher walking intensity compared with overground walking. However, this study[120] found no differences in the kinematic gait variables that typically indicate gait instability (shorter step lengths and double-limb support times and wider step widths), and therefore did not provide a clear explanation for the observed differences in metabolic intensity with each walking condition. It should be noted that none of these studies included a treadmill habituation period. In contrast, at least three other studies[78,81,121] have reported that the metabolic intensity of treadmill versus overground walking at a given speed did not differ, all with protocols that also did not include a treadmill habituation period. Additionally, in the secondary analysis conducted by Ludlow & Weyand[21] of ten publications representing 419 participants, the model goodness-of-fits of three speed-based metabolic equations (calibrated during treadmill walking) were reportedly similar when applied to mean VO_2 values measured during overground walking when compared to treadmill walking. In summary, there is conflicting evidence as to whether gait and metabolic intensity differ when walking on a treadmill versus overground. More research is needed to determine whether such walking conditions should be considered when modeling the metabolic intensity of walking, and how inherent differences may influence the cadence-intensity relationship.

2.2.4. Summary of Metabolic Intensity of Walking

The movements that underlie walking are characterized by the gait cycle, comprised of alternating single- and double-limb support phases.[49] The greatest metabolic intensity during walking is associated with the external work for raising the body's center of mass vertically during single-limb support, followed by the redirection of the body's center of mass during step-to-step transition support (when cadence is lower than normally self-selected) or the internal work for leg and arm swing (when cadence is higher than normally self-selected).[51] Humans tend to naturally select the cadence and step length combination at a given speed that minimizes these metabolic intensities.[20,45,58] One resultant feature of this metabolic optimization is a walk ratio that remains constant at normal-to-fast speeds of treadmill and unconstrained overground walking.[49,53,54]

A large body of literature published over the past century has examined how anthropometric and demographic predictor variables may influence the intensity of walking at a given speed. When mass-specific units of walking intensity are used (e.g. mL/kg/min), factors like BMI and percent body fat may still have some influence due to obesity-related differences in gait mechanics and proportions of metabolically active tissue. Such effects may only be observable in individuals with high levels of obesity.[61,70] There is more consistent evidence for an inverse relationship between height/leg length and intensity of walking at a given speed, reportedly due to taller individuals exhibiting longer step lengths, lower cadences, and thus lower rates of internal work at a given speed.[65,75,79,80] An influence of age on metabolic intensity of walking is only evident in adults ≥65 years of age;[77,86] these older adults are thought to employ more metabolically-taxing motor strategies in an attempt to preserve balance and stability, and to exhibit declines in coordination that result in a less efficient gait.[54,83-86] Finally, although studies have reported mixed results regarding the influence of biological sex on metabolic intensity of walking at a given speed,[70,78,87,95-98] controlling for sex-related difference in other variables (e.g., height, BMI, and percent body fat) can likely attenuate such effects.[23,36,75] Although there is evidence supporting the consideration of these predictors when modeling walking intensity, the support for an effect of each varies in strength, and may be dependent on the characteristics of the sample being examined.

The metabolic intensity of walking may also be influenced by walking condition, as defined herein as the constraints that are placed on walking parameters (e.g., speed, cadence, and step length) and the surface on which walking occurs (i.e., treadmill or overground). In overground unconstrained walking, self-selected gait parameters are strongly influenced by metabolic optimization.[20,45,49,55-57] When overground walking cadence is constrained through use of RACs (e.g., a metronome or music), increases in cadence produce proportionally smaller increases in step length and thus decreases in walk ratio and speeds at a given cadence.[45-47,122] There may also be an additional metabolic intensity of constraining cadence, associated with increased muscle activation to ensure proper timing of foot-strikes and maintain balance.[48] Walking on a treadmill has similarly been shown to result in differences in gait parameters, phase timing,[77,100-106] ground reaction forces,[107,108] and muscle activity.[107,109] Such changes may subside after a treadmill habituation period,[103,113] but are reportedly more pronounced in older adults even following habituation.[77,114] The mechanics of treadmill and overground walking should theoretically be the same.[115] Empirically-observed differences may still exist during treadmill walking due to momentary decreases in belt speed with each heel strike,[110,116] adaptations in motor navigation strategies for walking without the visual feedback provided by forward movement,[117] and the lateral constraints on foot placement needed for walking on a treadmill belt.[110] Investigations into the metabolic implications of such differences have had mixed results.[77,78,81,118-121] This evidence indicates that walking condition can influence metabolic intensity of walking, but more research is needed to confirm and further define the differences in walking intensity that may exist during overground unconstrained, overground cadence-constrained, and treadmill walking.

2.3. Speed-Based Metabolic Equations for Walking

There are many published studies, beginning as early as 1955[123], that have developed equations to predict the metabolic intensity of walking using speed as the primary predictor. Reviewing the methods used to derive these equations and conceptual models they are theoretically based on will help to inform the development of cadence-based models of walking intensity. In addition, the previously published speed-based metabolic equations provide a standard with which to compare the performance of future cadence-based metabolic equations. Six speed-based metabolic equations were selected for closer examination because of their popularity for use in real-world applications and/or reoccurrence in the academic literature examining the metabolic cost of walking. They are presented chronologically by year of publication in the sections that follow.

2.3.1. Cotes and Meade Equation

In order to advance the basic understanding of the metabolic intensity of walking, Cotes & Meade[80] published a 1960 study in which they described multiple relationships between gait variables. This is a seminal article that appears to be commonly cited in the field of gait mechanics in relation to the metabolic intensity of walking. It also included a metabolic equation that uses speed (*S*; m/min) to predict the energy expenditure of walking (*EE*; kcal/kg/min) as follows:

$$EE = 0.0386 \cdot 4.25^{-5} \cdot S^{2}$$

The data for calibrating this equation was collected from ten male participants (18-32 years of age, weight 52.9-74.6 kg, height 1.61-1.81 m) during treadmill walking at speeds ranging from 27-107 m/min (1.0-4.0 mph). The small size of this sample and its relative homogeneity in terms of age, height, and sex limit the generalizability of the reported speed-based metabolic equation.

It appears that Cotes & Meade[80] developed this equation by simply calculating the least squares regression of the relationship between the square of walking speed and energy expenditure. Although this metabolic equation is simple and therefore easy to use, no rationale was provided for the use of a quadratic speed-intensity relationship or why no other terms were included, such as an intercept or leg length (which was included in other reported analyses from their study). Thus, the development and basic form of their equation was not well justified.

2.3.2. Workman-Armstrong Metabolic Equation

The Workman-Armstrong Equation published in 1963 is also commonly referenced in the metabolic cost of walking literature and related publications, mainly because of the insights and implications provided by its conceptual framework. In its simplified form, the Workman-Armstrong Equation predicts oxygen consumption (VO_2; L/min) from functions of height (H; in) and body mass [M; lb], and two different functions of speed [S; mph], in the following equation:[65,124]

$$VO_2 = [\mathrm{F}(H) \bullet \mathrm{F}_1(S)] \bullet [\mathrm{F}(M) \bullet \mathrm{F}_2(S)]$$

Where: $\mathrm{F(H)} = [H/(0.0136H - 0.375)]$ $\qquad$ $\mathrm{F}_1(S) = [1.92S^{0.176} - 1.445]$

$\mathrm{F}(M) = [M \bullet 10^{-5}]$ $\qquad$ $\mathrm{F}_2(S) = [0.85S^2 - 3.94S + 9.66]$

This equation was developed with metabolic data collected from a sample of 8 young men during treadmill walking,[65] and was revisited by Workman and Armstrong in a later publication.[124] Exact ages of participants and the treadmill speeds used were not reported. In addition, this equation may have reduced external validity because the sample used for its calibration was small and of the same sex and age range.

The conceptual framework of the Workman-Armstrong Equation consists of modeling walking intensity as the product of cadence and metabolic cost per step (i.e., L/min = [steps/min] • [L/step]). The cadence component ($\mathrm{F}[H] \bullet \mathrm{F}_1[S]$) is predicted with an inverse relationship to height (within the physiological range) and positive relationship to walking speed, resulting in taller individuals having a lower cadence and therefore metabolic intensity at a given speed, as discussed earlier (see section 2.2.2.2). The metabolic cost per step component of the Workman-Armstrong Equation ($F[M] \bullet F_2[S]$) is related directly to both body mass and walking speed.[65] The authors of this equation state it to be a basic model of walking in relation to metabolic intensity because of its ability to predict several walking characteristics (i.e., cadence, metabolic cost per step, and walking intensity) and describe how these variables are inter-related through height, speed, and body mass.[124] Additionally, the relationship between speed and metabolic intensity of walking is uncertain because different combinations of cadence and step length can result in different metabolic intensities of walking at a single speed.[56] The authors therefore suggested that the inclusion of height in the Workman-Armstrong Equation makes it more versatile, as it enables the prediction of step length and thus cadence at a given speed.[65] A later study similarly reported the Workman-Armstrong Equation to be more accurate and robust than other speed-based metabolic equations because of its inclusion of height.[81] The inclusion of height in an intuitive conceptual model of walking intensity is a strength of the Workman-Armstrong Equation for mechanical and theoretical applications. Conversely, the length and complexity of this equation limits its utility in health and fitness settings and therefore impedes its wide-spread adoption.

2.3.3. Van Der Walt and Wyndham Metabolic Equation

In 1973, van der Walt & Wyndham[64] also published an equation for predicting walking intensity that commonly appears in the metabolic cost of walking literature and related publications. This metabolic equation relates speed (S; km/h) and body mass (M; kg) to oxygen consumption (VO_2; L/min) as follows:[64]

$$VO_2 = [0.00599 \bullet M] + [0.000366 \bullet M \bullet S^2]$$

Van der Walt & Wyndham[64] derived this equation by applying a least squares regression to data they collected from six untrained young men (20-26 years of age) during level treadmill walking at 54-134 m/min (2.0-5.0 mph). The speed-based metabolic equation they reported, like those discussed above, has questionable generalizability because of the small and homogeneous sample used in its calibration. In addition, although their treadmill protocol only included walking speeds as slow as 54 m/min (2.0 mph), Van der Walt & Wyndham[64] extrapolated their predictions of oxygen consumption to 27 m/min (1.0 mph). Studies from which other metabolic equations[21,80,125] have been developed have included speeds ≤27 m/min for enabling accurate intensity predictions at such slow walking speeds.

In the development of this metabolic equation, the potential components considered as predictors of oxygen consumption included the main effect of body mass (M), the body mass-speed interaction (M•S), and this same interaction with a quadratic speed term (M•S^2). Van der Walt & Wyndham,[64] reportedly considered these three potential components because of their inherent likeliness to modify VO_2 during walking and their use for metabolic intensity predictions by previous authors.[64,80,88,126,127] After determining that a strong linear relationship existed between VO_2 (L/min) and body mass at each speed (r-values range = 0.85-0.95), a linear main effect of body mass was included (0.00599•M). This component essentially creates an individualized intercept for the speed-VO_2 relationship based on each participant's body mass, like a predicted standing metabolic rate, equal to 5.99 mL/kg/min. Next, the speed-VO_2 interaction with a quadratic term (0.000366•M•V^2) was included in the equation because it was found to explain 4.2% more of the variation in VO_2 than that with a linear speed term. The authors also reported that the inclusion of leg length in the final speed-based metabolic equation only explained an additional 0.53% of the remaining variance in VO_2 (p >0.05). However, this study's small sample size and narrow range in participant heights (1.68-1.87 m) may have limited its capacity to identify an effect of leg length. In addition, the authors' justification for considering certain components (M, $M{\bullet}S$, and $M{\bullet}S^2$) while excluding others (e.g., S or S^2) remains unclear. There also did not appear to be a systematic methodology behind the determination of which potential components to ultimately include in the final metabolic equation and the order in which they were included. Despite lacking this clear rationale, the relative simplicity of the equation by Van der Walt & Wyndham[64] does make it reasonably feasible for use by the general public.

2.3.4. The Pandolf Equation

The Pandolf Equation is frequently used in military applications because of its inclusion of terrain and external load as predictors, which may be important considerations when estimating metabolic intensity of walking across various landscapes (e.g., grass, sand, snow, etc.) while carrying backpacks and weapons. This metabolic equation predicts walking energy expenditure (E; Watts), with speed (S; m/s), grade (G; fractional grade), body mass (M; kg), external load (L; kg), and a terrain factor (n; terrain-specific constants derived empirically) in the following equation:[125]

$$E = 1.5{\bullet}M + 2.0[M+L][L/M]^2 + n[M+L][1.5{\bullet}S^2 + 0.35{\bullet}S{\bullet}G]$$

This equation was developed in 1977 using data collected during treadmill walking at speeds of 13-107 m/min (0.5-4.0 mph), aggregated across four studies[71,125,128,129] for a combined sample of 38 men 19-33 years of age. Although the Pandolf Equation was developed in a moderately-sized sample, its generalizability is still limited by the homogeneity of this sample in regard to participant sex and age.

As ultimately reported by Pandolf, Givoni, & Goldman,[125] the Pandolf equation was developed to have four theoretically-based components that comprised the metabolic intensity of walking: standing without the load ($[1.5 \cdot M]$), standing with the load ($[2.0(M+L)(L/M)^2]$), the horizontal cost of walking ($n[M+L][1.5 \cdot S^2]$), and the vertical cost of walking at a grade ($n[M+L][0.35 \cdot S \cdot G]$). The inclusion of external load and a terrain factor as predictors in the Pandolf Equation enhances its utility in military applications, where soldiers carry weapons and equipment while walking on various terrains. This prediction equation can then be used to estimate heat production, body temperatures, fuel requirements, and water requirements during military drills and missions.[130] This consideration of speed, grade, body mass, additional load, and terrain is clear strength of the Pandolf Equation. Still, its complexity and use of an outcome variable (Watts) that is not easily converted to metabolic intensity units used in public health recommendations (e.g., METs, VO_2, kcals, etc.)[11,69] limits the utility of the Pandolf Equation in applications related to improving health and fitness.

2.3.5. ACSM Metabolic Equation for Walking

The most widely recognized and used metabolic equation for walking is that which appears to have been first published in the second edition of the ACSM's Guidelines for Exercise Testing and Prescription[17] in 1980. The ACSM Metabolic Equation for Walking was presented previously (see Eq. 1 in section 1.1). To reiterate, at walking speeds of 50-100 m/min (1.9 to 3.7 mph), this linear equation is intended to predict oxygen consumption (VO_2; mL/kg/min) from walking speed (*S*; m/min) and grade (*G*; grade in decimal form) as follows:[18]

$$VO_2 = [0.1 \cdot S] + [1.8 \cdot S \cdot G] + 3.5 \qquad \text{Eq. 1}$$

This equation is based on results of two publications.[19,131] The study[19] used to develop the first ([0.1•*S*]) component of the equation only included three aerobically-trained men (two 23 years of age and the author, 42 years of age). The other equation component ([1.8•*S*•*G*]) was derived from a study[131] that reported a sample size of about 500 male Air Force personnel. Thus, while only the first study is quite limited in its sample size, the ACSM Metabolic Equation may not be generalizable to individuals outside the young, male demographic that was solely included in its subsequent calibration studies.

The ACSM Metabolic Equation can be divided into three components: an intercept (3.5) to account for resting metabolic rate, a linear speed component ([0.1•*S*]) for the horizontal effects of walking speed, and a speed-grade interaction component ([1.8 • S • *G*]) to describe the vertical influence of grade with inclined walking. The intercept, which represents the metabolic intensity at a speed of zero (i.e., quiet standing), is based on the standardized resting metabolic rate of 3.5 ml/kg/min.[44] The speed component is derived from a study by Dill[19] in which three men walked and ran at various speeds between 63-348 m/min (2.4-13.0 mph) on a treadmill. The metabolic intensity of walking 1 m/min on a level surface was determined to be 0.1 mL/kg/min, thus resulting in the coefficient of the speed component. Finally, the coefficient in the speed-grade interaction component of the ACSM Metabolic Equation was derived from a study of maximal aerobic capacity by Balke and Ware,[131] where ~500 men walked on a treadmill at 90 m/min (3.3 mph) while grade increased 1% every minute until voluntary exhaustion. In stating a secondary finding, that is, that oxygen consumption at a given workload did not vary between individuals, the authors reported that a coefficient of 1.8 could be used to approximate the average increase in oxygen consumption for each additional meter per minute of vertical work. Thus, the ACSM Metabolic Equation multiplies this coefficient by the rate of vertical work (i.e., the product of grade [decimal form] and speed [m/min]) to estimate the effect of grade on the metabolic intensity of walking.

The simplicity of the ACSM Metabolic Equation makes it easily implemented by the general public in treadmill-based applications and may explain its popularity and continued inclusion in the ACSM Guidelines for Exercise Testing and Prescription up until the 2014 edition.[18] Still, its application is reportedly limited to walking speeds of 50-100 m/min. Several factors may also reduce the accuracy of the ACSM Metabolic Equation. For example, it does not consider the effects of additional anthropometric and demographic variables that may affect the metabolic intensity of walking (see section 2.2.2.). In addition, although the standardized resting metabolic rate (3.5 mL/kg/min) appears to be an intuitive value for the intercept of a metabolic equation, it does not account for the additional metabolic cost for the balance and posture of standing. This additional metabolic cost of standing is further discussed below in the presentation of the Height-Weight-Speed Equation[21,23] (section 2.3.6.). Finally, the relationship between walking speed and metabolic intensity was shown to be curvilinear in a later secondary analysis[20] of the data published by Dill[19] used to calibrate the ACSM Metabolic Equation, as well as in several other publications.[23,132,133] The accuracy of the ACSM Metabolic Equation is therefore also compromised by its linear form.

2.3.6. Height-Weight-Speed Equation

One of the most recently developed speed-based metabolic equations is the Height-Weight-Speed Equation, ultimately published by Ludlow & Weyand[21] in 2016. This equation is based on a conceptual framework that provides valuable insights regarding the components of the metabolic intensity of walking. It predicts oxygen consumption (VO_2; mL/kg/min) from a measured or predicted resting metabolic rate (VO_{2rest}; mL/kg/min), walking speed (S; m/s) and height (H; m) in the following quadratic equation:[21]

$$VO_2 = VO_{2rest} + 3.85 + 5.97[S^2/H]$$

The Height-Weight-Speed Equation was first calibrated by Weyand et al.[23] but later refined in a secondary analysis by Ludlow & Weyand.[21] This secondary analysis ultimately included data from ten publications representing 409 total participants and 25 participant groups with wide ranges in mean age (5.2-40.7 years), height (1.0-1.8 m) and body mass (18.9-78.0 kg). These participants all completed bouts of treadmill walking at speeds ranging from 24-114 m/min (0.9-4.3 mph). In contrast to the metabolic equation calibration studies discussed above, the external validity of the Height-Weight-Speed Equation is inherently strengthened by the large size of this sample and its diversity in relation to participant age and body size.

The conceptual model for the Height-Weight-Speed Equation consists of three components: 1) the resting metabolic rate (VO_{2rest}), 2) an additional minimum metabolic rate (3.85), and 3) a speed-dependent contribution to walking metabolic intensity ($5.97[S^2/H]$). In this equation's original calibration studies,[21] resting metabolic rate (Component 1) was predicted for each participant based on their age, sex, body mass and height using the Schofield Equations.[134] The additional minimum walking metabolic rate (Component 2) accounts for the increases in metabolic intensity for standing and walking at any speed (e.g., balance, posture, increased pulmonary ventilation and blood pressure). This component was assumed to remain constant across walking speeds based on prior evidence[65,75,80] and calibrated using Ludlow & Weyand's literature-aggregated data set[21] to derive the value of 3.85 mL/kg/min above VO_{2rest}. Finally, the metabolic cost for the actual walking movement is represented by the speed-dependent component which results in greater metabolic intensities at faster walking speeds (Component 3). In the development of the Height-Weight-Speed Equation, Ludlow & Weyand[21] reported that its predictive accuracy improved significantly by the inclusion of a quadratic (versus linear) speed term and height as predictors. Thus, this speed-dependent component results in a quadratic speed-intensity and inverse height-intensity relationship in the Height-Weight-Speed Equation. The use of this simple, rational, and empirically-based conceptual model for developing the Height-Weight-Speed Equation could bolster its utility in both theoretical and real-world applications. In addition, its consideration of height and an individualized resting metabolic rate may improve the accuracy of this equation. However, requiring the measurement or estimation of resting metabolic rate may reduce its accessibility for use.

2.3.7. Summary of Speed-Based Metabolic Equations for Walking

As the project proposed herein aims to develop a cadence-based equation for predicting walking intensity, reviewing previously published speed-based metabolic equations has provided insights into their relevant conceptual models and enabled identification of their individual strengths and limitations. The intercepts included in some of the equations discussed conceptually represents the resting metabolic rate (as in the ACSM Metabolic Equation) or the resting metabolic rate plus the additional metabolic costs for standing (as in the Pandolf[125] and Height-Weight-Speed Equations[21]). The speed-dependent component included in all equations represents the metabolic intensity for the walking movement, which increases with increasing walking speed. The ACSM Metabolic Equation[18] is the only equation using a linear form for this component, while the rest indicate a curvilinear (quadratic[21,64,80,125] or exponential[124]) relationship between speed and intensity of walking. In this speed-dependent component, the Workman-Armstrong[124] and the Height-Weight-Speed Equation[21] both include an inverse effect of height on metabolic intensity of walking as reported to account for the lower cadence (and thus rate of internal work) selected by taller individuals at a given speed.

All of the metabolic equations discussed, excluding the Height-Weight-Speed Equation[21], have questionable external validity because they were derived from studies with samples that were small (≤10 participants)[18,64,65,80] and/or homogeneous (all young adult men).[18,64,65,80,125] Some of the speed-based equations are also limited in their development because they lack a clear conceptual basis or statistical methodology behind the variables, components, and model shapes they include.[18,64,80] While such rationale is notably absent from some equations, others that are based on coherent conceptual frameworks have limited utility in health and fitness settings because of their length and complexity.[124,125] In contrast, the Height-Weight-Speed Equation[21] exemplifies a metabolic equation that uses a logical and empirically-based conceptual model while retaining the simplicity that enables it to be practically used by health professionals and members of the public. Still, even this equation is limited in its application because of its reliance on speed-controlled treadmill walking. A cadence-based metabolic equation could be more easily implemented during overground walking and thus in the settings more common in daily living.

2.4. Cadence and Metabolic Intensity

Although many studies have examined and modeled the relationship between speed and intensity of walking, there are currently only 18 studies that examine the cadence-intensity relationship in adults, with the first published in 2005.[40] Of these 18 studies, three are review articles[39,41,42] one measures the cadence and metabolic intensity of self-selected brisk walking in inactive older adults,[135] and the remaining 14 quantify the relationship between walking intensity and cadence in controlled conditions.[27-38,40,43] The methodologies and results of these 14 studies are compared and contrasted in the sections that follow in order to illustrate the discrepancies in their: 1) sample characteristics, 2) metabolic testing protocols, and 3) statistical analyses used. These study details are also cataloged in Table 1. Considering such methodological inconsistencies is vital for comparing and synthesizing the results of these studies and identifying knowledge gaps. Next, the influences of anthropometric and demographic predictor variables on the cadence-intensity relationship is reviewed. Lastly, the findings of the three review articles are summarized.

2.4.1. Cadence and Absolutely-Defined Intensity

Of the 14 publications identified that examined the relationship between cadence and metabolic intensity in controlled conditions, 12 studies calibrated cadence-based models of absolutely-defined intensity by using indirect calorimetry to measure oxygen consumption during treadmill or overground walking. One study[34] more specifically modeled the relationship between cadence and energy expenditure (kcal/min), while the rest[27,31-33,36,38-43,135] aimed to determine cadence thresholds associated with absolutely-defined moderate and vigorous intensity (3 and 6 METs, respectively). The methods and results of this subset of articles are compared and contrasted in this section. Further details regarding the sample characteristics, metabolic testing procedures, and statistical analyses of these 12 studies are provided in Table 1.

Almost all of these studies used regression analysis to model the cadence-intensity relationship and determine cadence thresholds. Several studies included additional predictors in their regression equations (i.e., height, leg length, BMI) but calculated single thresholds by inputting the mean of their sample for the respective predictor variable. This confounds direct comparisons between studies because the thresholds reported by each are influenced by the characteristics of their sample. To therefore control for these variables, the sex-specific average US adult values for height and BMI that are provided by the Centers for Disease Control[94] were inserted into each regression model that considered these predictors. As has been used previously,[136] a similarly representative measure for leg length was determined using values derived from the US Third National Health and Nutrition Examination Survey (NHANES III)[137] collected from 1988-1994 in the following equation: ([average standing height] – [average seated height]). In order to avoid extrapolation, 6 MET cadence thresholds were only calculated for studies where such a threshold was originally reported, or if the mean intensity reached by participants in the highest intensity bout was ≥6 METs. All cadence thresholds are presented in Table 2 with indications of whether they were calculated using reported regression models and which values were then used.

Table 1: Studies Quantifying the Cadence-Intensity Relationship in Controlled Conditions.

Study First Author and Year	Sample Characteristics	Metabolic Testing Protocol	Statistical Analysis and Final Model Predictor Variables
Tudor-Locke 2005[40]	50 healthy adults; 50% women; age range 18-49 years	Treadmill walking at 80.5-107.2 m/min (3.0-4.0 mph) and running at 160.9 m/min (6.0 mph) set using a treadmill	Linear standard regression modeling with cadence and sex
Marshall 2009[33]	97 healthy adults; 59.8% women; 32 ± 11 years of age	Treadmill walking at 64-110 m/min (2.4-4.1 mph)	ROC analysis Linear standard and mixed regression modeling with cadence and sex
Beets 2010[31]	20 healthy adults; 55.6% women; 26 ± 5 years of age	Overground walking at 30-91 m/min (1.1-3.4 mph) set using a concurrent researcher walking to set pace	Nonlinear (quadratic) mixed regression modeling with METs, leg length, and BMI *outcome variable of cadence
Abel 2011[27]	19 healthy adults; 52.6% women; 29 ± 7 years of age	Treadmill walking at 54-107 m/min (2.0-4.0 mph) and running at 134.1-187.7 m/min (5.0-7.0 mph)	Linear and nonlinear (exponential) standard regression modeling with cadence and sex
Harrington 2011[32]	62 healthy adults; 100% women; 18.5 ± 3.4 years of age	Treadmill walking at 53-117 m/min (2.0-4.4 mph)	Validation of linear, cadence-based MET prediction equation used by the activPAL accelerometer software
Nielson 2011[34]	100 healthy adults; 50% women; 23 ± 4 years of age	Treadmill walking at speeds eliciting cadence of 90-120 steps/min	Linear mixed regression modeling with cadence, sex, BMI, and step length *outcome variable of kcal/min
Rowe 2011[36]	75 healthy adults; 50.7% women; 33 ± 12 years of age	Overground walking at same cadence measured during treadmill bouts at 54-107 m/min (2.0-4.0) mph, set using a metronome	Linear mixed regression modeling with cadence alone and with cadence and height
Agiovlasitis 2012[28]	18 adults with DS and 22 healthy adults; 43% women; 26 ± 6 years of age	Overground walking at self-selected normal pace and 30-90 m/min (1.1-3.4 mph) set using a concurrent researcher walking to set pace	Nonlinear (quadratic) mixed regression modeling with cadence, height and group (DS or healthy)
Wang 2013[43]	226 healthy adults; 48.2% women; 22 ± 1 years of age	Overground walking at 64.4-107.3 m/min (2.4-4.0 mph) set using ground markers and a timer	ROC analysis stratified by sex
Agiovlasitis 2014[29]	24 adults with MS, 24 healthy adults); 50% women; 43 ± 12 years of age	Treadmill walking at 54 -107 m/min (2.0-4.0 mph)	Nonlinear (quadratic) mixed regression modeling cadence, height, and group (healthy, minimal walking impairment, or mild-moderate walking impairment)

Peacock 2014[35]	29 healthy older adults, 100% women; 71 ± 12 years of age	Treadmill walking at a self-selected slow, normal, and fast pace	Linear mixed regression modeling with cadence, sex, and age
Rowe 2014[37]	17 adults with a unilateral transtibial amputation, 11.8% women; 52 ± 13 years of age	Treadmill walking at 50% HR_{max} and a speed ~1 MET higher or lower	Linear standard regression modeling with cadence alone
Agiovlasitis 2016[30]	58 adults with MS, 82.8% women; 51 ± 9 years of age	Overground walking at self-selected normal pace and speeds 13 m/min (0.5 mph) slower and 13 m/min faster set using a concurrent researcher walking to set pace	Linear mixed regression modeling with cadence, height, and group (mild, moderate, or severe MS)
Serrano 2017[38]	121 healthy older adults, 59.5% women; 69 ± 8 years of age	Overground walking at 40% $VO_{2reserve}$ set using verbal cues and real-time monitoring	Linear standard regression modeling with self-selected normal cadence and body mass *outcome variable of cadence at 40% $VO_{2reserve}$

Note: All models haven an outcome variable of METs unless otherwise noted.

Overall, cadence thresholds associated with 3 METs ranged from 74-117 steps/min. The range for 6 MET cadence thresholds was even greater, at 120-173 steps/min. It should be noted that adults tend to transition from walking to running at cadences >140 steps/min,[138] yet running bouts were included in only one[40] of these studies (which reported 6 MET thresholds of 125-136 steps/min). The substantial variability observed in these cadence thresholds may be due to between-study differences in sample characteristics, metabolic testing procedures, and statistical analyses used in these studies.

2.4.1.1. Sample Characteristics

Healthy and relatively young samples (mean ages 21.7-41.0 years) were included in 75% (9/12) studies[27-29,31,33,34,36,40,43] calibrating cadence thresholds associated with absolutely-defined intensity levels. These studies had samples sizes ranging from 19-226 participants and were ≥41% female. The one study[34] modeling the relationship between cadence and kcal/min stated that their data supported a minimum cadence threshold of

100 steps/min for absolutely-defined moderate intensity walking but did not report an exact threshold or regression with which one could be determined. The rest reported cadence thresholds for 3 METs (or regressions from which they were derived) that ranged from 91-120 steps/min. The highest of these thresholds (112 steps/min in men, 120 steps/min in women) may be artificially inflated because Beets et al.[31] had originally measured leg length as the distance from the greater trochanter to the floor (with shoes), whereas US NHANES III reference mean leg length values were determined as the difference between standing and seated height;[137] thus the sample mean leg lengths reported by Beets et al.[31] (men = 92 cm, women = 86 cm) were notably greater than those used in the regression (men = 84 cm, women = 77 cm). Considering this, almost all (6/7) other articles[27-29,36,40,43] reported a 3 MET cadence threshold of 93-108 steps/min (93-104 steps/min for men, 99-108 steps/min for women). Cadence thresholds for 6 METs could be calculated for six studies[27,29,33,36,40,43] in young and healthy participants, and these values ranged from 120-165 steps/min, with most (4/6)[27,29,40,43] ranging from 120-148 steps/min (127-141 steps/min for men, 130-148 step/min for women). Therefore, the exact cadence thresholds found to be associated with 3 METs tended to be 100 ± 8 steps/min for young healthy adults, while there was more limited data indicating 6 MET cadence thresholds of 135 ± 15 steps/min. Additionally, the higher ends of these ranges of cadence thresholds were observed in women while the lower ends were observed in men (Table 2).

Participants with a disability or of older age were included in 42% (5/12) studies.[28-30,35,37] Four studies included participants with a disability and all reported lower cadences needed for attaining moderate intensity compared with young and healthy

Table 2: Cadence Thresholds with Respective Study Methods/Samples.

Study First Author and Year	TM or OG	Statistical Analysis: Regression Model Form	Statistical Analysis: Standard or Mixed Regression	Young/healthy, Older, or Disability Status	Moderate Intensity Thresholds (steps/min): Men	Moderate Intensity Thresholds (steps/min): Women	Vigorous Intensity Thresholds (steps/min): Men	Vigorous Intensity Thresholds (steps/min): Women
Tudor-Locke 2005[40]	TM	Linear	Standard	Young/healthy	96 [a]	107 [a]	125 [a]	136 [a]
Marshall 2009[33]	TM	ROC analysis		Young/healthy	102	115	NA	NA
		Linear	Standard		92	91	141	163
			Mixed		101	111	130	134
Beets 2010[31]	OG	Nonlinear	Mixed	Young/healthy	112***	120***	NA	NA
Abel 2011[27]	TM	Linear	Standard	Young/healthy	97	104	120	130
		Nonlinear			94	99	125	135
Nielson 2011[34]	TM	Linear	Mixed	Young/healthy	Concur with ≥100		NA	
Rowe 2011[36]	OG	Linear [b]	Mixed	Young/healthy	101*	108*	158*	165*
		Linear [c]			Overall: 103		Overall: 161	
Agiovlasitis 2012[28]	OG	Nonlinear	Mixed	Young/healthy	93*	102*	NA	
				DS	Overall: 92**		Overall: 132**	
Wang 2013[43]	OG	ROC analysis		Young/healthy	104	107	127	137
Agiovlasitis 2014[29]	TM	Nonlinear	Mixed	Young/healthy	96*	107*	141*	148*
				MS minimal	93*	102*	132*	138*
				MS mild-moderate	91*	99*	124*	130*
Peacock 2014[35]	TM	Linear	Mixed	Older (65 years)	86*	100*	NA	NA
				Older (75 years)	75*	91*	NA	NA
Rowe 2014[37]	TM	Linear	Standard	Unilateral TTA	Overall:86		NA	
Agiovlasitis 2016[30]	OG	Linear	Mixed	MS mild	96*	102*	166*	173*
				MS moderate	85*	91*	155*	162*
				MS severe	74*	80*	144*	151*
Serrano 2017[38]	OG	Linear	Standard	Older	115 [d]	120 [d]	NA	

Notes: Cadence thresholds were either reported within studies or calculated using reported regression models. All are indicative of walking at absolutely-defined moderate or vigorous intensity (3 or 6 METs) except where otherwise noted.

TM = treadmill; OG = overground; DS = Down Syndrome; MS = multiple sclerosis; ROC = receiver operating characteristic; TTA = transtibial amputation

* based on average US adult heights[94]; ** based on average height of subset of sample with DS[28]
*** based on average US adult BMI[94] and leg length (NHANES III)[139];
****based on average US adult body masses[94] and normative older adult self-selected cadences[140]
[a] threshold determined with data collected during walking and running;
[b] model including height and cadence; [c] model including cadence alone;
[d] threshold for relatively-defined moderate intensity (40% $VO_{2reserve}$)

adults. Specifically, in adults with DS,[28] unilateral transtibial amputation,[37] and MS,[29,30] 3 MET cadence thresholds were as low as 92, 86, and 74 steps/min, respectively (Table 2). Similarly, the only study[35] conducted with older adults (60-87 years of age) reported that 75-year-old men and women had 3 MET cadence thresholds of 75 and 91 steps/min, respectively. All of these cadence thresholds determined with samples of disabled and older participants are lower than those with young, healthy adults (i.e., 100 ± 8 steps/min, calculate from above). Thus, heterogeneity of study samples may explain some of the variability in the cadence-intensity relationship and resulting differences in specific thresholds.

2.4.1.2. Metabolic Testing Protocols

Of the 12 studies quantifying the relationship between cadence and absolutely-defined intensity, seven[27,29,33-35,37,40] collected metabolic data during treadmill walking while the other five[28,30,31,36,43] used data collected while walking overground. The walking speeds implemented in three of the treadmill-based studies were not controlled across all participants (i.e., used self-selected slow, normal, and fast speeds[35] or speeds that elicited a desired cadence[34] or heart rate[37]). The ranges of speeds used by the remaining four treadmill-based studies[27,29,33,40] are relatively similar, with slowest and fast speeds of speeds of 54-81 m/min (2.0-3.0 mph) and 107-110 m/min (4.0-4.1 mph) respectively.

Each of the five studies conducted during overground walking constrained either walking speed or cadence. Speed was constrained in one study[43] using floor markings and a timer and in three studies[28,30,31] by instructing participants to match the speed of a "pacer" who walked ahead of them with a speed-measurement device. Two of these overground-based studies[28,31] implemented constrained walking speeds that were slower than any of the speeds used in the treadmill-based studies, ranging from about 30-90 m/min (1.1-3.4 mph). Still, there do not appear to be any systematic differences in cadence thresholds reported by overground versus treadmill-based studies, or in those that included slower walking speeds (Table 2).

The one study[36] of overground walking that did not constrain speed used an RAC method (a metronome) to constrain cadence. This study reported cadence thresholds on the higher end of those associated with 3 METs (101 steps/min for men, 108 steps/min for women) and 6 METs (158 steps/min for men, 165 steps/min for women; Table 2). These greater cadence thresholds indicate a lower metabolic intensity of walking at a given cadence, which is an unexpected finding given the evidence that adding constraints to gait parameters increases metabolic intensity of walking.[47,48] Alternatively, during cadence-constrained walking, the rate of increase in step length due to faster RAC tempos (i.e., eliciting increases in cadence) was lower than that associated with the same increases in cadence during unconstrained or speed-constrained walking. This reduction in the walk ratio would result in a lower speed at a given cadence (see section 2.2.3.),[45-47] which could lead to greater cadences needed to attain 3 and 6 METs during cadence-constrained walking. Although using RACs to entrain cadence may be a useful tool for prescribing walking intensities in health and research settings, only one study[36] was identified that has examined the cadence-intensity relationship under this walking condition. Further, the potentially lower walking intensity at a given cadence indicated in this study conflicts with what is expected given that constraining gait increases walking intensity at a given speed.[47,48] In addition, the ability to use cadence as a proxy for metabolic intensity would be useful for researchers measuring ambulatory PA levels with accelerometers in the free-living setting. Although all five of these overground-based studies have constrained either walking speed or cadence, no studies have examined the cadence-intensity relationship during true overground unconstrained walking (e.g., self-selected slow, normal or fast walking) as would be observed in purposeful walking undertaken in a free-living context. Therefore, more research is needed to examine the cadence-intensity relationship during overground cadence-constrained and unconstrained walking.

2.4.1.3. Statistical Analyses

Cadence thresholds associated with absolutely-defined levels of intensity were determined in these studies using Receiver Operating Characteristic (ROC) analysis and several variants of regression analyses. In this context, threshold determination through ROC analysis first entails plotting the true positive rate (i.e., proportion of data points predicted to be ≥3 METs when actually ≥3 METs) against the false positive rate (i.e., proportion of data points predicted to be ≥3 METs when not actually ≥3 METs) across all possible cadence thresholds. The threshold with the highest true positive rate and lowest false positive rate is then selected as the optimal cadence threshold, thus maximizing both sensitivity and specificity. ROC analysis was the only statistical method used by Wang et al.[43] and was included in the study by Marshall et al.[33] Cadence thresholds for 3 METs reported by the former study were 104 and 107 steps/min for men and women respectively, while those of the latter study were 102 and 115 steps/min respectively. These values are within the upper end of the sex-specific cadence thresholds reported across studies for young, healthy adults (Table 2). Further, when Marshall et al.[33] used standard regression analyses with the same data, the 3 MET cadence thresholds they derived in the original samples of men and women were 92 and 91 steps/min, respectively. This provides direct evidence that the determination of cadence thresholds is influenced by the statistical analysis used. Specifically, cadence thresholds determined using ROC analysis have tended to be higher than those derived from regression analysis, with differences of 10-24 step/min reported even when the same data is used.[33]

Regression analysis was used in ten studies[27-31,33,35-37,40] to determine cadence thresholds associated with absolutely-defined levels of intensity. The regression models they included differed in their use of a linear[30,33,35-38,40] versus curvilinear[28,29,31] model. In addition, some of these studies[27,33,37,40] used standard regression analysis while others[28-31,33-36] used mixed modeling to develop regression models. Mixed modeling can be used when the assumption of data independence (required for standard regression analysis) is violated, such as when the data include multiple datapoints (i.e., bouts) from each participant. By including participant as a "random effect" in a mixed model, the nonindependence of the data (e.g., inter-individual variability in the cadence-intensity relationship) is accounted for.[141] Such inclusion of random effects in regression models is important for accurately testing statistical hypotheses and assessing *p*-values when data consist of repeated-measures.[142]

The different model shapes and regression analysis types (standard versus mixed) used in studies of the cadence-intensity relationship correlate with trends in the goodness-of-fits (R^2 values) they report. In the seven studies[30,33,35-38,40] that used linear regression, R^2 values ranged from 0.23-0.85, indicating a wide range in model performance. Further, the variability explained by cadence in studies[27,37,40] that used standard linear regression analyses (R^2 = 0.55-0.85) was greater than when linear mixed modeling was used (R^2 =

0.23-0.50).[30,33-36] Three studies[28,29,31] used curvilinear (quadratic) regression analysis after the authors visually evaluated the shape of the cadence-intensity relationship. Curvilinear (exponential) models were also used by Abel et al.[27] because their R^2 values were greater by 0.08 and 0.06 for men and women, respectively, than models with linear form. These studies indicate that the relationship between cadence and walking intensity has a curvilinear form. If the cadence-intensity relationship is truly curvilinear then the goodness-of-fit of a linear model would (theoretically) be the lowest at more extreme low and high cadences. Interestingly, two of the studies[27,28] using a curvilinear model were also those including the slowest walking speeds (Table 1) and presumably the lowest cadences, which may have thus contributed to their decision to use a curvilinear model. The R^2 values observed by Abel et al.[27] with curvilinear regression models (0.91 in men, 0.79 in women) were also the largest reported in any of these studies. While Abel et al.[27] used standard regression analysis, the curvilinear regression models included in the other studies[28,29,31] were developed using mixed modeling and reported R^2 values ranging from 0.43-0.68 (or 0.63-0.68 when excluding the study[29] with less explained variability potentially from including both healthy adults and adults with MS). In summary, because the cadence-intensity relationship appears to be curvilinear,[27-29,31] the use of a curvilinear model may improve the performance of regression models, especially at slow walking speeds and cadences.

The cadence thresholds derived as proxies for levels of metabolic intensity can also be affected by the variant of regression analysis used. For example, Abel et al.,[27] used both linear and curvilinear regression analysis to model the same metabolic data. The use of a linear model resulted in 3 MET cadence thresholds that were 3 and 5 steps/min higher for men and women, respectively, while the curvilinear model derived 6 MET thresholds that were greater by 5 steps/min for both sexes. Similarly, Marshall et al.[33] determined 3 MET cadence thresholds in their study using both standard regression analysis and mixed modeling. The mixed modeling analysis resulted in consistently higher cadence threshold, with magnitudes of 9 and 20 steps/min for men and women respectively. These examples provide direct evidence that the variant of regression analysis used to model the cadence-intensity relationship can influence the cadence thresholds reported. Because this relationship appears to be curvilinear[27-29,31] it is important for future studies to use curvilinear regression models to most accurately represent the relationship between cadence and walking intensity. In addition, mixed modeling should be used when testing statistical hypotheses and assessing *p*-values with these models to account for the non-independence of repeated-measures data.[141]

2.4.2. Other Studies of Cadence and Intensity in Controlled Conditions

Two additional publications[32,38] have examined the cadence-intensity relationship but were not discussed above (section 2.4.1) because they did not report results related to the relationship between cadence and absolutely-defined intensity. Instead, Serrano et al.[38] aimed to determine cadence thresholds associated with a relative measure of moderate intensity (i.e., metabolic intensity relative to an individual's maximal capacity),[69] defined as 40% $VO_{2reserve}$ (determined from prior fitness testing). In this study, 121 healthy older adults (60% women, mean age = 68.6 years) walked overground with a portable indirect calorimeter while a researcher monitored their oxygen consumption and directed them to walk faster or slower until 40% $VO_{2reserve}$ was reached. Participants then maintained this pace and intensity for two minutes while their cadence was determined. The authors reported the best standard regression model (that with the highest R^2 value) for predicting a participant's cadence at 40% $VO_{2reserve}$ based on their individual characteristics, which ultimately included a linear, inverse effect of body mass and linear, positive effect of self-selected walking cadence. The cadence thresholds reported herein for this regression model (included in Table 2) are based on the average body masses of U.S. adult men and women,[94] and sex-specific normative values of self-selected walking cadence for older adults (with ages comparable to the original study's sample).[140] These cadence thresholds associated with relatively-defined moderate intensity (115 steps/min for men, 120 steps/min for women) are discernibly higher than those associated with 3 METs (100 ± 8 steps/min; Table 2). As the average 40% $VO_{2reserve}$ value for these older adults was >3 METs (3.3 ± 0.8 METs in women, 3.9 ± 1.0 METs in men), it would be expected that a higher cadence would be needed to reach relatively-defined moderate intensity. Moreover, the 2011 ACSM Position Stand[69] reported that 40% $VO_{2reserve}$ is generally equivalent to 4.8, 4.0, and 3.2 METs in young, middle-aged, and older adults, respectively. Because 40% $VO_{2reserve}$ therefore tends to be an intensity >3 METs, cadence thresholds are expected to be higher when associated with relatively- versus absolutely-defined intensity, with even greater differences evident in younger (and generally more fit) individuals.

The final study measuring cadence and walking intensity in controlled conditions aimed to test the validity of the linear cadence-based equation used by the activPAL accelerometer's software to predict walking intensity (METs). To do so, Harrington et al.[32] recruited 62 young, healthy female participants (15-25 years of age) and measured their oxygen consumption during level treadmill walking at speeds of 53-117 m/min (2.0-

4.4 mph). A significant difference between indirect calorimetry-measured and activPAL-predicted METs was reported at every speed tested (all values of p <0.001), with an overall mean difference of 0.5 METs (p <0.001). Although the prediction equation used by the activPAL was therefore not valid, there was still a significant correlation between measured METs and activPAL-measured cadence (r = 0.59, p <0.001). This study therefore still supports the ability for cadence to be used to predict metabolic intensity of walking. It also demonstrates a potential application of this research – to use the measurement of free-living cadence patterns, as enabled by the time-stamped nature of accelerometry, to assess levels of ambulatory metabolic intensity in surveillance- and intervention-based research.

2.4.3. Predictor Variables for the Cadence-Intensity Relationship of Walking

The 14 studies that quantified the cadence-intensity relationship under controlled conditions also considered the effects of anthropometric and demographic predictor variables. These additional variables included BMI,[28,31,33,34,38] height and leg length,[28-31,35-38] disability status,[28-30,37] age,[29,35,38] and biological sex.[27-29,33,34,36,40,43]

2.4.3.1. BMI

The effect of BMI on the cadence-intensity relationship was discussed in five studies.[28,31,33,34,38] Beets et al.[31] found BMI to be the strongest predictor of METs at a given speed (p <0.05). Their regression included a positive main effect of BMI and negative BMI-MET interaction for predicting the cadence (outcome variable) for attaining a desired MET level (explanatory variable). This resulted in a relationship between BMI and METs that was positive at lower intensities (e.g., 3 METs) and inverse at higher intensities (e.g., 6 METs). Similarly, Nielson et al.[34] reported that including a positive main effect of BMI and positive BMI-cadence interaction significantly improved predictions of walking energy expenditure (both p <0.0001); this model suggests that intensity of walking at any given cadence increases with increasing BMI. Still, it is important to note that this study used units of metabolic intensity that were expressed in terms of kcal/min) and body mass was not controlled for analytically. Evidence for a positive relationship between metabolic intensity of walking and BMI was also provided by Serrano et al.,[38] who reported a significant correlation between the cadence for walking at relatively-defined moderate intensity (40% $VO_{2reserve}$) and participant BMI (r = -0.24, p = 0.012). A possible confounding relationship between BMI and fitness (and thus the value of 40% $VO_{2reserve}$) was not assessed, and their prediction equation ultimately did not include BMI because body mass was more strongly correlated with walking cadence for reaching moderate intensity (r = -0.36). Although none of these studies[31,34,38] provided rationale for the observed influences of BMI on the cadence-intensity relationship, mechanisms by which BMI modifies the speed-intensity relationship of walking were discussed previously (see section 2.2.2.1). Briefly, individuals with a higher BMI have an increased metabolic intensity of walking at a given speed because of obesity-related mechanical inefficiencies in gait and changes in body mass distribution.[61,70] In contrast to these findings, Marshall et al.[33] reported differences in cadence thresholds stratified by weight status (normal weight, overweight, or obese) that were relatively small and inconsistent across the three statistical methodologies used. Adding BMI as a predictor also did not significantly improve the cadence-based regression model of walking intensity reported by Agiovlasitis et al.[28] which included a subsample of adults with DS. The mixed evidence from these studies indicates more research is needed to determine the significance and direction of BMI's influence on the cadence-intensity relationship.

2.4.3.2. Height and Leg Length

As discussed previously, the strong linear relationship between height and leg length (r = 0.90)[31] makes considerations of their effects in models of walking intensity nearly identical (see section 2.2.2.2). Height was included as a predictor in six studies[28-30,35,36,38] and leg length was included in one.[31] All of these studies reported that taller individuals needed to walk at lower cadences to attain the same levels of absolutely-defined intensity. More specifically, their regression equations indicated that a 10 cm increase in height a would increase intensity at a given cadence by 0.2-0.7 METs, and an individual with a 5 cm longer leg length would require a cadence 6 steps/min lower to reach the same MET level.[31] Both Rowe et al.[36] and Peacock et al.[35] reported that the addition of height to their model explained significantly more variability in VO_2 than cadence alone (p <0.05 and p <0.01 respectively). This influence of height on the cadence-intensity relationship is likely mediated by step length, where the positive correlation between height and step length at a given speed (r = 0.55-0.74 depending on the speed)[27,36] would result in higher cadences and rates of internal work (for limb swing) in shorter individuals. Further, when height was not correlated with stride length in adults with unilateral transtibial amputations (r = 0.10, p = 0.58), Rowe et al.[37] found that adding height as a predictor in their model no longer explained more variation in VO_2 than cadence alone (p >0.05). A similar mediating effect of step length was previously discussed regarding the influence of height on the speed-intensity relationship (see section 2.2.2.2).[65,80] In summary, several studies have concluded that accounting for the inverse relationship between height and the cadence needed to attain a specific level of walking intensity enables more accurate and individualized cadence prescriptions than a single heuristic value (e.g., 100 steps/min for 3 METs), and should be further investigated.[27,31,36]

2.4.3.3. Disability Status

Disability status was considered in the three studies by Agiovlasitis and colleagues that included adults with either DS[28] or MS.[29,30] The study[28] including adults with DS demonstrated that this population is shorter in stature (subsample mean = 154 cm) than the average US adult (men = 176 cm, women 162 cm).[94] As height is a predictor in their reported regression equation, the cadence thresholds presented herein for adults with DS (Table 2) are based on the mean height of this subsample instead of the average US adult, as used previously (see section 2.4.1). Despite the fact that a shorter stature normally results in higher cadence-intensity thresholds,[31,35,36,38] the 3 MET cadence threshold calculated for adults with DS was lower than those derived for non-DS adults of average height (a difference of 1 step/min in men and 10 steps/min in women; Table 2). As indicated in their reported regression model, this result was due to adults with DS having a 0.8 MET greater walking intensity than adults without DS when controlling for cadence and height. Adults with MS were also reported to have cadence thresholds for 3 and 6 METs that were 5 and 17 steps/min lower, respectively, than those of healthy participants.[28] Each increase in MS-related disability status (i.e., mild to moderate or moderate to severe level of disability; determined using the Expanded Disability Status Scale[143]) was also associated with a 1.6 MET increase in walking intensity at a given cadence.[30] In addition, Rowe et al.[37] reported that the cadence threshold associated with 3

METs in adults with unilateral transtibial amputations was 86 steps/min. Although this study did not include a healthy control group for a direct comparison, this cadence threshold is considerably lower than the 100 ± 8 step/min thresholds commonly reported in studies with young healthy adults.[27-29,36,40,43] Thus, an elevated cadence-intensity relationship has been observed consistently in studies including populations with disabilities, indicating that disability status is an important predictor to include when predicting the walking intensity of individuals who are not ostensibly healthy.

2.4.3.4. Age

The influence of age on the cadence-intensity relationship was considered in three studies[29,35,38] examining the cadence-intensity relationship, with contradictory findings. In a sample of older adults (60-87 years of age), Peacock et al.[35] found a significant positive relationship between age and metabolic intensity (METs) at a given cadence (p <0.01). Their regression model indicated that 75-year-old men and women have 3 MET cadence thresholds of 75 and 91 steps/min respectively, with every 10-year increase in age decreasing these thresholds by ~10 step/min. In the study by Serrano et al.,[38] a non-significant negative trend (r = -0.17, p = 0.069) between age and the cadence needed to attain relatively-defined moderate intensity (40% $VO_{2reserve}$) was reported in their sample of older adults (≥55 years of age), but the possible confounding effect of age on fitness (and thus the value of 40% $VO_{2reserve}$) was not controlled for in the analysis. Conversely, age did not contribute significantly to cadence-based regression models of walking intensity in the study conducted by Agiovlasitis and Motl[29] with a sample of middle-aged adults (mean age = 42 years) who were healthy or had MS. As previously discussed (see section 2.2.2.3), studies regarding the speed-intensity relationship of walking have only reported an influence of age with older adults (age ≥65 years).[77,85,86] The findings reported here similarly support the use of age as a predictor in cadence-based predictions of walking intensity in older adults, whereas it likely does not have a significant effect in younger adult populations. Because few studies have examined such an influence, future research is needed to confirm these findings.

2.4.3.5. Biological Sex

The effects of sex were originally considered in five studies[27,33,36,40,43] by calibrating sex-specific cadence thresholds associated with absolutely-defined intensity levels. The thresholds reported within these articles were higher for women versus men, with differences ranging from 3-13 steps/min and 10-11 steps/min for 3 and 6 MET cadence thresholds, respectively. Despite observing such differences, Marshall et al.[33] still did not support the use of sex-specific cadence thresholds because they found that considerable variability remained in the cadence-intensity relationship even after controlling for sex. Two studies by Agiovlasitis and colleagues[28,29] similarly reported that sex did not contribute significantly to their regression models of walking intensity, although these models already included height. Conversely, a statistically significant effect of sex on cadence thresholds was reported by Abel et al.[27] The metabolic intensity of walking (VO_2 in L/min) at a given cadence from 80-120 steps/min was also reported by Nielson et al.[34] to be higher in men versus women by 0.20-0.36 L/min. Although this was partially related to differences in body mass, men also tended to walk at faster speeds at a given cadence (i.e., had greater step lengths) because they were taller and increased step length to a greater proportion than female participants, who primarily increased their cadence. This greater speed at a given cadence reportedly also contributed to their lower cadence thresholds needed for attaining levels of walking intensity. The notion that height and step length mediates sex differences in the cadence-intensity relationship was further supported by Rowe et al.[36] in a secondary analysis of the data published by Tudor-Locke et al.[40] and Marshall et al.[33] In this analysis, it was determined that these studies had male-to-female ratios in reported cadence thresholds that were inversely proportional to their male-to-female ratios in height. In concurrence with these findings and as discussed previously (see section 2.2.2.4.), studies that have developed speed-based metabolic equations for walking have reported sex to no longer be a significant predictor after controlling for height.[23,75] This evidence suggests that the tendency for men to be taller than women translates to correspondingly greater step lengths, speeds, and metabolic intensities at a given cadence, thereby explaining sex differences in cadence thresholds needed for attaining moderate and vigorous intensity walking.

2.4.4. Cadence Review Articles

Three review articles are published regarding the relationship between cadence and metabolic intensity of walking.[39,41,42] The first, published by Tudor-Locke & Rowe,[42] formulated the early evidence for using cadence to represent ambulatory PA patterns in free-living adults. A later review article by Slaght et al.[39] aimed to provide an updated summary of the literature regarding the recommended cadence threshold for reaching moderate intensity in adults with an additional focus on the effects of additional predictor variables. The most recent review article was published by Tudor-Locke et al.[41] in 2018 to present the state of evidence regarding minimum threshold values associated with desired outcomes and cross-sectional reference values for cadence-based metrics. The following sections summarize the findings of these three reviews as related to observational studies of cadence, cadence-based intervention studies, and laboratory-based studies of the cadence-intensity relationship.

2.4.4.1. Observational Studies of Cadence

The reviews by Tudor-Locke & Rowe[42] and Tudor-Locke et al.[41] included the methodologies and results of cross-sectional studies examining associations between free-living cadence patterns and health outcomes. Seven accelerometers capable of measuring cadence during free-living were reviewed by Tudor-Locke & Rowe [42] for use in such studies, and were shown to have generally high accuracy at normal walking speeds (mean absolute percent errors <3% at speeds ≥81 m/min [3.0 mph]). The review by Tudor-Locke et al.[41] also summarized the three metrics used to express free-living cadence patterns: 1) mean cadence over 24-hours (deemed inappropriate because of the influence of a large amount of time at zero cadence), 2) time at or above cadence thresholds (100 steps/min) or in *cadence bands* (i.e. time at 1-19, 20-39, 40-59, steps/min etc.), and 3) *peak cadence indicators* (7-day average of the highest 1-minute cadence of each the day or averages of the highest, not necessarily consecutive, 30 or 60 minutes in each day).

Results of these observational studies reported by Tudor-Locke & Rowe[42] included a weighted average normal walking cadence of 115.2 steps/min from eight studies that covertly observed pedestrians, as an indicator of normal purposeful cadence in ostensibly healthy adults. Still, it was found that individuals with chronic disease or disability may have difficulty walking at 100 steps/min and healthy adults spend much of their waking hours (13.5 hrs/day) sedentary (zero cadence) or at low cadences (1-59 steps/min), with only about seven minutes of their day at ≥100 steps/min.[42] The 2018 review by Tudor Locke et al.[41] presented population-specific values and trends for peak cadence indicators from a limited number of observational studies, with the authors acknowledging that the state of the evidence was immature. All three reviews[39,41,42] called for future research to further establish normative data for free-living cadence-based metrics based on large and diverse samples. Reported limitations of using cadence-based metrics to represent free-living PA patterns include the inability to quantify non-ambulatory PA and the misrepresentation of brief movement patterns (e.g., a cadence of 100 steps/min maintained for 30 seconds) when analyzing cadence using 1-minute epochs of step accumulation.[41,42] The use of 1-minute epochs was conversely justified for the discrimination of sporadic movements from the persistent patterns of purposeful walking or running.[41] The observational studies of free-living cadence patterns summarized in these reviews demonstrate the feasibility and utility of using cadence-intensity research in PA measurement applications.

2.4.4.2. Cadence-Based Intervention Studies

Three methods for implementing and monitoring cadence-based recommendations in interventions were discussed across the three studies: 1) counting aggregated steps in a continuous walking bout and dividing by time elapsed,[39,41,42] 2) the use of RAC to entrain cadence, [39,41,42] and 3) monitoring instantaneous (i.e. “real-time”) cadence with accelerometer-based technologies.[42] In the first review by Tudor-Locke & Rowe[42] only one PA intervention was identified that monitored cadence, and this intervention resulted in an improved heart rate response to exercise. The next review published by Slaght et al.[39] included two interventions, both of which found that groups provided with recommendations pertaining to both volume of steps (steps/day) and cadence (implemented with the aggregated steps divided by time method) had a significantly greater increase in moderate-to-vigorous intensity physical activity (MVPA) accumulated in >10-min bouts, as compared to a groups with step volume recommendations alone. In the most recent review by Tudor-Locke et al.,[41] five PA intervention studies including cadence recommendations (also implemented by aggregating a number of pedometer-counted steps in a certain length of time) were found to generally increase participants' speed of walking and engagement in continuous bouts of PA, but not to increase daily step counts or time in MVPA. Additionally, the review identified four intervention studies using cadence-based metrics to analyze accelerometer data that together provided preliminary evidence that cadence-based metrics are readily sensitive to change in PA interventions.

Although nine cadence-related intervention studies were ultimately identified in the most recent review, Tudor-Locke et al.[41] reported that these interventions had a generally high risk of bias (i.e., flaws in their design, conduct, or analysis that could lead to systematic error in their results[144]). Both this review and that by Slaght et al.[39] stated that more high-quality intervention studies are still needed to establish effective strategies for implementing cadence-based recommendations and determining their long-term effects on MVPA. For example, none of these previous intervention studies have attempted to use RACs or "real-time" monitoring of cadence to implement cadence recommendations. Strengths of using cadence metrics instead of accelerometer activity counts as an indicator of metabolic intensity in PA interventions were listed and included: 1) accessibility and ease of prescribing and measuring cadence, 2) capability for monitoring "real-time" cadence for instantaneous feedback and modification of PA metabolic intensity, 3) simplicity of cadence for facilitating the translation of knowledge to the public, and 4) the ability to combine steps/day, cadence indices, and time at zero cadence to comprehensively monitor PA volume, intensity, and sedentary time.[39,41,42] Thus, these review articles collectively summarize preliminary evidence demonstrating the potential for using cadence-based recommendation as an efficacious method for prescribing and monitoring walking intensity in PA interventions.

2.4.4.3. Laboratory-Based Studies of Cadence

Each of these review articles presented their own syntheses of contemporary publications examining the relationship between cadence and metabolic intensity under controlled conditions, similar to that previously discussed in detail herein. The initial review by Tudor-Locke & Rowe[42] aggregated data from five laboratory-based studies[27,31,33,36,40] that quantified the cadence-intensity relationship in ostensibly healthy adults and reported the overall linear correlation to be very strong (r = 0.93). All studies that were identified also consistently supported 100 steps/min as a reasonable heuristic (i.e., evidence-based, practical, rounded value) threshold indicative of absolutely-defined moderate intensity walking.[42] This 100 steps/min heuristic threshold for 3 METs (in ostensibly healthy adults) was also consistently supported in the later review by Slaght et al.,[39] and again in the most recent review by Tudor-Locke et al.[41] which ultimately included nine pertinent laboratory-based studies.[27,31,33-36,40,43,135] As previously discussed and shown in Table 2, Tudor Locke et al.[41] found that moderate intensity cadence thresholds not in concurrence with the 100 steps/min heuristic were only reported in a study conducted with unilateral transtibial amputees (threshold of 86 steps/min)[37] and a study where moderate intensity was differentially defined as 40% of $VO_{2reserve}$ (threshold of 115 steps/min).[38] Tudor-Locke et al.[41] also cited the results of three studies[27,40,43] that suggested 130 steps/min may be a reasonable heuristic cadence threshold for absolutely-defined vigorous intensity walking.

Although consistent evidence was reported for these heuristic cadence thresholds, all three review articles acknowledged substantial inter-individual variability in the cadence-intensity relationship. The initial review by Tudor-Locke & Rowe[42] attributed this unexplained variability to differences in age and stature. In addition, Slaght et al.[39] stated that other variables, such as BMI and biomechanically-focused factors (e.g., sway, balance, plantar pressure parameters, stance time, etc.), need to be examined in order to adequately individualize cadence thresholds for walking at desired intensities. The authors strongly supported considering such variables by reporting that only 45% of adults in the study by Marshall et al.[33] reached 3 METs when walking at 100 steps/min as well as citing three studies[35,38,145] to support that a cadence threshold greater than 100 steps/min may be needed for older adults to reach absolutely-defined moderate intensity. The most recent review by Tudor-Locke et al.[41] conversely concluded that there was not enough evidence to suggest that older adults need higher cadences to reach a given level of absolute intensity. This section of their review included two of the three studies[35,38] that were originally cited by Slaght et al.[39] The age-related study[145] not included by Tudor-Locke et al.[41] reported that older adults had higher cadences during normal walking cadence and in free-living, but metabolic intensity was not actually measured. Of the two studies of older adults cited by Tudor-Locke et al.,[41] one[38] concluded that a higher cadence threshold (115 steps/min) was associated with relatively-defined moderate intensity (40% $VO_{2reserve}$). A personal communication between Tudor-Locke and co-authors on the other study[35] revealed that the exact cadence threshold indicated by the data was 99/steps/min.[41] Despite stating that there was not enough current evidence to suggest an effect of age and recognizing the validity and utility of single heuristic cadence thresholds for translating public health guidelines, Tudor-Locke et al.[41] still acknowledged notable inter-individual variability in the cadence-intensity relationship. The authors recommended considering stature-related variables to individually calibrate cadence-based recommendations. In summary, all three reviews identified ≥100 steps/min as a reasonable heuristic value for absolutely-defined moderate intensity walking, but also recognized a need for future research to further individualize cadence-based recommendations.

2.4.5. Summary of Cadence and Metabolic Intensity

Although there is extensive literature modeling the speed-intensity relationship, there are a limited number of publications quantifying the relationship between walking cadence and intensity. Articles aiming to determine cadence thresholds associated with absolutely-defined moderate and vigorous intensity have wide ranges in values (74-117 steps/min and 120-173 steps/min respectively; Table 2). When considering only such studies that included young and ostensibly healthy adults (Table 1), most 3 MET cadence thresholds are 100 ± 8 steps/min[27-29,36,40,43] and most 6 MET cadence thresholds are 135 ± 15 steps/min.[27,29,40,43] The variability in cadence thresholds thus tends to be dramatically lower within this limited population. The protocols of studies examining the relationship between cadence and absolutely-defined intensity have included treadmill and overground walking (Table 1) with only two studies[28,31] including speeds as slow as 30 m/min (1.1 mph). No trends in cadence thresholds appear to be related to these differences in metabolic testing protocols. In the two studies[33,43] using ROC analysis, the reported cadence thresholds appear to be greater than those derived from the remaining studies that used various forms of regression analysis (Table 2). Even when applied to the same data, the use of different statistical analyses (i.e., ROC versus regression analysis,[33] standard versus mixed modeling,[33] or linear versus nonlinear regressions[27]) result in different values and thus influence variability in cadence thresholds. It is therefore important for future studies choosing regression analysis to use a curvilinear model to represent the cadence-intensity relationship[27-29,31] and mixed modeling when testing statistical hypotheses and assessing *p*-values.[141]

The one study[36] conducted during overground walking with cadence constrained using RAC reported relatively high cadence thresholds for attaining 3 and 6 METs (Table 2). This finding is unexpected given that the metabolic intensity of walking has shown to increase when gait parameters are constrained.[47,48] Still, this reduced metabolic intensity could be the result of decreases in walk ratio, step length, and thus walking speed at a given cadence, as previously reported during RAC-constrained walking.[45-47] In addition, all of the remaining studies[28,30,31,43] conducted during overground walking constrained speed. More research is therefore needed to further investigate the cadence-intensity relationship during overground cadence-constrained and unconstrained walking.

Of the anthropometric and demographic predictor variables considered in studies of the cadence-intensity relationship, there is the strongest evidence for an influence of height and leg length. Taller individuals were again found to select greater step lengths, leading them to walk with a lower cadence at a given speed,[27,36] and resulting in lower cadence thresholds needed for them to attain levels of absolutely-defined intensity.[28-

[31,35,36,38] Fewer studies have investigated an influence of BMI when examining the cadence-intensity relationship. Those reporting a statistically significant effect have only shown weak and possibly confounded evidence,[31,34,38] while others have reported no influence of BMI.[28,33] Studies including adults with disabilities have relatively consistently reported lower cadence thresholds associated with 3 METs (74-96 steps/min in men, 80-102 steps/min in women),[28-30,37] indicating that disability status is an important predictor of walking intensity in special populations. Articles[27,33,36,40,43] that performed sex-specific analyses have also consistently reported that women exhibit greater cadences associated with levels of absolutely-defined intensity. Still, such differences are likely attenuated after controlling for height.[23,36,75] Finally, an influence of age on cadence thresholds for absolutely-defined intensity may exist in older adults,[35] but more evidence is needed to establish this relationship.

Three review articles[39,41,42] have attempted to summarize the results of observational, intervention, and laboratory-based studies that examined walking cadence. The observational studies they included demonstrate the feasibility and utility of using cadence-intensity research in PA measurement applications.[41,42] Still, all three reviews[39,41,42] call for further research to establish normative values for free-living cadence-based metrics. Similarly, preliminary evidence was summarized for the efficacy of using cadence-based recommendations to prescribe and monitor walking intensity in PA interventions, but more high-quality intervention studies are reportedly needed.[39,41] Finally, laboratory-based studies have consistently supported ≥100 steps/min to be a reasonable heuristic cadence threshold indicative of moderate intensity walking in ostensibly healthy adults. As substantial inter-individual variability was consistently observed in the cadence-intensity relationship, all review articles called for future research that advances the individualization of cadence-based recommendations through the inclusion of additional predictors.[39,41,42]

CHAPTER 3

METHODS

The purpose of this thesis was to develop metabolic equations that predict metabolic intensity (oxygen consumption; mL/kg/min) from cadence using a large treadmill walking dataset (Study One) and cross-validate these equations during overground unconstrained and cadence-constrained walking conditions (Study Two). More specific objectives included to: 1) develop a metabolic equation that uses cadence as the only predictor (a *simple* equation), 2) develop a metabolic equation that uses cadence and the possible additional predictors of height, leg length, body mass, BMI, percent body fat, sex and age (a *full* equation), and 3) cross-validate these cadence-based metabolic equations under different walking conditions (i.e., overground unconstrained walking and overground cadence-constrained walking) in an independent sample.

This thesis comprises secondary data analyses from two datasets. The cadence-based metabolic equations were developed in Study One using a dataset that included a larger, more representative sample of adults across the lifespan (21 to 85 years of age). As this dataset was collected during treadmill walking, the cadence-based metabolic equations were cross-validated under different walking conditions in Study Two using a dataset collected with a separate, smaller sample of adults (21 to 40 years of age) during overground unconstrained and cadence-constrained walking. The methods used in Study One and Study Two are described in sections 3.1 and 3.2, respectively.

3.1. Study One: Development of Cadence-Based Metabolic Equations

Study One, involving the development of simple and full cadence-based metabolic equations, was a secondary analysis of the data collected as part of the

NIH/NIA funded R01 CADENCE-Adults Study (NCT02650258). Results for the primary aim of the CADENCE-Adults Study are published elsewhere.[146]

3.1.1. Participants

The CADENCE-Adults Study had a planned enrollment of 260 ostensibly healthy, ambulatory adults. This sample was intended to be age- and sex-balanced by including 10 men and 10 women from each 5-year age group between 21-85 years of age (e.g., 21-25 years, 26-30 years, etc.). Data collection was divided into three cohorts for logistical purposes over a number of years: Cohort 1 (adults 21-40 years old; n = 80) was completed in 2016,[146] Cohort 2 (adults 41-60 years old; n = 80) was completed in 2017, and recruitment and testing for Cohort 3 (adults 61-85 years old; n = 100) was planned for completion in 2019. All data available prior to March 1, 2019 were included in the analyses herein. All procedures were approved by the University of Massachusetts Amherst Institutional Review Board, and all participants read and signed informed consent documents.

Exclusion criteria for the Cohort 1 participants were: use of a wheelchair, having other impairments that prevented normal ambulation, BMI $<18.5 kg/m^2$ or $>40 kg/m^2$, current tobacco use, stage 2 hypertension, previous history of cardiovascular disease or stroke, conditions or medications that could affect heart rate response to exercise, pacemakers or other implanted medical devices, hospitalization for mental illness within the previous 5 years, and pregnancy. Exclusion criteria for participants in Cohorts 2 and 3 additionally included: dizziness or balance impairment at rest or with exercise, shortness of breath at rest or during mild exertion, treatment for kidney disease with dialysis, severe liver damage, chronic lung problems that made it difficult to breathe, and treatment of cancer with chemotherapy that affected breathing or heart rate.

3.1.2. Measures

Biological sex and age were self-reported. Standing height was measured to the nearest 0.1 cm with a wall-mounted stadiometer (ShorrBoard Portable Height-Length Measuring Board; Weigh and Measure LLC, Olney, Maryland USA). Seated height was also measured with a stadiometer to the nearest 0.1 cm while participants were seated on a bench with legs and hands hanging freely. Seated height reflects the difference between the floor-to-crown measure and the static height of the bench. Leg length was then calculated by subtracting seated height from standing height. Body mass was measured to the nearest 0.1 kg using a Tanita scale (DC-430U; Tanita Corporation, Tokyo, Japan). BMI was then derived by dividing body mass by height squared (kg/m^2). Percent body fat was also measured by the Tanita scale using bioelectrical impedance analysis, a purpose for which it has previously been validated.[147] All measures were performed twice, and if values differed by ≥0.3 cm for height or ≥0.1 kg for body mass, a third measure was taken. The two closest measurements were then averaged.

Metabolic intensity was determined using a portable indirect calorimeter (Jaeger Oxycon Mobile; CareFusion BD Germany 234 GmbH, Höchberg, Germany) which has been previously validated against the Douglas bag methods.[148] The indirect calorimeter was calibrated as recommend by the manufacturer prior to each data collection session. Oxygen consumption (VO_2; mL/kg/min) measures were collected breath-by-breath and transmitted to the Oxycon Mobile receiver unit connected to a laptop, with which values were monitored during testing. A self-reported rating of perceived exertion (RPE) was also evaluated in the final minute of each walking bout using the Borg Scale.[149]

For a criterion measure of steps (direct observation), a researcher counted the total steps taken in each walking bout using a hand-tally counter. High agreement (intraclass correlation 0.96-1.0) between hand-counted step counts of two observers has been reported previously.[150,151] In addition to this real-time count, a video camera was aimed at the feet of participant during each bout for backup recording of hand-counted steps. The speed output by the treadmill was used to determine walking speed.

3.1.3. Metabolic Testing Procedure

Participants arrived at the laboratory after having fasted for at least four hours. Before beginning the protocol, they sat in a chair stationed on the treadmill for a minimum of five minutes and stood for at least two minutes in order to establish baseline oxygen consumption. Participants then began the treadmill walking protocol by walking for five-minute bouts at 0% grade, each separated by at least two minutes of standing rest. The treadmill speed of the first bout was set at 13.4 m/min (0.5 mph) and the speed of each subsequent bout increased in 13.4 m/min increment. The test was terminated following the completion of a bout where participants: 1) naturally selected to run, 2) attained a heart rate ≥75% of their age predicted heart rate maximum (220-age), 3) indicated a Borg RPE >13, or 4) chose to stop the protocol. The protocol could also be terminated if research staff were concerned for the participant's safety.

3.1.4. Data Processing

Metabolic data for each participant were downloaded from the memory storage card located directly in the data exchange unit of the Oxycon Mobile. These data and all values of hand-counted steps were then imported into MATLAB (The MathWorks, Natick, MA) for initial data processing and management using custom scripts. The metabolic intensity of each five-minute bout was calculated as the average VO_2 during minutes 2:45-4:45. Hand-counted steps were divided by bout duration in minutes (hand-count / five minutes) for the criterion measure of cadence. These data and all participant characteristic data were exported from MATLAB for conducting the secondary analyses conducted herein.

3.1.5. Statistical Analysis

All statistical analyses were performed using R-Studio (version 3.5.1, R Foundation for Statistical Computing, Vienna, Austria). Statistical significance was set at $\alpha \leq 0.05$.

Aim 1: Determine if a linear or curvilinear model more accurately describes the relationship between cadence and metabolic intensity of treadmill walking, using data previously collected from a large sample of men and women across the adult lifespan.

> ***H_1*****:** A curvilinear (quadratic) model will fit the cadence-intensity relationship significantly better than a linear model.

The model that best fits the cadence-intensity relationship should describe the within-person pattern of change in VO_2 with changes in cadence.[142] Thus, the cadence (explanatory variable) and VO_2 (outcome variable) relationship was first plotted for participants individually. Visual inspection of these plots provided a preliminary evaluation of the linearity of the cadence-intensity relationship. A likelihood-ratio test was then performed to test for significant differences in the goodness-of-fit of a linear ($VO_2 = \alpha + \beta\bullet$[cadence]; null hypothesis) versus quadratic ($VO_2 = \alpha + \beta\bullet$[cadence]

+ $\lambda \cdot [\text{cadence}]^2$; alternative hypothesis) model. This use of a linear or quadratic model aligns with those used in previous studies of the cadence-intensity relationship.[27-31,33,35-37,40] Because multiple bouts performed by each participant were included in the data (i.e., data points were not independent), the models entered into this likelihood-ratio test were developed using mixed modeling with random intercepts.[141] This regression modeling analysis allowed intercept coefficients (α) to vary between participants, thus accounting for the non-independence of data (e.g., inter-individual variability in the cadence-intensity relationship) when testing statistical hypotheses with the model.[142] Random intercept models were developed in R using the 'lmer()' function of the 'lme4' package.

Aim 2: To develop simple and full cadence-based metabolic equations by calibrating regression models that predict metabolic intensity of treadmill walking, using the data from this same large sample of men and women across the adult lifespan.

$\boldsymbol{H_{2.1}}$**:** Cadence alone will be a significant predictor of metabolic intensity in the simple equation, with root mean square error (RMSE) and mean absolute error (MAE) values ≤1 MET when cross-validated within the original sample.

$\mathbf{H_{2.2}}$**:** The full equation will minimally include the additional predictor of leg length, which will result in increased predictive accuracy.

The simple cadence-based metabolic equation was derived by fitting the least squares regression model that predicted VO_2 from cadence. Although mixed modeling was used to account for the non-independence of data in the likelihood-ratio test, the simple cadence-based metabolic equation was derived by fitting a standard regression model. Mixed modeling was necessary when testing statistical hypotheses and evaluating models to account for the data having inter-individual and intra-individuals variability.[142]

Standard regression modeling was used to develop the cadence-based metabolic equations because: 1) they were used for predictions and not in hypothesis testing, 2) the use of standard regression did not have a large influence on the equation coefficients, and 3) it enabled the full equation to be developed with the model selection procedures discussed below. The simple cadence-based metabolic equation was therefore derived by using the 'lm()' function of the 'stats' package in R to fit a standard least squares regression model, with the form (linear or quadratic) determined in Aim 1, to the data of all participants. The full cadence-based metabolic equation was subsequently developed using *best subsets regression analysis*. This method of model development considers every model possible with the specified predictors and selects that with the greatest goodness-of-fit.[152] Best subsets regression has shown to produce prediction models that out-perform those developed using stepwise regression procedures.[153] Although goodness-of-fit can be evaluated by common criteria such as R^2 and residual sum of squares, these measures of the model's fit to the training (i.e., calibration) dataset may not reflect its error in a separate testing dataset, which can result in overfitting.[154] In contrast, the *predicted residual sum of squares* (PRESS) statistic represents the error of a model during cross-validation, where data are divided into separate model training and model testing datasets, and better indicates the testing (i.e., predictive) error of a model.[152] The PRESS statistic was therefore the most appropriate selection criteria for deriving an equation for the purpose of predictions.[155] Thus, the full-cadence based metabolic equation was derived through best subsets regression analysis with the PRESS selection criterion, using the 'bestglm()' function of the 'bestglm' package in R. Height, leg length, body mass, BMI, percent body fat, sex and age (main effects and two-way interactions) were included as candidate predictor variables. The resulting full cadence-based metabolic equation was then tested for collinearity between its predictor variables by ensuring that all variance inflation factors were <10.[156]

To obtain an unbiased evaluation of the predictive accuracies of the cadence-based metabolic equations,[152] repeated k-fold cross validation (k = 5, 10 repetitions) was performed with the original treadmill-based calibration dataset. In this cross-validation technique, participants were first randomly allocated to five groups (folds). The cadence-based metabolic equation being tested was then trained with participants' data from four of the five folds. The remaining data fold then served as the testing data set. Specifically, participants' cadence data from the remaining fold was inserted into the model and the equations measures of predictive error were calculated (specific measures discussed in section 3.1.4.1). Four more repetitions of this sequence of training and testing the equation was performed so that ultimately all folds served as the testing dataset at one point during the process. Randomization of participants to folds and equation training and testing were then repeated for nine more repetitions, and accuracy and bias measures were averaged across folds and repetitions. This k-fold cross-validation process was performed for both cadence-based metabolic equations using custom R scripts.

The predictive capacity of the ACSM Metabolic Equation was also evaluated using the treadmill walking metabolic data. Because the method of cross-validation influences the predictive error values observed,[157] directly applying this equation to the data would not produce results that could be compared with the k-fold cross-validated RMSE, MAE, and bias values of the simple and full cadence-based metabolic equations. Therefore, k-fold cross-validation (with k = 5 and 10 repetitions) was similarly used to test the ACSM Metabolic Equation. Specifically, the sample was divided into testing and training folds in the same manner. Then, instead of calibrating a regression on the training folds, the ACSM Metabolic Equation was applied to each testing fold within each repetition.

3.1.5.1. Predictive Error Measures

The performance of the simple and full equations and ACSM Metabolic Equation were evaluated with several different measures of predictive error. These predictive error measures can first be categorized as unscaled or scaled. *Unscaled* measures of predictive error (root mean square error [RMSE], mean absolute error [MAE], and bias) are expressed in the original units of VO_2 (mL/kg/min) because they were calculated using error values calculated as follows: measured VO_2 - predicted VO_2. Unscaled predictive error measures are also presented in METs (1 MET = 3.5mL/kg/min) and were included because their units allow unscaled values to be easily interpreted. To further illustrate their practical significance, unscaled predictive error measures were also converted to kcals/hr (1 MET = 1 kcal/kg/hr) using sex-specific US average body mass values (88.8 kg for men and 76.4 kg for women).[94]

Scaled measures of predictive error (root mean square percentage error [RMSPE], mean absolute percentage error [MAPE], and percent bias) are expressed as percentages because they were calculated using error values calculated as follows: (measured VO_2 - predicted VO_2) / measured VO_2. Scaling predictive error measures (i.e., making them relative to the measured VO_2 value) can be beneficial because it contextualizes error values with the intensity at which they were observed. For example, an unscaled error of 1 MET may have different implications if observed when walking at 3 METs (scaled error = 33%) versus when exercising at 10 METs (scaled error = 10%). As this example demonstrates, an unscaled error value equates to a lower scaled value if is observed at a higher intensity versus at a lower intensity.[158]

These unscaled and scaled measures also both included are measures of bias and measures of accuracy. *Bias* (bias/percent bias) is used to indicate the direction of error,[158] where the calculation of bias used herein (measured VO_2 - predicted VO_2) results in positive bias values for underpredictions and negative bias values for overpredictions. However, the summation of positive and negative bias values can result in a mean bias that is lower than the individual error values. For example, if a metabolic equation underpredicts intensity by 0.5 METs in one bout (bias = 0.5 METs) and then overpredicts intensity by 0.5 METs in the next bout (bias = -0.5 METs) the mean bias will be zero ([0.5 METs + -0.5 METs] / 2 = 0 METs). For this reason, measures of accuracy (RMSE/RMSPE and MAE/MAPE) were also calculated. *Accuracy* reflects the overall difference between measured and predicted values[158] by making all error values positive (either by using their absolute values [MAE/MAPE] or squaring them [RMSE/RMSPE]) and then calculating their average.

Lastly, there are differences between the two measures of predictive accuracy that were evaluated. Because MAE/MAPE is simply calculated by averaging the absolute values of error, it gives each error value equal weight. Because RMSE/RMSPE is determined by squaring error values, averaging them, and *then* calculating the square root, this measure of accuracy gives errors with a greater absolute value more weight than those with smaller absolute values.[159,160] It has been recommended that studies report both MAE/MAPE and RMSE/RMSPE when evaluating predictive error.[159] However, MAE was used as a direct reflection of the average error of metabolic equations (whereas RMSE can be greatly influenced by outliers).[159,160]

3.2. Study Two: Cross-Validation of Cadence-Based Metabolic Equations

In Study Two, the simple and full cadence-based metabolic equations developed in Study One were cross-validated using an independent dataset representing unconstrained and cadence-constrained overground walking conditions that were collected in 2017. A publication reporting the results of the study for which this dataset was originally collected was in preparation at the time of this analysis. The purpose of this secondary analysis was distinct from that of the original study.

3.2.1. Participants

A sample of 10 men and 10 women 21-40 years of age were recruited for the original study. Exclusion criteria for these participants were the same as those for Cohort 1 of the CADENCE-Adults study (see section 3.1.1.)

3.2.2. Measures

The following measures were obtained for each participant using the same equipment and protocols as described above (section 3.1.2.): age, sex, height, leg length, body mass, BMI, and percent body fat. The same methods discussed previously were also used to measure oxygen consumption, heart rate, RPE, and hand-counted steps (with redundant video recording) during metabolic testing. Overground walking speed was determined using a portable, pressure-sensitive electronic walkway (GAITRite, CIR Systems, Inc., Franklin, NJ, USA), which has been validated against video-based and manual (i.e., dividing a measured distance by the time it takes to walk that distance) measures of walking speed (intraclass correlations of 0.96 and 0.95, respectively).[161] This

7 m long, 0.9 m wide electronic walkway was placed on a straightaway of the walking course (described later), and speed was averaged over multiple crossings performed by participants during each trial.

3.2.3. Metabolic Testing Procedure

The metabolic testing procedure of the original study consisted of three bouts of unconstrained overground walking (self-selected slow, normal, and fast walking paces) and three bouts of cadence-constrained overground walking with foot-strikes entrained to the tempos of music (80, 100, and 125 beats/min). A single song ('Staying Alive' by the BeeGees) was used for constraining cadence in all trials, with its tempo modulated to the desired beats/min using the Tempo Magic (Lolo, LLC) smartphone app. This app adjusted the tempo of a song while attenuating changes in pitch, thus controlling for potential changes in physiological measures due to song- or pitch-specific responses.

Participants again arrived at the laboratory after fasting for at least four hours. Before beginning metabolic testing, they were briefly orientated to the task of walking with a cadence constrained to the tempo of music. To do so, music was played through a pair of wireless Bluetooth headphones (Mpow 059, Bluetooth Headphones Over Ear, Cheung Sha Wan, Hong Kong) fitted over participants' ears. They were instructed to walk "as normally as possible" during cadence-constrained trials with foot-strikes synchronized with the music tempo. A researcher then counted (from one to four) in time with the song tempo to indicate when foot-strikes were intended to occur and visually demonstrated the synchronization of cadence to the music.

Prior to overground walking trials, participants completed a five-minute seated rest period followed by two minutes of standing rest. They then performed three trials of unconstrained overground walking at their self-selected slow, normal and fast paces (in that order) followed by three trials of walking with cadences constrained to song tempos of 80, 100, and 125 beats/min (in a randomized order). The unconstrained walking trials were performed in an incremental order to facilitate the intended increases in self-selected pace. However, increases in cadence during cadence-constrained walking have shown to produce smaller increases in walking speed (due to smaller increases in step length) than with the same increases in cadence during treadmill or unconstrained overground walking.[45-47] The order of cadence-constrained walking trials was therefore randomized to elicit the naturally selected walking speed with each song tempo, without a consistent influence of trial order. Each trial was separated by five minutes of rest that began after participants returned to a standardized starting location. The course around which participants walked consisted of a 40 m indoor loop in a large, uncarpeted room. The corners of the loop were curved to minimize potential effects of turning on walking parameters and participants walked over the GAITRite electronic walkway along one of the two straightaways located on the loop's two longer sides.

3.2.4. Data Processing

Initial data processing and management were conducted in MATLAB using custom scripts. Similar to Study One, metabolic intensity was calculated as the average VO_2 during minutes 2:45-4:45 of each trial and hand-counted steps were divided by trial duration to determine cadence. Walking speed was averaged across all crossings of the GAITRite electronic walkway. All VO_2, cadence, speed, and participant characteristic data were exported from MATLAB for the secondary analyses conducted herein.

3.2.5. Statistical Analysis

Aim 3: To cross-validate these cadence-based metabolic equations across walking conditions (using previously collected unconstrained and cadence-constrained overground walking data) and compare their predictive accuracies to that of the ACSM metabolic equation.

***$H_{3.1}$*:** The cadence-based metabolic equations will remain valid for overground unconstrained walking with RMSE and MAE values ≤1 MET, but underpredict the metabolic intensity of overground cadence-constrained walking.

***$H_{3.2}$*:** The cadence-based metabolic equations will have greater predictive accuracies than the ACSM metabolic equation.

To cross-validate the simple and full cadence-based metabolic equations developed in Study One, their ability to predict the metabolic intensity of overground unconstrained and cadence-constrained walking was evaluated. Each equation was used to determine a predicted value of VO_2 for each of these overground walking trials by inputting hand-counted cadences and (for the full equation) the respective participant characteristics. The ACSM Metabolic Equation (Eq.1) was also used to predict VO_2 of unconstrained and cadence-constrained walking trials by inputting 0% for grade and the walking speeds measured with the GAITRite electronic walkway. The predictive accuracy of each metabolic equation was then evaluated by comparing predicted VO_2 values to those measured through indirect calorimetry, and calculating RMSE, RMSPE, MAE, and MAPE. Predictive bias (measured - predicted VO_2) and percent bias was also calculated to determine direction of error. Each metric was determined separately for each metabolic equation and walking trial. Predictive accuracy and bias measures were compared between unconstrained and cadence-constrained walking by averaging values across trials within each walking condition. Predictive error values were also converted to kcals/week (1 MET = 1 kcal/kg/hr) using sex-specific US average body mass values (88.8 kg for men and 76.4 kg for women)[94] to further depict their practical significance.

Systematic bias in metabolic equation predictions and their agreement with criterion-measured VO_2 was also evaluated using Bland-Altman analysis, where the bias (i.e., error) for each prediction of metabolic intensity was plotted against the average of the predicted and criterion-measured VO_2.[162,163] Modified Bland-Altman plots, where bias was plotted against criterion-measured (instead of the average of predicted and measured) VO_2, were used to confirm any observed trends (e.g., increasing bias with increasing VO_2). This method was not used for the primary analyses, however, because these modified Bland-Altman plots will always appear to show a relation between bias and measurement magnitude.[164] When calculating 95% confidence intervals for bias and 95% limits of agreement, the necessary modifications were applied to account for repeated measures.[165]

CHAPTER 4

RESULTS

4.1. Study One: Development of Cadence-Based Metabolic Equations

At the time of this secondary analysis (March 2018), data collection for the CADENCE-Adults Study was still ongoing. The results presented herein are representative of the 197 participants with completed data as of that time.

4.1.1. Analytic Sample

Data collected for four participants were invalid due to equipment malfunctions. The remaining 193 participants were included in the analyses. The analytical sample was comprised of 76 adults from Cohort 1 (21-40 years of age), 80 adults from Cohort 2 (41-60 years of age) and 37 adults from Cohort 3 (61-85 years of age). The characteristics of these participants are further detailed in Table 3. A total of 1456 treadmill walking bouts conducted at speeds of 13.4-134.1 m/min (0.5-5.0 mph) were available for analysis. Further details describing these treadmill walking bouts are provided in Table 4.

Table 3: Study One Participant Characteristics.

	All (*N* = 193)	**Cohort 1 (*n* = 76)**	**Cohort 2 (*n* = 80)**	**Cohort 3 (*n* = 37)**
Female (%)	52%	50%	50%	62%
Age (years)	45.9 ± 15.2 [21-81]	30.4 ± 5.8 [21-40]	50.2 ± 5.9 [41-60]	68.5 ± 4.7 [62-81]
Height (cm)	170 ± 9 [149-194]	171 ± 9 [149-194]	171 ± 9 [150-190]	166 ± 8 [151-183]
Body Mass (kg)	74 ± 14 [48-129]	73 ± 14 [52-119]	76 ± 14 [48-129]	73 ± 13 [48-103]
BMI (kg/m^2)	25.6 ± 3.8 [18.6-37.6]	24.8 ± 3.4 [19.4-36.9]	26 ± 4 [19.0-37.6]	26.3 ± 3.9 [18.6-36]
Leg Length (cm)	80.0 ± 5.4 [65.7-94.5]	79.7 ± 5.8 [65.7-94.5]	80.7 ± 5.2 [66.6-92]	79.2 ± 4.9 [70.3-91.9]
Body Fat (%)	27.6 ± 8.8 [5.2-50.7]	24.7 ± 7.4 [8.3-38.6]	29.0 ± 8.5 [5.2-47]	30.7 ± 10.3 [9.8-50.7]

Values are presented as mean ± SD [range]

Table 4: Treadmill Walking Bout Descriptions.

Speed	n Bouts Completed	VO_2 (mL/kg/min)	Cadence (steps/min)	Step Length (cm)
13.4 m/min [0.5 mph]	193	7.3 ± 1.2	52 ± 17	28.2 ± 7.4
26.8 m/min [1.0 mph]	189	8.2 ± 1.2	70 ± 12	39.2 ± 6.2
40.2 m/min [1.5 mph]	189	9.1 ± 1.2	85 ± 10	47.8 ± 4.8
53.6 m/min [2.0 mph]	188	10.1 ± 1.1	97 ± 8	55.8 ± 4.2
67.1 m/min [2.5 mph]	187	11.6 ± 1.3	106 ± 7	63.6 ± 3.9
80.5 m/min [3.0 mph]	184	13.9 ± 1.5	114 ± 7	70.9 ± 4.0
93.9 m/min [3.5 mph]	167	17.0 ± 1.9	121 ± 7	77.9 ± 4.5
107.3 m/min [4.0 mph]	116	21.3 ± 2.4	129 ± 8	83.5 ± 4.9
120.7 m/min [4.5 mph]	38	26.7 ± 3.6	138 ± 9	87.9 ± 5.4
134.1 m/min [5.0 mph]	5	31.1 ± 3.8	145 ± 9	92.4 ± 5.4

Values are presented as mean ± SD unless otherwise noted

4.1.2. Development of Cadence-Based Metabolic Equations

Upon visual inspection, participant-level plots of the relationship between cadence and metabolic intensity consistently appeared to be curvilinear. This observation was confirmed by a likelihood-ratio test. Specifically, the quadratic model provided a significantly better fit to the cadence-intensity relationship than the linear model ($p < 0.0001$), with marginal R^2 values of 0.81 and 0.65, respectively. A quadratic cadence term was therefore included in all further models of the cadence-intensity relationship.

Fitting a maximal likelihood regression model for predicting oxygen consumption (VO_2; mL/kg/min) from cadence (C; steps/min) resulted in the following simple cadence-based metabolic equation:

$$VO_2 = 13.93 + [-0.25*C] + [0.0022*C^2] \qquad \text{Eq. 2}$$

In this equation, cadence alone was a significant predictor of metabolic intensity of walking ($p < 0.0001$). Figure 1A shows the fit of the simple cadence-based metabolic equation to the treadmill walking metabolic data collected herein. The results of k-fold

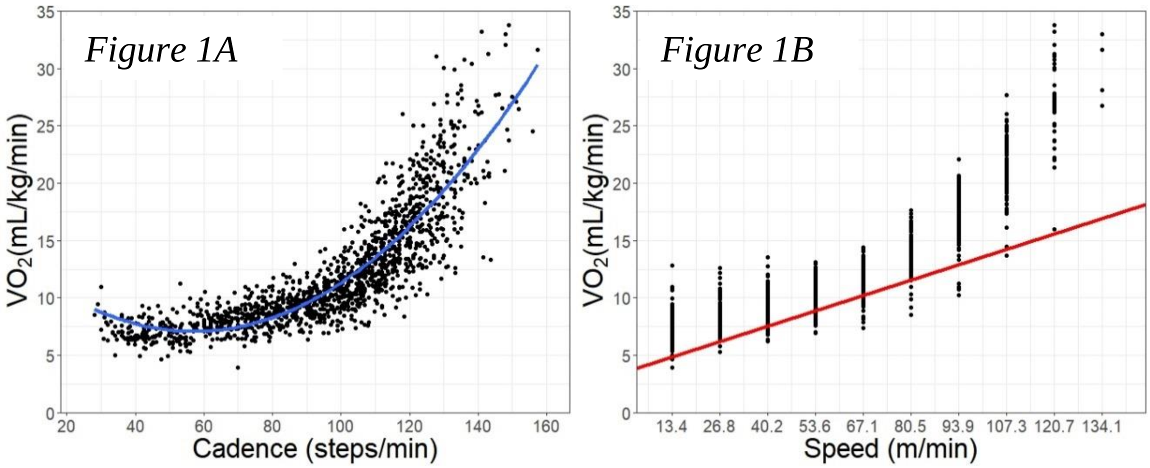


Figure 1: Fits of the Simple Equation (1A) and ACSM Metabolic Equation (1B) to the Treadmill Walking Data.

cross-validation with the simple cadence-based metabolic equation in these data are presented in Table 5.

The performance of best-subsets regression analysis additionally included the predictors of sex (*Sex*; equal to 1 for men and 0 for women), age (*A*; years), leg length (*LL*; cm), and BMI (*BMI*; kg/m^2), as well as cadence's interactions with leg length, sex, BMI, and age. This resulted in the following full-cadence based metabolic equation:

$$VO2 = 10.15 + [93.45*C] + [73.78*C^2] + [-0.08*LL] + [-1.01*Sex] + [0.08*Age] + [0.0016*C*LL] + [0.0163*C*Sex] + [-0.001*C*BMI] + [-0.0011*C*Age] \quad \text{Eq. 3}$$

All coefficients in this model had VIF values ≤5. In the k-fold cross-validation, the full cadence-based metabolic equation had a slightly (0.2 mL/kg/min) lower RMSE and MAE than the simple cadence-based metabolic equation and a similar magnitude of bias (difference <0.01 mL/kg/min).

Table 5: Predictive Error of the Metabolic Equations During Treadmill Walking.

Equation	RMSE*	RMSPE	MAE*	MAPE	Bias*	% Bias
Simple	2.5 ± 0.3	20 ± 2%	1.8 ± 0.2	14 ± 1%	<0.1 ± 0.3	<1 ± 3%
Full	2.3 ± 0.3	18 ± 2%	1.6 ± 0.2	13 ± 1%	<0.1± 0.3	<1 ± 2%
ACSM	4.2 ± 0.3	33 ± 1%	3.0 ± 0.2	24 ± 1%	3.0 ± 0.2	24 ± 1%

Note: values determined through repeated k-fold cross-validation (k=5, 10 repetitions)
Values are presented as mean ± SD
*Units are mL/kg/min

When the ACSM Metabolic Equation (Eq. 1) was applied to the treadmill walking dataset through k-fold cross-validation, it demonstrated greater predictive error than both cadence-based metabolic equations, especially in regard to bias (Table 5). Specifically, the ACSM Metabolic Equation's RMSE, MAE, and magnitude of bias were greater than those of the simple equation by 1.7, 1.3, and 3.0 mL/kg/min, respectively, and those of the full equation by 1.9, 1.4, and 3.0 mL/kg/min, respectively. As shown by its fit to the treadmill walking data in Figure 1B and the Bland-Altman plot in Appendix A, the ACSM Metabolic Equation appeared to underpredict metabolic intensity of walking with increasing magnitude as walking speed increased.

The kcal/hr equivalents of these predictive error values, when converted using average US body mass values (88.8 kg for men and 76.4 kg for women),[94] are provided in Appendix B. The simple equation's RMSE and MAE values were 64 and 45 kcals/hr, respectively, for the average American man, and 55 and 38 kcals/hr, respectively, for the average American women. The full equation had a 5 kcal/hr lower RMSE for both men and women and MAE values that were lower by 4 kcals/hr for the average American men and 3 kcals/hr for the average American women. With the ACSM Metabolic Equation, RMSE values for the average American man and woman (106 and 91 kcals/hr, respectively) were 36-47 kcal/hr greater than with the simple and full equations, and MAE values (77 and 66 kcals/hr, respectively) were greater by 28-36 kcals/hr. Additionally, while the biases of the simple and full equations were ~0 kcals /hr, the ACSM Metabolic Equation's biases were equivalent to 75 and 64 kcal/hr for the average American man and woman, respectively.

4.2. Study Two: Cross-Validation of Cadence-Based Metabolic Equations

4.2.1. Analytic Sample

All data collected during overground unconstrained and cadence-constrained walking were valid for analysis. The study recruitment design was not intentionally age-balanced and the 10 men and 10 women who participated tended to have ages in the ages in the younger end of the 21-40-year-old recruitment range (mean age = 23.7 years, age range = 21-29 years). The characteristics of this sample are reported in Table 6. All participants had complete data for each overground unconstrained and cadence-constrained walking trial.

Descriptions of the gait parameters and metabolic intensities observed during each of these trials are provided in Table 7. Increases in average VO_2, speed, cadence, and step length were observed with each increase in self-selected pace during unconstrained trials and song tempo during cadence-constrained trials (Table 7). In addition, the MAPE values for the cadences observed during cadence-constrained walking, versus those representing perfect entrainment with the music tempos, were 7.5 ± 8.3%, 5.0 ± 4.1%, and 3.1 ± 2.4% for trials conducted at 80, 100, and 125 BPM, respectively.

Table 6: Study Two Participant Characteristics.

	All (*N*=20)	**Men (*n*=10)**	**Women (*n*=10)**
Age (years)	23.7 ± 2.7 [21-29]	22.7 ± 1.8 [21-27]	24.7 ± 3.1 [21-29]
Height (cm)	173 ± 9 [161-195]	177 ± 8 [170-195]	168 ± 7 [161-181]
Body Mass (kg)	72 ± 16 [50-115]	79 ± 18 [60-115]	64 ± 9 [50-78]
BMI (kg/m^2)	23.8 ± 3.9 [18.3-33.2]	24.8 ± 3.9 [19.9-33.2]	22.7 ± 3.7 [18.3-29.4]
Leg Length (cm)	81.2 ± 5.7 [72.7-95.1]	83.9 ± 5.6 [77.9-95.1]	78.5 ± 4.5 [72.7-88.9]
Body Fat (%)	23.5 ± 8.3 [6.4-35.7]	17.4 ± 6 [6.4-24.7]	29.6 ± 5.3 [20.2-35.7]

Values are presented as mean ± SD [range]

Table 7: Unconstrained and Cadence-Constrained Walking Trial Descriptions.

Walking Condition	Trial	VO_2 (mL/kg/min)	Speed (m/min)	Cadence (steps/min)	Step Length (cm)
Unconstrained	Slow	10.0 ± 1.5	56.1 ± 10.5	91.7 ± 9.3	60.3 ± 6.1
	Normal	12.4 ± 2.2	75.8 ± 9.0	107.0 ± 5.3	70.5 ± 6.4
	Fast	16.8 ± 2.9	97.1 ± 10.0	118.8 ± 6.8	81.7 ± 7.4
Cadence-Constrained	80 BPM	10.9 ± 1.5	56.1 ± 10.6	86.0 ± 6.7	65.0 ± 8.1
	100 BPM	13.2 ± 1.9	77.1 ± 8.8	105.0 ± 4.1	73.3 ± 6.6
	125 BPM	17.8 ± 2.2	98.8 ± 8.6	125.4 ± 5.0	79.2 ± 7.9

Values are presented as mean ± SD

4.2.2. Cross-Validation Across Walking Conditions

The cadence-based metabolic equations developed in Study One were cross-validated across walking conditions by applying them to the data collected during overground unconstrained and cadence-constrained walking trials. The ACSM Metabolic Equation was similarly applied to this data for comparison. The fit of the simple cadence-based metabolic equation and ACSM Metabolic Equation to this data are shown in Figures 2A and 2B, respectively. Predictive error measures for these three equations are

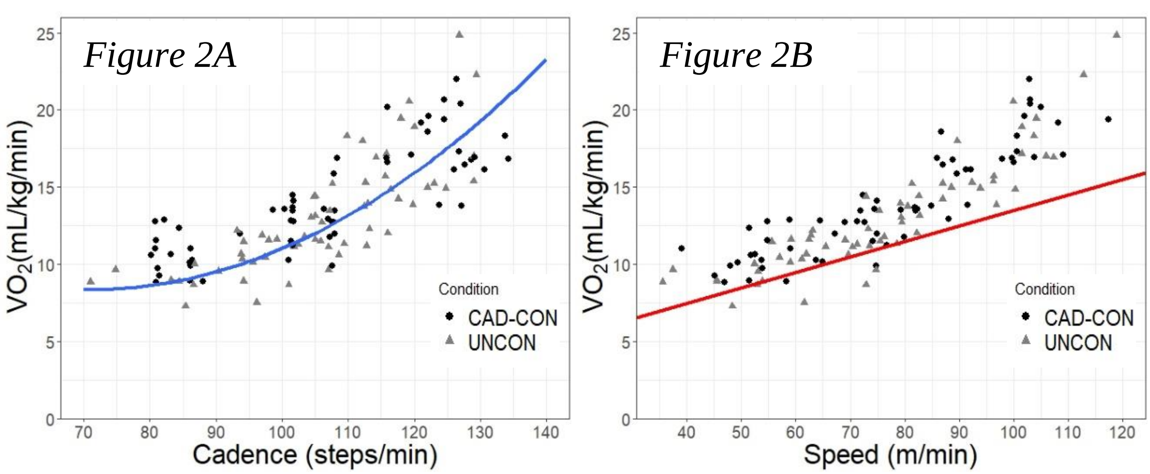


Figure 2: Fits of the Simple Equation (2A) and ACSM Metabolic Equation (2B) to the Overground Walking Data.

CAD-CON = overground cadence-constrained; UNCON = overground unconstrained compared between walking conditions in Table 8 and Figures 3A and B, and between individual overground walking trials in Table 9.

4.2.2.1. Trends Between Walking Conditions

To compare metabolic equation performance during unconstrained versus cadence-constrained walking, measures of predictive error were averaged across trials within each of these walking conditions. The resulting RMSE and MAE values for the simple and full cadence based metabolic equations were 1.7-2.5 mL/kg/min during both overground walking conditions (Table 8), which is equivalent to 44-62 and 37-54 kcal/hr for the average US man and women, respectively. These predictive error values were similar (0.3 mL/kg/min lower to 0.4 mL/kg/min higher) to those observed in Study One during treadmill walking (Figure 3A). Scaled measures of predictive accuracy for the simple and full equations were also similar between treadmill and overground walking conditions (≤4% differences in RMSPE and MAPE; Figure 3B). Whereas the cadence-based metabolic equations had approximately no bias during treadmill walking, there were slight tendencies for the simple equation to underpredict (i.e., had positive bias values) and the full equation to overpredict (i.e., had negative bias values) walking intensity during both overground unconstrained and cadence-constrained walking (bias magnitudes ≤0.9 mL/kg/min and percent bias magnitudes ≤7%). When the ACSM Metabolic Equation was applied to the data collected during overground unconstrained and cadence-constrained walking, its RMSE and MAE values (2.2-3.3 mL/kg/min; 55-84 and 48-73 kcal/hr for the average man and women, respectively) and magnitudes of bias (2.0-2.7 mL/kg/min; 51-69 and 44-59 kcal/hr for the average man and women, respectively) were consistently lower than during treadmill walking (Figure 3A).

Figure 3A

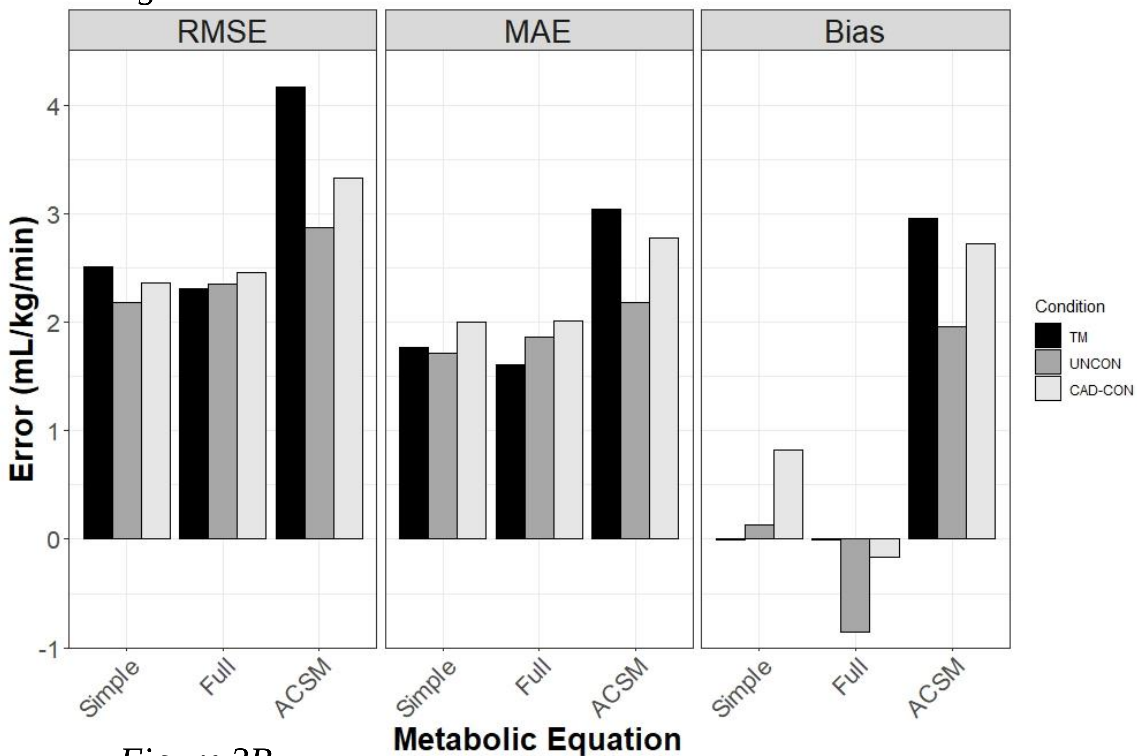


Figure 3B

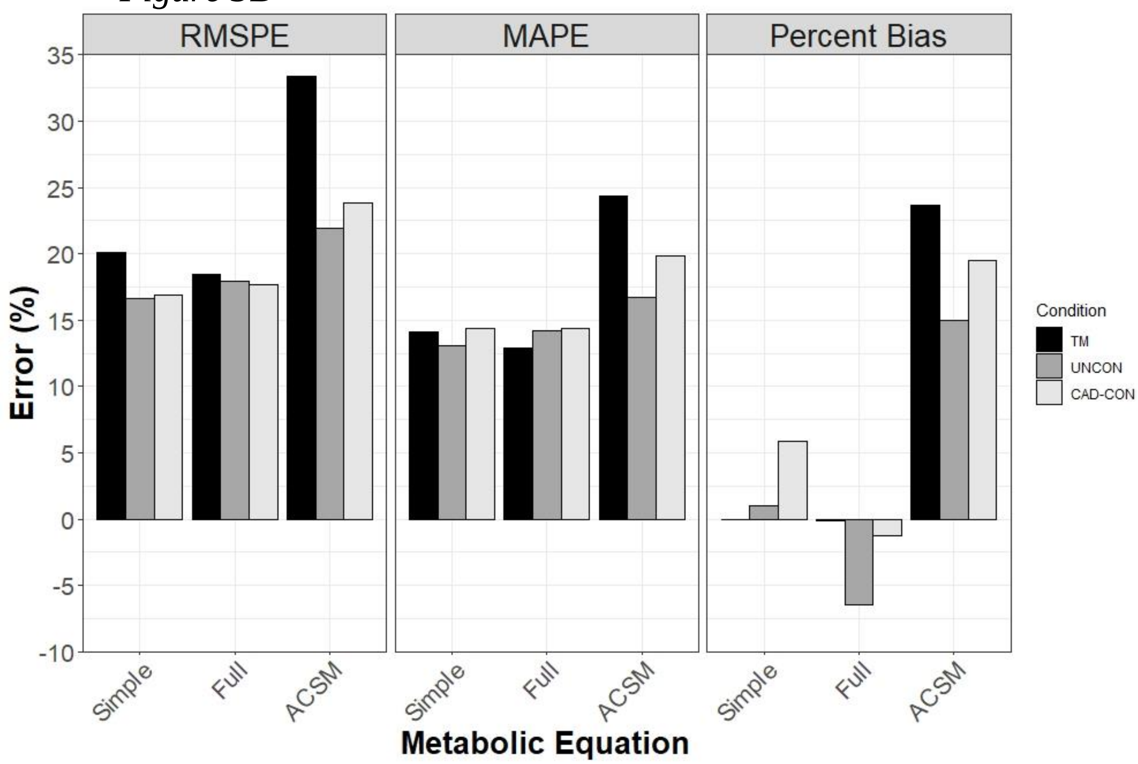


Figure 3: Unscaled (3A) and Scaled (3B) Measures of Predictive Error for Metabolic Equations Walking.

TM = treadmill; UNCON = overground unconstrained; CAD-CON = overground cadence-constrained

Table 8: Predictive Error of Metabolic Equations in Each Walking Condition.

Condition	RMSE (mL/kg/min) RMSPE (%)			MAE (mL/kg/min) MAPE (%)			Bias (mL/kg/min) Percent Bias (%)		
	Simple	**Full**	**ACSM**	**Simple**	**Full**	**ACSM**	**Simple**	**Full**	**ACSM**
TM	2.5±0.3	2.3±0.3	4.2±0.3	1.8±0.2	1.6±0.2	3.0±0.2	0.0±0.3	0.0±0.3	3.0±0.2
	20±2	18±2	33±1	14±1	13±1	24±1	0±3	0±2	24±1
UN-CON	2.2±2.7	2.4±2.7	2.9±3.9	1.7±1.4	1.9±1.4	2.2±1.9	0.1±2.2	-0.9±2.2	2.0±2.1
	17±20	18±20	22±30	13±10	14±11	17±14	1±17	-7±17	15±16
CAD-CON	2.4±2.4	2.5±2.8	3.3±3.7	2.0±1.3	2.0±1.4	2.8±1.8	0.8±2.2	-0.2±2.5	2.7±1.9
	17±18	18±20	24±26	14±9	14±10	20±13	6±16	-1±18	19±14
All OG	2.3±2.6	2.4±2.7	3.1±3.8	1.9±1.3	1.9±1.4	2.5±1.9	0.5±2.2	-0.5±2.4	2.3±2
	17±19	18±20	23±28	14±10	14±11	18±14	4±16	-4±17	17±15

Note: TM values are the same as those reported in Study One
Values are presented as mean±SD
TM = treadmill; UNCONS = overground unconstrained; CAD-CON = overground cadence-constrained; All OG = all overground

These differences in predictive error were slightly greater between treadmill and unconstrained (0.9-1.3 mL/kg/min) versus treadmill and cadence-constrained (0.2-0.9 mL/kg/min) walking. Similar trends were observed when the ACSM Metabolic Equation's predictive error was assessed using scaled measures, with RMSPE, MAPE, and percent bias values that were 8-11% lower during unconstrained and 4-10% lower during cadence-constrained walking, as compared to the treadmill walking condition in Study One. Therefore, there is no evidence that the cadence-based metabolic equations (and ACSM Metabolic Equation) had reduced predictive capacities when applied to the data collected during overground unconstrained or cadence-constrained walking.

When comparing predictive accuracy between the two overground walking conditions, RMSE and MAE values were slightly greater during cadence-constrained walking for both cadence-based metabolic equations (by 0.1-0.3 mL/kg/min) and the ACSM Metabolic Equation (by 0.4-0.6 mL/kg/min). When converted to kcals/hr for the average man and women, RMSE and MAE values were greater during cadence-constrained versus unconstrained walking by 2-7 kcals/hr for the simple and full equations and 10-15 kcal/hr for the ACSM Metabolic Equation. This indicates that all metabolic equations had lower predictive accuracy during cadence-constrained versus unconstrained walking, but only marginally (Figure 3A). Magnitudes of bias were also 0.7 mL/kg/min higher during the cadence-constrained walking condition for the simple equation and ACSM Metabolic Equation, while the full equation had a 0.7 mL/kg/min greater magnitude of bias during unconstrained walking. As can be seen in Figure 3A, these same (0.7 mL/kg/min) changes in bias during cadence-constrained walking accentuated the tendency of the simple equation and ACSM Metabolic Equation to underpredict metabolic intensity during unconstrained walking (i.e., made their biases more positive) but reduced the tendency of the full equation to overpredict metabolic intensity during unconstrained walking (i.e., made its bias less negative).

The use of scaled predictive error measures appeared to attenuate many of these (already small) differences in metabolic equation performance between overground walking conditions (Figure 3B). The RMSPE and MAPE of the simple and full equations were approximately the same (differences ≤1%) between unconstrained and cadence-constrained walking. The ACSM Metabolic Equation's RMSPE and MAPE remained marginally greater during cadence-constrained versus unconstrained walking, with differences of 2 and 3%, respectively. Differences in percent bias between cadence-constrained and unconstrained walking conditions mirrored the trends previously reported in (unscaled) bias. Specifically, magnitudes of percent bias during cadence-constrained walking were greater (4-5% more positive) with the simple equation and

ACSM Metabolic Equation but lower (6% less negative) with the full equation, compared to during unconstrained.

4.2.2.2. Comparison of Metabolic Equations

To compare predictive error between the three metabolic equations, results were first averaged across all trials and walking conditions. The resulting overall predictive error values were consistently the lowest for the simple cadence-based metabolic equation (Table 8), with 0.6-1.9 mL/kg/min and 5-14% greater unscaled and scaled measures for the ACSM Metabolic Equation but only marginally (0.1 mL/kg/min and ≤1%) higher predictive error for the full equation. The ACSM Metabolic Equation therefore also had greater overall unscaled and scaled predictive error measures than the full equation (differences of 0.6-1.9 mL/kg/min and 4-14%). The greater bias of the ACSM Metabolic Equation is visually apparent in its fit to the data (Figure 2B; further discussed in section 4.2.2.4).

The three metabolic equations were also compared when results were averaged across trials within each walking condition. During unconstrained and cadence-constrained walking, unscaled and scaled measures of predictive error remained 0.3-2.6 mL/kg/min and 3-18% higher for the ACSM Metabolic Equation than either cadence-based metabolic equation. When converted to kcals/hr for the average US man and woman, during both unconstrained and cadence-constrained walking, the ACSM Metabolic Equation had 11-25 kcal/hr greater RMSE, 7-19 kcal/hr greater MAE, and 26-84 kcal/hr greater magnitudes of bias than the simple and full equations (Appendix B). The simple and full equations had similar scaled and unscaled predictive accuracy measures during both of these walking conditions (differences ≤0.2 mL/kg/min and

≤1%). Differences in bias (and percent bias) between the cadence-based metabolic equations were slightly larger, with that of the simple equation lower by 0.7 mL/kg/min (6%) during unconstrained walking but that of the full equation lower 0.7 mL/kg/min (5%) during cadence-constrained walking.

4.2.2.3. Trends by Self-Selected Pace and Music Tempo

During the unconstrained walking condition, increases in self-selected walking pace were accompanied by increases in RMSE and MAE values, with maximum differences (i.e., differences between equation- and walking condition-specific lowest and highest trial values [slow- versus fast-paced trials in this instance]) ranging from 1.1-2.8 mL/kg/min for all three metabolic equation (Table 9). The magnitude of bias also increased with increasing self-selected walking pace for the simple equation and ACSM Metabolic Equation (maximum differences of 0.9 and 2.7 mL/kg/min, respectively), whereas the full equation's magnitude of bias was the greatest during self-selected normal-paced walking with a maximum difference (slow- versus normal-paced trials) of 1.0 mL/kg/min. Scaled measures of predictive error (RMSPE, MAPE, and percent bias magnitude) for the simple equation and ACSM Metabolic Equation also increased with increasing self-selected walking pace, with maximum differences of 4-5% and 9-13%, respectively (Table 9). For the full equation, however, these scaled measures of predictive error were highest during normal-paced walking (maximum differences of 3-9%).

When metabolic equations were applied to cadence-constrained walking trials, only the ACSM Metabolic Equation demonstrated a consistent increase in RMSE, MAE, and bias unscaled measures of predictive error with increasing music tempo (maximum

Table 9: Predictive Error of Metabolic Equations in Each Overground Unconstrained and Cadence-Constrained Walking Trial.

Trial	RMSE (mL/kg/min) RMSPE (%)			MAE (mL/kg/min) MAPE (%)			Bias (mL/kg/min) Percent Bias (%)		
	Simple	**Full**	**ACSM**	**Simple**	**Full**	**ACSM**	**Simple**	**Full**	**ACSM**
Slow	1.3±1.6	1.7±2.3	1.4±1.4	1±0.9	1.2±1.1	1.2±0.8	0.0±1.4	-0.7±1.6	0.9±1.1
	13±16	17±23	14±14	10±9	12±11	12±8	0±14	-7±16	9±11
Nor-mal	2.0±2.1	2.5±2.6	2.1±2.7	1.6±1.1	2.0±1.5	1.7±1.4	-0.5±1.9	-1.5±2	1.3±1.7
	16±17	20±21	17±22	13±9	16±12	14±11	-4±16	-12±16	11±14
Fast	2.9±3.2	2.8±2.9	4.2±4.8	2.5±1.6	2.4±1.5	3.6±2.2	0.9±2.9	-0.4±2.8	3.6±2.2
	17±19	17±17	25±28	15±9	14±9	22±13	5±17	-3±17	22±13
80 BPM	2.2±2.5	2.1±2.3	2.1±2.2	1.9±1.3	1.7±1.2	1.8±1.1	1.8±1.3	1.3±1.6	1.8±1.2
	21±22	19±21	20±20	17±12	15±11	17±10	17±12	12±15	16±11
100 BPM	1.8±2	1.9±1.9	2.4±2.4	1.5±1.1	1.7±0.9	2.1±1.3	0.8±1.7	-0.2±1.9	1.9±1.5
	14±15	14±14	18±19	11±8	13±7	16±10	6±13	-2±15	15±11
125 BPM	2.9±2.6	3.2±3.3	4.8±4.1	2.6±1.1	2.7±1.8	4.4±1.8	-0.1±2.9	-1.6±2.9	4.4±1.8
	16±15	18±19	27±23	15±6	15±10	25±10	-1±16	-9±16	25±10

All values are presented as mean±SD

differences [80 versus 125 BPM trials] of 2.3-2.5 mL/kg/min for each measure). Conversely, there was a consistent negative relationship between music tempo and bias magnitude for the simple equation, with a maximum difference of 1.7 mL/kg/min. The only other notable trend in unscaled predictive error measures among cadence-constrained trials was the consistently lower RMSE, MAE, and bias magnitude for both the simple and full cadence-based metabolic equations at 100 BPM (maximum differences 1.0-1.4 mL/kg/min for each measure and equation). When scaled measures of predictive error were evaluated, there were no consistent trends (positive or negative) with increasing music tempo of cadence-constrained trials (Table 9)**.** However, with the singular exception of the percent bias magnitude for the simple equation, each metabolic equation's RMSPE, MAPE, and percent bias magnitudes were the lowest during the 100 BPM trial. These maximum differences in scaled measures between cadence-constrained trials ranged from 3-10% for the cadence based metabolic equations and 8-10% for the ACSM Metabolic Equation, which also consistently had the highest values in the 125 BPM trial. In summary, while predictive error tended to increase with increasing self-selected walking pace in the unconstrained walking condition the simple and full cadence-based metabolic equations tended to have the lowest predictive error in the 100 BPM (as opposed to 80 BPM) trial.

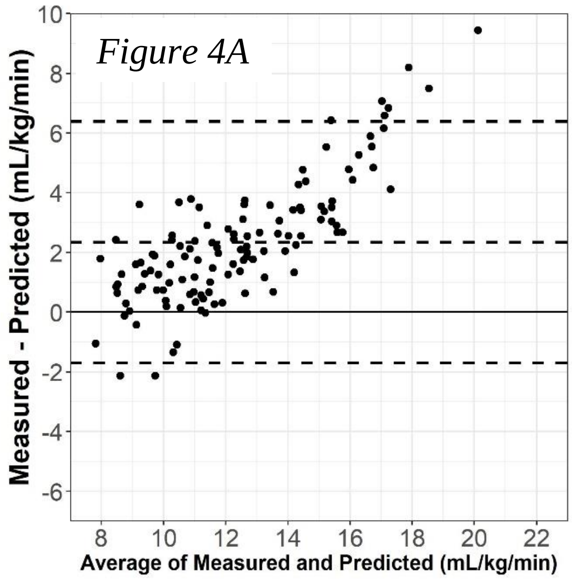
4.2.2.4. Bland-Altman Analysis

Shapiro-Wilk tests verified that the participant-level average differences between measured and predicted VO_2 were normally distributed with each metabolic equation. The Bland-Altman plots subsequently created to show the bias (measured - predicted VO_2) of each metabolic equation are presented in Figures 4A-C. Each equation's mean bias, 95% confidence interval for mean bias, and 95% limits of agreement are also provided in Table 10. Appendix C includes Bland-Altman plots for each equation stratified by walking condition, although there did not appear to be any differences in systematic bias between overground unconstrained and cadence-constrained walking conditions. The simple cadence-based metabolic equation tended to slightly underpredict walking intensity while the full equation tended to slightly overpredict walking intensity (mean biases of 0.5 and -0.5 mL/kg/min, respectively). Still, neither of these cadence-and there were no apparent trends in bias with increasing walking intensity (Figures 4B and 4C). Conversely, the ACSM Metabolic Equation significantly

Table 10: Results of the Bland-Altman Analysis for Each Metabolic Equation.

Equation	Mean Bias [95% CI]	95% LoA
Simple	0.5 [-0.3 to 1.3]	-3.9 to 4.9
Full	-0.5 [-1.3 to 0.3]	-5.2 to 4.2
ACSM	2.3 [1.8 to 2.9]	-1.7 to 6.4

Note: analysis included all data collected during unconstrained and cadence-constrained walking
All units are mL/kg/min
LoA = limits of agreement; CI = confidence interval



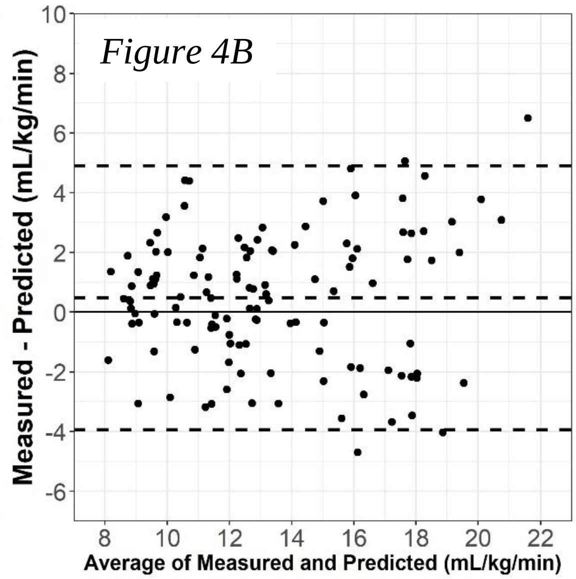
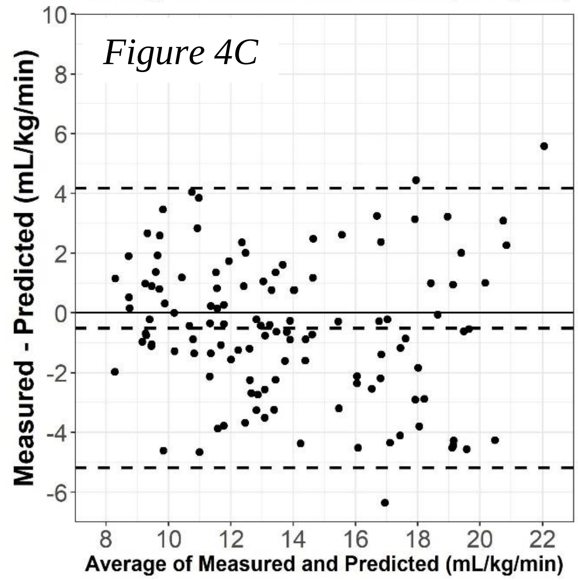


Figure 4: Bland-Altman Plots for the ACSM Metabolic Equation (4A), Simple Equation (4B), and Full Equation (4C) With the Overground Walking Data.

Note: figures include all data collected during unconstrained and cadence-constrained walking; Measured = VO_2 measured with indirect calorimetry; Predicted = VO_2 predicted by metabolic equation



underpredicted metabolic intensity(mean bias [95% confidence interval] of 2.3 [1.8-2.9] mL/kg/min) and there was a clear increase in its bias as metabolic intensity increased (Figure 4A). This observation was confirmed by a modified Bland-Altman plot where bias was plotted against measured VO_2 (Appendix D).

CHAPTER 5

DISCUSSION

Although metabolic intensity is an important component of PA to consider in exercise programming and measurement, it can be difficult to quantify and convey to the general public. Therefore, the purpose of this thesis was to develop metabolic equations that predict metabolic intensity (oxygen consumption; mL/kg/min) from cadence using a large treadmill walking dataset (Study One) and cross-validate these equations during overground unconstrained and cadence-constrained walking conditions (Study Two). The metabolic equation that is currently most well-known is the speed-based equation published in the ACSM Guidelines for Exercise Testing and Prescription since 1980 (Eq.1).[17] Because cadence can be easily measured and prescribed during overground walking, the metabolic equations developed herein (Eq. 2 and 3) are more practical for researchers, health professionals, and members of the general public to use. In addition, given the aforementioned limitations of the study from which the ACSM Metabolic Equation's speed component was originally derived,[19] the cadence-based metabolic equations developed herein are based on a larger, age- and sex-balanced sample of adults across the lifespan. The use of this sample for calibrating a metabolic equation suggests a greater potential to produce accurate and generalizable results. This conclusion is further supported by the simple and full equations' ~50% lower RMSE and MAE and ~200% lower bias than the ACSM Metabolic Equation in this large, heterogeneous sample.

5.1. The Cadence-Intensity Relationship During Treadmill Walking

5.1.1. The Simple Cadence-Based Metabolic Equation

As hypothesized in Study One, a quadratic model describing the cadence-intensity relationship provided a significantly better fit than a linear model. The marginal R^2 value of this quadratic mixed regression model (0.81) indicated that there was a strong relationship between cadence and metabolic intensity of treadmill walking. Moreover, the simple cadence-based metabolic equation achieved the hypothesized level of predictive accuracy, with RMSE and MAE values that were ≤1 MET during treadmill walking (0.7 and 0.5 METs, respectively). As MAE is a better indicator of average error,[166] the simple equation therefore predicted treadmill walking intensity within 0.5 METs, on average. This is equivalent to an error of 45 kcals/hr for the average American man and 38 kcals/hr for the average American women (Appendix B). This equation also demonstrated almost no bias (magnitude <0.01 METs). The strength of the cadence-intensity relationship observed with these data is somewhat similar to that observed by Abel et al.[27] (R^2 = 0.79), Beets et al.[31] (R^2 = 0.68), and Tudor-Locke et al.[40] (R^2 = 0.80-0.83). Comparatively weaker relationships were reported by Peacock et al.[35] (R^2 = 0.50), Marshall et al.[33] (R^2 = 0.23-0.35), and Rowe et al.[36] (R^2 = 0.34). The lower R^2 values reported in each of these latter three studies may be due to their use of a linear regression model, whereas Abel et al.[27] and Beets et al.[31] used curvilinear models. Although a linear regression model was used by Tudor-Locke et al.,[40] it may not have affected the observed R^2 values because participants completed only two walking bouts.

It should be noted that Study One's sample included fewer older adults (37 adults in Cohort 3), relative to young and middle-aged adults (76 and 80 adults for Cohorts 1 and 2, respectively). If there was a substantial effect of age on the cadence-intensity relationship, including fewer older adults in the calibration sample may have produced a simple equation that is more accurate in younger/middle-aged adults but less accurate in older adults. Still, the data used to develop and evaluate the simple equation in Study One were collected from a large sample of adults 21-81 years of age who varied in height by a factor of 1.3, body mass by a factor of 2.7, and BMI by a factor of 2.0. The utilization of this large, heterogeneous sample suggests that the simple equation (and its predictive error reported in Study One) will be generalizable to the vast majority of ostensibly healthy adults. This generalizability, along with its inclusion of cadence as the only input, make the simple equation a practical and valid tool for use in public health. However, while these features are advantageous for public health applications, they may also limit the simple equation's ability to provide precise, individualized predictions and prescriptions of walking intensity for a specific sub-population or individual.

5.1.2. The Full Cadence-Based Metabolic Equation

The rationale for developing both a simple and a full cadence-based metabolic equation was to provide two complementary tools for predicting walking intensity; one would be easier and more accessible to use (the simple equation), while the other (the full equation) required users to measure and/or input anthropometric and demographic variables but would theoretically produce individualized and therefore more accurate results. With these two options, researchers, health professionals, and members of the general public could choose the cadence-based metabolic equation that best aligns with their specific application, resources, and level of knowledge.

Using best subsets regression analysis, a full cadence-based metabolic equation was created that included leg length, age, BMI, and sex as additional predictors of walking intensity. This indicates that the model including these variables had the lowest cross-validated measure of residual sum of squares (i.e., PRESS statistic) for metabolic intensity predictions. As hypothesized, the full cadence-based metabolic equation had a lower RMSE and MAE than the simple equation during treadmill walking (Table 5). However, this <0.1 MET (0.2 mL/kg/min) difference in predictive accuracy between simple and full cadence-based metabolic equations has negligible practical significance. For example, most people would have a metabolic intensity of 8.7-12.3 mL/kg/min when walking at the 3 METs (10.5 mL/kg/min) cadence threshold determined by the simple equation, and of 8.9-12.1 mL/kg/min when walking at that provided by the full equation (according to their MAE values). These ranges are both equivalent to ~2.5-3.5 METs. Additionally, the observed differences in treadmill walking RMSE and MAE values between the simple and full equation equate to differences of only 3-5 kcal/hr for the average American man and woman. Furthermore, the simple cadence-based metabolic equation had several lower measures of predictive error than the full equation during the overground walking conditions (further discussed in section 5.2.1). Therefore, while the full cadence-based metabolic equation has additional barriers to its application and a higher user burden, it conveys little added benefit compared to using the simple equation.

Although including these additional predictor variables did not enable the full equation to predict walking intensity appreciably better on average than the simple equation (<0.1 MET differences in predictive accuracy), it did result in more substantial differences in predictions of metabolic intensity at a given cadence between individual

Table 11: Metabolic Intensity Predictions with the Simple and Full Cadence-Based Metabolic Equations.

Cadence	Simple Equation	Full Equation							
		Sex		*Age*		*Leg Length*		*BMI*	
		M	F	Min	Max	Min	Max	Min	Max
80 steps/min	8.3	8.4	8.1	8.5	8.2	7.7	9.1	9.1	7.2
100 steps/min	11.3	11.5	10.9	12.2	10.6	10.4	12.7	12.4	10
120 steps/min	16.2	16.6	15.6	17.8	14.8	15.0	18.2	17.6	14.8

Note: full equation predictions with one characteristic input as indicated and all others defaulted to male and Study One sample mean values
All units are mL/kg/min
M = Male; F = Female; Min = Study One sample minimum; Max = Study One sample maximum

participants. To quantify these differences, Table 11 presents each metabolic intensity predicted by the full equation when an individual has the minimum or maximum age, leg length, or BMI value of the Study One sample (or sex is set to male or female). Only one characteristic is set to such values while the remaining characteristics are controlled for by inputting the respective mean value for the Study One sample (Table 3) and male for sex. For example, the effect of age was examined by using the full equation to predict walking intensity for two individuals: one with the youngest and the other with the oldest age of Study One's sample, while both had a sex of male and a leg length and BMI equal to the Study One sample means. These predictions are provided for cadences of 80, 100, and 120 steps/min to represent the range of cadences measured during self-selected slow to fast walking trials (Table 7) and also includes the self-selected cadences of older adults, even during dual-task walking (i.e., spelling words backwards while walking).[145] In this analysis and at this range of cadences, the full equation predicted metabolic intensities that differed by 0.4-0.9 METs between the shortest and longest-legged individual, 0.1-0.8 METs between the oldest and youngest individual, 0.5-0.8 METs between the individuals with the lowest and highest BMI, and 0.1-0.3 METs between a man and woman. The full equation may therefore be advantageous for predicting walking intensity when an individual has more extreme anthropometric and/or demographic characteristics (i.e., older adults and very tall and/or obese individuals). Each of these variables' effect on the cadence-intensity relationship and the potential underlying mechanisms are discussed in the following sections.

5.1.2.1. Leg Length

Leg length and height have a positive relationship with step length at a given speed.[65,75,79,80] The longer step length of taller individuals results in lower cadences and rates of internal work (i.e., work for swinging limbs) at a given speed, and has been cited in several studies[63,65,79] to explain the inverse relationship between height and walking intensity (see section 2.2.2.2). In addition, seven studies[28-31,35,36,38] have reported a positive effect of height or leg length on the cadence-intensity relationship (i.e., increasing intensity are a given cadence with increasing height/leg length; see section 2.4.3.2). Similarly, leg length was included in the full cadence-based metabolic equation with a positive effect on predicted metabolic intensity that was greater at higher cadences due to a cadence-leg length interaction. This resulted in a difference between predictions for the shortest- and longest-legged individuals that was 0.4 MET (1.4 mL/kg/min) at 80 steps/min and 0.9 METs (3.3 mL/kg/min) at 125 steps/min (Table 11). The positive effects of leg length and height on the cadence-intensity relationship observed in previous studies[28-31,35,36,38] and herein may also be explained by increases in step length with increasing stature, as a greater step length would enable taller individuals to walk faster and perform more external work (i.e., work for accelerating the body's center of mass) at a given cadence, resulting in a greater metabolic intensity.

Table 12: Correlations Between Participant Leg Length and Cadence at Each Speed of Treadmill Walking.

Outcome Variable & Value		13.4 m/min	26.8 m/min	40.2 m/min	53.6 m/min	67.1 m/min	80.5 m/min	93.9 m/min	107.3 m/min	120.7 m/min	134.1 m/min
Cadence	***r***	-0.04	-0.15	-0.31	-0.46	-0.55	-0.61	-0.64	-0.71	-0.64	-0.91
	p	0.55	0.04	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	0.03

r = correlation coefficient; *p* = *p*-value

To further explore whether this mechanism may have caused the effect of leg length on the cadence-intensity relationship observed herein, the correlations between cadence at each treadmill walking speed and participant leg length and height were evaluated. Table 12 includes the correlation coefficients and *p*-values for these cadence-leg length relationships at each speed. Values were similar when height was considered as an alternative to leg length. At each speed ≥26.8 m/min (1.0 mph), there was a significant inverse correlation (p <0.05) between cadence and the leg length/height of each participant. These correlations generally strengthened as speed increased, with moderate-to-strong negative correlations (r ≤-0.50) at speeds ≥67.1 m/min (2.5 mph) and strong negative correlations (r ≤-0.70) at 107.3 and 134.1 m/min (4.0 and 5.0 mph). The correlations between cadence at a given speed and participant leg length and height at speeds ≥67.1 m/min (2.5 mph) were also comparable to those reported in previous studies (-0.66 to -0.77).[65,75,79,80] These findings provide confirmatory evidence that taller individuals had longer step lengths (and lower cadences) than shorter individuals at several of the same speeds. These taller individuals therefore tended to walk at a faster speed with the same cadence, which likely resulted in the positive effect of leg length on walking intensity in the full cadence-based metabolic equation. Furthermore, the increasing strength of this correlation with increasing walking speed indicates that taller individuals' step length was increasingly longer than that of shorter individuals at increasingly faster speeds. This is consistent with the full equation including a cadence-leg length interaction that resulted in a greater effect of leg length at higher cadences and provides additional evidence that step length mediated the influence of leg length on the cadence-intensity relationship.

5.1.2.2. Age

Several previous studies[54,83-86] have reported that older adults walk with a greater metabolic intensity than young and middle-aged adults walking at the same speed. This has been attributed to age-related declines in coordination and the motor strategies employed by older adults for preserving balance and stability (see section 2.2.2.3). In the only study that has examined the relationship between cadence and absolutely-defined intensity in older adults, Peacock et al.[35] similarly reported a positive effect of age on metabolic intensity (i.e., increasing age resulting in an increased walking intensity) at a given cadence. Studies[67,75,79,87,88] comparing only young and middle-aged adults, however, have not found such age-related differences in metabolic intensity of walking. Therefore, to further examine age's influence on walking intensity, a *post hoc* analysis of the treadmill walking dataset was conducted with participants stratified by age cohort (Cohort 1 [21-40 years], Cohort 2 [41-60 years], Cohort 3 [61-85 years]). Specifically, a quadratic least squares regression was fit to the cadence-intensity relationship for each cohort and are shown in Figure 5. These cohort-specific regressions were also used to derive cadences associated with

Table 13: Cadences Associated with Metabolic Intensities of Walking from Cohort-Specific Quadratic Regressions of the Cadence-Intensity Relationship.

Age Cohort	3 METs	4 METs	5 METs	6 METs
Cohort 1	95	110	122	131
Cohort 2	95	112	125	136
Cohort 3	100	119	133	145

All units are steps/min

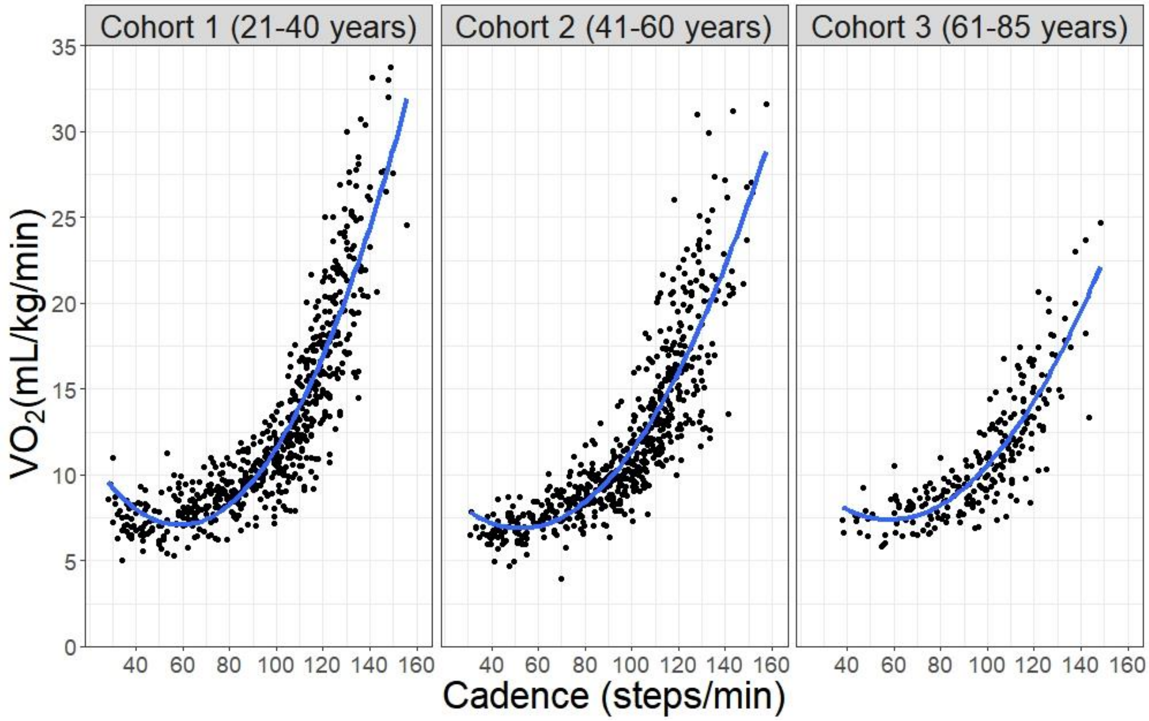


Figure 5: Cadence-Intensity Relationships During Treadmill Walking Stratified by Age Cohort.

walking at various metabolic intensities, which are presented in Table 13. The cadence-intensity relationship appeared to be similar between Cohorts 1 and 2 (0-5 step/min differences in cadences for attaining 3-6 MET). Conversely, Cohort 3 required cadences that were 5-14 steps/min higher than Cohorts 1 and 2 to walk at the same intensity from 3-6 METs (Table 13). These findings align with the 0.3-3.0 mL/kg/min lower metabolic intensity at a given cadence (from 80-120 steps/min) predicted for the youngest (21 years of age) versus oldest (81 years of age) participant in Study One when also controlling for leg length, BMI, and sex (Table 11). These age-related differences were the greatest at the highest metabolic intensities and cadences examined, with a 9 steps/min greater difference between Cohort 1 and Cohort 3 cadence thresholds for 6 METs versus 3 METs (Table 13) and a 2.7 mL/kg/min greater difference between VO_2 predictions with the minimum and maximum age at 80 versus 120 steps/min (Table 11).

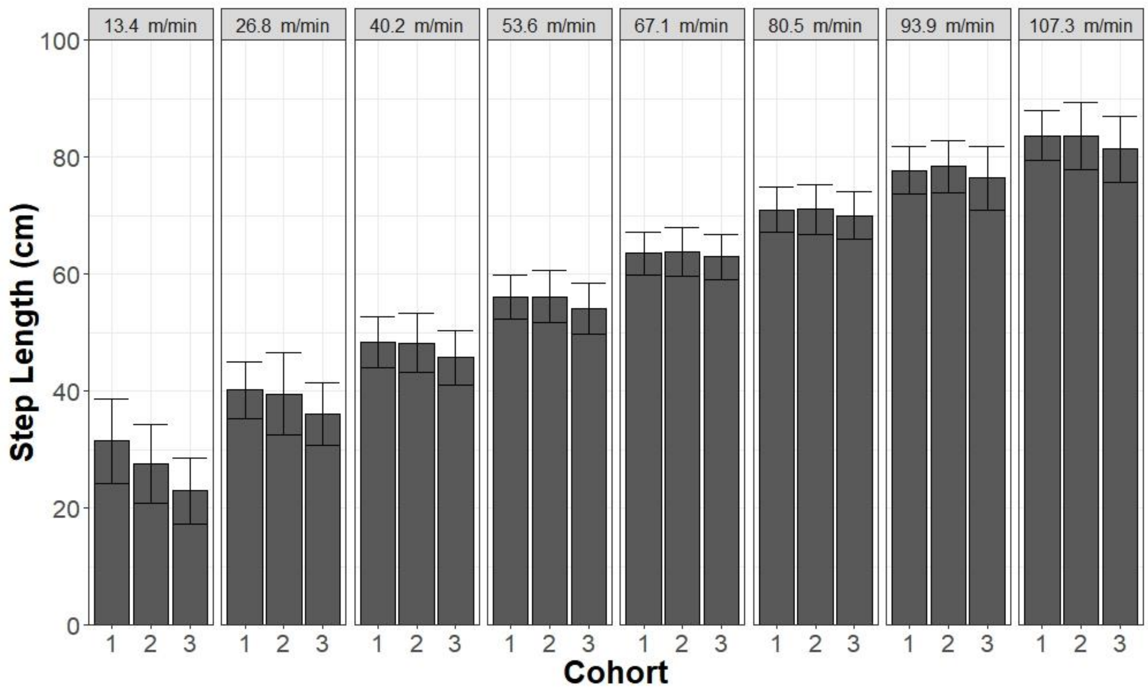


Figure 6: Average Step Length of Participants at Each Speed of Treadmill Walking Stratified by Age Cohort.

Note: error bars represent SD

The negative effect of age on metabolic intensity at a given cadence demonstrated in this *post hoc* analysis and included in the full cadence-based metabolic equation appears to conflict with previous evidence of a positive effect of age on the speed-intensity relationship.[54,83-86] However, this positive effect of age has partially been attributed to older adults walking with a significantly shorter step length and greater cadence at a given speed than young adults, in order to reduce single-limb support time and increase stability.[86] As shown in Figure 6, the average step lengths of older adults (Cohort 3) in this study were also lower (by 1-9 cm) at each speed than those of younger and middle-aged adults (Cohorts 1 and 2). The relatively shorter step lengths of Cohort 3 were especially pronounced at slower walking speeds, with differences of 4-9 cm at speeds <40.2 m/min (1.5 mph) when compared to Cohorts 1 and 2. This shorter step length indicates that older adults had a higher cadence and performed more internal work at a given speed, which aligns with the previously reported positive effect of age on the speed-intensity relationship.[54,83-86] The shorter step lengths of Cohort 3 participants also reconciles the negative effect of age on the cadence-intensity relationship observed herein; older adults tended to attain a given cadence at a slower speed and therefore while performing less external work than young or middle-aged adults. For example, the treadmill walking speed where at least half of participants reached cadences ≥100 steps/min was 53.6 m/min (2.0 mph) for Cohort 3 but 67.1 m/min (2.5 mph) for Cohorts 1 and 2. Although the data collection and analysis is not yet complete for that last age group (and outside the purposes of this thesis), we can anticipate that the average metabolic intensity associated with 100 steps/min will be lower when compared to younger participants in Cohorts 1 and 2. The article by Peacock et al.[35] that reported a positive effect of age on the cadence-intensity relationship in older adults did not provide any information pertaining to participants' step lengths or cadences at a given speed. As their sample was smaller (n = 29) and consisted exclusively of older adults that self-reported being physically-active, it is possible that they did not exhibit age-related differences in step length. Therefore, the present study provides the first evidence suggesting that older adults may require a greater cadence to obtain a given walking intensity. Because the full equation accounts for this potential effect of age on the cadence-intensity relationship, it may provide more accurate predictions of walking intensity in older adults, compared to the simple equation.

5.1.2.3. BMI

Prior studies[61,70].have reported that class II obese participants (BMI 35.0-39.9 kg/m^2) walked with greater metabolic intensities at a given speed than participants with lower BMIs. This was attributed to obesity-related mechanical inefficiencies in gait and changes in body mass distribution (see section 2.2.2.1). However, the full equation developed herein predicted greater walking intensities at a given cadence with lower BMIs, with an increasing magnitude of effect with increasing cadence (Table 11). This suggested influence of BMI is based on the Study One's sample which included 96 normal weight, 75 overweight, and 22 obese participants. Therefore, a positive BMI-intensity relationship due to obesity-related mechanical inefficiencies may not have been observed in this sample because a majority (89%) of participants were not obese. Additionally, there is evidence that walking intensity at a given speed may increase with decreasing body fat percentage due to fat-free mass having a greater metabolic demand than fat mass during PA.[76,78] This mechanism may have also caused the negative effect of BMI on metabolic intensity in the full equation. The full equation having accounted for this inter-individual variability in the cadence-intensity relationship by including BMI instead of percent body fat may reflect the inaccuracy of bioelectrical impedance for measuring body composition.[167]

A significant effect of BMI on the cadence-intensity relationship was also reported by Nielson el.[34] and Beets et al.[31] Contrary to the results of the current study, Nielson el.[34] reported that this effect of BMI was positive and greater at higher cadences but no potential mechanism for this effect was proposed. Although Beets et al.[31] indicated that BMI had a positive effect on walking intensity at lower intensities (e.g., 3 METs), similar to the full equation, they reported a negative cadence-BMI interaction that resulted in a negative effect of BMI at higher intensities (e.g., 6 METs).

In the current study, average step lengths did not differ between BMI categories by more than 3 cm at each treadmill walking speed. Compared to the 4-9 cm differences in step length observed between age cohorts (see section 5.1.1.2), the smaller magnitude of these differences indicate there were not BMI-related differences in gait parameters at a given speed. Therefore, the effect BMI exhibited on walking intensity at a given cadence, indicated by the full equation, was likely related to non-kinematic factors such as differences in the proportion of metabolically active tissue that comprised individuals' body mass.

5.1.2.4. Biological Sex

There is conflicting evidence regarding the influence of sex on the speed-intensity relationship (see section 2.2.2.1). When men and women were walking at the same speed, several studies[78,87,95,96] have reported that metabolic intensity was higher in men while others[70,97,98] have reported metabolic intensity to be higher in women. These differences may be attenuated when sex-related differences in percentage body fat and height are controlled statistically and/or by study design.[23,36,75,78] Studies[27,33,36,40,43] comparing the cadence-intensity relationships of men and women have consistently reported that men require lower cadences than women to reach 3 and 6 METs (by 3-13 steps/min and 10-11 steps/min, respectively). However, there is strong evidence that accounting for men's greater average height, relative to women, also eliminates their higher metabolic intensity at a given cadence.[28,29,36]

In the full cadence-based metabolic equation, the inclusion of sex as a predictor resulted in men having a higher predicted metabolic intensity at a given cadence compared with women. Although the direction of this effect was consistent with the results of other studies,[27,33,36,40,43] the full equation controls for leg length by including it as another predictor variable. This indicates that the observed effect of sex herein was independent from differences in stature between men and women. To further explore this unexpected finding, likelihood-ratio tests were used to compare quadratic mixed regression models of the cadence-intensity with and without sex as a predictor. When the original (null) model only included cadence, the addition of sex resulted in significantly better model fit (p <0.001). However, when the null model included cadence and leg length (i.e., when the model controlled for leg length), it was not further improved by including sex as a predictor (p = 0.28). In addition, the full equation's predictions of metabolic intensity at a given cadence differed only marginally between men and women (0.1-0.3 MET differences at 80 -120 steps/min [Table 11]). These findings suggest that there was not a significant independent effect of sex on the cadence-intensity relationship. Therefore, although selecting the model with the lowest PRESS statistic was a rational approach for developing the full equation, a more parsimonious model that did not include sex may have exhibited a similar predictive capacity.

5.2. Overground Unconstrained and Cadence-Constrained Walking

5.2.1. Effects on Equation Predictive Error and Metabolic Intensity

The cadence-based metabolic equations were developed using the data collected during treadmill walking to attempt to maximize their accuracy and generalizability, as this dataset included a larger and more heterogenous sample than the overground walking dataset. However, there is evidence that treadmill walking ground reaction forces,[107,108] muscle activity,[107,109] and gait timing[77,100-106] may differ from those observed during overground walking (see section 2.2.3). Still, as was hypothesized, the simple and full cadence-based metabolic equations remained valid when applied to data collected during overground unconstrained walking, with RMSE and MAE values <1 MET (≤0.7 METs). These values also equated to 37-60 kcals/hr for the average American man and women. Moreover, both cadence-based metabolic equations had a predictive accuracy during overground unconstrained walking that was similar (RMSE and MAE values 0.1 MET higher to 0.1 MET lower) to that observed during treadmill walking (differences ≤8 kcals/hr [Appendix B]). This suggests that the cadence-intensity relationship of treadmill walking did not differ appreciably from that of overground unconstrained walking and supports the cadence-based metabolic equations' generalizability to this more commonly performed walking condition.

Previous studies have shown that constraining cadence during overground walking may result in different gait parameters[45-47] and an elevated metabolic intensity[47,48] compared to unconstrained walking (see section 2.2.3). This evidence led to the hypothesis that the cadence-based metabolic equations would underpredict the metabolic intensity of cadence-constrained walking. However, both equations maintained their predictive accuracies during the cadence-constrained walking condition, with RMSE and MAE values that remained ≤1 MET (44-62 kcals/hr for the average American man and women) and similar (0.1 MET higher to 0.1 MET lower) to those observed during treadmill walking (differences ≤10 kcals/hr [Appendix B]). The simple and full cadence-based metabolic equations therefore appear to remain valid for determining metronome or music tempos to use when making cadence-based prescriptions of walking intensity.

Although the small differences in predictive accuracy between walking conditions are unlikely to be practically significant, there was a consistent trend for the simple and full equations to be less accurate during cadence-constrained versus unconstrained walking (RMSE and MAE values greater by <0.1-0.2 MET). There was also an interesting trend in bias between the two overground walking conditions; during cadence-constrained walking, the simple equation and ACSM Metabolic Equation were more likely to underpredict walking intensity (0.2 MET more positive bias) while the full equation was less likely to overpredict walking intensity (0.2 MET less negative bias). Both of these results could be explained by a slight (0.2 MET) elevation in walking intensity at any given cadence during cadence-constrained walking. This is similar to what was originally hypothesized. However, the small magnitude of this elevation in walking intensity did not result in practically significant effects on the simple equation's predictive accuracy and, because the full equation already tended to overpredict metabolic intensity (during unconstrained walking), these higher metabolic intensities actually reduced its magnitude of bias.

These findings align with the results reported by Wezenberg et al.,[48] who compared the metabolic intensity of normal treadmill walking (i.e., walking with only speed constrained by the treadmill) to that when additional constraints were simultaneously placed on cadence and step length (see section 2.2.3). While all trials were conducted at the same walking speed and with the same average cadences and step lengths, the authors reported that VO_2 was elevated by 8% when cadence and step length were constrained to be constant, and by 13% when they were constrained to be a real-time mimicry of their normal treadmill walking trial (i.e., exhibiting the same variability). The researchers concluded that these constraints on walking resulted in motor control-related demands (i.e., a modified ankle stabilization strategy and greater preparatory and antagonistic muscle activation) that increased metabolic intensity, even without differences in gait parameters. In the present study, a constraint was placed only on cadence (and not step length or speed) using an auditory signal from a popular commercial song to better represent a real-world application of this research. This may explain why the percent bias of the cadence-based metabolic equations differed only by ~5% between unconstrained and cadence-constrained walking conditions (Table 8), as opposed to the 8-13% increase in metabolic intensity observed by Wezenberg et al.[48] Still, the tendency of the metabolic equations to underpredict VO_2 by more (or overpredict VO_2 by less) during cadence-constrained walking suggests that entraining cadence to music tempos similarly resulted in motor control-related demands that slightly increased walking intensity at a given cadence.

The motor control-related demands of cadence-constrained walking may also underly the different trend in predictive error values observed among trials of overground unconstrained versus overground cadence-constrained walking. As the self-selected pace of unconstrained walking trials increased, predictive error of the simple and full cadence-based metabolic equations consistently increased. However, an analogous increase in predictive error with increases in music tempo was not observed in the cadence-constrained condition; predictive error was generally the lowest in the 100 BPM rather than the 80 BPM trial. This unexpected finding may be related to the prescribed cadence of 100 steps/min being closest to participants' preferred walking cadence (average cadence of 107 steps/min during the self-selected normal-paced trial; Table 7). Entraining cadence to the music tempos that represented greater deviations from participants' preferred cadence (i.e., to music tempos of 80 and 125 BPM) may have required more metabolically costly motor control-related demands (per step), resulting in greater differences between cadence-constrained and unconstrained walking intensities at these cadences.

As was found during treadmill walking, the predictive accuracies of the simple and full cadence-based metabolic equations were similar during both overground walking conditions (differences in RMSE and MAE <0.1 MET [≤0.2 mL/kg/min]). Compared to the full equation, the simple equation had actually exhibited slightly (≤0.2 mL/kg/min) lower RMSE and MAE values during overground unconstrained and cadence-constrained walking. This provides further evidence that use of the full equation does not have the intended benefit of producing more accurate predictions of walking intensity, despite requiring the additional input of individualized anthropometric and demographic predictor variables.

5.2.2. Effects on Walk Ratio

In addition to having independent effects on walking intensity, constraining a gait parameter may influence the other gait parameters that are unconstrained and self-selected. Specifically, studies[45,46] have reported that there are no to small increases in step length with increases in speed and cadence during cadence-constrained walking (see section 2.2.3). For example, Laurent & Pailhous[46] demonstrated that a 27% increase in cadence over four different RAC tempos was accompanied by only an 8% increase in cadence. This results in a decreasing walk ratio over a speed/cadence range of cadence-constrained walking, whereas there is strong evidence that the walk ratio remains constant during treadmill and unconstrained overground walking due to simultaneous and proportionally equivalent increases in cadence and step length.[49,53,54] To examine if such

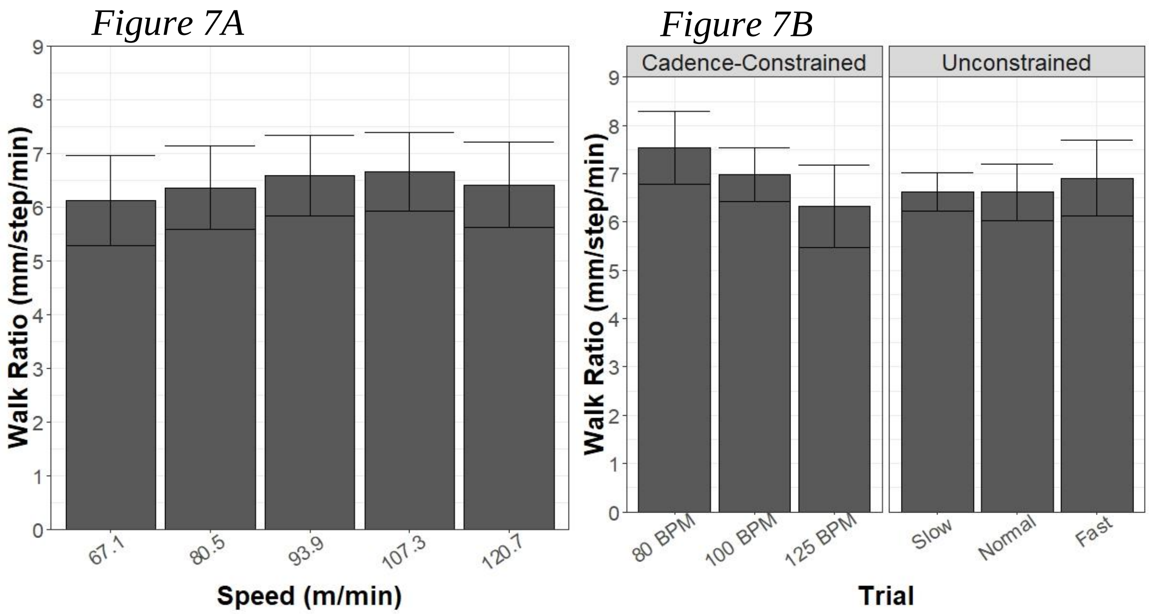


Figure 7: Average Walk Ratio for Each Treadmill (7A) and Overground (7B) Walking Trial.

Note: error bars represent SD

trends were present in the data collected herein, a *post hoc* repeated-measures analysis of variance (ANOVA) was used to test whether the walk ratio differed between trials in the unconstrained walking condition and the cadence-constrained walking condition. After applying Greenhouse-Geisser corrections to adjust for non-sphericity, there was a significant change in walk ratio during cadence-constrained walking (p <0.001), but not during unconstrained walking (p >0.05). As shown in Figure 7B, the average walk ratio of participants during cadence-constrained walking decreased as music tempo (and therefore walking speed [Table 7]) increased. These findings indicate that there were proportionally smaller increases in step length than in cadence during the cadence-constrained walking condition. The walk ratio also did not appear to change across the speeds of treadmill walking where the walk ratio has previously been shown to remain constant (60-120 m/min; Figures 5A),[53,54] although a repeated measures ANOVA could not be conducted because all participants did not complete the same number of treadmill walking trials. Nonetheless, the differences between minimum and maximum walk ratios observed during treadmill walking (0.5 mm/step/min) and overground unconstrained walking (0.3 mm/step/min) were similar and comparatively smaller than that observed during the cadence-constrained walking condition (1.2 mm/step/min). This finding demonstrates an influence of constraining cadence on gait parameters. While previous studies[45-47,122] have observed a decreasing walk ratio when entraining cadence to incrementally faster metronome tempos, the results reported herein demonstrate that this effect also exists when entraining cadence to a popular commercial song, as may be used to prescribe cadence-based recommendations for walking intensity. However, the proportionally smaller increases in step length during cadence-constrained walking suggests that participants were walking at slower speeds at a given cadence than during treadmill or overground unconstrained walking. While this implies there would be a reduction in metabolic intensity, the evidence discussed above indicates that this reduction in speed was compensated for by the additional metabolic cost of the motor-control related demands for entraining cadence to the tempo of music.

5.2.3. Age Discrepancy Between Study One and Study Two Participants

While the cadence-based metabolic equations were calibrated in participants representing ages across the adult lifespan (Study One), the data collected during

Table 14 Predictive Error of Simple and Full Equations After Re-Calibrated with Only Study One Cohort 1 Participant Data.

Walking Condition	RMSE (mL/kg/min)		MAE (mL/kg/min)		Bias (mL/kg/min)	
	Simple	Full	Simple	Full	Simple	Full
All OG	2.3 ± 2.6	2.4 ± 2.8	1.9 ± 1.4	2.0 ± 1.5	0.0 ± 2.3	-0.2 ± 2.4
UNCON	2.2 ± 2.5	2.3 ± 2.6	1.8 ± 1.3	1.8 ± 1.4	-0.3 ± 2.2	-0.6 ± 2.2
CAD-CON	2.5 ± 2.7	2.6 ± 2.9	2.0 ± 1.4	2.1 ± 1.5	0.4 ± 2.4	0.1 ± 2.6

All values are presented as mean ± SD
All OG = all overground; UNCONS = overground unconstrained; CAD-CON = overground cadence-constrained; TM = treadmill

overground unconstrained and cadence-constrained walking (Study Two) was limited to a sample of adults <30 years of age. These latter data were sufficient for accomplishing Study Two's aim of cross-validating the cadence based metabolic equations across walking conditions. Nonetheless, the results of Study Two would be strengthened by providing evidence that the reported predictive error values were not affected by the discrepancy in age between calibration and cross-validation samples.

Based on the aforementioned age-discrepancy, a *post-hoc* analysis was conducted to determine whether eliminating this age discrepancy changed the results of Study Two. Specifically, the simple and full cadence-based metabolic equations were re-calibrated (i.e., least squares regression models were fit) using only the treadmill walking data from Cohort 1 (adults 21-40 years of age). These re-calibrated cadence-based metabolic equations were then applied to the data collected during overground unconstrained and cadence-constrained walking in the same manner as in Study Two. The resulting predictive error values are provided in Table 14. When re-calibrated in this younger subsample and applied to the overground walking conditions, the simple and full equations had RMSE, MAE, and bias values that were similar to those originally reported in Study Two (all differences ≤0.1 MET; Table 8 and Table 14). Therefore, re-calibrating the cadence-based metabolic equations in participants with ages similar to those included in the cross-validation dataset did not affect the results. This *post hoc* analysis uses the data available to provide some evidence that the wider age range of the Study One sample did not have a notable influence on metabolic equation predictive error during the overground walking conditions in young adults (Study Two).

This discrepancy in age may still have implications for the interpretation of the results reported herein. As discussed previously (see section 5.1.1.), the cadence-based metabolic equations were developed in a sample that included proportionally fewer older adults(n = 37 for Cohort 3), compared to young and middle-aged adults (n = 76 for Cohort 1 and n = 80 for Cohort 2). This may have resulted in Study Two's predictive error values being lower and more similar to those reported in this *post hoc* analyses, compared to if the cadence-based metabolic equations were calibrated in a sample including more older adults. Additionally, overground unconstrained and/or cadence-constrained walking may have differences effects on the cadence-intensity relationship in older adults (i.e., an age-walking condition interaction). If so, Study Two's results may not be generalizable to older adults.

5.3. The ACSM Metabolic Equation

The ACSM has promoted the use of the ACSM Metabolic Equation since the second edition of the ACSM Guidelines for Exercise Testing and Prescription was published in 1980.[17] The ongoing dissemination of this equation is surprising given the erroneous predictions of metabolic intensity it has demonstrated previously[21,22] and herein, with RMSE and MAE values of ~1 MET or greater (Table 5) and 66-106 kcal/hr for the average American man and women (Appendix B) during treadmill walking. The ACSM Metabolic Equation also underpredicted walking intensity with a mean bias that was ~1 MET during treadmill walking and significantly different than zero during the overground walking conditions (Table 11). This systematic underprediction of walking intensity is visually apparent in the ACSM Metabolic Equation's fits to the treadmill walking and overground walking data (Figures 1B and 2B, respectively) and aligns with the results of previous validation studies.[21,22] For example, when applied to data from 409 participants aggregated from 10 studies, the ACSM Metabolic Equation underpredicted VO_2 with an SEE of 1.3 METs.[21] Another study[22] similarly reported that the ACSM Metabolic Equation underpredicted the intensity of treadmill walking at 81 m/min (3.0 mph) with SEE values of 1.2-1.7 METs. Although the direction of error was the same, these previous two studies appear to have reported a greater magnitude of underprediction potentially due to differences in sample characteristics and treadmill walking protocols, or their use of SEE instead of k-fold cross-validated RMSE, MAE, and bias.

The Bland-Altman plot presented in Figure 4A demonstrates that the bias of the ACSM Metabolic Equation increased in a seemingly linear pattern with increasing metabolic intensity of overground unconstrained and cadence-constrained walking. As shown in Appendix D, the ACSM Metabolic Equation's predictive bias also increased with increasing walking intensity during treadmill walking. The use of a linear model is a likely reason for this apparent trend, as several previous studies have reported that the speed-intensity relationship is curvilinear.[21,64,80,124,125] Similarly, in the data collected herein, including a quadratic term in a mixed regression model representing the relationship between treadmill speed and walking intensity significantly improved model fit (p <0.0001), as evaluated by a likelihood-ratio test. The ACSM Metabolic Equation may also be inaccurate because it includes a speed component that was developed with data from only three trained men.[19] The use of such a small, homogeneous calibration sample suggests that the ACSM Metabolic Equation may not be generalizable to women, adults of various ages, and populations with wider ranges in stature and BMI. This limited generalizability could also explain why the ACSM Metabolic Equation's predictive accuracy in Study One (with the more heterogenous sample) was consistently and noticeably lower than in Study Two, with 0.3-1.3 mL/kg/min differences in RMSE and MAE (Figure 3).

The results of the current study provide additional evidence that the ACSM Metabolic Equation underpredicts walking intensity by ~1 MET or more. In addition to demonstrating the limitations of this well-known equation in a large, heterogenous sample, the current study provides alternative metabolic equations that demonstrated ≥50% (≥1.4 mL/kg/min; 28-47 kcal/hr for the average American adult) lower RMSE and MAE values, and ~200% (3.0 mL/kg/min; 64-75 kcal/hr for the average American adult) lower magnitudes of bias than the ACSM Metabolic Equation during treadmill walking. Accordingly, adoption of these cadence-based metabolic equations would enable more accurate quantification and prescription of walking intensity, which may ultimately result in better adherence to walking programs[7-10] while ensuring that the health benefits of PA are accrued as anticipated.[2-6] Furthermore, walking speed is difficult to prescribe without a treadmill. For example, determining walking speed can require expensive and potentially problematic GPS technology[24] or walking a measured distance in a measured amount of time. Alternatively, cadence can be prescribed in almost any setting using a metronome or music and easily monitored by counting steps (with direct observation or a wearable device) and dividing by time. Therefore, in addition to demonstrating greater predictive accuracy, these cadence-based metabolic equations are simpler and more accessible for researchers, health professionals, and members of the general public to use.

5.4. Strengths and Limitations

A primary strength of this thesis was the use of a large, age- and sex-balanced sample of 21-81-year-old adults for the development of the cadence-based metabolic equations. The use of such a sample suggests that these equations, and their predictive accuracies reported in Study One, will be generalizable to healthy men and women of all ages. In comparison, several speed-based metabolic equations have been previously developed with considerably smaller and more homogeneous samples (section 2.3).[19,21,64,80,124,125] Additionally, previous studies[28-31,35,36,38] have highlighted the importance of accounting for anthropometric and demographic characteristics when using cadence to predict walking intensity. Not only were these variables considered herein, but the large and heterogeneous sample used for Study One included sufficient variability in participant characteristics to identify any existing effects. Additionally, multiple approaches were taken to evaluate potential influences of participant anthropometric and demographic characteristics on the cadence-intensity relationship. For example, the primary analysis examined whether including individual characteristics reduced metabolic equation predictive error for participants on average and an additional *post hoc* analysis was conducted to quantify the practical influence of each characteristic on metabolic intensity predictions (Table 11). Another strength of the methodology applied in Study One was the use of k-fold cross-validation for testing the cadence-based metabolic equations and the PRESS statistic to develop the full equation. These cross-validated measures of predictive error reflect the capacity of metabolic equations to predict walking intensity in data not included in the calibration sample (i.e., independent data), as directly relevant to research and health applications. The generalizability of the cadence-based metabolic equations was further strengthened by evaluating their predictive accuracies during overground unconstrained and cadence-constrained walking. This analysis provided explicit evidence for the validity of the cadence-based metabolic equations during potential real-world applications.

A limitation of this thesis was that the data available at the time of these analyses were incomplete for Cohort 3. Whereas 20 adults were included from each 5-year age group from 21-60 years of age (excluding the 3 participants with invalid data), data were only available for 10-13 adults per 5-year age group from 61-75 years of age, 2 adults 76-80 years of age, and 1 adult 81-85 years of age. This may have reduced the influence of age in the full equation and the results reported in Study One. Additionally, a *post hoc* analysis conducted herein (section 5.1.1.2) suggested that an effect of age on the cadence-intensity relationship existed in older but not young or middle-aged adults (Table 13). The inclusion of age in the full cadence-based metabolic equation may therefore reduce its accuracy in young and middle-aged adults, in whom age did not appear to have an effect. Nonetheless, this inclusion of age is unlikely to have an appreciable effect (e.g., a 0.1 MET difference in full equation predictions for a 30- versus 50-year-old adult at 100 steps/min) except when predicting walking intensity in older adults, as intended. The discrepancy in age between the sample in Study One and Study Two sample is a limitation that was partially addressed by showing that the results of the latter study did not differ when both samples were comprised of young adults (see section 5.2.3). Still, it is possible that walking condition (i.e., treadmill versus overground unconstrained versus overground cadence-constrained) has a greater influence on the cadence-intensity relationship in older adults. If such an age-walking condition interaction exists, the cadence-based metabolic equations could have a lower predictive accuracy during overground unconstrained and/or cadence constrained walking in older adult than was apparent in Study Two. Lastly, based on previous studies[21,22] reporting the ACSM Metabolic Equation to have a predictive error of >1 MET, we hypothesized that the cadence-based metabolic equations would be accurate relative to an RMSE and MAE threshold of 1 MET. However, the practical significance (e.g., health implications, effects on adherence to prescribed PA programs) of exhibiting predictive error above versus below this (or any) threshold is difficult to determine. For this reason, the accuracy of each cadence-based metabolic equation was compared to that of the ACSM Metabolic Equation in the same datasets. The cadence-based metabolic equations developed herein demonstrated greater accuracy than the ACSM Metabolic Equation, therefore advancing the methods available for quantifying and prescribing walking intensity.

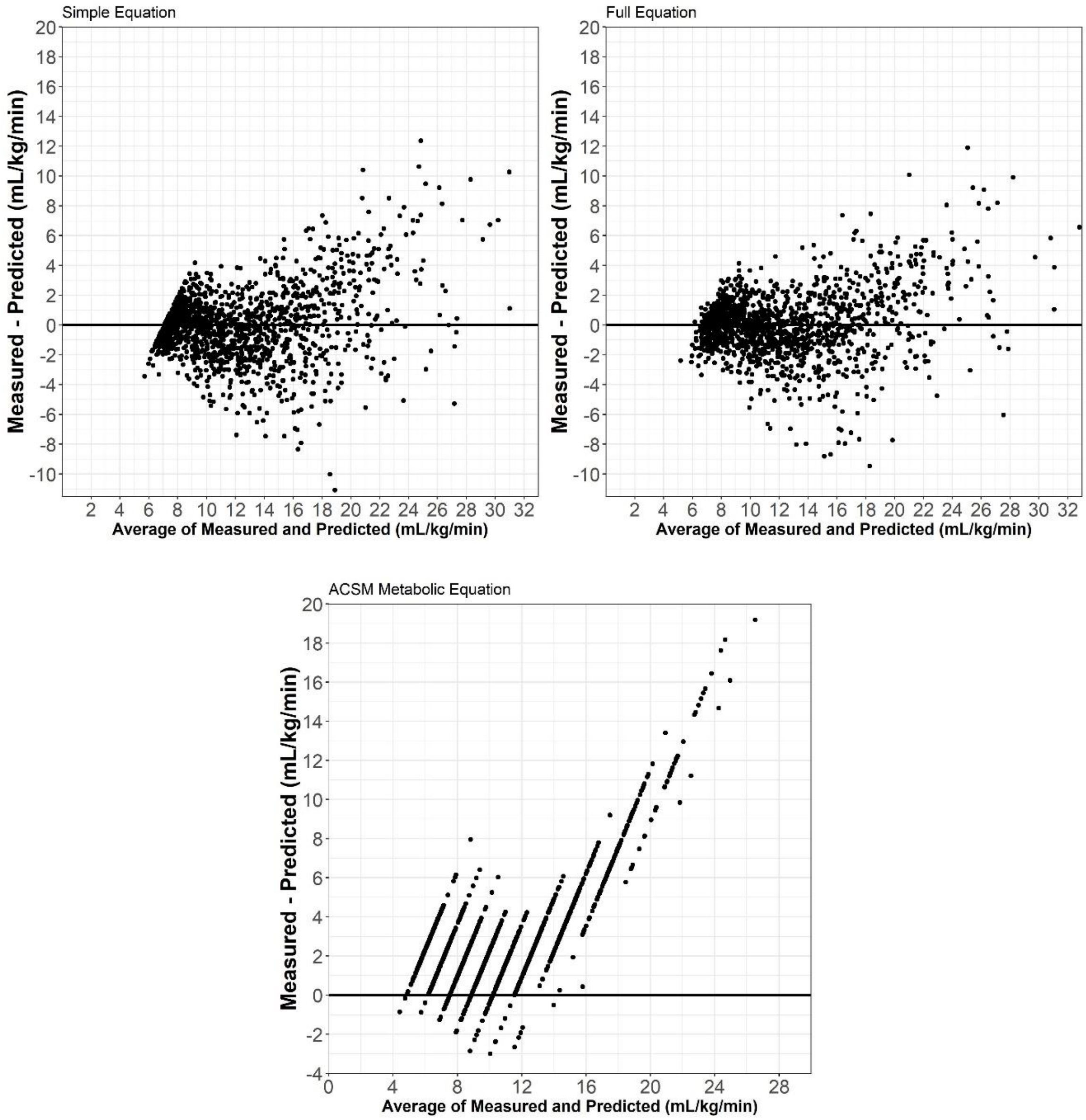
5.5. Conclusion and Future Directions

Metabolic intensity is an important consideration for ensuring that PA programs elicit the desired health benefits[2-6] while still remaining enjoyable[7] and maintaining adherence.[10] Although measuring metabolic intensity is often problematic, cadence can be easily assessed using a timer and the direct observation of steps. Using only these cadence values, the simple cadence-based metabolic equation (Eq. 2) can predict walking intensity with reasonable accuracy (within 0.5 METs, on average; within 45 kcals/hr for the average American man and 38 kcals/hr for the average American women). Contrary to what was hypothesized, this predictive accuracy was not improved by including leg length, age, BMI, and sex as additional predictors in the full cadence-based metabolic equation (Eq. 3). Using the simple equation is therefore not only easier and more practical for public health applications, but it also predicts walking intensity with comparable accuracy to the full equation, on average. The full equation may have utility, however, in adults with exceptionally short or tall statures, high levels of obesity, or an older age (>60 years of age). The predictive accuracies of the cadence-based metabolic equations also did not change when cross-validated across walking conditions. This provides explicit evidence that these equations are valid for predicting treadmill and overground unconstrained walking intensity and can be used when developing cadence-based walking prescriptions that are implemented using metronome or music tempos. Furthermore, when averaged across treadmill walking bouts, the simple and full cadence-based metabolic equations predicted walking intensity with ≥50% greater accuracy and ~200% less bias than the ACSM Metabolic Equation. Therefore, these cadence-based metabolic equations enable more accurate quantification and prescription of walking intensity while employing a metric that is accessible to researchers, health professionals, and members of the general public.

Given that the sample included in Study One included a limited number of older adults (3 adults >75 years of age), further research is needed to examine and quantify the effect of age on the cadence-intensity relationship. This older age group may also particularly benefit from cadence-based walking prescriptions that are developed using relative measures of metabolic intensity (e.g., percent $VO_{2Reserve}$ or heart rate maximum). These knowledge gaps may be addressed following the completion of the CADENCE-Adults Study.[146] Additionally, after conducting the first known comparison of the cadence-intensity relationship across walking conditions, Study Two provided preliminary evidence that walking intensity is slightly elevated during cadence-constrained walking (section 5.2.1). Future studies examining the effect of constraining cadence on the cadence-intensity relationship are needed to 1) confirm these findings, 2) examine this effect in middle-aged and older adults (and its practical significance), and 3) evaluate the persistence of this potential elevation in metabolic intensity during longer (>5 min) walking bouts. Finally, future walking interventions and PA surveillance studies are needed to implement these cadence-based metabolic equations and determine whether they actualize their potential to be acceptable and efficacious tools for conveying, prescribing, and quantifying walking intensity.

APPENDIX A

A. BLAND-ALTMAN PLOT FOR EACH METABOLIC EQUATION DURING TREADMILL WALKING



Note: 95% limits of agreement not calculated because of unequal number of bouts completed by each participant Measured = VO_2 measured with indirect calorimetry; Predicted = VO_2 predicted by ACSM metabolic equation

APPENDIX B

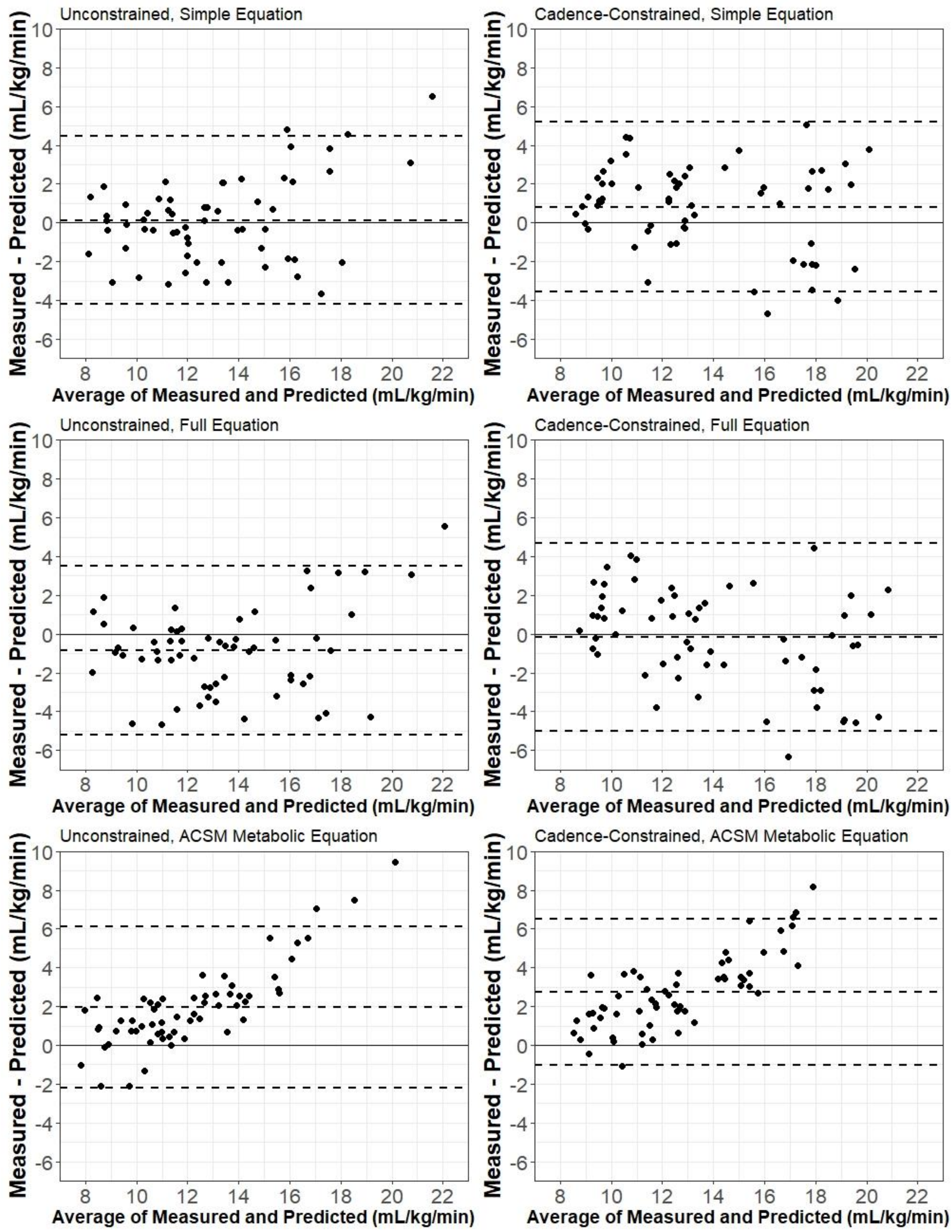
B. PREDICTED ERROR VALUES FOR EACH METABOLIC EQUATION WHEN CONVERTED TO KCAL/HR

Measure	Walking Condition	Men*			Women*		
		Simple	Full	ACSM	Simple	Full	ACSM
RMSE	TM	64 ± 7	59 ± 7	106 ± 8	55 ± 6	50 ± 6	91 ± 7
	UNCON	55 ± 68	60 ± 67	73 ± 99	48 ± 58	51 ± 58	63 ± 86
	CAD-CON	60 ± 62	62 ± 71	84 ± 93	51 ± 53	54 ± 61	73 ± 80
MAE	TM	45 ± 4	41 ± 4	77 ± 5	38 ± 4	35 ± 4	66 ± 5
	UNCON	44 ± 34	47 ± 37	55 ± 48	37 ± 30	41 ± 32	48 ± 41
	CAD-CON	51 ± 32	51 ± 36	70 ± 47	44 ± 27	44 ± 31	60 ± 40
Bias	TM	0 ± 9	0 ± 7	75 ± 6	0 ± 8	0 ± 6	64 ± 5
	UNCON	3 ± 56	-22 ± 56	50 ± 54	3 ± 48	-19 ± 48	43 ± 46
	CAD-CON	21 ± 57	-4 ± 63	69 ± 49	18 ± 49	-4 ± 54	59 ± 42

All units are kcals/hr
Values are presented as mean ± SD
TM = treadmill; UNCONS = overground unconstrained; CAD-CON = overground cadence-constrained
*calculated using sex-specific US average body mass values (88.8 kg for men and 76.4 kg for women)[94]

APPENDIX C

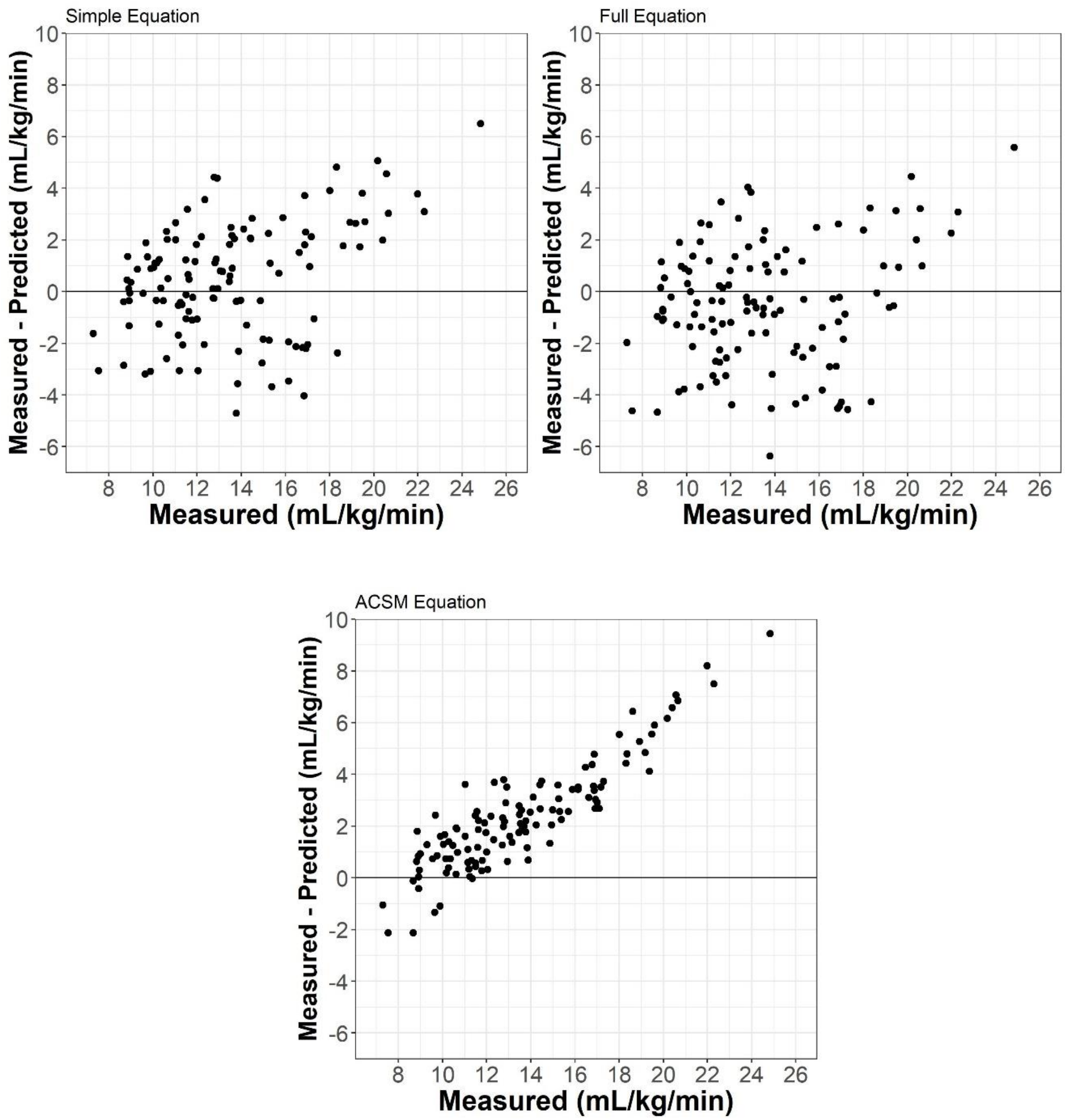
C. BLAND ALTMAN PLOTS FOR EACH METABOLIC EQUATION DURING EACH OVERGROUND WALKING CONDITION.



Measured = VO_2 measured with indirect calorimetry; Predicted = VO_2 predicted by metabolic equation

APPENDIX D

D. MODIFIED BLAND-ALTMAN PLOT FOR EACH METABOLIC EQUATION DURING OVERGROUND WALKING



Note: modified because criterion-measured VO_2 of each bout is plotted on the x-axis (instead of the average of measured and predicted VO_2)

Measured = VO_2 measured with indirect calorimetry; Predicted = VO_2 predicted by ACSM metabolic equation

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