AN ENERGY BALANCE FRAMEWORK FOR EVALUATING SELF-REPORTED METHODS FOR ESTIMATING WEIGHT CHANGE IN INDIVIDUALS

A Dissertation

Presented to

The Faculty of the Department

of Health and Human Performance

University of Houston

In Partial Fulfillment

Of the Requirements for the Degree of

DOCTOR OF PHILOSOPHY

By

Che Young Lee

August 2020

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ABSTRACT

Weight change is explained by energy imbalance between energy intake (EI) and energy expenditure (EE). Because changes in EI and EE affect each other in a dynamic way, energy deficit that is produced by changes of physical activity energy expenditure (PAEE) or EI are often smaller than predicted. However, there are sources of error in estimating energy deficit such as measures of PAEE and EI (both objective and subjective methods) as well as confounding factors that affect inconsistent estimates of EB. Subjective self-reported data have been used to collect data in large populations due to the advantages of requiring few resources and the data require little processing, but they have low reliability and validity compared to objectively measured methods. Thus, it is necessary to find and develop methods to improve the accuracy of self-reported EI and EE measurement with accounting for possible confounding factors such as initial body composition, PA history, energy balance status, and racial differences. We hypothesized that the accuracy of weight change estimation would be improved by accounting for the variability attributable to these factors at the individual level.

Therefore, this dissertation sought to identify methods to improve accuracy of estimating energy balance using self-reported EE and EI data by evaluating how various self-reported measures account for the possible confounding factors. This dissertation 1) tested accuracy for a range of predicted weight change estimation after a prescribed exercise intervention using measured and self-reported data and comparing to the observed weight changes, 2) examined how initial energy balance before participating in the exercise intervention affects the accuracy of energy balance estimates, and 3) examined the

association of racial differences with accuracy of estimation for weight changes to the intervention.

This dissertation found the predicted weight change estimations among the variety of self-reported PAEE methods were fairly consistent, with the predicted weight change by PAEE estimation using RPE being the most accurate self-reported method for estimation of PAEE used to predict weight changes after the prescribed intervention, followed by the combination of objectively measured HR and self-reported RPE. In addition, individuals showed considerable variability of estimated EB status before participating in the intervention and a small amount of positive EB before participating in the prescribed activity on average. The accuracy of predicted weight changes was improved by accounting for individual variability such as initial body composition, PA level, and especially baseline EB status. Finally, this dissertation observed racial differences of body size and composition at baseline, but race did not affect prediction of weight changes after accounting for these differences in predicting change in body weight.

The findings of this dissertation indicate that accuracy of self-reported measures can be improved to be more feasible for use and analysis in large population research settings, primarily reducing bias and improving precision by accounting for individual variability in baseline characteristics and using a validated prediction model. Investigators need to consider including individual variability at baseline to improve estimation of expected energy deficit and the development of effective weight management intervention programs.

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CHAPTER 1

1. INTRODUCTION

1.1 BACKGROUND AND RATIONALE

Obesity has been considered as a growing problem in the United States (US). About two third of adults are classified as overweight or obese, which is defined as having body mass index (BMI) greater than 25 kg/m^2 and 30 kg/m^2, respectively [1]. US adults are gaining 0.5 to 1 kilogram per year on average [2].

Weight gain is explained by energy imbalance, consistently excess energy intake (EI) over energy expenditure (EE), which is called positive energy balance (EB). In order to lose weight, therefore, it is necessary to produce negative EB, in which EE exceeds EI [3]. For losing weight, intervention programs aim to increase physical activity energy expenditure (PAEE), decrease EI, or achieve a combination of both. Since changes in EI and EE affect each other in a dynamic way, production of energy deficit by changes of PAEE or EI are often smaller than predicted [4-6], and may ultimately result in failure of weight loss goal achievement in individuals. Why does not predicted weight loss with increase of PAEE in particular seem to match with the actual weight loss? What are the possible confounding factors that result in inconsistent estimates of EB and predicted weight loss for PAEE interventions?

First, there are errors for estimating energy deficit (difference between EI and EE) for weight management depending on the measures of EE and EI used. Several objective and self-reported measurement methods have been validated and used to estimate EI and EE [7]. Objectively measured PAEE methods such as doubly labeled water (DLW), accelerometers, and pedometers are more likely to provide accurate measures of PA but also are challenging to distribute among large numbers of free-living individuals and expensive in terms of personnel, equipment, and processing costs [8]. Self-reported dietary intake via recall or food frequency questionnaires for EI and physical activity (PA) logs and categorical physical activity level (PAL) ratings for PAEE have been used to collect data in large populations, because they have the advantages of requiring few resources (e.g., staff and equipment), and the data require little processing and are thus immediately available [9, 10]. However, they may also have poor reliability and validity [11]. Especially, using a categorical general rating of PAL would have limitations due to different fitness levels among individuals. The rating of perceived exertion (RPE) scales is a valid method of rating intensity and can be feasibly collected on a large population to estimate heart rate, and thus it may help improve estimation of PAEE by using mode and duration of activities with RPE. With the growing number of epidemiology studies among free-living large populations, self-reported data is more feasible to collect and analyze. Thus, it is desirable to find and develop methods to improve the bias (systematic error) and precision (random error) of self-reported measurement to estimate EE and EI.

In addition to the measurement challenges, individual variability in EI and EE behaviors before participating in weight loss intervention should be considered as confounding factors when the effects of weight loss intervention are examined. Most studies have examined weight changes after an intervention that increases PAEE, decreases dietary intake, or does a combination of both to achieve a negative EB. Successful intervention programs are considered as those producing more weight reduction. However, initial body composition and specific changes in energy stores (fat mass [FM] and fat free mass [FFM]) also affect the rate and amount of weight changes and EB in individuals. In particular, weight loss induced by increasing PAEE to increase total daily energy expenditure (TDEE) would vary in individuals depending on initial FM and FFM [12]. At the same caloric intervention-induced negative EB, a person with higher initial FM would lose more weight eventually but take longer to reach a new EB state, compared to a person with lower initial FM [13, 14].

Initial energy balance status and PA history before entering a weight loss intervention program would also affect weight changes. Most studies of intervention programs for weight management assume, explicitly or implicitly, that participants are in EB (i.e., weight stable) and have the same PA level at baseline (i.e., sedentary or inactive). However, there could be considerable variability based on lifestyle among participants. For example, a person who is in positive EB at the start of intervention may lose less weight than would be expected by the caloric value of the intended negative EB of the intervention. For this person, the intervention program needs to produce a larger energy deficit by adding more PA or reducing caloric intake to offset the initial positive EB to achieve the intended negative EB for weight loss.

Moreover, a sedentary person may replace sedentary behaviors with the intervention PA, which results in a net increase in PAEE and TDEE. This person would lose weight if EI remains unchanged. An active person, however, may replace some or all of their habitual exercise EE with the intervention PA, which would result in a much smaller net increase in PAEE and TDEE than expected. Even if the active person adds the intervention PA without reducing their other exercise activities, there seems to be an upper limit on PA's contribution to increasing TDEE. This limit is due to compensatory reduction of other activity (non-exercise PAEE) and metabolic adaptations, such that at increasing amounts of PAEE and TDEE does not increase proportionately and may eventually reach a plateau at which adding more PAEE has no effect on TDEE [5, 15]. There is also compensatory increasing in EI in response to increase in PAEE [16]. Therefore, the information about the initial FM, EB, and PA status of individuals would be helpful to design an intervention of appropriate magnitude to achieve their weight loss goals.

Racial differences should also be considered as a potential source of individual variability when predicting EB. Racial disparities in prevalence of obesity [17, 18] and racial differences of body composition [19, 20], chronic diseases [21, 22], and behaviors [23] have been observed by many studies. These racially distributed physiological and behavioral differences would affect energy balance and its influence on energy stores, and ultimately results in different weight gain, loss, or maintenance among racial groups. Indeed, the effects of increased PAEE on weight and body composition changes vary considerably across different racial groups [24]. This result may be explained partly by various genetic factors among different racial groups that may be associated with exercise adoption and adherence [25] or physiological differences in response to prescribed exercise types and dose independent of effects of race-associated differences in body composition, energy balance (i.e., average rate of weight change), and PA, which also vary by race. Thus, to examine the racial differences response to intervention, it is necessary to control for each individual's initial (habitual) activity level and baseline energy balance and body composition.

The purposes of this dissertation were to 1) examine the accuracy and reliability of EB prediction using self-reported EE and EI data and identify potential factors related to systematic and random error (bias and precision), 2) investigate the effects of energy balance status at baseline on body weight changes after a 15-week prescribed exercise intervention, and 3) explore racial differences of weight changes response to the intervention.

1.2 RESEARCH AIMS

The primary goal of this study was to seek accurate and reliable way to predict energy imbalance in individuals, as indicated by weight changes, using self-reported EE and EI data and quantifying change in total PAEE during a prescribed exercise intervention while accounting for possible confounding factors that influence EB estimation (e.g., baseline body composition and energy balance). To achieve this goal, three studies were separately conducted. Figure 1 shows rationale, aim, and approach of each study to achieve the overall goal.

Figure 1. Overview of the proposed study

Overall Aim: To seek accurate and reliable way to predict energy imbalance in individuals by quantifying total PAEE using self-reported EE data and accounting for possible confounding factors that influence EB estimation

	Study 1	**Study 2**	**Study 3**
Rationale	• Necessary to find methods to improve the accuracy and reliability of self-reported measurement for estimating EB and weight changes	• Lack of study to consider initial EB status before participating in interventions • Need to control initial individual variability to examine the effects of intervention program on weight changes	• Unknown role of racial differences on body mass after controlling for individuals variability (initial body composition, EB status, and PA history)
Aim	• Predicting energy imbalance by estimating PAEE before and after prescribed exercise program using self-reported data • Testing reliability of self-reported PAEE and EI to estimate weight changes associated with increasing PAEE	• Investigating the effects of initial energy balance status on body weight after a prescribed exercise, accounting for initial PA history and body composition	• Examining the effects of racial differences on body weight changes after a prescribed exercise, accounting for baseline body composition, energy balance status, and PA history
Approach	• Using NIDDK Body Weight Planner program to predict PAEE and weight changes • Using HRPAS and self-reported activity logs with RPE to estimate actual PAEE and weight changes • Comparing the predicted PAEE and weight changes with actual PAEE and weight changes	• Estimating EB status before participating in a prescribed exercise intervention using self-reported weight history data • Estimating weight changes after the intervention program using methods in Study 1 with baseline EB status	• Estimating body weight changes after the prescribed exercise using the same steps with Study 2 • Comparing differences of body weight changes after the intervention program among different racial groups

PAEE: physical activity energy expenditure; EE: energy expenditure; EB: energy balance; EI: energy intake; NIDDK: the National Institute of Diabetes and Digestive and Kidney Diseases; HRPAS: heart rate physical activity score; RPE: rating of perceived exertion; PA: physical activity

In study 1, the research aim was to predict energy imbalance as indicated by change in body weight in sedentary individuals by estimating TDEE including resting EE (REE; calculated by an equation), PAEE (daily non-exercise and exercise), and other components (thermic effects of food [TEF; 10% of TDEE] and adaptive thermogenesis [AT; 14% of TDEE]) at baseline. The change in PAEE after participating in a prescribed exercise program was quantified using a variety of self-reported data and collected HR data during a 15-week exercise intervention and used to predict weight change. In addition, the accuracy (bias and precision) of using the various methods of self-report to estimate PAEE and the available self-reported EI data to estimate weight changes associated with the PA intervention were evaluated.

Hypothesis 1: Self-reported PAEE with rating of perceived exertion (RPE) would be the most accurate self-report method (lowest bias and best precision) in predicting weight change following the intervention.

In study 2, the research aim was to investigate the effects of different baseline energy balance status on body weight change following a prescribed exercise program, thus improving the accuracy of the methods identified in Study 1.

Hypothesis 1: Including energy balance status at baseline would decrease bias and increase the precision of predicted weight changes after the prescribed exercise intervention.

In study 3, the research aim was to examine the effects of race on weight change response to the prescribed exercise program, thus improving the accuracy of the methods in Studies 1 and 2.

Hypothesis 1: Changes in weight after 15-week of exercise program would differ among racial groups after controlling for initial body composition, changes in EI, and baseline energy balance.

1.3 OUTLINE

Chapter 1 is the Introduction of the dissertation. In this chapter, a brief background and the rationale of the study, overall aims and aims of each study, and the research questions and hypotheses are included.

Chapter 2 is the Literature Review, including explanation of current research on energy balance theory and weight changes in individuals, how energy balance is estimated and interpreted, Hall's model for estimation of weight changes in response to changes in energy balance, intervention programs for weight management based on energy balance theory, and factors potentially related to individual variability in energy balance and weight changes.

Chapter 3 is the Methodology. In this chapter, study design and methodology of each study are explained.

Chapter 4 is the Manuscript 1 that describes research regarding Study 1.

Chapter 5 is the Manuscript 2 that describes research regarding Study 2.

Chapter 6 is the Manuscript 3 that describes research regarding Study 3.

Chapter 7 is the Conclusion that summarizes findings of the dissertation and describes strengths, limitations, and future directions for research.

1.4 IMPORTANT TERMS AND ABBREVIATIONS

%HRR: percent of heart rate reserve

%VO2max: percent of the maximum rate of oxygen consumption during exercise

BMI: body mass index (kg/m^2)

BMR: basal metabolic rate (kcal/kg/day)

DLW: doubly labeled water

DXA: dual-energy x-ray absorptiometry

EB: energy balance

EE: energy expenditure

EI: energy intake

FFM: fat free mass (kg)

FFQ: food frequency questionnaire

FM: fat mass (kg)

HR: heart rate

HRmax: age-predicted maximum heart rate

HRex: average heart rate during exercise

HRPAS: heart rate physical activity scores

IPAQ: international physical activity questionnaire

MET: metabolic equivalent

MVPA: moderate to vigorous physical activity

NIDDK: National Institutes of Digestive and Diabetes and Kidney Diseases

PA: physical activity

PAEE: physical activity energy expenditure (kcal/day)

PAL: physical activity level

PAR: physical activity rating

REE: resting energy expenditure (kcal/day)

RMR: resting metabolic rate (kcal/kg/day)

RPE: rating of perceived exertion

TDEE: total daily energy expenditure (kcal/day)

TEF: Thermic effect of food

TIGER: Training Intervention and Genetics of Exercise Response

VO_2max: maximum rate of oxygen consumption

VO_2ex: rate of oxygen consumption during exercise

CHAPTER 2

2. LITERATURE REVIEW

2.1 ENERGY BALANCE THEORY AND WEIGHT CHANGES

Energy balance (EB) refers to the theory of maintaining the balance between the amount of energy intake (EI) and energy expenditure (EE). When one is consistently more than the other, it becomes energy imbalance, and then weight gain or loss will occur. More simply, positive energy balance, when EI exceeds EE, will result in weight gain (increase in energy stores in the form of body mass), whereas negative EB, when EE exceeds EI, will result in weight loss.

The original concept of EB was expressed in static terms. As attributed to Wishnofsky, based on his interpretation of the published results of a study of 13 subjects with obesity who were placed on a monitored diet [26], a cumulative negative EB of 3,500 kcal is needed to lose one pound of body weight, and the negative EB may be attained by decreasing EI or increasing EE or a combination of both [27]. For example, if a person wants to lose ten pounds of his weight, equivalent to 35,000 kcal in static EB terms, it could be achieved by daily 350 kcal reduction of EI for 100 days. Use of Wishnofsky’s estimate in this manner assumes that a change in one component (EE or EI) does not change or affect the other component [28].

The static concept of EB and Wishnofsky’s estimate have been under criticisms for issues of inaccuracy and overestimation of predicted weight loss [29], leading to modeling of EB as a dynamic process. The dynamic concept of EB explains how changes in factors on one component (i.e., EI) influence factors on the other component (i.e., EE), acknowledging that numerous biological and behavioral factors regulate both sides [28]. In other words, EB is dynamic with non-linear relationships and responses between EI and EE, meaning that sustained changes in one component cause changes in the other. In the example above, the person with an initial 350 kcal/day negative EB would actually lose less than expected amount of weight for the period, or it would take longer than 100 days. Table 1 shows the factors that regulate and influence EE and EI in dynamic ways (adapted from [30-32]).

Table 1. The factors that regulate and influence EE and EI.

Energy Intake (EI) Examples	**Energy Expenditure (EE) Examples**
• MVPA alters EI and food selection	• RMR increases with FFM
• Bigger body size (body mass) increases EI	• REE increases with total body weight
• Ghrelin (hormone) increases appetite	• TEF is increased by high EI
• Increases of PA increases EI	• High intensity PA increases sedentary time
	• Low EI decreases EE

MVPA: moderate to vigorous physical activity; EI: energy intake; PA: physical activity; RMR: resting metabolic rate; FFM: fat free mass; REE: resting energy expenditure; TEF: thermic effect of foods

In the dynamic concept of EB, one component change for weight change will affect the other component with biological and behavioral compensation. Restricted caloric intake without changing activity results in rapid weight loss at the beginning with negative EB by decreasing body mass stores of carbohydrate, protein, and fat and water with those components [16]. By losing body mass through caloric restriction alone, however, both FFM and FM decrease, which affect, resting metabolic rate (RMR) and resting energy expenditure (REE) (and thus total daily energy expenditure). In addition, the thermic effect of food (TEF) also decreases due to lower food consumption. Decreases in these components, RMR/REE and TEF, decreases total daily energy expenditure (TDEE) [28]. Decreased EI also may lead to a behavioral decrease in PAEE as a EE response to lack of energy for activities [33]. Combining all of these effects, particularly the decrease in TDEE, the energy deficit will be smaller than expected from the caloric value of the EI restriction. This decrease in energy deficit results in slower than expected weight loss as time increases; the weight loss is nonlinear for a fixed decrease in EI. As these compensations continue, at some point the negative energy deficit will disappear and EB will be reached at a new stable body mass.

Substantially increased EE (i.e., high intensity exercise) results in behavioral compensatory changes in EE, such as decrease of other moderate to vigorous physical activity (MVPA) or increase of sedentary time due to fatigue [34-36]. Consequently, the net increase in kcal/day from EE will be smaller than the value of the additional exercise [4], and these compensatory effects increase with the total amount of added PAEE. In addition, increased TDEE may alter energy demand and stimulate appetite hormones (i.e., ghrelin) and daily food intake, resulting in an increase of EI [37-39]. These adaptations and responses may elicit a smaller energy deficit than the value of the added PAEE, which ultimately results in failure to obtain the expected weight loss.

Changes in body composition (i.e., relative amounts of FM and FFM) by exercise lead to changes in EI and EE. In general, a 1 kg-for-1 kg increase in FFM and decrease in FM will increase RMR, which would increase TDEE [40, 41]. Because metabolically 1 kg change of FFM requires more energy than a 1 kg change of FM [42], whereas the energy density is much higher in FM than in FFM, the change in FM is more than the change FFM. More simply, it is more efficient to build or catabolize FM than FFM when either storing energy or using body mass as energy stores. Thus, exercise interventions for increasing FFM and RMR have been utilized to lose weight while maintaining or increasing FFM [43]. However, a recent review study suggested that increased FFM by exercise ultimately increase EI at EB, negative EB, and positive EB status [44]. For example, FFM while body weight maintaining stimulates increased appetite due to its higher energy demands, which is balanced to some extent by leptin inhibition from FM signaling. Therefore, the association of FFM with EI is mediated by RMR [44]. Increased FFM while losing body weight may increase EI due to disproportionally decreased FM and thus, energy demand and drive to eat to preserve and restore FFM. Finally, increased FFM while gaining body weight may increase appetite and an increase in FM, which could lead to development of insulin and leptin resistance. Thus appetite increases by increased tonic stimulation with decreased inhibitory system, which results in increased ghrelin hormone with decreased leptin that works for decrease appetite [44]. Again, the increased EI by changes in body composition may bring out smaller energy deficit than intended. Even though the created negative EB is smaller, however, maintaining FFM during weight loss has several benefits such as maintaining REE and decreasing proportion of FM, which is more likely to be successful for long-term weight loss and prevention of weight regain due to required less energy deficit [45].

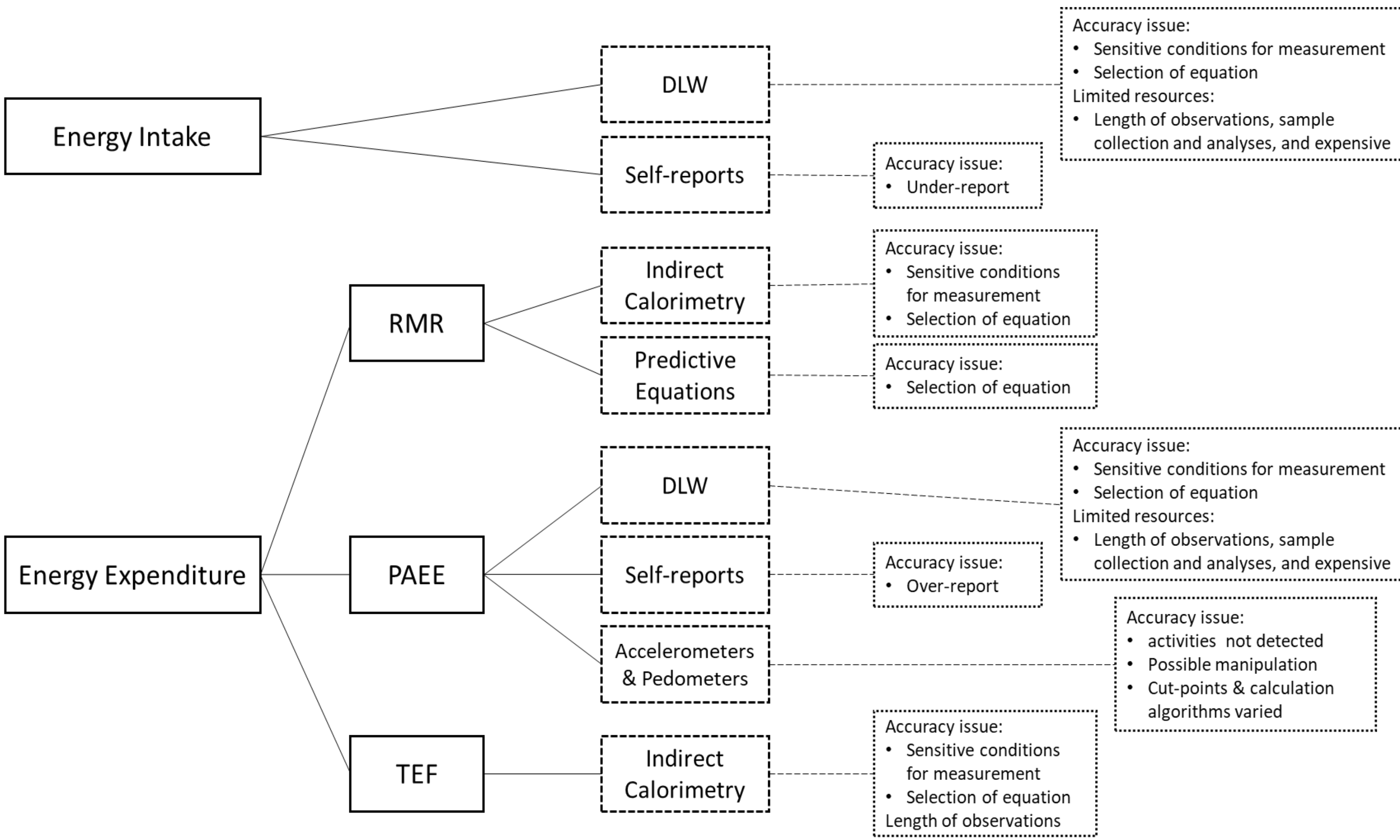
2.2 ENERGY BALANCE COMPONENTS, ESTIMATION, AND INTERPRETATION

To determine EE and EI for estimation of EB and prediction of weight changes, several methods and analytical procedures are available. Each method of measurement for

EE and EI components are described in Figure 2 (adapted from Fernandez-Verdejo, 2019 [7]).

EI is commonly assessed using self-reports such as 24-hours dietary recall, food record or dairy, and food frequency questionnaires. The 24-hours dietary recall, measuring the collection of foods consumed during the last day [46], has been used due to easy to administer [7]. However, this method needs trained interviewers and responders and is not able to measure habitual food intake using a single day of food consumption only. An average of three 24-h recalls or combination of randomly selected weekdays and weekend are recommended [47]. Food record or diary, recording the amount of all foods and beverage consumptions on daily basis for 3 to 14 days, is able to capture quantitative food consumption information by measured or weighed foods and beverage before consumption. However, it is hard to capture participants' habitual food intake since food intake may be altered during the recording period [48]. Although the food frequency questionnaires (FFQ), asking frequency of food consumptions over a specific time period (i.e., a typical week, month, or year), is one of several validated methods of dietary assessment, this method has issues of quantification for not listed food items in the questionnaire and feasibility and accuracy for recall of many days [49]. Overall, EI using those self-reported assessments commonly results in under-reporting of EI. A study showed that the average rate of under-reported EI was 28% and 15% with FFQ and 24-h recalls, respectively, among Americans [50], which is equivalent to 300 to 700 kcal/day for EI between 2000 and 2500 kcal/day. A review study also reported that self-reported 24-h recall data tended to be under-reported 16% on average when comparing with estimated EI assessed by doubly labeled water (DLW), with the assumption that estimated EE by DLW is equal to EI in weight stable individuals [51]. For this under-reporting problem, Goldberg's cut-off is suggested to use for screening of EI data [51]; if a ratio of reported EI to basal metabolic rate (BMR) is less than 1.55, the report is deemed infeasible since the EI would be below minimal TDEE as estimated using body weight [52].

Figure 2. Measurement of EE and EI and main issues



RMR: resting metabolic rate; PAEE: physical activity energy expenditure; TEF: thermic effect of foods; DLW: doubly labeled water

EE can be assessed by combination of resting energy expenditure (REE), PAEE, and TEF, which account for about 60%, 30%, and 10% of TDEE, respectively [53]. REE is estimated by measuring RMR (kcal/kg/day) using indirect calorimetry or predictive equations. Indirect calorimetry estimates substrate oxidation by measurement of gas changes between oxygen consumption (VO_2) and carbon dioxide production (VCO_2) to estimate EE using conversion equations [54]. For this method, it is suggested that individuals need to fast for more than 7 hours, rest for at least 30 minutes before testing [55], refrain from smoking (>2.5 hours before testing), refrain from caffeine/stimulants consumption (>4 hours before testing), and no exercise (>24 to 48 hours before testing, depending on intensity of exercise) to remove influence on confounding factors for estimation [7]. With such sensitive testing conditions being required to conduct indirect calorimetry, using predictive equations to calculate metabolic rate (kcal/day) is another possible error to determine individual REE or RMR [7]. Depending on what equations are using, the intra-individual difference can be up to 167 kcal/day [7], which could be critical amount of error for estimating long-term EE and EB.

Predictive equations for estimating REE are easier and inexpensive as compared with indirect calorimetry. However, the results could be less accurate and estimation of REE varies by the selection of the equation. There have been several equations for different populations, such as Italians [56, 57], Spaniards [58], North Europe athletes [59], and all populations [60], Central Americans [61], etc. Therefore, the equation should be selected for the respective population, but there will be prediction error regardless of what equation is used. In this study, the predictive equation from Mifflin et al., (1990) was used to estimate REE in individuals. This equation was tested among normal weight and obese subjects by comparing with indirect calorimetry data [62]. Mifflin's equation has been validated [63] and used [14] by researchers for estimation of REE. The equation of Mifflin et al. (1990) for REE (kcal/day) is as following [62]:

$$REE\ (Women) = 10 \times weight\ (kg) + 6.25 \times height\ (cm) - 5 \times age\ (yr) - 161 \quad \text{(Eq. 1)}$$

$$REE\ (Men) = 10 \times weight\ (kg) + 6.25 \times height\ (cm) - 5 \times age\ (yr) - 5 \quad \text{(Eq. 2)}$$

PAEE can be measured by doubly labeled water (DLW), self-report, accelerometer, and pedometer. DLW has been recognized as a golden standard to measure TDEE under free-living conditions [60]. DLW method is measuring the difference between the elimination rates of the stable isotopes, deuterium (^2H) and oxygen (^{18}O), consumed by the participant as water. The rate of CO_2 production can be estimated by this difference and used to calculate EE [64]. PAEE using DLW can be estimated by subtracting REE and TEF from the TDEE. However, there are limitations for conducting DLW such as length of observation interval, cost, and sample collection analysis procedure [65]. The TDEE to REE ratio is an index of PA, which represents the energy requirements of physical activity as multiples of REE and is known as Physical Activity Level (PAL, Table 2) [60].

Table 2. PAL categorization [66]

Level of Activity	**PAL**
Sedentary or Light Activity	1.40-1.69
Active or Moderately active	1.70-1.99
Vigorous or Vigorously active	2.00-2.40

Self-report methods for PA such as International Physical Activity Questionnaire (IPAQ), self-reported PA level, and physical activity rating (PAR) are commonly used to estimate PAEE. Using IPAQ, metabolic equivalent (MET) of the reported activities are estimated basking about occupational, transport, household, and leisure activities and sedentary behaviors for the past 7 days. The MET, the ratio between the rate of activity EE to the rate of EE at rest [60, 67, 68], with rest being 1 kcal/kg/hour and 3.5 ml of oxygen per kilogram per minute, which is approximately equivalent to the energy cost of sitting quietly. Therefore, PAEE can be estimated using MET, time of each activity, and body weight [69].

Self-reported PA level category as described by Hall et al. [14] is used to estimate PAEE by individuals reporting their activity levels from 1.4 to 2.3 (Table 3). Hall's self-reported categorical PAL consists of two parts: work/school activity (very light, light, moderate, and heavy; 0 to 3) and leisure time activity (very light, light, moderate, active, and very active; 0 to 4).

Table 3. Hall's self-reported PAL categories

		Leisure time physical activity				
Work/School physical activity		0	1	2	3	4
	0	1.4	1.5	1.6	1.7	1.9
	1*	**1.5**	**1.6**	**1.7**	**1.8**	**2.0**
	2	1.6	1.7	1.8	1.9	2.2
	3	1.7	1.8	1.9	2.1	2.3

*Participants of this study were sedentary college students, and thus "1; Light" for Work/School physical activity is expected (bolded).

One version of the PAR has seven-point scales of activity levels to categorize individual's level of PA, originally developed for use in regression equations for estimating aerobic capacity without exercise testing [70]. PAR 7-point scale ranges from 0 to 7;

0 = None (Avoids walking or exercise)

1 = Minimal activity (Walks for pleasure, routinely uses stairs, occasionally exercises sufficiently to cause heavy breathing or perspiration)

2 = Moderate activity (Participation in recreation or work requiring modest PA for 10-60 minutes per week)

3 = Moderate activity (Participation in recreation or work requiring modest PA over 1 hour per week)

4 = Vigorous activity (Runs less than 1 mile per week or spends less than 30 minutes per week in comparable PA)

5 = Vigorous activity (Runs 1-5 miles per week or spends 30-60 minutes per week in comparable PA)

6 = Vigorous activity (Runs 5-10 miles per week or spends 1-3 hours per week in comparable PA)

7 = Vigorous activity (Runs more than 10 miles per week or spends more than 3 hours per week comparable PA) [70].

Although these self-reported PAEE or TDEE data are inexpensive to use and easily distributed to large populations, self-reported data for PA also have issues with accuracy, especially over-reported PA, leading to biased estimates of EE [7, 11].

In this study, PAR was converted to self-reported PA level categories for estimation of EE using the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) online calculator described by Hall et al. [14]. Since the inclusion criteria require participants of this study to be sedentary university students, lifestyle PAEE would be ranging from 1.5 to 1.6 of PAL at baseline, assuming "Light" for work/school activity and "Very Light" or "Light" for leisure time activity. The PAEE of the exercise intervention was added to the leisure time activity component, with an assumption that work/school activity is unchanged (Table 4).

Table 4. PAR, Hall's self-reported PAL, and associated PAL categories

PAR	Hall's self-reported leisure time PAL category	PAL ratio (TDEE/RMR)^
0	Very Light	1.5
1, 2	Light	1.6
3, 4	Moderate	1.7
5	Active	1.8
6, 7	Very Active	2.0

PAR: physical activity rating; PAL: physical activity level; TDEE: total daily energy expenditure; RMR: resting metabolic rate
^In the current study, PAL ratio is estimated by "Light" for Work/School activities with Leisure time activities from "Very Light" to "Very Active".

However, because individuals have different fitness levels, using a categorical rating of overall PA has limitations. For example, if two people who rated their activities as a "very active" have different fitness levels, the person who has lower fitness (i.e., lower aerobic capacity, perhaps walks regularly) likely would do relatively lower intensity, frequency, or duration of activity, resulting in a lower PAEE, compared to a person who has higher fitness (i.e., higher aerobic capacity, perhaps runs regularly). The rating of perceived exertion (RPE) scales have been used for quantitative measured of perceived exertion during PA. RPE is a valid method of rating intensity that is highly correlated with heart rate and VO_2, and can be feasibly collected on a large population [71, 72]. Thus, RPE may help improve estimation of PAEE by using RPE with each self-reported activity and duration in combination with each person's estimated aerobic capacity to provide a caloric estimate of the activity. Borg's RPE [72] was used as self-reported intensity of exercise in this study. The Borg's RPE scale ranges from 6 (no exertion at all) to 20 (maximal exertion), as described in Table 5.

Table 5. Borg's Rating of Perceived Exertion

Rating	Perceived Exertion
6	No exertion
7	Extremely light
8	
9	Very light
10	
11	Light
12	
13	Somewhat light
14	
15	Hard
16	
17	Very Hard
18	
19	Extremely hard
20	Maximal exertion

Accelerometers and pedometers are commonly used to assess EE objectively. Accelerometers count accelerations in three orthogonal axes over a fixed time interval. Pedometers count movements of device sensors resulting from steps (e.g., walking or running). These are small devices, and thus easy to carry and wear for assessment of free-living activity. Although accelerometers have been validated by comparing to DLW estimates and have been used for many studies, count cut-points for indicating intensity of different activities can differ by the various calculation algorithms; children require different cut points than adolescents and adults, for example. Accelerometry is less reliable for the quantification of some activities such as cycling and swimming, since most of the algorithms were developed while participants were walking and running – the acceleration parameters differ greatly for non-gait activities. Finally, the accelerometer counts can possibly be manipulated (intentionally or unintentionally) by participants to produce activity counts in the absence of meaningful body movement [7].

Finally, TEF, the energy required for ingestion and digestion of foods, can be directly measured by indirect calorimetry. Like RMR, using indirect calorimetry has issues of sensitivity to conditions for assessment, long duration of measurement (up to 6 hours after consumption), and variable accuracy of caloric calculation when using different calibration equations [7]. TEF is the smallest component of TDEE, only accounting for about 10% [40, 53]. This study will also use a fixed value of 10% for TEF when calculating EE. Although this may not accurately reflect inter-person differences (i.e., a person who consumes more protein has higher TEF than a person who consumes more carbohydrates [73]), its bias in TDEE estimation would be negligible since it is a constant proportion of the sum of the REE estimate and a PAEE estimate using any of several methods.

2.3 PREDICTION OF ENERGY IMBALANCE AND WEIGHT CHANGES USING HALL'S MODEL

Weight changes can be predicted by an imbalance between EE and EI over time. There are several mathematical models for prediction of weight changes following changes of EE and EI. The simplest is the previously described Wishnofsky estimate based on the static concept of an energy deficit of 3,500 kcal to lose one pound of body weight [29]; this estimate is now widely acknowledged as being inaccurate. Acknowledging that weight changes always include changes in both FM and FFM, Forbes evaluated the cross-sectional interrelationship between in FM and FFM and reported that FFM varies as a function of FM in a consistent and predictable way, such that the magnitude of the FFM changes is inversely related to the initial FM [74]. This association can be used to predict the proportions of total weight change attributable to FM and FFM, which can be converted into caloric equivalents for each type of mass change, thus representing energy balance during the period observed.

These models, however, do not account for dynamic physiological adaptations to accurately predict weight changes over time, which produces a nonlinear change in weight for an intervention of fixed caloric value. Thomas et al. (2011) developed a mathematical model using a system of differential equations to predict weight changes as interrelated, dynamic FFM and FM changes [75]. However, her model was concerned with EI changes and did not include EE changes [76]. Finally, in a series of articles Hall developed a system of differential equations representing dynamic associations among metabolic processing of macronutrients (carbohydrate, fat, and protein) and predicting body composition and mass changes [77-79]. Hall and his colleagues also provides a web-based dynamic simulation using this weight change model for individual adults that predicts weight changes over time in response to behavioral changes such as increased PA or decreased caloric intake [14]. In the model, changes of body composition along with weight changes were considered following Forbes equation, which included the inter-relationship between FFM and FM updated for large changes in weight [80].

In this study, predicted body mass changes after the exercise intervention were estimated using the equations from the NIDDK Body Weight Planner program by Hall et al. [14]. This program calculates expected weight changes with changes in EI and/or PAEE by entering information such as height, body weight, fat mass or percentage, age, sex, and physical activity level. Since the current study included an exercise intervention, using Hall's model to predict how changes of PAEE affects weight changes and FFM and FM changes. Therefore, Hall's equations below for estimation of PAEE changes (Eq. 3), expected body weight changes until reach a new EB by exercise intervention (Eq. 4), and final body weight changes (Eq. 5) considering body composition changes (Eq. 6) are mainly used for the three studies:

$$PAEE\ (kJ/kg/day) = [(1-\beta_{TEF}) \times PAL - 1]REE/BW \qquad \text{(Eq. 3)}$$

$$\Delta BW = \frac{(1-\beta)\Delta EI - (BW_1 \times \Delta PAEE)}{PAEE_1 + \Delta PAEE + \gamma_{FFM} - \phi(\gamma_{FFM} - \gamma_{FM})} \qquad \text{(Eq. 4)}$$

$$\Delta BW_t = \Delta BW - \Delta BW e^{-t/\tau} \qquad \text{(Eq. 5)}$$

$$\tau = \frac{\eta_{FM} + \rho_{FM} + \alpha(\eta_{FFM} + \rho_{FFM})}{\gamma_{FM} + PAEE_2 + \alpha(\gamma_{FFM} + PAEE_2)} \qquad \text{(Eq. 6)}$$

Equation 3 is estimating total PAEE, including both spontaneous PAEE and exercise EE. The predictors are TEF (β_{TEF} = 0.1 representing 10% of TDEE), PAL (amount of work or school activity, i.e., all non-spontaneous PA, plus exercise activity), REE (resting EE estimated from equations in Mifflin et al. [62]), and body weight (BW). $PAEE$ is represented as a multiple of REE, divided by body weight and removing TEF (PAL scaled by 1–β_{TEF}) and REE (by subtracting 1 from PAL). The unit is kcal//kg/day, and thus it is in a metric comparable among persons of different body weights, conceptually similar to metabolic equivalents (METs) to describe exercise intensity (kcal/kg/hr). A PAL = 1.0 represents REE (excluding all EE related to movement), and a sedentary person with no non-spontaneous PA (e.g., desk job, avoids exercise) would have ~1.5 PAL.

Equation 4 estimates expected total body weight change when a new energy balance (stable weight) is attained following changes of EI or PAEE. The predictors are β (proportion of TDEE attributable to both TEF, 0.10, and adaptive thermogenesis (AT), 0.14, so β = 0.24), changes of EI (kcal/day) and PAEE (kcal/kg/day), initial body weight (kg) and PAEE (kcal//kg/day), contribution of FFM and FM to REE (γ_{FFM} = 92 kJ/kg/day and γ_{FM} = 13 kJ/kg/day, respectively), and ϕ representing the change in FM divided by change in body weight ($\phi = \Delta FM/\Delta BW$). This equation includes changes in EI and PAEE, effects of TEF and AT, and body composition changes. Because ϕ increases with initial FM and the γ_{FFM} > γ_{FM}, the difference in the right side of the denominator becomes smaller with larger FM, so the expected final ΔBW is larger for larger FM.

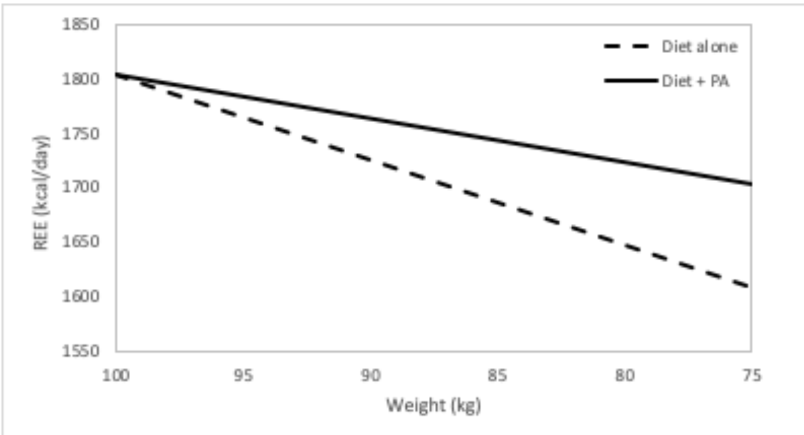
Equation 5 is estimating amount of body weight change after a specific time period (t in days) using an exponential decay model. The components are total ΔBW from Equation 4, time (~105 days for the TIGER study), and τ (timescale constant). The characteristic timescale of weight change, τ, is defined by Equation 6 and depends on the cost of fat and protein synthesis (η_{FFM} = 960 kJ/kg and η_{FM} = 750 kJ/kg, respectively), metabolizable energy density of mass change (ρ_{FFM} = 7,600 kJ/kg and ρ_{FM} = 39,500 kJ/kg, respectively), contribution of FFM and FM to REE (γ_{FFM} = 92 kJ/kg/day and γ_{FM} = 13 kJ/kg/day, respectively), PAEE of the intervention, and body composition change ($\alpha = C/FM$; where Forbes parameter, C = 10.4, divided by initial FM). The time constant (tau: τ) decreases when PAEE increases, meaning both the amount and rate of weight change increases.

2.4 INTERVENTION FOR WEIGHT MANAGEMENT USING ENERGY BALANCE

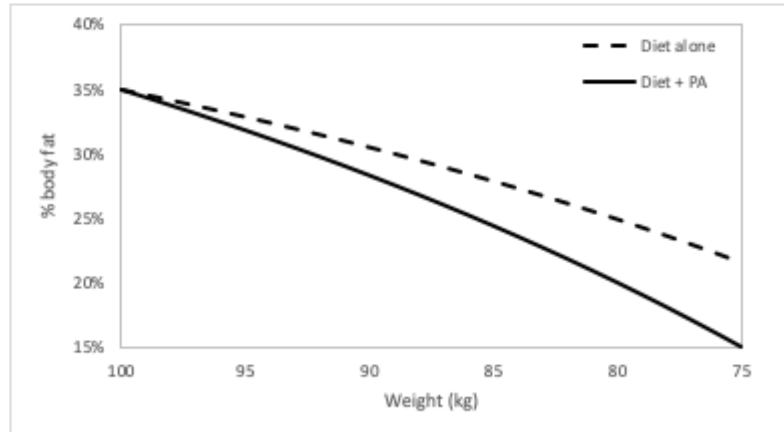
Restricted calorie intake (EI), increased PA (EE), or a combination of both have been implemented for weight management. Decreasing EI and increasing EE are not only modifiable behaviors to control weight at the individual level [81], but are also consistent with EB theory, particularly the producing of negative EB to induce weight loss [82, 83]. Diet (i.e., low fat and carbohydrates diet, daily calorie intake reduction) has been recognized as more effective for weight loss compared to PA alone intervention [84]. However, the weight loss by diet alone intervention decreases FFM, RMR, and TEF, which results in a substantial decline of TDEE [28, 85]. In terms of weight loss intervention that produces a large energy deficit, a PA only intervention would be less effective than diet only intervention, but PA helps individuals maintain FFM during weight loss [86]. In particular, PA has been recognized as a fundamental strategy for significant maintenance of health [84] and less weight gain [87], since weight gain in US adults has been associated with the decline of PA and incline of sedentary time in individuals over the past century [88]. Indeed, multiple studies have investigated that increased level of PA is associated with less weight gain compared to lower PA level [87, 89-91]. Because an accompanying loss in FFM can frequently be observed while weight loss, it is important that maintaining FFM or at least attenuating its decrease with PA. Similarly, diet with PA interventions compared to diet only could facilitate maintenance of weight loss by maintaining TDEE [92] with minimizing loss of FFM and thus maintain higher RMR [28, 43]. The Figure 3 presents these dynamic changes of REE and body composition with weight loss by diet alone and diet with PA interventions.

Figure 3. Weight loss by diet alone and diet with PA

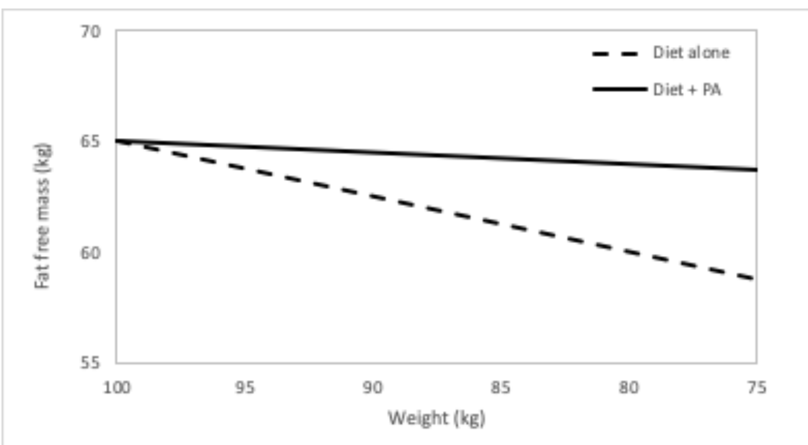
(a)



(b)



(c)



The figure 3 shows a simulated comparison of the same caloric negative EB for diet alone vs. diet + PA in changes of REE (a), percent of body fat (b), and fat free mass (c) by weight loss. The simulation assumes that 75% of weight change is FM during diet alone and 95% during diet + PA. Compared with diet alone, diet + PA preserves FFM and results in higher REE (a), lower percent of body fat (b), and maintaining fat free mass (c) for the same amount of weight loss.

However, interventions of increased PA and decreased calorie intake for weight control are not always successful. For example, individuals may lose less weight, maintain, or even gain weight or regain the lost weight after the intervention. In addition, the effects of weight management intervention are varied among individuals even if they all participate in the same intervention.

Some reasons that expected weight loss may be less than predicted are behavioral compensation and physiological adaptation in both daily EE and EI when behaviors are changed [93]. As previously mentioned, in a dynamic concept of EB, a high intensity of PA causes compensatory increases in EI due to energy needs for the PA, changes in body composition (e.g., increase in FFM), and increases sedentary behaviors due to fatigue [94]. Also, restricted food consumption results in compensatory decreases in EE [95] and increases in appetite [96], which may result in failure to maintain the decrease in EI (i.e., non-adherence to diet protocol). Weight loss can be achieved by behavioral changes, but weight loss is difficult to maintain because of the interdependent relationships between EE and EI, which may reduce the net energy gap over time. The energy gap eventually reaches 0 and plateaus at a new energy balance and body weight (i.e., weight loss no longer occurs). These mechanisms may result in failure of intended weight loss or weight regain or both. Therefore, to achieve a specific amount of weight loss and maintain the new weight, permanent changes and modifications of both calorie intake and PA are recommended [97].

Small incremental changes of each behavior have been recommended for successful long-term weight control in individuals [98]. Sudden, large changes of behavior may lead to compensatory behaviors and metabolic adaptations to maintain energy balance [97]. Also, small incremental changes are more sustainable than large lifestyle changes, so the desired health behaviors are more likely to be maintained [99]. The prescribed exercise intervention program in this study is aligned with this recommendation. Considering the participants of this study are sedentary college students, adding vigorous PA of 30 minutes per day for 3 days per week for 15 weeks (equivalent to 100 to 150 kcal/day) is a reasonable dose of prescribed exercise to expect good compliance) with minimal compensatory behaviors and adaptations.

Lastly, another potential reason for inconsistent effects of increased PA and/or decreased calorie intake for weight management interventions is individual variability. Individual variability such as physiological (i.e., FFM and FM) and behavioral (i.e., diet and PA) differences affect energy imbalance (weight changes), which leads to different positive or negative EB in individuals. For example, a person who has more initial FM would lose more weight compared to a person who has less initial FM by the same intervention [13, 14] due to a higher proportion of weight change from FM, which is equivalent to preservation of FFM, which has a higher metabolic rate [40]. In addition, for a person who is gaining weight over a long term (i.e., years), the sustained positive EB would accumulate FM, which increases appetite by inducing insulin and leptin resistance, while also accumulating FFM, which increases drive to eat by increased RMR [44], leading to sustained weight gain over time. Thus, because of the positive energy balance producing sustained weight gain at the start of an intervention, he or she would lose less weight than expected weight loss by a PA or diet intervention for producing negative EB. Therefore, unsuccessful weight loss programs could result from insufficient negative EB by not considering individual variability before entering the intervention program. More detailed contents for individual variability will be addressed in the next section.

2.5 INDIVIDUAL VARIABILITY IN ENERGY BALANCE AND WEIGHT CHANGES

Along with the compensatory mechanisms to create smaller energy deficit than expected, individual variability in energy balance at baseline is another potential reason for inconclusive effects of increased PA for weight management interventions. Baseline body composition and mass, energy balance status (i.e., a person is gaining or losing weight or weight stable), and physical activity and racial differences are possible confounding factors that affect weight changes (change in tissue energy stores) after an intervention program.

Body composition such as the relative proportions of FM and FFM is one of the physiological differences that affects changes among individuals. Since FFM and FM are both highly associated with REE and RMR but FFM has a much larger contribution, different initial FM and FFM affects variability in REE, RMR and TDEE, and ultimately weight changes [42]. Given that REE is the largest component of EE, accounting for about 60% to 70% of TDEE, for two people who have the same body weight, a person with higher proportion of FFM will have higher TDEE compared to a person with lower proportion of FFM [40, 41], because FFM has a much higher metabolic demand than FM [42].

Body mass and composition before participating in a weight loss program also affects the results. Changes in mass and body composition directly reflects changes in EB. In particular, if a person is at positive EB over time (i.e., gaining mass), a weight loss program may change the balance to be negative (i.e., losing weight) but if the intervention is insufficient to entirely offset the initial positive EB, the post-intervention EB may remain positive (i.e., continue to gain weight but at a lower rate than before intervention) or become flat (i.e., neither losing nor gaining weight during the intervention). If a person is at negative

EB before a weight loss intervention, the slope of the negative trend would be enhanced by the weight loss intervention, resulting in greater weight loss than expected. As evidence of this effect, a previous study demonstrated that participants who had lost weights immediately before an intervention showed greater weight loss after the intervention compared to participants who had not lost weight or who had gained weight before the intervention [100]. Considering baseline weight trajectory would be helpful to determine prescribed exercise dose of an intervention. For a given intervention that intends to induce a negative EB, for example, a person who is in positive EB at the start of the intervention will require more behavior change (to induce a larger caloric change) than a person who is in EB (weight stable) at the start. If the dose of intervention is insufficient to offset the entire positive energy gap, this person would not lose weight or may even continue to gain weight during the intervention, although at a rate lower than before the intervention.

When providing an exercise intervention to promote weight changes, individuals' PA history before the intervention should also be considered. Research investigations involving PA may attract persons who are already currently active ("like to exercise"), or who have been active in the past, introducing potential self-selection bias (i.e., few truly sedentary persons). To minimize selection bias, several studies have assessed the baseline PA in individuals using IPAQ or PAR to exclude the individuals who are already more active than their intervention or who are actively participating other exercise programs [101-103]. Many studies, however, do not include the estimate of baseline PA and PAL as a factor in their analyses, instead assuming that all participants have the same PAL.

The PA history may influence the intervention effect in two ways. First, an active person may replace some or all of their existing exercise EE with the intervention PAEE, resulting in a much smaller net increase in PAEE than expected. By contrast, a sedentary person is more likely to replace sedentary behaviors with the intervention activity, and thus have a greater net increase in PAEE as well as a greater potential change in weight. Second, even if the active person adds the intervention PA to their previous exercise activities, there may be a limit on PA's contribution to increasing TDEE by compensation of other activity (changes in time spent in sedentary and light activities) [15] and metabolic processes of EI [3, 4, 29]. Therefore, TDEE would reach a plateau such that further increasing PAEE has little to no effect [5]. If the intervention that creates smaller energy deficit than a person's initial activity level, moreover, this person would lose less weight than expected compared to sedentary person.

Finally, racial differences may affect energy balance, which could lead to different weight loss, maintenance, or gain among racial groups for the same intervention. Racial differences in physiological factors such as body composition (relative proportions of FM and FFM) have been observed in many studies [19, 20, 104], which would result in different responses to exercise intervention, as described previously. The different response to exercise intervention may also be related to genetic factors that affect adherence or adaptation to the intervention [25]. A recent review reported that for a given intervention African Americans consistently do not receive the same weight loss benefit as compared to other racial groups [105]. However, to our knowledge, the racial differences have been demonstrated by only comparing racial groups for outcomes after participating in the same interventions, without consideration of individuals' baseline body composition, baseline energy balance status, and PA history. These factors affect weight change response to PA and are known to differ between races. Analyzing race differences after adjusting for these factors would identify any remaining racial differences in response or adaptation to PA. Once these other factors are identified, investigators and practitioners would be able to develop and distribute adaptable intervention programs that can be optimized to promote weight loss and health for diverse populations.

CHAPTER 3

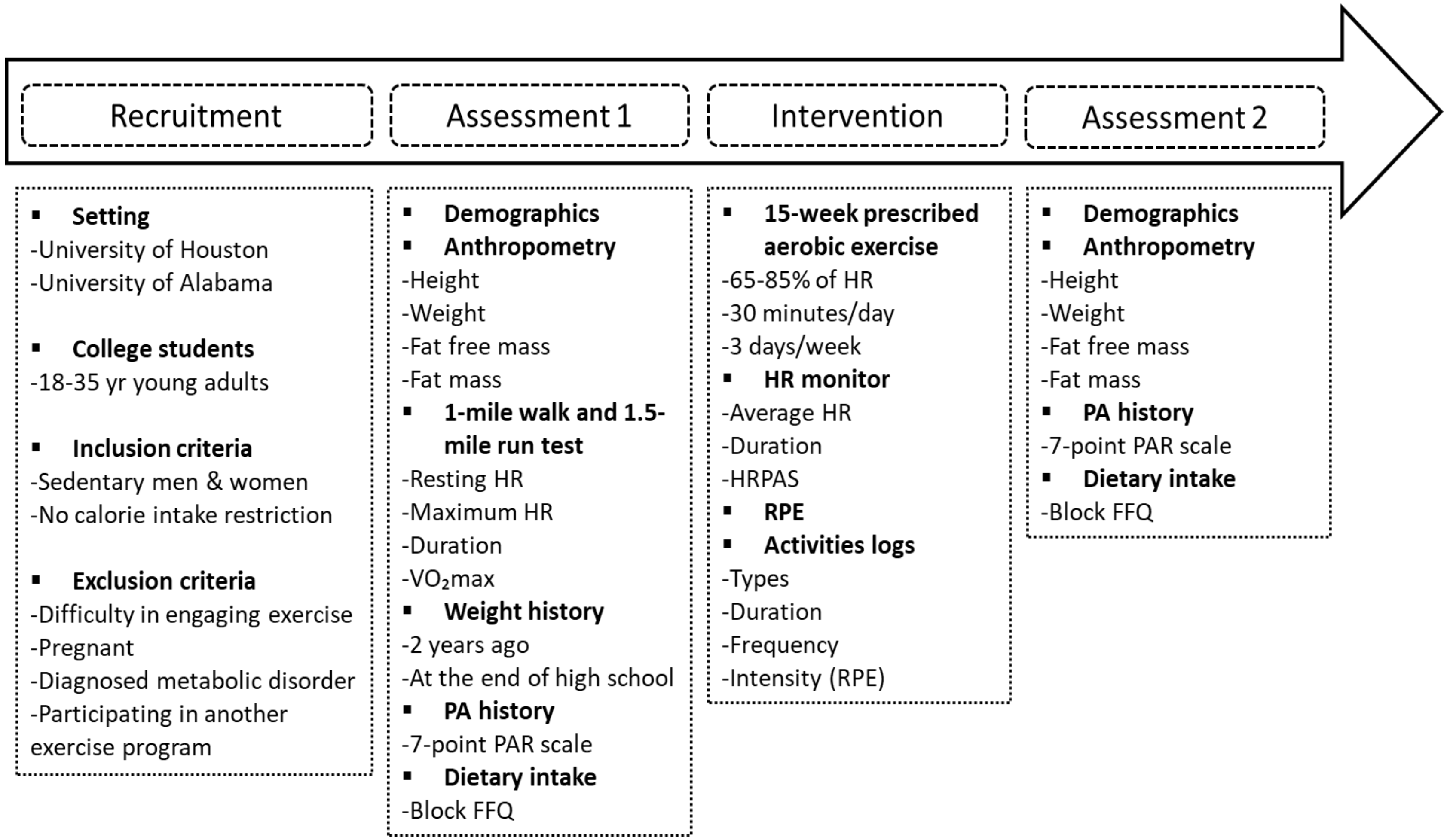
3. METHODOLOGY

3.1 STUDY DESIGN OVERVIEW

This dissertation involved secondary analyses of the data from the Training Intervention and Genetics of Exercise Response (TIGER) study [106]. The primary goal of the TIGER study was to identify genetic factors that influence on metabolism and adiposity response to the intervention in diverse college students. Between 2003 and 2015, the TIGER study implemented a program of regular prescribed exercise via a 1-semester, 3 days per week course taken for college credit. The TIGER study had one cohort each semester and two phases across a total of 10 years, with some updating and revision of methods in the second phase (i.e., adding measures, using updated versions of questionnaires, etc.). However, the design of the TIGER study was guided by social cognitive, self-determination, and self-schema theory to motivate students participating in PA and exercise [107, 108]. Data collection for the TIGER study has ended, but data analyses and dissemination are ongoing. Figure 4 depicts the timeline for the study.

The primary goal of this dissertation was to identify the most accurate and reliable way to estimate energy balance in individuals using self-reported EE and EI data, while identifying and accounting for possible confounding factors. This dissertation consisted of three studies to achieve this goal: 1) determining accuracy (bias) and reliability (precision) for a range of estimates of energy balance as determined by body weight changes after the TIGER exercise intervention using observed and self-reported data, 2) examining the effects of energy balance status at baseline on accuracy of energy balance estimates, and 3) exploring the association of race with accuracy of estimation for weight changes to the intervention.

Figure 4. Overall timeline of the TIGER study



HR: heart rate; VO_2max: maximum rate of oxygen consumption; PA: physical activity; PAR: physical activity rating; FFQ: food frequency questionnaire; HRPAS: heart rate physical activity score; RPE: rating of perceived exertion

3.1.1 PARTICIPANTS AND ELIGIBILITY

Participants of the TIGER study were 18-35 years old sedentary college students recruited from University of Houston (2003-2010) and University of Alabama at Birmingham (2011-2015). Participants were recruited via advertisements in the local and university newspapers, flyers, and other media. A five-minute presentation was also delivered in the several large lecture classes to explain the purpose, procedure, and eligibility of the study, and to encourage students considering enrolling in the study the following semester. The potential participants were sedentary students who had not exercised more than 30 minutes per week for the past month and who were not limiting caloric intake. Potential participants who were interested in this study contacted research staff who explained the study activities in detail and conducted eligibility screening. When the participants enrolled the study, they also enrolled in a 3-hour college credit course that included all of the measurement sessions as well as the prescribed exercise sessions.

Participants were excluded if they had difficulties in engaging in exercise, had diagnosed metabolic disorders, were pregnant (by self-report or pregnancy test), or were already participating in a regular exercise program within the past month (by self-reported physical activity rating). The study was approved by the Institutional Review Boards of the participating institutions, and all participants signed informed consent before data were collected.

3.1.2 MEASURES

The TIGER measures of interest for this study included demographics, anthropometry, fitness testing, dietary intake, prescribed and non-prescribed exercise, and weight history prior to enrolling in TIGER (Table 6).

Table 6. Measures of the study

Measurement	Variables	Instruments
Demographics	Age	Questionnaire
	Sex	
	Race	
Anthropometry	Height	Stadiometer (SECA Road Rod, Hanover, MD)
	Weight	Digital scale (SECA 770, Hanover, MD)
	Fat free mass	DXA (Hologic, Bedford, MA)
	Fat mass	
1 mile walk or 1.5 mile run test	Resting & Maximum HR	HR monitor (Polar Electro, Lake Success, NY)
	Duration (min) of test	
Dietary Intake	Calorie intake	Block Food Frequency Question (FFQ)
Prescribed activity	Heart rate (HR)	HR monitor (Polar Electro, Lake Success, NY)
	RPE (Phase 2 only)	Borg's Rating of Perceived Exertion (6-20 scale)
Other activities (Phase 2 only)	Mode	Online activity log; all activity, prescribed or otherwise, was to be logged describing mode, duration, intensity (e.g., jogging pace) and RPE
	Duration	
	Frequency	
	Intensity (RPE)	
PA History	PAR	0-7 point Physical Activity Rating
Weight History	Weight of 2 years ago (Phase 1), or Weight at the end of high school (Phase 2)	Questionnaire

DXA: dual-energy x-ray absorptiometry; HR: heart rate; PAR: physical activity rating

Anthropometry

Height was measured using a stadiometer (SECA Road Rod, Hanover, MD) and recorded in centimeters (cm) to the nearest 0.1 cm. Weight was measured using a digital scale (SECA 770, Hanover, MD) and recorded in kilogram (kg) to the nearest 0.1 kg. Fat mass (FM) and fat free mass (FFM) were assessed using dual-energy x-ray absorptiometry (DXA) (Hologic, Bedford, MA). Height and weight were measured at two time points, before and after the 15-week prescribed activity intervention, but weight was measured at two interim time points during the intervention period (four measurements total).

Resting heart rate and 1 mile walk and 1.5 mile run test

The resting heart rate (HR) was measured after participants were sitting at rest for at least 5 minutes. The resting HR was measured for 20 seconds three times and recorded as the average of the three measurements. Participants then performed a 1 mile walk or 1.5 mile run test. The maximum HR during performance (beats/min) and duration of the walk or run test (min) were recorded. VO_2max (ml O_2/kg/min) from maximal walk and run test was estimated using the equations by Kline et al. [109] and Baumgartner et al. [110] (revised from [111]), respectively.

$$VO_2max\ (walk) = 132.853 - (0.0769 \times weight) - (0.3877 \times age) + (6.315\ [if\ male]) - (3.2649 \times Time) - (0.1565 \times HR) \quad \text{(Eq. 7)}$$

$$VO_2max\ (run) = 3.5 + 483/time \quad \text{(Eq. 8)}$$

However, this field test with untrained sedentary participants may have limitations for estimating maximal oxygen consumption during the walk and run test. The estimated VO_2max using the equations above (Eq. 7 and 8) may be not appropriate to use if the test was not representative of the true maximum effort of the participants. Therefore, the Astrand-Ryhming single state method of estimating VO_2max was used [112]:

$$VO_2max = \frac{VO_{2ex}(HR_{max} - k)}{HR_{ex} - k} \quad \text{(Eq. 9)}$$

where k = 63 for men and 73 for women. HR_{max} is age-predicted maximum HR (220 – age), and HRex is HR at the end of the walk or run test. The VO_{2ex}, oxygen consumption during the exercise test, as determined by the walk or run speed, can be used to estimate VO_2max using the Equation 9.

Self-reported food intake

Dietary intake was assessed using Block Food Frequency Questionnaire (FFQ, NutritionQuest, Berkeley, CA) before and after the intervention [113]. Participants were asked to report the frequency of consumption of 102 food items. The frequency that each food item was consumed during a typical week was rated using nine categories, ranging from “never” to “every day”. Total food intake was converted to a weekly calorie intake (kcal) using the Block’s standard scoring service (https://nutritionquest.com/assessment/pricing-and-ordering/).

Self-reported physical activity

Physical activity rating (PAR) was assessed by having participants rate their activity levels, ranging from 0 (None; No activity) to 7 (Vigorous; Runs over 10 miles or 3 hours of comparable PA per week) [70]. Participants also reported all physical activities during the entire intervention period, including the TIGER-prescribed exercise as well as additional activity outside of TIGER sessions using an online activity log. The modes (i.e., running, elliptical, weight lifting, etc.) and duration of exercise were reported by participants as well as intensity by a rating of perceived exertion (RPE) ranging from 6-20 for each activity [72]. The RPE of self-reported activity was reported only by participants in Phase 2.

Weight History

Weight history was reported by participants using a questionnaire. The two different study phases (i.e., Phase 1: University of Houston; Phase 2: University of Houston and University Alabama at Birmingham) used different questions about weight history. Participants reported their body weights either of 2 years ago (Phase 1) or when they were at the end of high school (Phase 2).

3.1.3 Prescribed Exercise Intervention

The TIGER study implemented 15-week prescribed aerobic exercise, 3 days per week for 30 minutes per day at a sustained 65%-85% of age and sex-specific predicted maximum heart rate reserve [114]. Participants had a choice of mode of aerobic exercise, including treadmill, stair climber, stationary bicycle, or elliptical trainer. They could choose the same or a different mode for each session. Exercise sessions were monitored by recording attendance and issuing a HR monitor for each session, but the activity was not supervised during the session, which resulted in variability in frequency, duration, and intensity of exercise.

During every session of the prescribed activity, heart rate (HR) was monitored using HR monitors (Polar Electro, Lake Success, NY). The recorded HR data during the prescribed activity were downloaded for each participant after each session. Then, this recorded HR data was matched with participants' attendance records. For either missing or unusable average HR data for each session due to a malfunction of the HR monitor, the data were imputed using the within-participant distributions of HR and duration across other valid sessions, which requires at least 60% of all possible exercise session for each subject [115].

3.2 METHODOLOGY FOR STUDY 1

In Study 1, several methods of predicting energy balance, as indicated by predicted change in body mass following an exercise intervention, were compared to actual change in body mass. Changes in body mass represent positive (mass gain) or negative (mass loss) energy balance; a short-term exercise intervention that introduces new PAEE should result in a negative energy balance if no other behaviors change.

Predicted body mass changes after the exercise intervention were estimated using the equations from the NIDDK Body Weight Planner online calculator, as described in the appendix of Hall et al. [14]. This program calculates expected weight changes for adults with changes in EI and/or PAEE by entering information such as height, body weight, fat mass or percentage, age, sex, and physical activity level (PAL), which is expected to be 1.5 to 1.6 at baseline for the sedentary TIGER participants. Using the equations by Hall (2011), participants' expected weight changes after exercise intervention would be expected to increase PAL to 1.7-2.0. The equation for estimating PAEE [14] (Eq. 3) is:

$$PAEE\ (kJ/kg/day) = [(1 - \beta_{TEF}) \times PAL - 1]REE/BW \qquad \text{(Eq. 3)}$$

β_{TEF} is 0.1, the thermic effect of food, approximated as 10% of TDEE. REE was calculated using equations by Mifflin et al.(1990) [62].

The baseline PAEE ($PAEE_1$) was estimated using self-reported PAR at baseline by converting into PAL, the metric required to use the equations of Hall et al. The PAEE during 15 weeks ($PAEE_2$) was estimated by converting into PAL using five different methods: 1) categorizing into PAL using Hall's PAL categories for 15-week prescribed activity, 2) categorizing into PAL using self-reported PAR after 15-week prescribed exercise, 3) calculating PAL as a ratio (TDEE/RMR) rather than a category by using compendium MET values of the prescribed and self-reported activity with body mass (kg), and duration (min) for each reported activity to estimate PAEE [68, 69], 4) calculating PAL ratio using the self-reported RPE for the prescribed and self-reported activity the participant's estimated aerobic capacity and duration for each reported activity to estimate PAEE, 5) calculating PAL ratio using measured HR for prescribed activity plus RPE for non-prescribed activity.

For the first method, Hall's PAL categories were used to estimate the amount of PAEE including only the prescribed activity. Hall's PAL method uses two sections that describe activity: PA at work or school, and PA at leisure time [14]. Because participants in this study were sedentary college students, "Light" activity was assumed for PA at work or school, and "Active" for PA at leisure time (for prescribed activity), which indicates a 1.8 PAL for all participants during the intervention.

For the second method, self-reported PAR by participants after the 15 weeks of only the prescribed exercise was used to estimate PAEE. Using Table 3, it was expected that PAR was converted into a PAL ranging from 1.7 to 2.0 depending on the individual variability of self-reported frequency and intensity of the prescribed activity.

From the third method, the prescribed activity and activities other than the prescribed activity was included to estimate total amount of PAEE and PAL. Mode and duration of activity were used to identify the respective compendium MET value, which was then combined with body weight to estimate calories expended for each activity [68, 69]. For example, if an individual who has 70 kg of body weight does a walking activity at 3.5 mph (4.3 METs) for 30 minutes, the caloric value is 158 kcal, using the equation:

$$METs \times 3.5 \times body\ weight\ (kg)/200 = kcal/min \quad \text{(Eq. 10)}$$

30 minutes of walking at 3.5 mph (4.3 METs):

4.3 × 3.5 × 70 /200 = 5.26 kcal/min × 30 min = 158 kcal

The calculated PAEE (kcal) was added to the estimated baseline TDEE kilocalorie value and divided by REE to calculated total PAL. For example, if a person who is sedentary has 1500 kcal/day of REE, this person's TDEE is 2400 kcal (sedentary activity is 1.6 PAL = REE*1.6 = 1500*1.6 = 2400), or 100 kcal/hr. This person does 1 hour and 500 kcal of exercise per day, replacing 1 "normal" hour (100 kcal) with 1 "exercise" hour (500 kcal). The new TDEE is 2400 – 100 + 500 = 2800 kcal. To estimate PAL, the 2800 kcal/day is divided by 1500 kcal/day, which is 1.87 PAL. If the 1 hour of 500 kcal exercise is done only 3 days/week, the revised TDEE = [2400*4 (non-exercise days) + 2800*3 (exercise days)]/7 = 18,000/7 = 2571 kcal/day, or 2571/1500 = 1.71 PAL. This approach was also used for the fourth and fifth methods, which compute PAEE using RPE alone and then HR measures plus RPE, respectively, to estimate PAEE.

In the fourth method, self-reported RPE for prescribed and other activities was used to estimate PAEE using the participant's estimated maximum aerobic capacity from the 1-mile walk and 1.5-mile run test and the self-reported duration for each reported activity. The RPE was used to estimate the percent of heart rate reserve ($\%HRR$) and $\%VO_2max$ using the equation:

$$\%HRR = \%VO_2max = (RPE - 6)/14 \quad \text{(Eq. 11)}$$

where RPE is ranged from 6 to 20, which is 0% to 100% of HRR. Then, the Astrand-Ryhming single stage method, which estimates VO_2max in mlO_2/kg/min using exercise VO_2 (VO_{2ex}), $\%HRR$ ($\%VO_2max$), and VO_2max was used [112]:

$$VO_{2ex} = \%VO_2max \times VO_2max \qquad \text{(Eq. 12)}$$

where the VO_2max was estimated from the 1 mile walk test or 1.5 mile run test using Equation 9.

The averaged HR during activity (HR_{ex}) was estimated using the equation:

$$HR_{ex} = \%HRR\ (\%VO_2max) \times (HR_{max} - k) + k \qquad \text{(Eq. 13)}$$

where k = 63 for men and 73 for women, and HR_{max} is the age-predicted maximum heart, adapted from the Equation 9 and 13. For example, if a man who has 200 bpm of maximum HR and reports 15 of RPE, this person's HR during the activity (HR_{ex}) was:

$$HR_{ex} = (RPE - 6)/14 \times (HR_{max} - k) + k$$

$$= (15 - 6)/14 \times (200 - 63) + 63 = 151 \text{ bpm}$$

Then, the estimated VO_{2ex} (ml/kg/min) can be converted into kcal/min: 1) multiply mlO_2/kg/min by the individual's body weight in kg, then divide by 1000 (mlO_2/min to LO_2/min), and 2) LO_2/min multiply 5 (LO_2/min to kcal/min, 5 kcal per LO_2). Using the same example above of the man who has 70kg of body weight and 40 ml/kg/min of VO_2max who runs for 30 minutes, the expended kilocalories of activity (kcal) estimated from RPE was:

$$kcal = \frac{VO_2max \times [(RPE - 6)/14] \times kg \times min \times 5}{1000} \qquad \text{(Eq. 14)}$$

$= 40\ mlO_2/kg/min \times [(15 - 6)/14] \times 70\ kg \times 30 \times 5\ /\ 1000$

$= 270\ kcal$

As showed in the example in the third method, calculated PAEE (kcal) of every activity was added into kilocalorie value of PAL at work or school ("Light" activity) and divided by REE to calculated total PAL, as well as TDEE (kcal/day).

To estimate PAEE with the fifth method, measured HR for prescribed activity and RPE for non-prescribed activities were used to estimate PAEE. The averaged measured HR and total duration (min) for prescribed activity were used to estimate $\%VO_2max$, and expended kilocalorie (kcal) for the prescribed exercise across the entire intervention period using the equation:

$$kcal = \frac{VO_{2max} \times (Averaged\ HRex - k) \times kg \times min \times 5}{(220 - age - k) \times 1000} \qquad \text{(Eq. 15)}$$

For example, if a man who is 20 years old and has 70kg of body weight and 40 ml/kg/min of VO_2max participated in the prescribed exercise with an average HR and total minutes of exercise of 160 bpm and 2,500 minutes, respectively:

$$kcal = \frac{40\times(160-63)\times70\times2500\times5}{(220-20-63)\times1000} = 24{,}781\ kcal$$

Therefore, the expended prescribed EE (kcal/day) was divided by the total number of days of prescribed exercise, 24,781/ 70 days = 354 kcal/day. The estimation of PA other than prescribed TIGER exercise was estimated using self-reported RPE for each activity that was calculated as kcal using individual's VO_2max, $\%VO_2max$, duration of activity, same as the fourth method.

Using Hall's equation (Eq. 4) below, expected total weight change was estimated if the same exercise dose continues over an indefinite period of time until reaching a new stable body weight (i.e., energy balance = 0), first without an estimate of change in EI (ΔEI =0) and then with an estimate from the TIGER data. The estimate without ΔEI assumes diet was unaffected, such that all changes in body weight are attributable to the exercise intervention. Although the TIGER study intended to increase PA by prescribed activity while maintaining dietary intake, it is possible that EI changed due to dynamic inter-relationships between EE and EI after increasing PAEE. Previous research has observed dietary changes following a prescribed exercise intervention [116]. Thus, including ΔEI may increase the accuracy of the estimate, if EI changed during the intervention. Failing to account for ΔEI may be a substantial source of error when evaluating effects of PA interventions on body weight. The ΔEI was computed as the difference between baseline and 15-week EI estimates from the Block FFQ.

$$\Delta BW = \frac{(1-\beta)\Delta EI-(BW_1\times\Delta PAEE)}{PAEE_1+\Delta PAEE+\gamma_{FFM}-\phi(\gamma_{FFM}-\gamma_{FM})} \qquad \text{(Eq. 4)}$$

Then, body weight changes after 15 weeks of TIGER intervention (i.e., the portion of the total change in Eq. 4 expected to occur in the initial 15 weeks) were estimated using the equations below, which represent the exponential decay function predicting BW at time = t and the characteristic time constant (τ) for the predicted nonlinear rate of weight loss given the initial body weight and body composition, and the change in PAEE. Each parameter of the equations is described in the Table 7.

$$\Delta BW_t = \Delta BW - \Delta BW e^{-t/\tau} \qquad \text{(Eq. 5)}$$

$$\tau = \frac{\eta_{FM}+\rho_{FM}+\alpha(\eta_{FFM}+\rho_{FFM})}{\gamma_{FM}+PAEE_2+\alpha(\gamma_{FFM}+PAEE_2)} \qquad \text{(Eq. 6)}$$

Table 7. Definition and description of each parameter of the equations (Eq. 4, 5, and 6)

Parameters	**Definition and Description**
$\boldsymbol{\beta}$	$\beta = \beta_{AT} + \beta_{TEF}$ (β_{AT} = 0.14, β_{TEF} = 0.1, and thus, β = 0.24), β_{AT} is 0.14, the proportion of TDEE attributable to adaptive thermogenesis
$\boldsymbol{\Delta EI}$	The difference of EI between at baseline (EI_1) and 15-weeks (EI_2)
$\boldsymbol{\Delta PAEE}$	The difference of PAEE between at baseline ($PAEE_1$) and 15-week ($PAEE_2$)
$\boldsymbol{\Delta BW}$	Expected change in BW (kg) until reach a new weight stable by the same exercise dose
$\boldsymbol{\phi}$	Composition of body weight change = $\Delta FM/\Delta BW$ = $FM_1/(C + FM_1)$, where FM_1 is initial FM, C = 10.4 is the Forbes parameter [14, 74]
$\boldsymbol{\Delta BW_t}$	ΔBW_t represents body weight at time= t (days after the baseline)
t	*t* is the time, a number of days (e.g., *t* = 105 days for 15 weeks)
$\boldsymbol{\tau}$	τ is time constant of weight change (Eq. 6)
$\boldsymbol{\eta_{FM}}$	η_{FM} is 750 kJ/kg, representing cost of fat synthesis
$\boldsymbol{\eta_{FFM}}$	η_{FFM} is 960 kJ/kg, representing cost of protein synthesis
$\boldsymbol{\rho_{FM}}$	ρ_{FM} is 39,500 kJ/kg, representing energy density of 1-kg change in FM
$\boldsymbol{\rho_{FFM}}$	ρ_{FFM} is 7600 kJ/kg, representing energy density of 1-kg change in FFM
$\boldsymbol{\alpha}$	α is C/FM (Forbes parameter, C = 10.4) divided by initial FM, representing the association of ΔFFM to ΔFM
$\boldsymbol{\gamma_{FFM}}$	γ_{FFM} is 92kJ/kg/day, representing the contribution of FFM to REE
$\boldsymbol{\gamma_{FM}}$	γ_{FM} is 13kJ/kg/day, representing the contribution of FM to REE

Statistical analysis

Descriptive statistics were conducted to quantify participants' demographics (i.e., age and sex), anthropometry (i.e., height, weight, FFM, and FM), and PAR at baseline, as well as changes of weight, FFM, FM, and PAR between before and after the 15-week prescribed activity intervention. Paired t-tests were utilized to test the accuracy of the frequency, duration, and intensity of self-reported methods (3 and 4) for the TIGER prescribed activity by comparing with the observed frequency, duration, and intensity. All values were presented as mean and standard deviation (SD).

The observed weight changes during 15 weeks were estimated using the simple difference ($kg_{final} - kg_{baseline}$) as well as a fixed effects regression model. Each participant (i = 1 to N) has 4 body weight measurements during the intervention period, and thus we can estimate the rate of weight change (i.e., kg/day) over that same period. The intercept (representing expected body weight at baseline) and slope (representing kg/day body weight change) of a regression line describing weight change were included as fixed effects parameters in the fixed effects model. The actual days from baseline for each participant's body weight measurements were used as the day (t = 0 [baseline day] to D [last measurement day for participant i]) scale.

$$Weight_{it} = Intercept_i + (Slope_i * day_t) + e_{it} \qquad \text{(Eq. 16)}$$

The residuals, e_{it}, represents the deviations of each participant from their individual regression line at time t.

This model provides a participant-specific slope (rate of weight change, kg/day) estimate as well as the participant-specific standard error (SE) of that rate, both of which will be saved to the data file. The slope estimates were used to estimate expected weight change during the intervention period as slope (kg/day) × days between first and last measurement.

The fixed effects regression method estimates average (linear) rate of weight change and removes random, day-to-day fluctuations in body weight (the e_{it}), thus minimizing measurement error (a potentially substantial source of error when using the simple post-pre difference), and is consistent with the concept of dynamic weight change in energy balance theory. Specifically, weight is a function of average energy balance over an extended period of time (weeks to months) rather than energy balances on an given specific days, so weight change is best represented as a rate (kg/day) and not a simple difference between two points in time. The average difference of the slope-predicted body weight change and the simple post-pre estimate represents bias (systematic error) of the simple post-pre estimate, and the SD of the differences represents imprecision (random error) of the simple post-pre estimate. All analyses were conducted using STATA (STATA 15, Stata Corp., College Station, TX).

The optimal estimate had the lowest bias and lowest SD of differences (i.e., high precision), which were evaluated by descriptively comparing the relative magnitudes of bias and SD among the 5 estimates. Among the five methods for estimating PAL, the 5th method, using the self-reported data with measured HR, was expected to be the most accurate (i.e., lowest bias and best precision). Therefore, the method with the most accurate predicted weight change among other four methods that are using only self-reported data was used with the fifth method in Study 2 and 3.

3.3 METHODOLOGY FOR STUDY 2

Study 2 examined how baseline EB affects weight changes after the TIGER exercise intervention. In particular, participants who are in positive energy balance at baseline (i.e., a weight gain trajectory, consistent with the general US population) may experience less weight change than expected for the caloric value of the intervention. The intervention may only partly offset the amount of baseline positive energy balance. Expected weight changes from the TIGER prescribed activity and self-reported PA during the intervention period were estimated by the most accurate self-report method determined in Study 1. The fifth method, using observed HR, was also used as it is the only method using an objective measure of the prescribed exercise. The steps for estimation of PAEE, PAL, and associated expected weight changes with the addition of baseline EB were the same as Study 1.

The additional step for Study 2 was estimating baseline EB using each participant's weight history. The baseline EB satus before participating in exercise intervention was calculated by using the adapted equations of Hall et al. (2011) [14]. Baseline EB is a function of weight change, and more specifically the change in body composition, the relative changes in FM and FFM, since FM has a much higher energy density than FFM. Consequently, a defensible, valid estimate of change in FM (ΔFM) and FFM (ΔFFM) is required.

Using Hall et al.'s (2007) notion and equation for history of changes of body weight before intervention (ΔBW_b):

$$\Delta BW_b = \Delta FFM_b + \Delta FM_b \qquad \text{(Eq. 17)}$$

where ΔFFM_b and ΔFM_b are history of changes of FFM and FM at baseline, respectively. And,

$$\mathit{\Delta} FM_b = FM_2 - FM_1 \qquad \text{(Eq. 18)}$$

where FM_1 and FM_2 are the historical and baseline FM, repectively.

Forbes's equation can provide an estimate of the relative change in FFM and FM, although it describes the cross-sectional relationship between FFM and FM across differences in body weight and as such represents change in body composition for infinitesimal differences in weight. Because baseline EB status in individuals is represented by relatively large, longitudinal changes of body mass and composition, using Forbes's original equation is not applicable. Therefore, Hall expanded upon the concept of Forbes's original equation to predict body composition change for a given change of body weight ($\mathit{\Delta} BW_b$, by weight history prior to baseline; i.e., from weight of 2 years ago or at the end of high school to baseline) and current FM (FM_2) using the Lambert W function, W, to solve a transcendental equation predicting historical FM (FM_1) [117].

$$FM_1 = 10.4W\left[\frac{1}{10.4} \times exp\left(\frac{\Delta BW_b}{10.4}\right) \times FM_2 \times exp\left(\frac{FM_2}{10.4}\right)\right] \qquad \text{(Eq. 19)}$$

Using the respective energy densities associated with mass changes (ρ_{FFM} and ρ_{FM}), baseline EB in kilocalorie (kcal) was estimated as [(7,600 × $\mathit{\Delta} FFM$ + 39,500 × $\mathit{\Delta} FM$) × 0.239]/(365 × 2 years). Finally, using the equation below, the total expected body weight changes with inclusion of initial EB status (EB) in the numerator was estimated. Description of other parameters of the equations are the same with the Table 7.

$$\Delta BW = \frac{(1-\beta)(\Delta EI)-(BW_1 \times \Delta PAEE)+EB}{PAEE_1+\Delta PAEE+\gamma_{FFM}-\phi(\gamma_{FFM}-\gamma_{FM})} \quad \text{(Eq. 20)}$$

Then, the Equations 5 and 6 were used to predict weight changes after 15-week prescribed exercise intervention. The process for estimating weight change during the TIGER prescribed intervention was the same as in Study 1, but the modified ΔBW value from Equation 20 was used.

Comparison of weight change using Equation 5 with observed weight change after 15-week prescribed exercise intervention was utilized to examine whether considering initial EB status individuals is more accurate for estimation of body weight changes. Same as with Study 1, the fixed effects regression method was used to estimate rate of weight change after the prescribed exercise intervention, which was used with the simple post-pre difference as the criteria for evaluating bias and SD.

3.4 METHODOLOGY FOR STUDY 3

Study 3 examined whether racial differences explains any remaining variability in weight changes associated with exercise intervention, after accounting for body composition, changes in EI, and baseline EB status, by using the estimates from Study 1 and Study 2. To compare racial differences, participants were categorized into five racial groups: 1) Non-Hispanic White (NHW), 2) Non-Hispanic Black (NHB), 3) Hispanic, 4) Asian, and 5) Asian Indian. Asian Indian was separated from Asian, since unique anthropometric differences have been observed [118]. Participants were excluded if they indicated their race as Multiracial or Others due to non-homogeneity and uncertainty of race and racial influences in those groups.

The Study 1 and Study 2 estimates of PAEE and associated predicted weight changes after the intervention were used. Then, analysis of variance (ANOVA) tests were used to compare racial groups on bias, defined as the differences of the observed body weight change (Both the rate estimated by the fixed effects model and the simple post-pre weight difference) and the predicted body weight changes after 15-week prescribed exercise intervention.

If the race variable is significant, then race accounts for systematic variance in observed weight change that is unexplained by differences in body composition, effects of the exercise intervention, changes in EI, and baseline EB.

CHAPTER 4

4. MANUSCRIPT 1: PREDICTING WEIGHT CHANGES USING SELF-REPORTED ACTIVITY DATA DURING EXERCISE INTERVENTION

4.1 INTRODUCTION

About two third of adults in the United States (US) are classified as overweight or obese by body mass index (BMI) [1]. Weight gain occurs when energy intake consistently exceeds energy expenditure according to the energy balance theory. In this theory, producing negative energy balance (EB), in which energy expenditure exceeds energy intake, is needed to result in weight loss in individuals [3].

Almost one-half (49.1%) of adults in the US have tried to lose weight within the last 12 months [119]. Interventions for increasing physical activity energy expenditure (PAEE), reducing energy intake (EI), or combination of both, have been considered for weight loss. However, individuals have failed to achieve weight loss goals, in part because changes of PAEE or EI results in adaptations that produce a smaller than expected energy deficit [4-6]. In particular, weight change with change in PAEE does not seem to match the caloric value of the physical activity (PA) to the extent seen in weight change after reducing EI by the same amount calories [5]. In addition, there are sources of errors in estimating energy deficit for weight control that depend on the measure of PAEE and EI used [7]. Specifically, self-reported measures have come under recent criticism over concerns of poor reliability and validity.

Self-reported questionnaires have been used to collect data in large populations because it is less expensive and resource-dependent, and data are immediately available for analyses [9, 10, 120]. However, self-reported EI tends to be under-reported, whereas self-reported PAEE tends to be over-reported [11]. These reporting errors lead to an estimate of negative energy balance considerably larger than the actual deficit, which can explain why the associated weight loss does not occur as expected.

Objectively measured PA such as accelerometry, pedometers, and doubly labeled water (DLW) also have limitations. Accelerometers and pedometers have different intensity cut-points for different activities and age groups, can possibly be manipulated by participants to produce activity counts in the absence of meaningful body movement, and are less reliable for the quantification of some activities (i.e., cycling, swimming, etc.) [121]. In addition, these devices are challenging to distribute among large numbers of free-living individuals and expensive in terms of personnel, equipment, and processing costs [8]. In the situation that assessment of large populations is required (e.g., population surveillance), subjective self-reported data is more feasible to collect, and thus researchers should try to develop and administrate more accurate and reliable ways to acquire information. Finding feasible and reliable ways to estimate energy deficit by PAEE and EI also would help individuals set their weight loss or maintenance goals and adjust amount of PAEE and EI to achieve the goals successfully.

Several methods of self-reporting PA exist. Most self-reported PA uses levels of activity (e.g., 0 to 7 scale) or reporting of specific activities with duration (minutes) with investigators using a compendium to estimate intensity of the activities [69]. The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) Body Weight Planner calculator includes a categorical general rating of physical activity level (PAL, a multiple of estimated basal metabolic rate) to estimate total daily caloric expenditure [14]. Due to different fitness levels in individuals, however, using categorical rating of overall PA would have limitations. For example, if two people who rated their activities as a “Very active” have different fitness levels, the person who has lower aerobic capacity (i.e., VO_2max) likely would do relatively lower intensity, frequency, or duration of activity, resulting in a lower PAEE, compared to a person who has higher aerobic capacity. The rating of perceived exertion (RPE) scales is a valid method of rating intensity and can be feasibly collected on a large population to estimate heart rate [72], and thus it may help improve estimation of PAEE by using activity (mode), RPE, and duration.

The purpose of this study was to predict energy imbalance, as estimated by body mass changes, in sedentary individuals who participated in an exercise intervention. Baseline total daily energy expenditure (TDEE) was computed using estimates of resting EE and daily non-exercise and exercise PAEE. TDEE during the intervention period was quantified using a variety of methods for self-reporting PA as well as objectively measured heart rate data collected during the prescribed exercise. In addition, the accuracy (bias and precision) of the various self-reported PA methods were computed by comparing body mass change predicted by each method to observed body mass change, while also incorporating the available self-reported EI data in the predictions. We hypothesized that self-reported PA with RPE would be the most accurate self-reported method in predicting body mass change following the exercise intervention.

4.2 METHODS

This study used the data from the Training Intervention and Genetics of Exercise Response (TIGER) study between 2003 and 2015. The TIGER study was designed to investigate genetic factors that influence on metabolism and adiposity response to a 15-week prescribed exercise intervention in diverse young adults. Details of the TIGER study are described elsewhere [106].

Participants

Participants in this study were 18-35 years old men and women (n=3,769) who were students enrolled at University of Houston (2003-2008) or University of Alabama at Birmingham (2010-2015). Participants were asked to complete questionnaires about demographics, medical history, diet, and PA at baseline, before initiating the prescribed exercise protocol. Participants were excluded if they had difficulties with engaging in exercise, had diagnosed metabolic disorders, were pregnant, or were already participating in a regular exercise program within the past month. The study was approved by the Institutional Review Boards of the participating institutions, and all participants signed informed consent before data were collected.

Anthropometry measures

Height was measured using a stadiometer (SECA Road Rod; SECA, Hanover, MD) and weight was measured with a digital scale (SECA 770; SECA, Hanover, MD). Height and weight recorded in centimeters (cm) to the nearest 0.1 cm and kilogram (kg) to the nearest 0.1 kg, respectively. Fat mass (FM) and fat free mass (FFM) were estimated by dual-energy x-ray absorptiometry (DXA) (Hologic, Bedford, MA). Height and weight were measured before and after the 15-week prescribed activity intervention, and weight was also measured at two interim time points during the intervention period (four measurements total).

VO_2max estimation

The resting heart rate (HR) was measured for 20 seconds three times and recorded as the average of the three measurements, in which participants were sitting at rest for at least 5 minutes prior to measurement. Then, participants were asked to perform 1-mile walk or 1.5-mile run test (i.e., walking or running at a steady pace), and exercise HR during performance (beat/min), and duration of test (minutes) were recorded during the test using HR monitors.

VO_2max (mlO_2/kg/min) from maximal walk and run test were estimated using the equations by Kline et al. [109] and Baumgartner et al. [110] (revised from [111]), respectively. However, this field test with untrained sedentary participants may have limitations for estimating maximal oxygen consumption during the walk and run test. Therefore, the Astrand-Ryhming single state method of estimating VO_2max using HR was also used [112].

Self-reported food intake and exercise

Dietary intake was assessed using Block Food Frequency Questionnaire (FFQ, NutritionQuest, Berkeley, CA) [113]. Participants were asked to report how often each item of foods was consumed during a typical week using nine categories, ranging from "never" to "every day", and each food intake was converted to a weekly calorie intake (kcal) or averaged daily calorie intake (kcal/day) using the Block's standard scoring service (https://nutritionquest.com/assessment/pricing_and_ordering/), validated from the previous studies [122, 123]. Using Goldberg's cut-off, we flagged the value of less than 1.55 for a ratio of reported EI to basal metabolic rate (BMR), which is suggested for infeasible and implausible values of reported EI data [52].

Physical activity rating (PAR) was assessed by having participants rate their activity levels, ranging from 0 (None; No activity) to 7 (Vigorous; Runs over 10 miles or 3 hours of comparable PA per week) [70]. Self-reported PAEE was assessed using an activity log in which participants reported physical activities other than the TIGER-prescribed exercise during the entire 15 weeks. The modes (e.g., running, elliptical, weight lifting) and duration of exercise were reported by participants as well as their RPE using the 6-20 Borg scale [71].

Exercise intervention and HR monitoring

Participants voluntarily participated in 15 weeks of aerobic exercise training, which was prescribed as 3 days per week for 30 minutes per day at a sustained 65-85% of age and sex-specific predicted maximum heart rate reserve [114]. Participants were permitted to select treadmill, stair stepper, stationary bike, or elliptical trainer as the activities, and they could select different activities for different sessions. Heart rate (HR) monitors (Polar Electro, Lake Success, NY) were used to monitor the participants' HR during the prescribed activity. Exercise sessions were monitored but the exercise was not individually supervised, which resulted in variation of frequency, duration, and intensity of exercise from the prescribed amounts. The recorded HR data during the prescribed activity were downloaded for each participant after each session. Then, this recorded HR data was matched with participants' attendance records, and we identified some missing or unusable data due to a malfunction of the HR monitor. For either missing or unusable average HR data for each session, the data were imputed using the within-participant distributions of HR and duration across other valid sessions, which required including only those subjects who had at least 60% of all possible exercise session for each subject to provide reasonable imputed values [115].

Estimation of predicted and actual energy balance

Predicted changes of energy intake and expenditure, which may result in energy balance (maintain body mass) or energy imbalance (loss or gain of body mass) after the 15-week of exercise intervention, were estimated using the equations from the NIDDK Body Weight Planner program [14]. This program allows users to plan caloric intake and expenditure to reach their weight goals by entering basic information such as height, weight, age, sex, and physical activity level (PAL). Because exercise intervention was included, the equations in Hall's model (2011) were used to estimate PAEE changes (Eq. 3), expected eventual body mass changes when a new EB is attained through exercise intervention (Eq. 4), and final body mass change (Eq. 4) with body composition changes (Eq. 6) [14]:

First, predicted PAEE was calculated using:

$$PAEE\ (kJ/kg/day) = [(1 - \beta_{TEF}) \times PAL - 1]REE/BW \qquad \text{(Eq. 3)}$$

The β_{TEF}, which is the thermic effect of food was set at a fixed 0.1 (representing 10% of TDEE) for all participants, and REE was estimated using the equations of Mifflin et al. (1990) [62], consistent with Hall's method [14] and current recommendations [63]. The baseline PAEE ($PAEE_1$) was estimated using self-reported PAR at baseline, converted into a PAL value. The estimated PAEE during the 15-week intervention ($PAEE_2$) was estimated by converting into PAL using five different methods: 1) categorizing into expected PAL for 15-week after adding the prescribed activity (1.8 PAL for all participants), 2) categorizing into PAL using self-reported PAR for the 15 week period (1.7-2.0 PAL), 3) calculating PAL as ratio (TDEE/REE) using body mass, duration of activities, and the compendium MET values of the prescribed and self-reported non-prescribed activity, 4) calculating PAL ratio using the self-reported RPE for the prescribed and non-prescribed activity with the participant's estimated maximum aerobic capacity and duration of activities, and 5) calculating PAL ratio using measured HR for prescribed activity and RPE (Method 4) for self-reported non-prescribed activity (Appendix 1).

Predicted body mass change was estimated in two stages. First, expected total body mass change that would occur over an indefinite period of time with permanent changes in EI or PAEE or both was calculated using Hall's Eq. 4:

$$\Delta BW = \frac{(1-\beta)\Delta EI-(BW_1 \times \Delta PAEE)}{PAEE_1+\Delta PAEE+\gamma_{FFM}-\phi(\gamma_{FFM}-\gamma_{FM})} \quad \text{(Eq. 4)}$$

The β is 0.24, according to the $\beta = \beta_{AT} + \beta_{TEF}$, where β_{AT} is a constant value of 0.14 representing the proportion of PAEE attributable to adaptive thermogenesis [14]**.** ΔEI (kJ/day) is the difference of EI between at baseline and 15-weeks. $\Delta PAEE$ *(kJ/kg/day)* is the difference of PAEE between at baseline ($PAEE_1$) and 15-week ($PAEE_2$). BW_1 (kg) is body weight at baseline, and $PAEE_1$ is PAR at baseline. γ_{FFM} and γ_{FM} are 92 kJ/kg/day and 13 kJ/kg/day, respectively, which are the constants for FFM and FM contributions to REE. The ϕ is estimated composition of body weight change, $FM_1/(C + FM_1)$, where FM_1 is initial FM, which was the DXA-measured FM at baseline, and C is 10.4, the Forbes parameter [74]. According to the equation, higher initial body fat results in more weight changes, since ϕ is increased by higher initial body fat and γ_{FFM} is larger than γ_{FM}, which results in a smaller denominator of the equation. This indicates that higher initial FM brings out more loss of FM for weight loss compared to higher initial FFM because FM has lower contribution to REE compared to FFM. Thus, the TDEE remains higher than if a higher proportion of the weight loss is FFM.

Second, body mass changes after the 15 weeks of TIGER intervention were estimated. Equation 3 represents the exponential decay function predicting ΔBW_t at a specific time *t* (in this study, *t* = 15 weeks = 105 days), which is only the initial part of the predicted ΔBW from Equation 2. The characteristic time constant (tau; τ) for the predicted nonlinear rate of weight loss accounting for changes in both body mass and composition following behavior change (i.e., ΔEI and ΔPAEE) computed using Equation 6.

$$\Delta BW_t = \Delta BW - \Delta BWe^{-t/\tau} \quad \text{(Eq. 5)}$$

$$\tau = \frac{\eta_{FM}+\rho_{FM}+\alpha(\eta_{FFM}+\rho_{FFM})}{\gamma_{FM}+PAEE_2+\alpha(\gamma_{FFM}+PAEE_2)} \quad \text{(Eq. 6)}$$

where η_{FM} is 750 kJ/kg and η_{FFM} is 960 kJ/kg, representing the cost of fat and protein synthesis, respectively. The ρ_{FM} is 39,500 kJ/kg and ρ_{FFM} is 7,600 kJ/kg, representing metabolizable energy density of mass change. $PAEE_2$ is PAEE of the intervention, which was estimated using the five methods described above. The α is C/FM; where the Forbes parameter, C = 10.4, is divided by initial FM. Thus, the τ decreases when $PAEE_2$ increases, indicating both the amount and rate of weight change increases.

Statistical analysis

All analyses were conducted using STATA (STATA 15, Stata Corp., College Station, TX). Descriptive statistics were conducted to quantify participants' demographics, anthropometry, and PAR at baseline as well as changes of body mass, FFM, FM, and PAR before and after the 15-week prescribed activity intervention. Paired t-test were utilized to test the accuracy of the frequency, duration, and intensity of self-reported methods for the prescribed activity in average by comparing with the observed data.

The observed body mass changes during 15 weeks was estimated for each participant using the simple difference ($kg_{final} - kg_{baseline}$) as well as a fixed effects regression model. Since each participant (i = 1 to N) has four body weight measurements during the intervention period, the rate of weight change (kg/day) can be estimated. The fixed effects model estimates body weight change (kg/day) as the slope of a regression line describing body mass change.

$$Weight_{it} = Intercept_i + (Slope_i * day_t) + e_{it} \quad \text{(Eq. 16)}$$

For each participant, the actual days from baseline for each of the body weight measurements were used as the final day (t) from baseline (t = 0) that weight was measured: expected final weight on day t = slope * t (days). For example, if slope is 0.01 kg/day, then the expected weight change on day 105 would be 0.01 * 105 = 1.05 kg. The residuals, e_{it}, represent the deviations of each participant from their individual regression line at time (t). The fixed effects regression slope provides averate rate of weight change and removes random, day-to-day fluctiations in body weight, and is consistent with the concept of dynamic weight change of the EB theory compared to using the simple difference between pre-post weights, which confounds true change and day-to-day fluctuations.

The average difference of the predicted and observed body mass changes represents bias (systematic error) of the predicted value, and the SD of the differences represents its imprecision (random error).

4.3 RESULTS

Total participants were 1,565 (men=515; women=1,050). Among 3,769 participants, this study excluded 269 participants outside the age criteria (18-35 yrs), 231 who did not have weight pre-post measurement, 1028 who did not perform 1-mile walk or 1.5-mile run test to obtain VO_2max because the test was not included for two study cohorts, and 93 who had an estimated VO_2max higher than 65 mlO_2/kg/min (very unlikely for sedentary person) or measurement errors (i.e., HR monitor malfunction). An additional 538 participants were excluded based on missing data on one or more variables.

Descriptive results

The baseline characteristics of participants were described in Table 8. Of 1,565 participants, 515 (33%) were men and 1,050 (67%) were women. All participants reported their physical activity rating (PAR) at baseline: 68.7% of participants were reported 0-4 of PAR scores, which indicates less than 1-mile run or less than 30 minutes of comparable PA per week (i.e., sedentary). Reported 0-4 of PAR scores at baseline in men and women were 55.8% and 75.0%, respectively.

Mean weight change after the 15-week prescribed exercise was -0.37 kg (SD=2.63). Self-reported PAR scores were increased after 15-week exercise intervention, with 78.7% of participants reporting 5-7, which indicates more than 1-5 miles of run or 30-60 minutes of comparable PA per week.

Table 8. Characteristics of participants at baseline (Mean±SD, or %)

	All (n=1,565)	Men (n=515)	Women (n=1,050)
Age (yr)	21.2±2.8	21.4±2.7	21.1±2.8
Height (cm)	166.8±9.1	175.3±7.1	162.5±6.6
Weight (kg)	73.2±19.4	83.6±19.3	68.1±17.2
FFM (kg)	49.9±12.6	63.2±10.5	43.4±7.2
FM (kg)	23.3±12.0	20.4±12.3	24.7±11.6
PAR (score)			
0	3.4%	1.0%	4.5%
1	26.1%	15.4%	31.3%
2	12.5%	9.3%	14.1%
3	18.3%	20.9%	17.0%
4	8.5%	9.3%	8.1%
5	15.9%	19.5%	14.2%
6	8.6%	13.4%	6.3%
7	6.7%	11.2%	4.5%

FFM: fat free mass; FM: fat mass; PAR: physical activity rating score

Comparison of measured and self-reported activity

The averaged frequency, duration, and intensity of exercise between measured activity data (HR monitors) and self-reported activity data (Activity Logs) were compared using paired t-tests (Table 9). For this comparison, only participants who completed activity logs were included (i.e., only Phase 2), and the dates of prescribed (HR measured) and reported activities were matched.

Table 9. Measured vs. self-reported activity data (Mean±SD), (n=1,012)

	HR data	**Activity Log**
Frequency (activities)	36.3±9.28	56.0±26.3
Duration (minutes)	37.8±4.4	33.1±6.8
Intensity (HR, bpm)	156.1±8.0	142.8±13.7

bpm: beat per minute

The results showed that the averaged frequency of activity was higher in the self-reported activity logs (diff=19.7, $p<.001$) compared to the HR data, since participants reported more than two activities in one session. Averaged duration per session were 4 minutes longer in the HR data compare to the activity logs ($p<.001$). For intensity, self-reported RPE in the activity logs were used to calculate HR (beat/min, bpm) using Astrand-Ryhming single stage method [112] (Appendix 1, the 4th method) to compare with the collected HR monitor data. Averaged HR during the activity in the self-reported activity logs were 13.3 bpm lower compared to measured HR data ($p<.001$), but had more variability (SD=13.7 in the activity log vs. SD=8.0 in the HR data).

Comparison of observed, expected, and predicted weight changes

The observed weight changes after 15-week prescribed exercise were estimated using two criterion measures: 1) simple difference of weights before and after the intervention and 2) the rate of weight change (kg/day) over the intervention period. The simple difference weight change (Simple ΔWT) was calculated using measured weights at baseline and after the intervention ($kg_{final} - kg_{baseline}$). The expected weight change, based on the rate of weight change (Rate of ΔWT), was estimated using the slope from the fixed effects regression approach for each participant. Then, the rate (kg/day) was multiplied by the number of days between baseline and final weight measurement to estimate the total weight change.

The predicted weight changes after 15-week prescribed exercise were estimated using the five methods of PAEE estimations: 1) Categorized PAL of prescribed activity (1.8 PAL for all participants), 2) Categorized PAL using PAR reported by participants, 3) PAL ratio (TDEE/REE) calculation using activity logs and compendium MET values for the reported activities, 4) PAL ratio calculation using RPE from activity logs, and 5) PAL ratio calculation using measured HR for prescribed exercise sessions and RPE from the activity log for non-prescribed activities (Appendix 1).

Average simple pre-post measured weight change was -0.23 kg (SD=2.55), and average expected weight change from the rate of change method was 0.29 kg (SD=2.81). The predicted weight changes for Method 1 to 5 were -3.82kg (SD=8.17), -5.44 kg (SD=8.29), -3.53 kg (SD=8.12), -3.43 kg (SD=8.12), and -2.77 kg (SD=8.23), respectively. Therefore, the self-reported methods to predict weight changes showed more weight loss than the observed weight changes.

Table 10. Comparisons of bias and precision in predicting weight change among PAEE estimation methods (n=581)

	Simple ΔWT		**Rate of ΔWT**	
	Mean	**SD**	**Mean**	**SD**
Observed ΔWT	-0.23	2.55	0.29	2.81
	Bias	**Precision**	**Bias**	**Precision**
Method 1	3.59	8.54	4.11	8.81
Method 2	5.20	8.58	5.73	8.95
Method 3	3.29	8.56	3.82	8.71
Method 4	3.20	8.57	3.73	8.72
Method 5	2.54	8.69	3.07	8.80

ΔWT: weight change; Bias: mean differences between observed ΔWT and predicted ΔWT by each method; Imprecision: SD differences between observed ΔWT and predicted ΔWT by each method; Method 1: categorized PAL of prescribed activity; Method 2: categorized PAL using PAR reported by participants; Method 3: PAL ratio (TDEE/REE) calculation using compendium MET values from activity logs; Method 4: PAL ratio calculation using RPE from activity logs; and Method 5: PAL ratio calculation using measured HR and RPE of activities

The comparisons of bias and imprecision among the five different PAEE estimation methods with observed weight changes are presented in Table 10. According to the results, Method 5, calculating PAL ratio using the objectively measured HR with the self-reported activity logs, was the lowest bias (lowest difference between observed and predicted weight changes) among the five different PAEE estimation methods. Method 4, calculating PAL ratio using the self-reported activity with RPE, was the lowest bias and SD (imprecision) among the entirely self-reported methods.

However, for calculation of predicted body weight changes using Equation 4, many values for the self-reported EI data using Block FFQ were noted to be implausible (i.e., under-reported by Goldberg's cut-off: ratio of reported EI to BMR < 1.55 [52]). Thus, the analyses were repeated with the ΔEI set to 0 in Equation 4, which indicates the assumption that EI did not change during the intervention period. Given that only a prescribed exercise intervention without dietary intervention was provided to participants, PAEE would be expected to change, but EI may not have changed. Without EI, the bias of the predicted weight changes for Method 5 was the lowest among all PAEE estimation methods, and Method 4 had the lowest bias among the entirely self-reported methods (Table 11), consistent with the results in Table 10. Compared to the results that included the reported ΔEI, all bias and imprecision estimates improved when the ΔEI measures were excluded (i.e., Rate of ΔWT: bias and precision of the 4th method were changed from 3.73 to 1.15 and 8.72 to 3.82, respectively).

Table 11. Comparisons of bias and precision in predicting weight change among PAEE estimation methods, without EI (n=581)

	Simple ΔWT		**Rate of ΔWT**	
	Mean	**SD**	**Mean**	**SD**
Observed ΔWT	-0.23	2.55	0.29	2.81
	Bias	**Precision**	**Bias**	**Precision**
Method 1	2.07	3.82	1.55	3.86
Method 2	3.71	4.45	3.18	4.26
Method 3	1.77	3.57	1.25	3.88
Method 4	1.68	3.49	1.15	3.82
Method 5	1.01	3.52	0.48	3.92

ΔWT: weight change; Bias: mean differences between observed ΔWT and predicted ΔWT by each method; Imprecision: SD differences between observed ΔWT and predicted ΔWT by each method; Method 1: categorized PAL of prescribed activity; Method 2: categorized PAL using PAR reported by participants; Method 3: PAL ratio (TDEE/REE) calculation using compendium MET values from activity logs; Method 4: PAL ratio calculation using RPE from activity logs; and Method 5: PAL ratio calculation using measured HR and RPE of activities

4.4 DISCUSSION

In this study, PAEE during the intervention was quantified using four different methods of self-reporting activity and an objective measure of HR during the 15-week prescribed exercise intervention. Then, the revised TDEE calculation from the increased PAEE and the available self-reported EI data was used to predict body mass changes by each method. Finally, the predicted body mass changes from each method after the intervention were compared to the observed body mass changes to examine the accuracy of self-reported data.

This study found that the average duration and intensity of the measured HR data was higher than self-reported data, although higher frequency (more activities) were also reported in the self-reported activity logs. Most previous studies indicated that self-reported PA tends to be over-reported compared to objectively measured PA [124]. One explanation of our inconsistent results with previous studies would be due to converting self-reported RPE to %HRR and average HR during activity using Astrand-Ryhming method [112], which could be misleading at lower intensity activity. For example, according to this method, an RPE of 6 would convert to 0% of HRR, which results in an activity HR estimate approximately equal to resting HR. In the self-reported activity logs, some participants reported an RPE of 6 for their warm-up sessions such as jogging, stretching, walking, etc. It is possible that a reported RPE of 6 (%HRR=0) does not represent the actual and measured HR during these activities, which would be expected to result in HR elevation above resting HR. Another explanation is that participants may have underreported their total durations of activities if they did two or more activities in one session. For the HR monitored sessions, total durations of activity were recorded in one data stream regardless of transitions of activities (i.e., 5 minutes of walking to 30 minutes of elliptical training, and to 10 minutes of stretching) during that one session, and thus, more than 45 minutes of activity duration should be recorded including the time between activity transitions or rests. On the other hand, only the activity minutes were recorded in the self-reported activity, and some warming up activities (i.e., 5 minutes of running track or 5 minutes of stair-steps before every session) were not reported.

This study found that the predicted body mass changes using a combination of measured HR data and self-reported activity logs with RPE showed the lowest bias and best precision. Method 4, PAL calculation using RPEs of intensity, was the most accurate entirely self-reported method to predict weight changes. Measured HR is known to be an accurate method of predicting individual's relative exercise intensity during the activity [125, 126], so Method 5 may be considered an objectively measured and accurate estimate of ΔPAEE due to the intervention. For the entirely self-reported methods, estimates of PAEE using %HRR and %VO_2max from RPE and individuals' estimated maximum aerobic capacity (Method 4) were close to the predictions of Method 5, and thus can be considered to be reasonably accurate (unbiased). Comparing the five different methods of PAEE estimation, Method 2, using categorical PAL from participants' reported PAR, was least accurate and resulted in a predicted weight change about 5 kg below the observed weight changes. The other 3 self-report methods of PAEE estimation showed relatively consistent predicted weight changes.

The validity of converting RPE to an approximate HR during activity has strong theoretical and empirical support [72]. If HR and aerobic capacity are known within reasonable accuracy, then an estimate of PAEE can be derived. Collecting RPE might be more feasible than instrumentation (e.g., HR monitors, accelerometers) in large interventions or population surveillance studies but still provide reasonably accurate estimates of PAEE and predicted weight change in response to PA intervention.

The RPEs could be useful for estimation of PAEE compared to calculation using compendium MET values of each activity. To calculate PAEE using compendium METs, participants have to report categorized intensity (i.e., light, moderate, vigorous) or specific performance information (i.e., pace (mph) for walking and running) [68, 69]. However, the pace data was not reported in the logs and many participants were missing running or walking distance, which could be combined with duration to estimate pace. Therefore, we used RPEs as categories of activity intensity (i.e., light=6 METs: running with RPE <12; 11.5 METs: running with RPE=14; 15 METs: running with RPE=18) for our compendium METs calculations. In practice, without the reported RPE values the compendium estimates (Method 3) would likely have greater inaccuracy than observed in the current study. In addition, continuous RPE values allow more granular variability than using only three categories of intensity (light, moderate, and vigorous) as described in the Compendium for many activities. There were also infeasible reported intensity values, such as having only a single intensity for elliptical training (i.e., = 5 METs), despite a wide range of other possible intensities for that activity. There were also unavailable categories in the compendium for some specific activities (i.e., Zumba, pole dancing). In these cases, and other situations, RPE with duration of activity can be used to calculate PAEE for the session, regardless of activity modes, which is an advantage over the compendium method. Recent studies also concluded that compendium METs values of activity can be accurately obtained using %HRR by measured HR [127]. Thus, RPE can be used instead of measured HR since properly reported RPE has been demonstrated to be highly consistent with prediction of HR and VO_2 [71, 128].

Using RPE and duration of activities to estimate PAEE was the most accurate entirely self-reported method for estimation of PAEE used to predict body mass changes after the prescribed intervention. Feasibility of RPE or other intensive self-reporting methods, however, can be a challenge. Understanding the advantages and limitations of each assessment method would allow investigators and practitioners to select methods appropriate for the purposes of their work, recognize the assumptions and limitations, and make appropriate conclusions and recommendations.

Table 12. Summary of PAEE estimation methods

	Assumptions	Advantages	Limitations
Method 1	-Participants are 100% compliant and have the exact same exercise dose throughout the intervention period	-Easy to calculate PAL	-Does not capture variability within participants (e.g., day-to-day or week-to-week) -Does not capture variability among participants
Method 2	-Reported PA level reflects average activity -Participants' PA was consistent during the entire intervention period	-More categories for PA level description compared to Method 1 -Captures variability among participants	-Does not capture variability within participants (e.g., day-to-day or week-to-week)
Method 3	-All reported PA is accurate in terms of mode and duration	-Easy to quantify caloric expenditure value using METs -Reflecting variability in intensity and duration -Captures variability within participants -Captures variability among participants	-Participants must report all PA sessions -Lack of intensity categories of mode, and thus lack of MET values, for some activities
Method 4	-All reported PA are accurate in terms of intensity (RPE) and duration	-Captures variability within participants -Captures variability among participants -No need to report mode of activity	-Participants must report all PA sessions -Need to train participants for accurate RPE rating
Method 5	-HR is accurately measured during the prescribed activity -All non-prescribed PA is accurately reported with respect to intensity (RPE) and duration	-Objectively measured activity (in part or entirely) -Captures variability within participants -Captures variability among participants -No need to report mode of activity	-Participants must wear HR monitor or self-report all PA sessions -Possible equipment errors (i.e., HR monitor malfunction) -Need to train participants for accurate RPE rating

Method 1: categorized PAL of prescribed activity; Method 2: categorized PAL using PAR reported by participants; Method 3: PAL ratio (TDEE/REE) calculation using compendium MET values from activity logs; Method 4: PAL ratio calculation using RPE from activity logs; and Method 5: PAL ratio calculation using measured HR and RPE of activities

The findings of this study should be interpreted considering certain limitations. The two different phases of this study collected some different measures (i.e., HR data, Fitness test, Activity logs, etc.) such that not all subjects could be included in all estimates, although a fairly large sample size was maintained. Duration reports in the self-reported activity logs were categorized (i.e., … 15, 20, 25, 30…., and more than 60 min), whereas the measured HR data provided exact durations to the minute, which introduced variability by reporting method. Self-reported EI data using Block FFQ had many implausible values leading to inflated bias and imprecision for body mass change estimation in our data; specifically, substantial under-reporting of EI led to large underestimating of change in body weight. After setting EI change to 0 in the equations and using only the PAEE estimates, the predicted body mass changes became more accurate. Unlike PAEE estimation, there was only one method to estimate EI in this study, so we were unable to compare accuracy of methods and sources of self-reported EI errors.

This study also has strengths and meaningful findings. First, this study included various self-reported methods for PAEE estimation and included objectively measured HR data for every prescribed exercise session, and we were able to compare each method to estimate predicted weight changes with the observed weight changes. From the first to fifth methods, more information was added, which led to better estimates, with Method 4 and 5 being the most accurate self-reported and self-reported + measured methods, respectively. Collecting a variety of information to quantify PAEE may reduce missing data and sources of error for self-reported data. For example, collecting and using RPE can be useful if mode of activity is missing when using the compendium MET values to rate activity. Second, this study used Hall's validated dynamic mathematical models that incorporate body weight, body composition, and behavior changes (PA, EI) to predict weight changes after the prescribed exercise intervention. Finally, the use of RPE for self-reported activity logs provided estimates with the lowest bias for caloric values of PAEE, as confirmed by a more accurate estimate of body mass changes.

This study compared the four different self-reported PA methods to estimate body mass changes after the prescribed exercise intervention. Except for self-reported PA category by PAR, we found that the predicted weight change estimations among the variety of self-reported PAEE methods were fairly consistent, and using more refined self-report measures produced increasingly more accurate predictions of body weight change. Although the self-reported measures have been considered to be substantially less accurate than objective measures, self-reported measures can be more feasible to use and analyze in large population research. Our results show that there are ways to reduce bias and errors and improve precision by using more detailed self-reported methods such as RPE or perhaps self-reported HR during activity, both of which are relatively easy to teach to participants, and recording of specific duration minutes and all activity sessions.

CHAPTER 5

5. MANUSCRIPT 2: THE EFFECTS OF INITIAL ENERGY BALANCE STATUS ON BODY WEIGHT CHANGES IN INDIVIDUALS AFTER EXERCISE INTERVENTION

5.1 INTRODUCTION

Lifestyle weight loss programs such as restricted calorie intake, increased physical activity (PA) and total daily energy expenditure (TDEE), or a combination of both have been implemented to lower obesity rate and improve individual health [84]. These weight loss programs create an energy deficit, when energy expenditure (EE) exceeds energy intake (EI), which is called as negative energy balance (EB) [82, 83]. However, the effects of weight loss programs that increase TDEE vary due to individual variability in body composition, PA history, and EB status (i.e., a person is gaining or losing weight or weight stable when the intervention begins).

First, different body composition such as fat mass (FM) and fat free mass (FFM) affects weight changes among individuals [12]. Because FM has a lower metabolic cost (contribution to resting energy expenditure (REE)) compared to FFM [40], higher initial FM at a given total body mass means that the REE is relatively lower. This differential results in higher proportion of FM loss during weight loss for a given energy gap (relative preservation of FFM), which also results in more total weight loss when reaching a new stable weight. With higher proportion of FM loss, however, the amount of FM (kg) has higher energy stored than FFM, which means it requires more energy to lose a kg of FM and total mass – the energy required to lose 1 kg of mass is higher than persons with lower FM. Thus, for a given energy gap, the rate of body mass change is lower, particularly after the initial few months of weight change. Therefore, for a sustained change in behavior, a person with higher initial FM will lose ultimately more weight before reaching a new EB state but would also need more time to reach the new plateau [13, 14].

Second, PA history may influence amount of exercise needed to achieve weight loss goals. PA history is often determined using categorical physical activity rating (PAR) [70] or the international physical activity questionnaire (iPAQ) [129]. A person with regular higher amount of pre-intervention PA than a new, prescribed exercise program (assuming they do only the prescribed activity during the intervention period and EI does not change) would not achieve their weight loss goal because their PAEE, and thus TDEE, would actually decrease. If this person was weight stable at baseline (i.e., in energy balance), he or she may even gain weight due to producing a positive EB from the intervention exercise program having less EE than their pre-intervention PA.

Finally, initial EB status before participating in the weight loss programs, as represented by weight change history, would be expected to affect subsequent weight change. A previous study showed that the relationship between baseline EB status and weight changes in the same direction and magnitude after the intervention [100]. For example, if an individual who is gaining weight (sustained positive EB) does not change their weight after the intervention because the activity of intervention equals the individual’s positive EB before the intervention, a net state of EB (weight stable) will result. Or, if individuals were losing weight (sustained negative EB), they may lose more weight than expected because energy deficit that the intervention created would be added to individuals’ the existing negative EB. However, to our knowledge, most previous studies of weight loss interventions assumed that participants were in EB (weight stable) or excluded persons who reported substantial recent weight change, although there could be considerable variability based on lifestyle among participants. For individuals with positive EB, in addition, it would be beneficial to account for initial EB status to adjust intervention dose for effective weight loss and to set appropriate expectations.

The purpose of this study was to examine how EB status at baseline is associated with body weight changes after the prescribed exercise intervention, controlling for initial body composition and PA history in individuals. We hypothesized that accounting for baseline EB status to estimate weight changes would more accurately predict actual weight changes following a prescribed exercise program in individuals.

5.2 METHODS

This study was a secondary analysis of data from the Training Intervention and Genetics of Exercise Response (TIGER) study. Between 2003 and 2015, the TIGER study implemented a longitudinal study to provide regular prescribed exercise and identify genes that influence physiological response in college-age individuals. Detailed study information have been described elsewhere [106].

Participants

Participants of this study were college men and women aged 18-35 years old and recruited from University of Houston (2003-2008) and University of Alabama at Birmingham (2010-2015). Participants were excluded if they were pregnant, had diagnosed metabolic disorders, or had difficulties in engaging in exercise intervention. The study was approved by the Institutional Review Boards of the universities, and informed consent was signed by participants before data collection.

Anthropometric measures

Height was measured before and after the 15-week exercise intervention using a stadiometer (SECA Road Rod, Hanover, MD) and recorded to the nearest 0.1 centimeter (cm). Weight was measured at four timepoints, baseline, two interim timepoints during the intervention, and after the intervention, using a digital scale (SECA 770, Hanover, MD) and recorded to the nearest 0.1 kilogram (kg). Fat mass (FM) and fat free mass (FFM) were assessed at baseline using dual-energy x-ray absorptiometry (DXA) (Hologic, Bedford, MA).

Dietary intake

Dietary intake was measured using Block Food Frequency Questionnaire (FFQ, NutritionQuest, Berkeley, CA) [113]. Using the Block's standard scoring method and service, habitual frequency of intake of 102 food items consumed during a typical week were obtained by participants (https://nutritionquest.com/assessment/pricing_and_ordering/), validated from the previous studies [122, 123]. The frequency of each food intake was converted to a weekly calorie intake (kcal/wk) and averaged daily calorie intake (kcal/day). For under-reported EI problems, we used Goldberg's cut-off, less than 1.55 for a ratio of reported EI to basal metabolic rate (BMR) is considered as implausible values of reported EI data [52].

Physical activity rating (PAR)

Participants rated their regular physical activity using the PAR scale, ranging from 0 (None; No activity) to 7 (Vigorous; Run over 10 miles of 3 hours of comparable PA per week) [70] at baseline and 15-week exercise intervention. PAR was converted to Hall's five categories of physical activity level (PAL) ranging from "Very Light" to "Very Active" [14].

PAL is defined as a ratio that individual's total daily energy expenditure (TDEE) in a day, divided by individual's resting metabolic rate (RMR) [130].

Activity Logs

Participants also reported all physical activities during the entire intervention period, including the TIGER-prescribed exercise as well as additional activity outside of TIGER sessions, using an online activity log. The modes (i.e., weight lifting, elliptical, running, etc.), duration (minutes), and intensity (rating of perceived exertion, RPE, ranging from 6 to 20 [72]) for each session were reported by participants.

Weight history

Weight history was self-reported by participants on a questionnaire at baseline. The two different study phases used different questions about weight history. Participants reported their body weight in the previous 2 years (Phase 1: University of Houston) or at the end of high school (Phase 2: University of Houston and University of Alabama at Birmingham). The historical change in weight was estimated as the difference between the measured baseline weight and this reported prior weight.

VO_2max estimation

Participants performed a 1-mile walk or 1.5-mile run test and the exercise HR during the test and duration of test were recorded. To estimate VO_2max (mlO_2/kg/min), the equations by Kline et al. [109] and Baumgartner et al. [110] were used for 1-mile walk and 1.5-mile run test, respectively. However, the Astrand-Ryhming method [112] was finally used to estimate VO_2max due to limitations for estimating maximal oxygen consumption during the test by untrained sedentary participants.

TIGER-prescribed exercise intervention

Participants participated in the 15-week of aerobic exercise intervention at a prescribed 65-85% of age and sex-specific predicted maximum HR reserve [114], 30 minutes or more per day, and 3 days per week. Different activities (i.e., treadmill, elliptical trainer, stair stepper, or stationary bike) were allowed to select for different sessions. During each session, participants wore a heart rate (HR) monitor (Polar Electro, Lake Success, NY), and the HR data were recorded and downloaded to compute averaged HR during the sessions for every participant. Invalid data such as the missing or unusable data due to HR monitor malfunction were imputed by using other valid sessions of the within-participant distributions of HR and duration [115].

Physical activity energy expenditure (PAEE) estimation

The PAEE at baseline ($PAEE_1$) and during the 15-week intervention ($PAEE_2$) were estimated using the equation by Hall et al. [14] (Eq. 3).

$$PAEE\ (kJ/kg/day) = [(1 - \beta_{TEF}) \times PAL - 1]REE/BW \qquad \text{(Eq. 3)}$$

where β_{TEF} is 0.1, representing the thermic effect of food, estimated as 10% of TDEE. PAL is ratio of TDEE, which includes the amount of work or school activity such as all non-spontaneous PA and exercise activity, divided by REE. The PAL of $PAEE_1$ was calculated using participant's PAR at baseline by converting into PAL. The PAL of $PAEE_2$ was calculated using participant's measured HR during the TIGER-prescribed activity and self-reported activity logs including mode, duration and RPE of each activity for non-prescribed activity (Appendix 1 of Study 1, the 4th and 5th methods). REE (kJ/day) is resting EE, estimated from equations in Mifflin et al. [62], and BW (kg) is body weight at baseline.

EB status at baseline calculation

EB status before participating in the prescribed exercise intervention was calculated by using each participant's weight history and the equations of Hall et al. (2007) below (Equation 2) [80], which incorporates Forbes's parameter [74]. The baseline EB (ΔBW_b) is a function of weight change, and more specifically the change in body composition, the relative changes in FM and FFM, since FM has a much higher energy density than FFM ($\Delta BW_b = \Delta FFM_b + \Delta FM_b$, where ΔFFM_b and ΔFM_b are history of FFM and FM change). Consequently, a reasonable estimate of change in FM (ΔFM) and FFM (ΔFFM) using only reported change in BW and current FM (via DXA) was required (i.e., $+\Delta FM_b = FM_2 - FM_1$, where FM_1 and FM_2 are the historical and baseline FM, respectively.).

$$FM_1 = 10.4W\left[\frac{1}{10.4} \times exp\left(\frac{\Delta BW_b}{10.4}\right) \times FM_2 \times exp\left(\frac{FM_2}{10.4}\right)\right] \qquad \text{(Eq. 19)}$$

Because baseline EB status in individuals is represented by relatively large, longitudinal changes of body mass and composition, Hall expended upon the concept of Forbes's original equation of cross-sectional association between FFM and FM to predict body composition change for a given change of body weight (ΔBW_b) and current FM (FM_2) using the Lambert W function to solve a transcendental equation predicting historical FM (FM_1) [117].

Estimation of predicted body weight changes

Predicted body mass changes after the TIGER-prescribed exercise intervention were estimated using the equations from the NIDDK Body Weight Planner program by Hall et al. [14]. Hall and his colleagues demonstrated a web-based dynamic simulation program and equations to estimate weight changes over time in response to changes of calorie intake and PA. According to his program and equations, initial body composition (FM and FFM) and physical activity level (PAL, TDEE divided by REE) were accounted for estimating weight changes (see Equation 4).

$$\Delta BW = \frac{(1-\beta)\Delta EI - (BW_1 \times \Delta PAEE)}{PAEE_1 + \Delta PAEE + \gamma_{FFM} - \phi(\gamma_{FFM} - \gamma_{FM})} \qquad \text{(Eq. 4)}$$

The predictors of Equation 3 are β (proportion of TDEE attributable to both TEF, 0.10, and adaptive thermogenesis (AT), 0.14, so β = 0.24), changes of EI (ΔEI, kJ/day) and PAEE ($\Delta PAEE$, kJ/kg/day), baseline body weight (BW_1, kg) and PAEE ($PAEE_1$, kJ//kg/day), contribution of FFM and FM to REE (γ_{FFM}= 92 kJ/kg/day and γ_{FM}= 13 kJ/kg/day, respectively), and ϕ representing composition of body weight change, $FM/(C + FM)$, where FM is baseline FM which was measured FM at baseline and C is 10.4, the Forbes parameter. Because ϕ increases with initial FM and the $\gamma_{FFM} > \gamma_{FM}$, the difference in the right side of the denominator becomes smaller with larger FM, so the expected final ΔBW is larger for larger FM.

However, EB status was not included to consider in this model, since Hall's Body Weight Planner program has been developed to estimate adjustment of caloric values or days for achieving weight goals in individuals. Therefore, the EB status before participating in prescribed exercise intervention program in each individual using Equation 19 was added (Eq. 20).

$$\Delta BW = \frac{(1-\beta)\Delta EI-(BW_1 \times \Delta PAEE)+EB}{PAEE_1+\Delta PAEE+\gamma_{FFM}-\phi(\gamma_{FFM}-\gamma_{FM})} \qquad \text{(Eq. 20)}$$

The expected total body weight change when a new energy balance (stable weight) was estimated using the adapted version of Hall's equation, Equation 4. Using Equation 19 and the respective energy densities associated with mass changes (ρ_{FFM} = 7,600 kJ/kg and ρ_{FM} = 39,500 kJ/kg), EB (kJ/day) was estimated as (7,600 × ΔFFM + 39,500 × ΔFM)/(365 × 2 years, or the number of days from the at the end of high school to baseline date).

Then, the amount of body weight change after the TIGER-prescribed exercise intervention was estimated using an exponential decay model (Eq. 5) with the characteristic timescale of weight change (τ) (Eq. 6).

$$\Delta BW_t = \Delta BW - \Delta BW e^{-t/\tau} \qquad \text{(Eq. 5)}$$

$$\tau = \frac{\eta_{FM}+\rho_{FM}+\alpha(\eta_{FFM}+\rho_{FFM})}{\gamma_{FM}+PAEE_2+\alpha(\gamma_{FFM}+PAEE_2)} \qquad \text{(Eq. 6)}$$

The τ was obtained by the cost of fat and protein synthesis (η_{FFM} = 960 kJ/kg and η_{FM} = 750 kJ/kg, respectively), metabolizable energy density of mass change (ρ_{FFM} = 7,600 kJ/kg and ρ_{FM} = 39,500 kJ/kg, respectively), contribution of FFM and FM to REE (γ_{FFM} = 92 kJ/kg/day and γ_{FM} = 13 kJ/kg/day, respectively), PAEE of the intervention, and body composition change ($\alpha = C/FM$; where Forbes parameter, C = 10.4, divided by FM at baseline [74]). The τ is decreased by increases of PAEE, meaning both the amount and rate of weight change increases.

Statistical analysis

Descriptive statistics for participants' baseline characteristics such as demographics (i.e., age and sex), anthropometry (i.e., height, weight, FFM, and FM), and PAR at baseline were conducted and presented as mean and standard deviation (SD).

The actual weight changes during the TIGER-prescribed exercise intervention was estimated using the simple difference ($kg_{final} - kg_{baseline}$). The fixed effects regression model was also used to estimate the rate of weight change over the intervention period (kg/day) using four body weight measurements during the intervention period in each participant (i). The intercept represents the expected body weight at baseline, slope represents the rate of body weight change (kg/day), day represents the actual days from baseline for each participant's body weight measurement in the fixed effects model. The residuals, e_{it}, indicates the deviations of each participant from individual regression line at time t.

$$Weight_{it} = Intercept_i + (Slope_i * day_t) + e_{it} \qquad \text{(Eq. 16)}$$

The participant-specific slopes were estimated by computation that correlation between weights and days of each measurement muliplied by the values from the SD of weights devided by the SD of days. The rate of weight change (kg/day) was then calculated by using muliplied by the number of days between pre- and post- weight measurement for the total weight change estimation. By comparing the actual weight changes with the rate of weight changes estimation using both Equation 4 and 20, we examined whether considering

EB status individuals would be more accurate for estimation of body weight changes. If the mean difference and the SD of individual weight change rate are smaller for Equation 20 compared to Equation 4, it was considered to be more accurate method.

All analyses were conducted using STATA (STATA 15, Stata Corp., College Station, TX).

5.3 RESULTS

Among the full sample (n=3,769), 269 participants who were not meet age criteria (18-35 years), 231 who did not have weight pre-post measurements, 1,028 who did not have VO2max data due to missing the 1-mile walk or 1.5-mile run test in two study cohorts, 93 who had estimated VO2max > 65 mlO_2/kg/min or measurement errors such as HR monitor malfunction, 559 who had missing data on demographics, DXA, Block FFQ, weight history, etc. were excluded. Therefore, total 1,544 of participants (men=509; women=1,035) were included in this study.

Descriptive results

The characteristics of participants at baseline are presented in Table 13. Self-reported physical activity rating (PAR) at baseline among all participants showed that 68.8% of participants reported 0-4 PAR scores, meaning they are sedentary, less than 1-mile run or less than 30 minutes of comparable PA per week. PAR scores reporting by men and women were different: reported 0-4 of PAR scores were at baseline in men and women were 56.0% and 75.1%, respectively, and thus women were more sedentary at baseline.

Table 13. Characteristics of participants (Mean±SD, or %)

	All (n=1,544)	Men (n=515)	Women (n=1,050)
Age (yr)	21.2±2.8	21.4±2.7	21.0±2.8
Height (cm)	166.8±9.0	175.3±7.1	162.6±6.6
Weight (kg)	73.2±19.4	83.6±19.4	68.0±17.2
FFM (kg)	49.9±12.6	63.2±10.6	43.4±7.2
FM (kg)	23.3±12.0	20.4±12.3	24.7±11.5
PAR (score)			
0	3.4%	1.0%	4.6%
1	26.1%	15.4%	31.4%
2	12.5%	9.3%	14.0%
3	18.2%	21.1%	16.9%
4	8.6%	9.3%	8.2%
5	15.9%	19.7%	14.0%
6	8.6%	13.1%	6.3%
7	6.7%	11.1%	4.6%

FFM: fat free mass; FM: fat mass; PAR: physical activity rating score

Predicted weight changes with EB status at baseline

Average weight changes at baseline among participants was 4.16 kg (SD=8.57) and averaged EB among participants were 155.04 kJ/day (SD=415.71), which indicates participants were in a small amount of positive EB at baseline, on average.

The predicted weight changes without baseline EB (using Equation 3) was -3.10 kg (SD=8.72), but it became -2.66 kg (SD=8.72) after including baseline EB status (using Equation 20) (Table 14).

Comparison of observed weight changes and predicted weight changes

Averaged simple ΔWT of pre-post measured weights was -0.24 kg (SD=2.55) and averaged rate of ΔWT among 4 timepoints measured weights was 0.28 kg (SD=2.81). The predicted weight changes without including EB status using RPE only and RPE with HR were -3.35 kg (SD=8.14) and -2.80 kg (SD=8.25), respectively. Predicted weight change with EB status using RPE only and RPE with HR were -2.96 kg (SD=8.09) and -2.30 kg (SD=8.19), respectively.

Table 14. Comparisons of the bias and precision between without vs. with EB status at baseline (n=577)

	Simple ΔWT		**Rate of ΔWT**	
Observed change without EB status	**Mean**	**SD**	**Mean**	**SD**
	-0.24	2.55	0.28	2.81
	Bias	**Precision**	**Bias**	**Precision**
RPE only	3.22	8.59	3.74	8.74
RPE + HR	2.56	8.71	3.08	8.83
	Simple ΔWT		**Rate of ΔWT**	
Observed change with EB status	**Mean**	**SD**	**Mean**	**SD**
	-0.24	2.55	0.28	2.81
	Bias	**Precision**	**Bias**	**Precision**
RPE only	2.73	8.54	3.25	8.70
RPE + HR	2.07	8.66	2.59	8.78

ΔWT: weight change; Bias: mean differences between observed ΔWT and predicted ΔWT by each method; Imprecision: SD differences between observed ΔWT and predicted ΔWT by each method

The bias and precision of predicted weight changes (Predicted ΔWT with or without Baseline EB status, RPE only or RPE + HR) compared to observed weight changes (Simple ΔWT and rate of ΔWT) after 15-week prescribed exercise intervention are compared in Table 14. The results showed that using RPE with HR for PAEE estimation was more accurate (lower bias) compared to RPE only, and including baseline EB status lower bias (systematic error) and imprecision (random error) compared to without EB status.

Table 15. Comparisons of the bias and precision between without vs. with EB status at baseline without EI data (n=577)

	Simple ΔWT		Rate of ΔWT	
Observed change without EB status	**Mean**	**SD**	**Mean**	**SD**
	-0.24	2.55	0.28	2.81
	Bias	**Precision**	**Bias**	**Precision**
RPE only	1.69	3.49	1.17	3.82
RPE + HR	1.02	3.52	0.51	3.93
	Simple ΔWT		**Rate of ΔWT**	
Observed change without EB status	**Mean**	**SD**	**Mean**	**SD**
	-0.24	2.55	0.28	2.81
	Bias	**Precision**	**Bias**	**Precision**
RPE ONLY	2.18	3.80	1.67	4.12
RPE + HR	1.52	3.83	1.00	4.22

ΔWT: weight change; Bias: mean differences between observed ΔWT and predicted ΔWT by each method; Imprecision: SD differences between observed ΔWT and predicted ΔWT by each method

Due to infeasible data of self-reported EI data using Block FFQ (i.e., under-reported problems such as less than 1.55 of EI to BMR ratio by Goldberg's cut-off [52]), we repeated the analyses with removed ΔEI from the Equation 4. Under this scenario, EI was assumed not to change (ΔEI=0) during the prescribed exercise intervention period. After removing EI, the bias (means differences between observed and predicted weight changes) and imprecision (SD differences) were lowered in both with and without baseline EB status inclusion. In contrast to the results when ΔEI was included, the models without baseline EB showed lower bias and SDs in both using RPE and RPE with HR for PAEE estimation, compared to modeling including EB status (Table 15).

5.4 DISCUSSION

This study examined whether predicted weight changes following a 15-week PA intervention are more accurately estimated by accounting for body composition, PA level, and baseline EB status. For this study aim, we used Hall's equations to predict weight changes with PAEE estimation using self-reported RPE and measured HR data, which account for baseline body composition and PA level. We also used an adapted equation using Forbes's principle of relative longitudinal changes in FFM and FM [74] and Hall's expanded dynamic changes of body mass and composition [80] to estimate EB status at baseline.

Using self-reported weight history of each participant, the amount of weight change from historical weight to current weight was estimated, and respective energy densities associated with predicted changes of FM and FFM (ρ_{FM} and ρ_{FFM}) were used to calculate the baseline EB in kJ/day. In this study, participants were in positive EB at baseline, which is consistent with a previous study reporting that on average adults are gaining weight (0.5 to 1 kg per year, on average) [2].

In our data, when individual's baseline EB was added, the predicted weight changes were closer to the observed weight changes (both simple difference of pre-post weights and predictions from rate of weight change estimates), which indicates that bias (systematic error) was lower after accounting for individual's baseline EB status. This study also found that PAEE estimation using both self-reported RPE and measured HR data had lower bias compared to using self-reported RPE only. This can be explained by the measured HR being an objective method, so it could be a more accurate indicator of intensity and duration of activity in individuals than a subjective method [7, 11].

To our knowledge, this is the first study to examine the effects of baseline EB status on weight changes after the intervention. Most weight loss intervention studies ask potential participants about recent weight changes and exclude those who report having had substantial recent weight changes [131, 132]. Thus, the included participants are assumed to be weight stable in most studies. However, in reality, there could be variability of EB status based on lifestyle among participants (i.e., gaining weight gradually over the college years, losing weight during the school year but gaining weights during the summer, trying to lose weight in a short period (i.e., “crash dieting” for a month or two) but regaining weight over time (i.e., the span of a year or more), etc.), and thus, most potential participants are unlikely to be weight stable. As our data showed, TIGER participants were mostly in positive EB, but considerable variability of estimated EB status before participating in the intervention was observed. These results indicate the prescribed actvity in this study resulted in inconsistent weight changes across the participants who had different estimated EB at baseline. Therefore, it may be inappropriate to provide the same intervention dose for all if a consistent response is desired (e.g., losing 3% BW). In particular, an intervention of a fixed magnitude for all participants may not be sufficient to create and energy deficit and achieve a weight loss goal among people who are in positive EB (weight gain trajectory). Considering baseline EB status using the information to estimate weight trajectory could be useful for optimizing effective interventions for weight management in large intervention studies.

This study also has limitations. There are possible errors to estimate weight changes and baseline BE from the self-reported methods of EI, PAEE, and weight history. EI data appeared to have many implausible values that adversely affected the estimates of body weight changes, as evidence by improved accuracy and precision of weight change prediction when removing EI change from the estimation process. PAEE estimation using self-reported RPE and measure HR also has limitations to accuracy such as missing activities to report, over- or under-reported durations of activity due to reporting duration in 5-min categories (15 min, 20 min, etc.) rather than actual minutes, HR monitor malfunctions, etc. Also, weight history was measured by asking for body weight 2 years ago or at the end of high school, which are subject to recall bias and thus it may add error to the predicted weight changes. A single time point of weight history may not be able to capture accurate the rate of weight change between the historical and current weight measurement. Future studies should consider including multiple, more recent timepoints of historical weight status such as 3-month, 6-month, and 12-month ago, which may reduce recall bias (recent periods are recalled more accurately than distant periods) and may provide better baseline EB estimation.

This study confirmed that accuracy and precision of predicted weight changes in individuals were improved by accounting for individual variability such as initial body composition, PA level, and especially EB status. Moreover, participants had variability of EB status at baseline, which affected the weight changes after the prescribed activity intervention. Our findings suggest that it is necessary to consider and account for possible EB status at baseline in individuals and evaluate variation in response to an intervention across different states of EB, rather than excluding participants who are not weight stable. This may help to develop effective weight management intervention programs for populations including persons in positive EB and realistic expectations for weight management.

CHAPTER 6

6. MANUSCRIPT 3: ESTIMATION OF WEIGHT CHANGES AMONG DIFFERENT RACIAL GROUPS: IS RACE A CONFOUNDING FACTOR TO PREDICT WEIGHT CHANGE AFTER PRESCRIBED EXERCISE PROGRAM?

6.1 INTRODUCTION

Health disparities have been recognized as a tremendous public health concern, particularly since racial minority populations are rapidly increasing in the United States [133]. Prevalence of obesity and its associated chronic diseases such as cardiovascular diseases and metabolic disorder varies across diverse populations due to genetic, environmental, and behavioral differences contributing to the development of obesity [17, 18].

Indeed, racial differences of body composition, chronic diseases, and behaviors have been observed. For example, for a given body size, on average African American (AA) men have more fat free mass (FFM) [20] and less fat mass (FM) [19] compared to Caucasian men, and Hispanic and AA women have higher body mass index (BMI) [104] and more FM [19] than Caucasian women. In addition, AAs tend to have higher risk of cardiovascular diseases [21, 22], lower cardiorespiratory fitness [45, 134], and higher prevalence of physical inactivity compared to Caucasians [23]. These racially distributed physiological and behavioral differences would affect energy balance (EB), which is associated with energy stores (body mass and composition) and ultimately results in different weight gain, loss, or maintenance among racial groups.

Increasing physical activity energy expenditure (PAEE) improves individual health with or without weight loss. However, the effects of increased PAEE on weight loss and body composition improvement (i.e., increased FFM decreased FM) are inconclusive due to individual variability across different racial groups [24]. Several studies showed racial differences in weight changes and body fat reduction after intervention [135-137], while other studies did not observe racial differences [20, 134, 138] . A recent study also reported that a particular racial group did not benefit from behavioral lifestyle intervention for weight loss [105]. This result may be explained by various genetic and epigenetic [139] factors among different racial groups that may be associated with exercise adoption and adherence [25] or physiological differences in response to prescribed exercise types and dose. In other words, the different outcomes of intervention programs would be expected when considering the racial differences of physiological and behavioral factors.

In addition, each individual has different activity levels and EB status (i.e., negative EB: weight loss; positive EB: weight gain; or EB: weight maintenance) before entering intervention programs, which affects response to new, added activity. Thus, using the same absolute exercise dose (duration and intensity of exercise) may not result in the same weight changes across racial groups. Controlling for each individual's initial (habitual) activity level and EB status along with body composition are key to examining the effects of exercise on weight changes across different racial groups. Understanding racial differences in response to changes in PA would help investigators and practitioners develop adaptable intervention programs for prevention and treatment of obesity in diverse populations, and ultimately to reduce racial disparities in obesity.

The purpose of this study is to examine the effects of race on estimation of weight changes response to 15-week of prescribed exercise intervention after accounting for initial body composition, PA history, and EB status. We hypothesized changes in weight after the prescribed exercise intervention would differ among racial groups, after controlling for initial body composition, energy balance, and PA level.

6.2 METHODS

Study design and participants

This study used data collected between 2003 and 2015 in the Training Intervention and Genetics of Exercise Response (TIGER) study [106]. Participants were ethnically diverse men and women aged 18-35 who enrolled in the study at University of Houston and University of Alabama at Birmingham. Eligible participants were sedentary students who were not limiting caloric intake and currently not participating in a regular exercise program within the past month. Participants were excluded from participating in TIGER study if they were pregnant, had metabolic disorders, difficulties engaging in prescribed exercise intervention. Participants self-identified as one of five categories of racial groups: 1) Non-Hispanic White (NHW), 2) Non-Hispanic Black (NHB), 3) Hispanic, 4) Asian, and 5) Asian Indian. Asian Indian was separated from Asian, since their anthropometric differences have been observed [118]. Participants were excluded from the current investigation if they indicated their race as Multiracial or Others due to difficulty in identifying specific association of race with responses to the intervention in this study. Informed consent was signed by participants before the data collection. The study was approved by the Institutional Review Boards of all involved institutions.

Measures

Height (cm) was measured at pre- and post-prescribed exercise intervention using a stadiometer (SECA Road Rod, Hanover, MD). Weight (kg) was also measured at pre- and post-prescribed exercise intervention, and additionally two interim timepoints during the intervention period using a digital scale (SECA 770, Hanover, MD). Body composition, fat mass (FM) and fat free mas (FFM), was assessed at baseline using Dual-energy x-ray absorptiometry (DXA) (Hologic, Bedford, MA).

1-mile walk or 1.5-mile run test was performed at baseline to estimate VO_2max (ml O_2/kg/min) of each participant. VO_2max was estimated using the recorded HR (beat/min) and duration (min) of the test with the equations by Kline et al. [109] for walk test and Baumgartner et al. [110] for run test. Because there is potential limitation to estimate maximal oxygen consumption by untrained sedentary participants during the field test, the equation underlying the method originally described by Astrand-Ryhming [112] was used to estimate the final VO_2max.

Dietary intake was assessed at pre- and post-prescribed exercise intervention using Block Food Frequency Questionnaire (FFQ, NutritionQuest, Berkeley, CA) [113]. Participants reported the frequency of consumption of 102 food items during a typical week using nine categories, ranging from “never” to “every day”. These values were converted to averaged daily calorie intake (kcal) using the Block’s standard scoring service (https://nutritionquest.com/assessment/pricing_and_ordering/), validated from previous studies [122, 123].

Weight history was assessed by participants using a questionnaire at baseline. The two different study phases (i.e., Phase 1: University of Houston; Phase 2: University of Houston & University of Alabama at Birmingham) used different questions about weight history. Participants reported their body weights either of 2 years ago (Phase 1) or when they were at the end of high school (Phase 2).

Self-reported physical activity rating (PAR) was assessed at pre- and post-prescribed exercise intervention by participants rating their activity level, ranging from 0 to 7 (None = no activity, to Vigorous = Run over 10 miles or 3 hours of comparable PA per week) [70]. The PAR was used to calculate physical activity energy expenditure (PAEE) at baseline by converting to physical activity level (PAL) of Hall and this colleagues' PAEE estimation methods [14].

Exercise Intervention and other activities

The TIGER prescribed exercise intervention consisted of 15-week of aerobic exercise for 30 minutes or more per day at 65%-85% of age- and sex-specific predicted maximum heart rate reserve, 3 times per week [114]. Participants selected activities among options including treadmill, elliptical trainer, stair stepper, or stationary bike for different sessions. During each session, heart rate (HR) was recorded using HR monitors (Polar Electro, Lake Success, NY), and participants were instructed on how to self-monitor HR during exercise to maintain their target HR (i.e., intensity). Then, average HR and duration of each session were used to estimate exercise dose. Possible missing or unusable HR data (i.e., HR monitor malfunction) were imputed using the valid within-participant distributions of HR and duration data. [115].

Participants were also allowed to participate in other physical activities in addition to the prescribed exercise and reported the additional activities using their activity logs. The types of activities as well as the duration and Borg's rating of perceived exertion (RPE) ranging from 6-20 were reported for each activity in the logs. PAEE was estimated by using RPE and predicted maximum HR to estimate the participant's percent of heart rate reserve [112] , which could be expressed as percent of VO_2max, with self-reported duration for each activity. The recorded average HR and total duration (min) during the prescribed activity were combined to estimate total PAEE during the entire intervention period.

Estimation of predicted body weight change

Predicted body weight changes after the 15-week prescribed exercise intervention in individuals were estimated using the National Institutes of Diabetes and Digestive and Kidney Diseases (NIDDK) Body Weight Planner program and equations by Hall and colleagues [14]. There are several steps for predicted body weight changes estimation: 1) PAEE estimation, 2) body weight change for a new steady state, and 3) body weight change estimation expected to occur during the intervention period only.

1) PAEE estimation

Using the equation below [14], the PAEE at baseline ($PAEE_1$) and during the prescribed exercise intervention ($PAEE_2$) were estimated.

$$PAEE\ (kJ/kg/day) = [(1 - \beta_{TEF}) \times PAL - 1]REE/BW \qquad \text{(Eq. 3)}$$

β_{TEF} indicates a constant value of 0.1, representing the thermic effect of food, estimated for all participants as 10% of TDEE. PAL represents the physical activity level ratio of TDEE divided by REE. For $PAEE_1$ estimation, participant's PAR at baseline was converted into PAL. For $PAEE_2$ estimation, participant's measured HR and duration during the prescribed activity and self-reported non-prescribed activity were used. Detailed process of PAEE estimation was described elsewhere (Appendix 1 of Study 1, the 4th and 5th method). REE (kJ/day) was estimated by using the equations in Mifflin et al. [62], and BW (kg) represents body weight at baseline.

2) Body weight change estimation for a new EB state

The expected total body weight change for a new EB state was estimated using the adapted version of Hall's equation (Eq. 20). This adapted version was created using Hall's equation [14] to account for EB status at baseline for body weight change estimation. The detailed concepts and processes of adapted version of the equation were described in Appendix 2.

$$\Delta BW = \frac{(1-\beta)\Delta EI-(BW_1 \times \Delta PAEE)+EB}{PAEE_1+\Delta PAEE+\gamma_{FFM}-\phi(\gamma_{FFM}-\gamma_{FM})} \qquad \text{(Eq. 20)}$$

β is 0.24, which are sum of the proportion of TDEE attributable to both TEF (0.10) and the adaptive thermogenesis (0.14). ΔEI (kJ/day) and $\Delta PAEE$ (kJ/kg/day) represent the changes of EI and PAEE between baseline and after the intervention, respectively. EB (kJ/day) represents baseline EB status, estimated using the respective energy densities associated with mass changes (ρ_{FFM} = 7,600 kJ/kg and ρ_{FM}= 39,500 kJ/kg) divided by days from historical weight to current weight. BW_1(kg) is the baseline body weight and $PAEE_1$(kJ//kg/day) is the baseline PAEE. γ_{FFM} and γ_{FM} are 92 kJ/kg/day and 13 kJ/kg/day, representing metabolic cost of FFM and FM to REE, respectively. ϕ represents composition of body weight change, $FM/C(C+FM)$, where FM is baseline FM and C is 10.4, the Forbes parameter.

3) Final body weight change estimation after the intervention

The final body weight change after the prescribed exercise intervention (i.e., the portion of the total change in Equation 2 expected to occur in the initial 15 weeks) was estimated using the Equation 5, which represent the exponential decay function predicting ΔBW at time = *t*. Conceptually, the total time to achieve final BW change is a function of the energy density of the mass change and the rate of weight change relative to TDEE [14, 140]. Using this concept, Equation 6 was derived as the characteristic time constant (τ) for the predicted nonlinear rate of weight loss given the initial body weight and body composition and $PAEE_2$.

$$\Delta BW_t = \Delta BW - \Delta BW e^{-t/\tau} \qquad \text{(Eq. 5)}$$

$$\tau = \frac{\eta_{FM}+\rho_{FM}+\alpha(\eta_{FFM}+\rho_{FFM})}{\gamma_{FM}+PAEE_2+\alpha(\gamma_{FFM}+PAEE_2)} \qquad \text{(Eq. 6)}$$

η_{FFM} and η_{FM} represent the cost of fat and protein synthesis, which are 960 kJ/kg and 750 kJ/kg, respectively. ρ_{FFM} and ρ_{FM} represent metabolizable energy density of mass change, which are 7,600 kJ/kg and 39,500 kJ/kg, respectively. γ_{FFM} and γ_{FM} represent contribution of FFM and FM to REE, which are 92 kJ/kg/day and 13 kJ/kg/day, respectively. The α is C/FM and C is Forbes parameter, 10.4, divided by FM at baseline [74]). When $PAEE_2$ increases, the τ decreases, which means the rate of weight change increases such that the total weight change is achieved more quickly.

Statistical analyses

For all statistical analyses, Stata (Stata 15, Stata Corp., College Station, TX) was used. Descriptive statistics such as participants' demographics (i.e., age, sex, and race), anthropometry (i.e., height, weight, FFM and FM), and PAR at baseline were conducted, representing as mean and standard deviation (SD).

The observed weight changes after the prescribed exercise intervention was estimated by the simple difference between final weight (kg) and baseline weight (kg). In addition, the fixed effects regression model was used to estimate the rate of weight change during the intervention (kg/day) from four time points of weight measurement in each participant (*i*).

$$Weight_{it} = Intercept_i + (Slope_i * day_t) + e_{it} \quad \text{(Eq. 16)}$$

The actual days from baseline for each body weight measurements were used as the day (*t*) from baseline (*t* = 0) using weight on day = slope * days for each participant (*i*). The slopes of each participant were estimated by correlation of weights with days between each measurement as well as the SDs of weights and days. For the rate of weight change after the 15-week intervention, the numbers of days between baseline and final weight measurement was multiplied. For instance, if slope is 0.01 kg/day and 15-week is 105 days, the race is 0.01 * 105 =1.05 kg. The e_{it} is residual, representing the deviations of each participant from their individual regression line at time (*t*).

Then, analysis of variance (ANOVA) tests were used to compare racial groups on bias, defined as the differences of the observed body weight change (Both the rate estimated by the fixed effects model and the simple post-pre weight difference) and the predicted body weight changes after 15-week prescribed exercise intervention.

6.3 RESULTS

In this study, 459 of men and 958 of women, total 1,417 participants, were included. Among participants who enrolled in the TIGER study (n=3,769), we excluded 269 participants who were not between 18-35 years of age, 231 who had missing on both pre and post weight measurements, 1,028 who did not have VO2max data due to missing the 1-mile walk or 1.5-mile run test in the two study cohorts, 93 who had VO2max > 65 or measurement errors such as HR monitor malfunction, and 559 who had missing data on demographics, DXA, Block FFQ, weight history, etc. Two-hundred fifty-two participants were further excluded for missing data on race or self-classifying of race as Multi-racial or others.

Descriptive results

Table 16 and 17 described the characteristics of participants at baseline. Average age, height, weight, fat free mass (FFM), fat mass (FM) of all participants were 21.2 years (SD=2.7), 166.8 cm (SD=9.0), 73.2 kg (SD=19.4), 49.9 kg (SD=12.6), and 23.3 kg (SD=12.0), respectively. Because there are sex and race differences in body size and composition, men and women with different races were described separately (Table 2). Average height of Non-Hispanic White (NHW) was significantly higher than Hispanic White (HW) (men: p=.001; women: p<.001), Asian Indian (AI) (men: p=.002; women: p=.001), and Asian (men: p=.001; women: p<.001) in both men and women. Average weight of NHW was significantly lower than NHB (p<.001) but higher than Asian (p<.001) in women; while average weight of NHW was not significantly different from other racial groups in men. In both men and women, average FFM of NHW was significantly lower than NHB (men: p=.001; women: p<.001), but higher than AI (men: p=.009; women: p=.001) and Asian (men: p=.022; women: p<.001). NHW men had significantly higher FM than NHB men (p=.029); while NHW women had significantly lower FM than NHB women (p=.001).

Table 16. Characteristics of participants (Mean±SD, or %)

	All (n=1,417)	Men (n=459)	Women (n=958)
Age (yr)	21.2±2.7	21.4±2.8	21.1±2.7
Height (cm)	166.8±8.9	175.3±7.0	162.7±6.6
Weight (kg)	73.6±19.6	84.1±19.4	68.5±17.4
FFM (kg)	50.0±12.6	63.4±10.7	43.6±7.3
FM (kg)	23.6±12.2	20.6±12.6	25.0±11.7
Race			
Non-Hispanic White (NHW)	43.0%	47.4%	40.8%
Hispanic White (HW)	16.0%	19.0%	14.5%
Non-Hispanic Black (NHB)	31.3%	21.8%	35.8%
Asian Indian (AI)	2.8%	3.5%	2.5%
Asian	7.0%	8.3%	6.4%

FFM: fat free mass; FM: fat mass; PAR: physical activity rating score

For baseline self-reported PA (PAR), NHB and Asian women significantly more reported 0-4 scores of PAR (sedentary to less active categories) than NHW women ($p<.001$, data not shown). Asian men had significantly higher baseline EB in kJ/day compared to NHW men ($p=.019$), and NHB women had significantly higher EB at baseline (kJ/day) compared to NHW women ($p=.001$) (data not shown).

Table 17. Characteristics of participants by sex and race

	Non-Hispanic White (NHW) (n=609)	Hispanic White (HW) (n=226)	Non-Hispanic Black (NHB) (n=443)	Asian Indian (AI) (n=40)	Asian (n=99)
Men (n=459)	n=218	n=87	n=100	n=16	n=38
Age (yr)	21.8±3.1	21.5±2.5	20.6±2.4	21.6±3.1	21.0±1.7
Height (cm)	176.6±6.7	173.4±7.0*	176.1±6.7	171.2±6.2*	171.8±7.2*
Weight (kg)	84.7±19.7	83.1±19.5	86.0±18.6	82.1±21.2	78.1±22.6
FFM (kg)	62.9±9.7	63.4±11.2	67.6±10.2*	56.2±10.4*	58.8±12.1*
FM (kg)	21.8±13.4	19.7±10.6	18.4±12.1*	25.9±12.0	19.3±12.7
Women (n=958)	n=391	n=139	n=343	n=24	n=61
Age (yr)	21.1±2.9	21.3±2.7	20.9±2.7	21.5±1.6	20.8±1.9
Height (cm)	164.4±6.3	159.1±5.9*	163.5±6.2	159.0±5.9*	158.2±6.4*
Weight (kg)	66.6±14.4	67.8±16.6	73.4±20.1*	57.3±11.5	62.9±9.7*
FFM (kg)	42.8±6.1	42.3±6.8	46.3±7.8*	38.6±6.9*	37.9±5.9*
FM (kg)	23.8±10.2	25.5±10.8	27.1±13.8*	24.3±9.2	19.4±7.2*

FFM: fat free mass; FM: fat mass; PAR: physical activity rating score; NHW (non-Hispanic White) is reference. *p<.05

PAEE estimation

The PAEE during the 15-week prescribed exercise intervention period was estimated using two methods: 1) the self-reported activity logs with RPE (RPE only) and 2) the measured HR data during the intervention and self-reported activity logs with RPE for other than prescribed activity (RPE + HR) using Equation 3. Averaged PAL (ratio of TDEE/REE) of RPE only and RPE+ HR were 1.67 (SD=0.06) and 1.64 (SD=0.04), respectively. Averaged PAEEs of RPE only and RPE + HR were 62.06 kJ/kg/day (SD=9.17) and 60.04 kJ/kg/day (SD=7.82), respectively (data not shown).

Observed and Predicted weight changes estimation

The observed weight changes between before and after the intervention (Simple ΔBW) was are -0.18 kg (SD=2.56) and the rate of weight change over the intervention period (Rate of ΔBW) was 0.32 kg/day (SD=2.81).

Predicted weight changes were estimated using Equation 5, 6, and 20 after estimating EB status at baseline using weight history data. According to the estimation of EB status before participating in the TIGER study, participants were gaining 4.31 kg (SD=8.43) in average from 2 years ago or the end of high school to baseline, and they had 154.81 kJ/day (SD=357.00) of positive energy balance in average. After inclusion of baseline EB status, estimation of predicted weight change using RPE only and RPE + HR were -2.95 kg (SD=8.07) and -2.29 kg (SD=8.18), respectively.

The differences of race and bias among observed and predicted weight changes

Table 18 shows the racial differences of observed weight changes (both Simple ΔBW and Rate of ΔBW) with predicted weight change (predicted ΔBW, using RPE only or RPE + HR).

Table 18. Racial differences of observed and predicted weight changes (n=550)

	Non-Hispanic White (NHW) (n=314)	Hispanic White (HW) (n=18)	Non-Hispanic Black (NHB) (n=175)	Asian Indian (AI) (n=13)	Asian (n=30)
Observed ΔBW					
Simple ΔBW	-0.27±2.5	0.44±1.9	-0.06±2.8	-0.57±2.1	-0.20±2.4
Rate of ΔBW	0.58±2.7	0.78±1.9	-0.11±3.1	0.26±2.3	-0.18±2.7
Predicted ΔBW					
RPE only	-2.70±6.5	-3.16±6.0	-3.46±9.7	-4.02±7.0	-2.04±13.2
RPE + HR	-1.97±6.5	-2.71±6.0	-2.86±9.9	-3.49±7.0	-1.58±13.4

ΔBW: Body weight change

Table 19 presents bias of predicted weight changes compared to observed weight changes by racial groups. The PAEE estimation using RPE with HR showed lower bias compared to RPE only for both Simple ΔBW and Rate of ΔBW among five racial groups. The racial differences of bias were tested using ANOVA, but there were no significant racial differences of bias.

Table 19. Bias among by racial groups (n=550)

	Mean	NHW (n=314)	HW (n=18)	NHB (n=175)	AI (n=13)	Asian (n=30)
Simple ΔBW	**-0.18**					
RPE only	2.77	2.43	3.59	3.39	3.45	1.84
RPE + HR	2.11	1.70	3.14	2.79	2.92	1.38
Rate of ΔBW	**0.32**					
RPE only	3.27	3.28	3.93	3.35	4.28	1.86
RPE + HR	2.61	2.55	3.48	2.75	3.75	1.40

ΔBW: Body weight change; NHW: non-Hispanic white; HW: Hispanic white; NHB: non-Hispanic black; AI: Asian

Since implausible EI data (i.e., Goldberg's cut-off: EI/BMR < 1.55) were found in this study, ΔEI was removed to improve estimation of predicted weight changes by PAEE changes (Equation 2). The analyses were repeated with the ΔEI set to 0 in Equation 4, which indicates the assumption that EI did not change during the intervention period. Given that only a prescribed exercise intervention without dietary intervention was provided to participants, PAEE would be expected to change, but EI may not have changed. The racial differences of bias without EI estimation were tested using ANOVA and presents in Table 20. According to the result, the bias of rate of ΔBW were significantly different between NHW and NHB for both RPE only and RPE + HR (p<.001).

Table 20. Bias among by racial groups, with ΔEI=0 (n=550)

	Mean	NHW (n=314)	HW (n=18)	NHB (n=175)	AI (n=13)	Asian (n=30)
Simple ΔBW	**-0.18**					
RPE only	2.19	1.94	1.68	2.67	1.63	2.59
RPE + HR	1.53	1.20	1.22	2.08	1.08	2.14
Rate of ΔBW	**0.32**					
RPE only	1.69	1.10	1.34	2.72*	0.79	2.57
RPE + HR	1.03	0.36	0.88	2.08*	0.24	2.11

ΔEI: Change in energy intake; ΔBW: Body weight change; NHW: non-Hispanic white; HW: Hispanic white; NHB: non-Hispanic black; AI: Asian; NHW (non-Hispanic White) is reference. *p<.05

6.4 DISCUSSION

The current study examined whether racial differences explain any remaining variability to predict weight changes following a 15-week of exercise intervention, after accounting for initial body composition, PA level, and EB status. The five different racial groups, non-Hispanic white, Hispanic white, non-Hispanic black, Asian Indian, and Asian, were included to predict observed weight changes with predicted body weight changes by quantifying PAEE using self-reported RPE and measured HR data.

This study observed racial differences of body size (i.e., height and weight) and composition (i.e., FFM and FM) at baseline in both men and women. Our findings were consistent with previous studies of racial differences in anthropometric measures [19, 20, 104]. In our assumption, these racial differences would affect weight changes response to

PAEE changes, which results in bias or imprecision to predict weight changes. However, there were no significant racial differences in bias of predicted weight changes using PAEE estimation of self-reported RPE and measured HR. The observed racial differences of body composition and weight at baseline in this study represents individual variability regardless of race or sex. Hall's equations account for the individual variation in initial body composition and PA level in prediction of weight changes following EI and/or PAEE changes [14] and do not include sex or race as factors. If race introduced substantial variation into the prediction, the bias should vary by race, but that did not occur. Therefore, weight changes can be explained by individual variability in physical and behavioral factors rather than race.

Because race may be associated with biological factors rather than physiological and behavioral factors that were accounted for weight change prediction in the Hall's equations [14], we hypothesized that race could be an additional potential factor explaining variability in response. That hypothesis was not supported. There were still differences (bias) between observed and predicted weight changes after accounting for the physiological factors, and thus, future studies are needed to investigate the errors of current prediction methods (i.e., PAEE estimation using a variety of self-reported and objective methods). In addition, the findings of baseline racial differences of body composition and size in this study can be considered as individual variability, so these individual-level factors could be used to develop and adapt dose of intervention for individuals regardless of race.

There were limitations of this study. First, categorizing into racial groups using self-report may not be accurate to represent biological differences among the racial groups, and small numbers of Asian Indian and Asian groups in this study limit comparisons with other racial groups. Second, measurement errors of self-reported EI, PAEE, and EB status (history of weight change) measures may affect accuracy of predicting weight changes following an intervention. Specifically, self-reported EI data using Block FFQ were found to be implausible for many participants in this study. When it was removed from the predicted weight change estimation, the racial differences of predicted weight changes were statistically significant, but it cannot be concluded that racial differences may affect weight changes in this study since EI reporting errors may be confounded with race. If EI had changed equally across the racial groups and then racial differences of weight changes appeared, it could be interpreted as being unexplained differences in effects of intervention among racial groups. Unfortunately, due to the implausibility (inaccuracy) for a large proportion of the EI data, race differences in ΔEI could not be tested with confidence. Future studies with two or more different methods to estimate EI changes to compare bias of EI methods to apply the least biased method to test racial differences.

Despite these limitations, this study included valid and reliable self-reported methods to estimate EI [50] and PAEE [72, 125] changes as well as well-developed and validated dynamic mathematical models to predict weight changes [14]. Our findings suggest that weight changes can be reasonably accurately predicted by considering initial body composition, PA level, and EB status alone, such that race does not appear to be a substantial factor in response.

CHAPTER 7

7. CONCLUSION

7.1 SUMMARY

Weight change is explained by changes of energy imbalance between energy intake (EI) and energy expenditure (EE). Increased physical activity energy expenditure (PAEE), restricted EI, or combination of both produce negative EB, and ultimately weight loss. Predicting weight changes can be estimated by quantifying the amount of energy deficit that is produced by PAEE and EI. However, there are sources of error in estimating energy deficit such as measures of PAEE and EI (both objective and subjective methods) as well as confounding factors that affect inconsistent estimates of EB. Self-reported data have been used to collect data in large populations based on the advantages of requiring few resources and feasibility, but also have reliability and validity issues. Thus, it is valuable and important to seek accurate and reliable way to predict weight changes using self-reported EE and EI data while accounting for possible confounding factors that influence EB estimation.

This dissertation project fulfilled three research aims: 1) improving estimation of predicted weight changes after participating in a prescribed exercise program using variety of self-reported physical activity (PA) data and examining the accuracy (bias and imprecision) of the PAEE estimation methods; 2) investigating the effects of different baseline energy balance (EB) status on weight change following a prescribed activity to improve the accuracy of the weight change estimation; and 3) examining the effects of race on weight change response to the prescribed activity to improve the accuracy of the weight change estimation.

For the first research aim, weight changes after 15-week prescribed exercise were predicted by using the five methods of PAEE estimations: 1) categorized PAL of prescribed activity (1.8 PAL for all participants), 2) categorized PAL using PAR reported by participants, 3) PAL ratio (TDEE/REE) calculation using activity logs and compendium MET values for the reported activities, 4) PAL ratio calculation using RPE from activity logs, and 5) PAL ratio calculation using measured HR for all prescribed exercise sessions and RPE from the activity log for non-prescribed activities. The findings of this dissertation indicate that the predicted weight change estimations among the variety of self-reported PAEE methods were fairly consistent, except for the substantially worse prediction using self-reported PA category by PAR (the second method). The predicted weight change by PAEE estimation using the fifth method, combination of measured HR and self-reported RPE, was the closest to observed weight changes, indicating lowest bias, as expected when incorporating an objective measure. Using RPEs during the activities was the most accurate self-reported method for estimation of PAEE used to predict body mass changes after the prescribed intervention. These observations suggest that self-reported RPE measures can be feasible to use and analyze in the large population research setting with training people for accurate reporting.

To examine the second research aim, the baseline EB status was estimated using self-reported weight history data and added to the equation that estimates the predicted weight changes. Our findings showed participants had a small amount of positive EB before participating in the prescribed activity on average but considerable variability of estimated EB status before participating in the intervention was observed. In addition, this dissertation confirmed that bias and precision of predicted weight changes in individuals were improved by accounting for initial EB status. These results suggest that it may be inappropriate to provide the same intervention dose for all participants if a consistent response is desired (e.g., losing 3% BW). Therefore, investigators need to consider individual variability in characteristics at baseline and incorporate that information to account and adjust for it in the development of effective weight management intervention programs.

Finally, for the third research aim, this dissertation examined whether racial differences explain any remaining variability to predict weight changes following a 15-week of exercise intervention, after accounting for initial body composition, PA level, and EB status. The five different racial groups, non-Hispanic white, Hispanic white, non-Hispanic black, Asian Indian, and Asian, were included to predict observed weight changes with predicted body weight changes by quantifying PAEE using self-reported RPE and measured HR data. This dissertation observed racial differences of body size (i.e., height and weight) and composition (i.e., FFM and FM) at baseline in both men and women. However, after accounting for body size and composition, race did not affect prediction of weight changes, either simple difference of before and after intervention or the rate of weight changes over the intervention period. These results indicate that weight changes can be explained by individual variability in initial body composition and PA level, without the need to include race as a factor. Therefore, weight changes can be reasonably accurately predicted by considering initial body composition, PA level, and EB status alone, such that race does not appear to be a substantial factor.

7.2 STRENGTHS AND LIMITATIONS

This dissertation project contributes novel findings to the investigation of feasible and reliable self-reported data use to predict weight change by changes of PAEE. A variety of valid and reliable self-reported methods and measured data were included and PAEE estimations to predict weight changes were compared to evaluate accuracy. For the accurate weight change prediction after a prescribed activity, possible confounding factors that affect weight change estimation were accounted for using well-developed and validated dynamic mathematical models. Then, the predicted weight changes were compared to the observed weight changes, such that bias and imprecision could be compared.

This dissertation was the first known study to examine the effects of baseline EB status on weight changes following the intervention. By assessing and accounting for the variability of EB status at baseline in individuals with initial body composition and PA level, the bias and precision of predicted weight change estimation were improved. Thus, considering baseline EB status using the information to estimate weight trajectory could be useful for effective interventions for weight management in individuals.

Among the study limitations, the most important was that the EI data appeared to have many implausible values that adversely affected the estimates of body weight changes, as evidence by improved accuracy and precision of weight change prediction when removing EI change from the estimation process. PAEE estimation using self-reported RPE and measure HR also has limitations to accuracy such as missing activities to report, HR monitor malfunctions, etc. The self-reported weight history was measured by asking for body weight 2 years ago or at the end of high school, which are subject to recall bias. Finally, categorizing into racial groups using self-report may not be accurate to represent biological differences among the racial groups, and there were small numbers of Asian Indian and Asian groups in this study limit racial group comparisons.

7.3 IMPLICATIONS AND FUTURE DIRECTIONS

This dissertation project includes important implications for research and practice. There are ways to reduce sources of error to estimate EE and EI and associated weight changes that may be adjusted to provide more accurate estimation. Indeed, adding more detailed self-reported information and accounting for more potential confounding factors (i.e., individual variability) resulted in improvement of accuracy for estimating PAEE. Investigators or practitioners should consider evaluating and incorporating baseline individual variability to develop exercise intervention programs and adapt exercise doses for effective weight management. In this dissertation project, EI data using the Block FFQ had many implausible values to predict weight changes. Only one method to self-report EI was available while there were various PAEE self-reported methods, so we were unable to compare accuracy of methods and sources of EI self-report errors. Future studies that include more self-report EI and EE methods will allow for comprehensive evaluation and identification of strategies for more feasible and reliable self-report methods to provide predictions with lower bias and imprecision.

Feasible and accurate (low bias, high precision) self-reported methods that can be easily applied in future epidemiology studies of the free-living large population would be of great value. Self-reported RPE is recommended as the most accurate self-reported method to quantify PAEE and estimate predicted weight change. Measured HR appeared to lower bias and imprecision, probably due to removing systematic errors of measurement due to self-report (i.e., over- or under-reported intensity and duration) and missing self-report of intensity or duration. However, there still could be possible errors for HR measures such as HR monitor malfunction during an activity. Therefore, for intervention studies in particular, it may be important to use multiple methods (including HR measurement or other objective measure), which can be helpful to reduce missing or unreliable data. Finally, reliable and accurate self-reported measures require training participants to report accurately and limit missing data when reporting.

REFERENCE

1. National Center for Health Statistics, N. *Normal weight, overweight, and obesity among adults aged 20 and over, by selected characteristics: United States, selected years 1988-1994 throuhg 2013-2016*. [cited 2019 July 22]; Available from: https://www.cdc.gov/nchs/hus/contents2017.htm#058.
2. Hill, J.O., et al., *Obesity and the environment: where do we go from here?* Science, 2003. **299**(5608): p. 853-5.
3. Thomas, D.M., et al., *Why do individuals not lose more weight from an exercise intervention at a defined dose? An energy balance analysis.* Obes Rev, 2012. **13**(10): p. 835-47.
4. Thomas, D.M. and Heymsfield, S.B., *Exercise: Is More Always Better?* Curr Biol, 2016. **26**(3): p. R102-4.
5. Pontzer, H., et al., *Constrained Total Energy Expenditure and Metabolic Adaptation to Physical Activity in Adult Humans.* Curr Biol, 2016. **26**(3): p. 410-7.
6. Maclean, P.S., et al., *Biology's response to dieting: the impetus for weight regain.* Am J Physiol Regul Integr Comp Physiol, 2011. **301**(3): p. R581-600.
7. Fernandez-Verdejo, R., Aguirre, C., and Galgani, J.E., *Issues in Measuring and Interpreting Energy Balance and Its Contribution to Obesity.* Curr Obes Rep, 2019. **8**(2): p. 88-97.
8. Satija, A., et al., *Objective measures are complementary to, rather than a replacement for, self-reported methods.* Int J Obes (Lond), 2015. **39**(7): p. 1179.
9. Lagerros, Y.T. and Lagiou, P., *Assessment of physical activity and energy expenditure in epidemiological research of chronic diseases.* Eur J Epidemiol, 2007. **22**(6): p. 353-62.
10. Shook, R.P., et al., *Energy Intake Derived from an Energy Balance Equation, Validated Activity Monitors, and Dual X-Ray Absorptiometry Can Provide Acceptable Caloric Intake Data among Young Adults.* J Nutr, 2018. **148**(3): p. 490-496.
11. Dhurandhar, N.V., et al., *Energy balance measurement: when something is not better than nothing.* Int J Obes (Lond), 2015. **39**(7): p. 1109-13.
12. Carpenter, W.H., et al., *Influence of body composition and resting metabolic rate on variation in total energy expenditure: a meta-analysis.* The American Journal of Clinical Nutrition, 1995. **61**(1): p. 4-10.
13. Hall, K.D. and Jordan, P.N., *Modeling weight-loss maintenance to help prevent body weight regain.* Am J Clin Nutr, 2008. **88**(6): p. 1495-503.
14. Hall, K.D., et al., *Quantification of the effect of energy imbalance on bodyweight.* Lancet, 2011. **378**(9793): p. 826-37.
15. Pontzer, H., *Constrained Total Energy Expenditure and the Evolutionary Biology of Energy Balance.* Exerc Sport Sci Rev, 2015. **43**(3): p. 110-6.
16. Blundell, J.E., et al., *Appetite control and energy balance: impact of exercise.* Obes Rev, 2015. **16 Suppl 1**: p. 67-76.
17. Mensah, G.A., et al., *State of disparities in cardiovascular health in the United States.* Circulation, 2005. **111**(10): p. 1233-41.

18. Wei, L. and Wu, B., *Racial and ethnic differences in obesity and overweight as predictors of the onset of functional impairment.* Journal of the American Geriatrics Society, 2014. **62**(1): p. 61-70.
19. O'Connor, D.P., et al., *Generalized equations for estimating DXA percent fat of diverse young women and men: the TIGER study.* Med Sci Sports Exerc, 2010. **42**(10): p. 1959-65.
20. Walts, C.T., et al., *Do sex or race differences influence strength training effects on muscle or fat?* Med Sci Sports Exerc, 2008. **40**(4): p. 669-76.
21. Kurian, A.K. and Cardarelli, K.M., *Racial and ethnic differences in cardiovascular disease risk factors: a systematic review.* Ethn Dis, 2007. **17**(1): p. 143-52.
22. Sundquist, J., Winkleby, M.A., and Pudaric, S., *Cardiovascular disease risk factors among older black, Mexican-American, and white women and men: an analysis of NHANES III, 1988-1994. Third National Health and Nutrition Examination Survey.* J Am Geriatr Soc, 2001. **49**(2): p. 109-16.
23. Egede, L.E. and Poston, M.E., *Racial/ethnic differences in leisure-time physical activity levels among individuals with diabetes.* Diabetes Care, 2004. **27**(10): p. 2493-4.
24. Brewis, A.A., *Obesity: Cultural and Biocultural Perspectives*. 2011: Rutgers University Press.
25. Herring, M.P., Sailors, M.H., and Bray, M.S., *Genetic factors in exercise adoption, adherence and obesity.* Obes Rev, 2014. **15**(1): p. 29-39.
26. Strang, J.M., McClugage, H.B., and Evans, F.A., *Further studies in the dietary correction of obesity.* The American Journal of the Medical Sciences, 1930. **179**(5): p. 687-693.
27. Wishnofsky, M., *Caloric equivalents of gained or lost weight.* The American journal of clinical nutrition, 1958. **6**(5): p. 542-546.
28. Manore, M.M., et al., *Dynamic Energy Balance: An Integrated Framework for Discussing Diet and Physical Activity in Obesity Prevention-Is it More than Eating Less and Exercising More?* Nutrients, 2017. **9**(8): p. 905.
29. Thomas, D.M., et al., *Time to correctly predict the amount of weight loss with dieting.* Journal of the Academy of Nutrition and Dietetics, 2014. **114**(6): p. 857-861.
30. Galgani, J. and Ravussin, E., *Energy metabolism, fuel selection and body weight regulation.* Int J Obes (Lond), 2008. **32 Suppl 7**: p. S109-19.
31. Acheson, K.J., et al., *Protein choices targeting thermogenesis and metabolism.* Am J Clin Nutr, 2011. **93**(3): p. 525-34.
32. Manore, M.M., Meyer, N.L., and Thompson, J.L., *Sport nutrition for health and performance*. 2009: Human Kinetics.
33. Redman, L.M., et al., *Metabolic and behavioral compensations in response to caloric restriction: implications for the maintenance of weight loss.* PloS one, 2009. **4**(2): p. e4377-e4377.
34. Church, T.S., et al., *Changes in weight, waist circumference and compensatory responses with different doses of exercise among sedentary, overweight postmenopausal women.* PloS one, 2009. **4**(2): p. e4515.
35. King, N.A., et al., *Individual variability following 12 weeks of supervised exercise: identification and characterization of compensation for exercise-induced weight loss.* International journal of obesity, 2008. **32**(1): p. 177.

36. Whybrow, S., et al., *The effect of an incremental increase in exercise on appetite, eating behaviour and energy balance in lean men and women feeding ad libitum.* British Journal of Nutrition, 2008. **100**(5): p. 1109-1115.
37. Pomerleau, M., et al., *Effects of exercise intensity on food intake and appetite in women.* The American journal of clinical nutrition, 2004. **80**(5): p. 1230-1236.
38. Stubbs, R.J., et al., *The effect of graded levels of exercise on energy intake and balance in free-living women.* International journal of obesity, 2002. **26**(6): p. 866.
39. Stensel, D., *Exercise, appetite and appetite-regulating hormones: implications for food intake and weight control.* Annals of Nutrition and Metabolism, 2010. **57**(Suppl. 2): p. 36-42.
40. Ravussin, E., et al., *Determinants of 24-hour energy expenditure in man. Methods and results using a respiratory chamber.* J Clin Invest, 1986. **78**(6): p. 1568-78.
41. Schulz, L.O. and Schoeller, D.A., *A compilation of total daily energy expenditures and body weights in healthy adults.* Am J Clin Nutr, 1994. **60**(5): p. 676-81.
42. Nelson, K.M., et al., *Prediction of resting energy expenditure from fat-free mass and fat mass.* Am J Clin Nutr, 1992. **56**(5): p. 848-56.
43. Stiegler, P. and Cunliffe, A., *The Role of Diet and Exercise for the Maintenance of Fat-Free Mass and Resting Metabolic Rate During Weight Loss.* Sports Medicine, 2006. **36**(3): p. 239-262.
44. Stubbs, R.J., et al., *Potential effects of fat mass and fat-free mass on energy intake in different states of energy balance.* European journal of clinical nutrition, 2018. **72**(5): p. 698.
45. Swift, D.L., et al., *Racial differences in the response of cardiorespiratory fitness to aerobic exercise training in Caucasian and African American postmenopausal women.* J Appl Physiol (1985), 2013. **114**(10): p. 1375-82.
46. Morgan, R., et al., *A comparison of dietary methods in epidemiologic studies.* American journal of epidemiology, 1978. **107**(6): p. 488-498.
47. Ma, Y., et al., *Number of 24-hour diet recalls needed to estimate energy intake.* Annals of epidemiology, 2009. **19**(8): p. 553-559.
48. Goris, A.H., Westerterp-Plantenga, M.S., and Westerterp, K.R., *Undereating and underrecording of habitual food intake in obese men: selective underreporting of fat intake.* The American journal of clinical nutrition, 2000. **71**(1): p. 130-134.
49. Barrett-Connor, E., *Nutrition epidemiology: how do we know what they ate?* Am J Clin Nutr, 1991. **54**(1 Suppl): p. 182s-187s.
50. Freedman, L.S., et al., *Pooled Results From 5 Validation Studies of Dietary Self-Report Instruments Using Recovery Biomarkers for Energy and Protein Intake.* American Journal of Epidemiology, 2014. **180**(2): p. 172-188.
51. Trabulsi, J. and Schoeller, D.A., *Evaluation of dietary assessment instruments against doubly labeled water, a biomarker of habitual energy intake.* American Journal of Physiology-Endocrinology And Metabolism, 2001. **281**(5): p. E891-E899.
52. Goldberg, G.R., et al., *Critical evaluation of energy intake data using fundamental principles of energy physiology: 1. Derivation of cut-off limits to identify under-recording.* Eur J Clin Nutr, 1991. **45**(12): p. 569-81.
53. Hall, K.D. and Guo, J., *Obesity energetics: body weight regulation and the effects of diet composition.* Gastroenterology, 2017. **152**(7): p. 1718-1727. e3.

54. Mtaweh, H., et al., *Indirect Calorimetry: History, Technology, and Application.* Frontiers in pediatrics, 2018. **6**: p. 257-257.
55. Fullmer, S., et al., *Evidence analysis library review of best practices for performing indirect calorimetry in healthy and non–critically ill individuals.* Journal of the Academy of Nutrition and Dietetics, 2015. **115**(9): p. 1417-1446. e2.
56. Lazzer, S., et al., *Prediction of resting energy expenditure in severely obese Italian males.* Journal of endocrinological investigation, 2007. **30**(9): p. 754-761.
57. Lazzer, S., et al., *Prediction of resting energy expenditure in severely obese Italian women.* Journal of endocrinological investigation, 2007. **30**(1): p. 20-27.
58. Camina, M.M., et al., *Proposal for a new formula for estimating resting energy expenditure for healthy Spanish population.* Nutricion hospitalaria, 2015. **32**(5): p. 2346-2352.
59. ten Haaf, T. and Weijs, P.J., *Resting energy expenditure prediction in recreational athletes of 18–35 years: confirmation of Cunningham equation and an improved weight-based alternative.* PloS one, 2014. **9**(10): p. e108460.
60. Joint, F., *Human energy requirements. Report of a Joint FAO/WHO/UNU Expert Consultation, Rome, 17-24 October 2001.* 2004.
61. Henry, C., *Basal metabolic rate studies in humans: measurement and development of new equations.* Public health nutrition, 2005. **8**(7a): p. 1133-1152.
62. Mifflin, M.D., et al., *A new predictive equation for resting energy expenditure in healthy individuals.* Am J Clin Nutr, 1990. **51**(2): p. 241-7.
63. Rosenbaum, M., et al., *Accumulating Data to Optimally Predict Obesity Treatment (ADOPT): Recommendations from the Biological Domain.* Obesity (Silver Spring), 2018. **26 Suppl 2**: p. S25-s34.
64. Prentice, A.M., *The doubly-labelled water method for measuring energy expenditure. Technical recommendations for use in humans*. 1990, International Atomic Energy Agency.
65. Westerterp, K.R., *Doubly labelled water assessment of energy expenditure: principle, practice, and promise.* Eur J Appl Physiol, 2017. **117**(7): p. 1277-1285.
66. *Human energy requirements: report of a joint FAO/ WHO/UNU Expert Consultation.* Food Nutr Bull, 2005. **26**(1): p. 166.
67. Garber, C.E., et al., *Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise.* 2011.
68. Ainsworth, B.E., et al., *2011 Compendium of Physical Activities: a second update of codes and MET values.* Medicine & science in sports & exercise, 2011. **43**(8): p. 1575-1581.
69. Ainsworth, B.E., et al., *Compendium of physical activities: an update of activity codes and MET intensities.* Med Sci Sports Exerc, 2000. **32**(9 Suppl): p. S498-504.
70. Jackson, A.S., et al., *Prediction of functional aerobic capacity without exercise testing.* Med Sci Sports Exerc, 1990. **22**(6): p. 863-70.
71. Borg, G., *Perceived exertion as an indicator of somatic stress.* Scand J Rehabil Med, 1970. **2**(2): p. 92-8.
72. Borg, G., *Borg's perceived exertion and pain scales*. Borg's perceived exertion and pain scales. 1998, Champaign, IL, US: Human Kinetics. viii, 104-viii, 104.

73. Glickman, N., et al., *The Total Specific Dynamic Action of High-Protein and High-Carbohydrate Diets on Human Subjects: Two Figures.* The Journal of nutrition, 1948. **36**(1): p. 41-57.
74. Forbes, G.B., *Lean body mass-body fat interrelationships in humans.* Nutrition reviews (USA), 1987.
75. Thomas, D.M., et al., *A simple model predicting individual weight change in humans.* Journal of biological dynamics, 2011. **5**(6): p. 579-599.
76. Thomas, D.M., et al., *A computational model to determine energy intake during weight loss.* The American journal of clinical nutrition, 2010. **92**(6): p. 1326-1331.
77. Hall, K.D., *Predicting metabolic adaptation, body weight change, and energy intake in humans.* American Journal of Physiology-Endocrinology and Metabolism, 2009. **298**(3): p. E449-E466.
78. Aarsland, A., Chinkes, D., and Wolfe, R.R., *Hepatic and whole-body fat synthesis in humans during carbohydrate overfeeding.* The American journal of clinical nutrition, 1997. **65**(6): p. 1774-1782.
79. Acheson, K., et al., *Glycogen storage capacity and de novo lipogenesis during massive carbohydrate overfeeding in man.* The American journal of clinical nutrition, 1988. **48**(2): p. 240-247.
80. Hall, K.D., *Body fat and fat-free mass inter-relationships: Forbes's theory revisited.* British journal of nutrition, 2007. **97**(6): p. 1059-1063.
81. Foreyt, J.P. and Goodrick, G.K., *Evidence for Success of Behavior Modification in Weight Loss and Control.* Annals of Internal Medicine, 1993. **119**(7_Part_2): p. 698-701.
82. Hall, K.D., et al., *Energy balance and its components: implications for body weight regulation.* The American Journal of Clinical Nutrition, 2012. **95**(4): p. 989-994.
83. Westerterp, K.R., *Physical activity, food intake, and body weight regulation: insights from doubly labeled water studies.* Nutr Rev, 2010. **68**(3): p. 148-54.
84. Brown, T., et al., *Systematic review of long-term lifestyle interventions to prevent weight gain and morbidity in adults.* Obesity Reviews, 2009. **10**(6): p. 627-638.
85. Heymsfield, S.B., et al., *Weight loss composition is one-fourth fat-free mass: a critical review and critique of this widely cited rule.* Obes Rev, 2014. **15**(4): p. 310-21.
86. Kohrt, W.M., et al., *American College of Sports Medicine Position Stand: physical activity and bone health.* Med Sci Sports Exerc, 2004. **36**(11): p. 1985-96.
87. Swift, D.L., et al., *The role of exercise and physical activity in weight loss and maintenance.* Progress in cardiovascular diseases, 2014. **56**(4): p. 441-447.
88. Hill, J.O., Wyatt, H.R., and Peters, J.C., *Energy balance and obesity.* Circulation, 2012. **126**(1): p. 126-132.
89. Besson, H., et al., *A cross-sectional analysis of physical activity and obesity indicators in European participants of the EPIC-PANACEA study.* International journal of obesity, 2009. **33**(4): p. 497-506.
90. Hankinson, A.L., et al., *Maintaining a high physical activity level over 20 years and weight gain.* Jama, 2010. **304**(23): p. 2603-2610.
91. May, A.M., et al., *Effect of change in physical activity on body fatness over a 10-y period in the Doetinchem Cohort Study.* The American journal of clinical nutrition, 2010. **92**(3): p. 491-499.

92. Redman, L.M., et al., *Metabolic and behavioral compensations in response to caloric restriction: implications for the maintenance of weight loss.* PLoS One, 2009. **4**(2): p. e4377.
93. Thomas, D.M., et al., *A mathematical model of weight change with adaptation.* Mathematical biosciences and engineering: MBE, 2009. **6**(4): p. 873.
94. Hafekost, K., et al., *Tackling overweight and obesity: does the public health message match the science?* BMC medicine, 2013. **11**(1): p. 41.
95. Dulloo, A.G. and Jacquet, J., *Adaptive reduction in basal metabolic rate in response to food deprivation in humans: a role for feedback signals from fat stores.* The American journal of clinical nutrition, 1998. **68**(3): p. 599-606.
96. Schwartz, M.W., et al., *Central nervous system control of food intake.* Nature, 2000. **404**(6778): p. 661.
97. Hill, J.O., Wyatt, H.R., and Peters, J.C., *The importance of energy balance.* European endocrinology, 2013. **9**(2): p. 111.
98. Yoo, S., *Dynamic energy balance and obesity prevention.* Journal of obesity & metabolic syndrome, 2018. **27**(4): p. 203.
99. Hill, J.O., *Can a small-changes approach help address the obesity epidemic? A report of the Joint Task Force of the American Society for Nutrition, Institute of Food Technologists, and International Food Information Council.* The American journal of clinical nutrition, 2008. **89**(2): p. 477-484.
100. Romanelli, R.J., et al., *Short-term weight trajectories and long-term weight outcomes from a lifestyle intervention in real-world clinical practice.* Transl Behav Med, 2019.
101. Berger, M.B., et al., *The Balance protocol: a pragmatic weight gain prevention randomized controlled trial for medically vulnerable patients within primary care.* BMC public health, 2019. **19**(1): p. 596-596.
102. Ambak, R., et al., *The effect of weight loss intervention programme on health-related quality of life among low income overweight and obese housewives in the MyBFF@home study.* BMC women's health, 2018. **18**(Suppl 1): p. 111-111.
103. Beleigoli, A.M., et al., *Online platform for healthy weight loss in adults with overweight and obesity - the "POEmaS" project: a randomized controlled trial.* BMC public health, 2018. **18**(1): p. 945-945.
104. Flegal, K.M., et al., *Prevalence of obesity and trends in the distribution of body mass index among US adults, 1999-2010.* Jama, 2012. **307**(5): p. 491-7.
105. Goode, R.W., et al., *African Americans in Standard Behavioral Treatment for Obesity, 2001-2015: What Have We Learned?* West J Nurs Res, 2017. **39**(8): p. 1045-1069.
106. Sailors, M.H., et al., *Exposing college students to exercise: the Training Interventions and Genetics of Exercise Response (TIGER) study.* J Am Coll Health, 2010. **59**(1): p. 13-20.
107. Bandura, A., *Health promotion by social cognitive means.* Health education & behavior, 2004. **31**(2): p. 143-164.
108. Ryan, R.M. and Deci, E.L., *Self-determination theory and the facilitation of intrinsic motivation, social development, and well-being.* American psychologist, 2000. **55**(1): p. 68.
109. Kline, G.M., et al., *Estimation of VO2max from a one-mile track walk, gender, age, and body weight.* Med Sci Sports Exerc, 1987. **19**(3): p. 253-9.

110. Baumgartner, T.A., et al., *Measurement for evaluation in kinesiology*. 2015: Jones & Bartlett Publishers.
111. Medicine, A.C.o.S., *ACSM's guidelines for exercise testing and prescription*. 2013: Lippincott Williams & Wilkins.
112. Åstrand, P.-O. and Ryhming, I., *A nomogram for calculation of aerobic capacity (physical fitness) from pulse rate during submaximal work.* Journal of applied physiology, 1954. **7**(2): p. 218-221.
113. Block, G., et al., *A DATA-BASED APPROACH TO DIET QUESTIONNAIRE DESIGN AND TESTING.* American Journal of Epidemiology, 1986. **124**(3): p. 453-469.
114. Jackson, A.S. and Ross, R.M., *Understanding exercise for health and fitness*. 1997: Kendall/Hunt Pub.
115. Miller, F.L., et al., *Exercise dose, exercise adherence, and associated health outcomes in the TIGER study.* Med Sci Sports Exerc, 2014. **46**(1): p. 69-75.
116. Joo, J., et al., *The influence of 15-week exercise training on dietary patterns among young adults.* Int J Obes (Lond), 2019.
117. Corless, R.M., et al., *On the LambertW function.* Advances in Computational mathematics, 1996. **5**(1): p. 329-359.
118. O'Connor, D.P., et al., *Ethnic bias in anthropometric estimates of DXA abdominal fat: the TIGER study.* Med Sci Sports Exerc, 2011. **43**(9): p. 1785-90.
119. Martin, C.B., et al., *Attempts to Lose Weight Among Adults in the United States, 2013-2016.* NCHS Data Brief, 2018(313): p. 1-8.
120. Terwee, C.B., et al., *Qualitative attributes and measurement properties of physical activity questionnaires: a checklist.* Sports Med, 2010. **40**(7): p. 525-37.
121. Hills, A.P., Mokhtar, N., and Byrne, N.M., *Assessment of physical activity and energy expenditure: an overview of objective measures.* Front Nutr, 2014. **1**: p. 5.
122. Boucher, B., et al., *Validity and reliability of the Block98 food-frequency questionnaire in a sample of Canadian women.* Public Health Nutrition, 2007. **9**(1): p. 84-93.
123. Johnson, B.A., et al., *Structured measurement error in nutritional epidemiology: applications in the Pregnancy, Infection, and Nutrition (PIN) Study.* Journal of the American Statistical Association, 2007. **102**(479): p. 856-866.
124. Walsh, M.C., et al., *Comparison of self-reported with objectively assessed energy expenditure in black and white women before and after weight loss.* Am J Clin Nutr, 2004. **79**(6): p. 1013-9.
125. Ceesay, S.M., et al., *The use of heart rate monitoring in the estimation of energy expenditure: a validation study using indirect whole-body calorimetry.* Br J Nutr, 1989. **61**(2): p. 175-86.
126. Christensen, C.C., et al., *A critical evaluation of energy expenditure estimates based on individual O2 consumption/heart rate curves and average daily heart rate.* Am J Clin Nutr, 1983. **37**(3): p. 468-72.
127. Caballero, Y., et al., *Simple Prediction of Metabolic Equivalents of Daily Activities Using Heart Rate Monitor without Calibration of Individuals.* Int J Environ Res Public Health, 2019. **17**(1).
128. Faulkner, J., Parfitt, G., and Eston, R., *Prediction of maximal oxygen uptake from the ratings of perceived exertion and heart rate during a perceptually-regulated sub-*

maximal exercise test in active and sedentary participants. Eur J Appl Physiol, 2007. **101**(3): p. 397-407.
129. van Poppel, M.N., et al., *Physical activity questionnaires for adults: a systematic review of measurement properties.* Sports Med, 2010. **40**(7): p. 565-600.
130. Joint, F.A.O.W.H.O.U.N.U.E.C.o.E., et al., *Energy and protein requirements : report of a Joint FAO/WHO/UNU Expert Consultation [held in Rome from 5 to 17 October 1981]*. 1985, World Health Organization: Geneva.
131. Rounds, T. and Harvey, J., *Enrollment Challenges: Recruiting Men to Weight Loss Interventions.* American Journal of Men's Health, 2019. **13**(1): p. 1557988319832120.
132. Voils, C.I., et al., *Recruitment and Retention for a Weight Loss Maintenance Trial Involving Weight Loss Prior to Randomization.* Obesity science & practice, 2016. **2**(4): p. 355-365.
133. Arroyo-Johnson, C. and Mincey, K.D., *Obesity Epidemiology Worldwide.* Gastroenterol Clin North Am, 2016. **45**(4): p. 571-579.
134. Ceaser, T.G., et al., *Association of physical activity, fitness, and race: NHANES 1999-2004.* Med Sci Sports Exerc, 2013. **45**(2): p. 286-93.
135. Brandon, L.J. and Elliott-Lloyd, M.B., *Walking, body composition, and blood pressure dose-response in African American and white women.* Ethn Dis, 2006. **16**(3): p. 675-81.
136. Svetkey, L.P., et al., *Effect of lifestyle modifications on blood pressure by race, sex, hypertension status, and age.* J Hum Hypertens, 2005. **19**(1): p. 21-31.
137. Wadden, T.A., et al., *One-year weight losses in the Look AHEAD study: factors associated with success.* Obesity (Silver Spring), 2009. **17**(4): p. 713-22.
138. Wilmore, J.H., et al., *Alterations in body weight and composition consequent to 20 wk of endurance training: the HERITAGE Family Study.* Am J Clin Nutr, 1999. **70**(3): p. 346-52.
139. McGee, S.L. and Hargreaves, M., *Epigenetics and Exercise.* Trends in Endocrinology & Metabolism, 2019. **30**(9): p. 636-645.
140. Chow, C.C. and Hall, K.D., *The Dynamics of Human Body Weight Change.* PLOS Computational Biology, 2008. **4**(3): p. e1000045.

APPENDIX 1

The PAEE during 15-week ($PAEE_2$) was estimated by converting into PAL using five methods.

1) **PAL categorization using Hall's PAL categories for 15-week prescribed activity**

   Hall's PAL categories were used to estimate the amount of PAEE including only the value of the prescribed activity, assuming all participants did exactly what was prescribed [14]. Hall's PAL method uses two sections that described activity: PA at work or school, and PA at leisure time. Because participants in this study were sedentary college students, "Light" activity will be assumed for PA at work or school, and "Active" for PA at leisure time for prescribed activity, which indicates a 1.8 PAL for all participants during the intervention.

2) **PAL categorization using self-reported PAR after the prescribed activity**

   Self-reported PAR by participants after the 15 weeks of only the prescribed exercise was used to estimate PAEE. Using the table below (Table 4), PAR was converted into a PAL ranging from 1.7 to 2.0 depending on the individual variability of self-reported frequency and intensity of the prescribed activity.

Table 4. PAR, Hall's self-reported PAL, and associated PAL categories

PAR	Hall's self-reported leisure time PAL category	PAL ratio (TDEE/RMR)^
0	Very Light	1.5
1, 2	Light	1.6
3, 4	Moderate	1.7
5	Active	1.8
6, 7	Very Active	2.0

PAR: physical activity rating; PAL: physical activity level; TDEE: total daily energy expenditure; RMR: resting metabolic rate
^In the current study, PAL ratio is estimated by "Light" for Work/School activities with Leisure time activities from "Very Light" to "Very Active".

3) **PAL calculation as a ratio (TDEE/REE) using compendium MET values of the prescribed and non-prescribed activity**

From the third method, the prescribed activity and activities other than the prescribed activity were included to estimate total amount of PAEE and PAL. Mode and duration of activity were used to identify the respective compendium MET value, which will then be combined with body weight to estimate calories expended for each activity ([68, 69]. For example, if an individual who has 70 kg of body weight does a walking activity at 3.5 mph (4.3 METs) for 30 minutes, the caloric value is 158 kcal, using the equation:

$$METs \times 3.5 \times body\ weight\ (kg)\ /200 = kcal/min \qquad \text{(Eq. 10)}$$

Therefore, 30 minutes of walking at 3.5 mph (4.3 METs) is

$4.3 \times 3.5 \times 70\ /200 = 5.26$ kcal/min $\times$ 30 min = 158 kcal.

4) PAL calculation as a ratio (TDEE/REE) using the self-reported RPE as intensity of the prescribed and non-prescribed activity

Self-reported RPE for prescribed and other activities was used to estimate PAEE using the participant's estimated maximum aerobic capacity from the 1-mile walk and 1.5-mile run test and the self-reported duration for each reported activity. The RPE was used to estimate the percent of heart rate reserve (%HRR) and $\%VO_{2max}$ using the equation:

$$\%HRR = \%VO_{2max} = (RPE - 6)/14 \qquad \text{(Eq. 11)}$$

where RPE is ranged from 6 to 20, which is 0% to 100% of HRR. Then, the Astrand-Ryhming single stage method, which estimates VO_2max in mlO_2/kg/min using exercise VO_2 (VO_2ex), %HRR ($\%VO_2max$), and VO_2max [112] was used:

$$VO_2ex = \%VO_2max \times VO_2max \qquad \text{(Eq. 12)}$$

where the VO_2max was estimated from the 1 mile walk test or 1.5 mile run test using Kline et al. [109] and Baumgartner et al. [110], respectively. The averaged HR during activity (HRex) was estimated using the equation:

$$HRex = \%HRR\ (\%VO_2max) \times (HRmax - k) + k \qquad \text{(Eq. 13)}$$

where k = 63 for men and 73 for women, and HRmax is the age-predicted maximum heart, adapted from the equations by the Astrand-Ryhming single stage method [112]. For example, if a man who has 200 bpm of maximum HR and reports 15 of RPE, this person's HR during the activity (HRex) will be:

$$HRex = (RPE - 6)/14 \times (HRmax - k) + k$$

$$= (15 - 6)/14 \times (200 - 63) + 63 = 151 \text{ bpm}$$

Then, the estimated VO_2ex (ml/kg/min) was converted into kcal/min: 1) multiply mlO_2/kg/min by the individual's body weight in kg, then divide by 1000 (mlO_2/min to LO_2/min), and 2) LO_2/min multiply 5 (LO_2/min to kcal/min, 5 kcal per LO_2).

$$kcal = \frac{VO_{2max} \times [(RPE - 6)/14] \times kg \times min \times 5}{1000} \quad \text{(Eq. 14)}$$

Using the same example above of the man who has 70kg of body weight and 40 ml/kg/min of VO_2max who runs for 30 minutes, the expended kilocalories of activity (kcal) estimated from RPE were

$$40\ mlO_2/kg/min \times [(15 - 6)/14] \times 70\ kg \times 30 \times 5\ /\ 1000 = 270\ kcal$$

5) PAL calculation as a ratio (TDEE/REE) using measured HR data for prescribed activity and RPE for non-prescribed activity

To estimate PAEE with the fifth method, both measured HR for prescribed activity and RPE for non-prescribed activities were used to estimate PAEE. The averaged measured HR and total duration (min) for prescribed activity was used to estimate $\%VO_2max$, and expended kilocalorie (kcal) for the prescribed exercise across the entire intervention period using the equation:

$$kcal = \frac{VO_{2max} \times (Averaged\ HRex - k) \times kg \times min \times 5}{(220 - age - k) \times 1000} \quad \text{(Eq. 15)}$$

For example, if a man who is 20 years old and has 70kg of body weight and 40 ml/kg/min of VO_2max participated in the prescribed exercise with an average HR and total minutes of exercise of 160 bpm and 2,500 minutes, respectively:

$$kcal = \frac{40 \times (160 - 63) \times 70 \times 2500 \times 5}{(220 - 20 - 63) \times 1000} = 24{,}781\ kcal$$

Therefore, the expended prescribed EE (kcal/day) was divided by the total number of days of prescribed exercise, 24,781/ 70 days = 354 kcal/day. The estimation of PA other than prescribed TIGER exercise was estimated using self-reported RPE for each activity that was calculated as kcal using individual's VO_2max, $\%VO_2max$, duration of activity, same as the fourth method.

For the third, fourth, and fifth methods, the calculated PAEE (kcal) was added to the estimated baseline TDEE kilocalorie value and divided by REE to calculated total PAL. For example, if a person who is sedentary has 1500 kcal/day of REE, this person's TDEE is 2400 kcal (sedentary activity is 1.6 PAL = REE*1.6 = 1500*1.6 = 2400), or 100 kcal/hr. This person does 1 hour and 500 kcal of exercise per day, replacing 1 "normal" hour (100 kcal) with 1 "exercise" hour (500 kcal). The new TDEE is 2400 – 100 + 500 = 2800 kcal. To estimate PAL, the 2800 kcal/day is divided by 1500 kcal/day, which is 1.87 PAL. If the 1 hour of 500 kcal exercise is done only 3 days/week, the revised TDEE = [2400*4 (non-exercise days) + 2800*3 (exercise days)]/7 = 18,000/7 = 2571 kcal/day, or 2571/1500 = 1.71 PAL.

APPENDIX 2

The baseline EB satus before participating in exercise intervention was calculated by using the adapted equations of Hall et al. (2011) [14]. Baseline EB is a function of weight change, and more specifically the change in body composition, the relative changes in FM and FFM, since FM has a much higher energy density than FFM. Consequently, a defensible, valid estimate of change in FM (ΔFM) and FFM (ΔFFM) is required.

Using Hall et al.'s (2007) [80] notion and equation for history of changes of body weight before intervention (ΔBW_b):

$$\Delta BW_b = \Delta FFM_b + \Delta FM_b \qquad \text{(Eq. 17)}$$

where ΔFFM_b and ΔFM_b are history of changes of FFM and FM at baseline, respectively.

And,

$$\Delta FM_b = FM_2 - FM_1 \qquad \text{(Eq. 18)}$$

where FM_1 and FM_2 are the historical and baseline FM, repectively.

Forbes's equation can provide an estimate of the relative change in FFM and FM, although it describes the cross-sectional relationship between FFM and FM across differences in body weight and as such represents change in body composition for infinitesimal differences in weight. Because baseline EB status in individuals is represented by relatively large, longitudinal changes of body mass and composition, using Forbes's original equation is not directly applicable. Therefore, Hall expanded upon the concept of Forbes's original equation to predict body composition change for a given change of body weight (ΔBW_b, by weight history prior to baseline; i.e., from weight of 2 years ago or at the end of high school to baseline) and current FM (FM_2) using the Lambert W function, $W,$ to solve a transcendental equation predicting historical FM (FM_1) [117].

$$FM_1 = 10.4W\left[\frac{1}{10.4} \times exp\left(\frac{\Delta BW_b}{10.4}\right) \times FM_2 \times exp\left(\frac{FM_2}{10.4}\right)\right] \qquad \text{(Eq. 19)}$$

Using the respective energy densities associated with mass changes (ρ_{FFM} and ρ_{FM}), baseline EB (kJ/day) can be estimated as [(7,600 × ΔFFM + 39,500 × ΔFFM) × 0.239]/(days from the reported historical and baseline weights). Finally, the total expected body weight changes with inclusion of initial EB status *(EB)* in the numerator can be estimated (Equation 20 in the main text).

$$\Delta BW = \frac{(1-\beta)(\Delta EI)-(BW_1 \times \Delta PAEE)+EB}{PAEE_1+\Delta PAEE+\gamma_{FFM}-\phi(\gamma_{FFM}-\gamma_{FM})} \qquad \text{(Eq. 20)}$$