A FRESH PERSPECTIVE ON FAT-LOSS AND BODY MEASUREMENT TECHNIQUES: THE EFFECTS OF TIME RESTRICTED FEEDING AND EXERCISE ON FAT-OXIDATION RATES AND COMMONLY USED FATNESS MEASUREMENTS.

LOREN YAVELBERG

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Abstract:

Currently employed techniques for weight management consist of; extreme caloric deprivation alone or in combination with exercise, exercise alone or medically invasive procedures, all of which have proven not to provide sustainable resolutions (Brownell et. al., 1987; Kramer et. al., 1989). Due to the significance of a growing global obesity epidemic, the need for customized PA and exercise prescriptions which potentially increase fat-oxidation rate (FOR) are critical. To formulate a successful solution, examining both the acute and chronic effects of varying exercise intensities and modalities on FOR alone and in conjunction with healthier eating habits (time-restricted feeding (TRF) will be informative. A growing body of evidence suggests that TRF could be a valuable tool for improving health in the general population due to reports of improving blood lipids (Klempel et al., 2012 & 2013; Varady et al., 2011) and glycaemic control (Barnosky et.al., 2014), reducing circulating insulin (Trepanowski & Bloomer, 2010), decreasing blood pressure (Trepanowski & Bloomer, 2010; Tinsley & La Brounty, 2015; Varady & Bhutani, 2009), decreasing inflammatory markers (Farajeh et al., 2012) and reducing fat-mass (FM) even during relatively short durations (8–12 weeks) (Varady & Bhutani, 2009). Currently, little is known about the synergistic effects of TRF supplemented with varying forms of PA on FOR. In order to successfully improve FOR in individuals living with obesity and overweightness, exercise intensity, modality, and duration must be considered for successful weight loss.

This series of investigations examined 1) Validated FOR at rest and during exercise, 2) The acute effects of TRF (12 & 16 hrs) and varying exercise intensities on FOR, 3) The short-term effects of intermittent fasting and continuous steady-state low-moderate intensity exercise on commonly used fatness measurements and FOR in middle-aged women, and 4) The importance of considering Body Mass Index in conjunction with VO_2max when evaluating the health and wellness of frontline fire suppression personnel.

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List of Abbreviations:

ATGLS: Adipose Tissue Triglyceride

BIA: Bio-electrical Impedance Analysis

BMI: Body Mass Index

BMR: Basal Metabolic Rate

CHO: Carbohydrate

FFA: Free Fatty Acids

FOR: Fat-Oxidation Rate

FOR_{max}: Maximum Fat-Oxidation Rate

FM: Fat Mass

HIIT: High-Intensity Intermittent Training

HR: Heart Rate

HRmax: Maximum Heart Rate

IF: Intermittent-Fasting

IMTG: Intramuscular Triglycerides

LISS: Low-moderate intensity steady-state

PA: Physical Activity

PAR-Q+: PA and Readiness Questionnaire for Everyone

PAPSQ: PA Participation and Sedentarism Questionnaire

%BF: Percent Body Fat

RER: Respiratory Exchange Ratio

TCA: The Citric Acid Cycle

TDEE/TEE: Total Daily Energy Expenditure

TRF: Time-restricted feeding

TRF12: Time-restricted feeding for 12 hours

TRF16: Time-restricted feeding for 16 hours

VO_2max: Maximum Oxygen Consumption

WHO: World Health Organization

EXECUTIVE SUMMARY:

With the rising financial burden of health care costs linked to battling an obesity epidemic, along with the associated co-morbidities, researchers must elucidate sustainable approaches to combat this global issue on both an individual and population basis. The World Health Organization (WHO) estimates that, within the next few years, non-communicable diseases will become the principal global causes of premature morbidity and mortality. Being overweight and obese increases the risk of morbidity from several pathologies: hypertension, type 2 diabetes, coronary heart disease, stroke, non-alcoholic fatty liver disease, osteoarthritis, sleep apnea, and several cancers. According to the WHO, worldwide, there are around 2 billion adults living with overweight and more than 1 billion living with obesity—650 million adults, 340 million adolescents, and 39 million children. These estimates were primarily based on the body mass index (BMI = body mass (kg)/height (m^2)) metric. The prevalence of obesity, as determined by BMI, has doubled or even risen threefold in less than two decades in adults and children; this is rising at concerning rates in some regions of the world (James, 2008; WHO, 2018; Betts et al., 2014). In the United States alone, total healthcare costs attributable to overweight and obesity will double every decade to $860.7–$956.9 billion by 2030, accounting for 16–18% of the total US healthcare costs (Wang et al., 2008). In Canada, in 2021, 53% of the population aged 18–34 self-reported their BMI as overweight or obese (30.8% overweight, 22.2% obese), while 69.4% of the population aged 35–49 self-reported their BMI as overweight or obese, with 36.6% reporting overweight and 32.8% reporting obese (Stats. Canada, 2021). Currently employed techniques for weight management consist of extreme caloric deprivation alone or in combination with physical activity (PA) and/or exercise, PA or exercise alone, or medically invasive procedures, all of which have proven to not provide sustainable solutions. Researchers speculate that focusing on improving the body's fat utilization rates could be a more effective approach.

This series of investigations examined: 1) validated fat-oxidation rates at rest and during exercise, 2) the acute effect of time-restricted feeding (12 and 16 hours) and varying exercise intensities on fat-oxidation rate; 3) the short-term effects of intermittent fasting and continuous steady-state low-moderate intensity exercise on commonly used fatness measurements and fat oxidation rates in middle-aged women; and 4) the importance of considering Body Mass Index in conjunction with VO_2max when evaluating the health and wellness of frontline fire suppression personnel.

MANUSCRIPT I: Validated Fat-Oxidation Rates at Rest and During Exercise in Postmenopausal Middle Eastern and Caucasian Women

During menopause and throughout aging, women are at an increased risk for a plethora of chronic conditions, many of which are related to the interruption of estrogen. The primary and secondary prevention benefits of habitual unstructured and structured PA are well documented. Fat-oxidation rates (FOR) at rest and during exercise have been reported to decrease through the menopausal transition.

The purpose of this study was to i) validate the treadmill-based indirect calorimetry FOR procedures and ii) compare resting FOR, FOR during incremental exercise, and FORmax, hormone levels of Middle Eastern (ME) and Caucasian (C) postmenopausal women for further understanding of the menopausal transition and the effects on FOR. It was hypothesized that the ME women would exhibit lower FOR at rest and different sub-maximal exercise intensities and, therefore, have a lower FOR_{max}, lower estrogen levels, and possess higher cardiometabolic risk factors compared to the C women.

Twenty-three middle-aged Middle Eastern (n = 11) and Caucasian (n = 12) women were recruited. An independent t-test was used to determine differences between the groups for: anthropometrics, menstrual characteristics, resting blood pressure (BP) and heart rate (HR), PA levels, blood lipid panel, blood hormone panel, glucose, resting VO_2, and VO_2peak. To assess the protocol's reliability, a subset of participants had their VO_2max and maximum fat-oxidation rate (FOR_{max}) determined on three separate occasions.

No significant differences between FOR at rest, during exercise, and/or other physical and physiological parameters were observed. There were no significant differences between the three separate trials for the VO_2 and FOR_{max} values.

The findings of this investigation support the use of this protocol in further investigations examining FOR_{max}. This study contributed to the ever-growing body of literature on FOR and women's health by exploring an ethnic group that has not been previously studied.

MANUSCRIPT II: The Acute Effect of Time-Restricted Feeding (12 and 16 Hours) and Varying Exercise Intensities on Fat Oxidation Rate: A Randomized Control Trial

Time-restricted feeding (TRF) is a dietary pattern alternating between fasting and feeding periods that has gained significant attention in recent years. The 16/8 approach consists of fasting for 16 hours and feeding for an 8-hour window, while the 12/12 method consists of fasting for 12 hours and feeding for a 12-hour feeding window. Limited research exists comparing the effects of these methods coupled with physical activity (PA). This investigation aimed to examine the acute effects of varying TRF durations (12 and 16 hours) and varying PA intensities on the fat-oxidation rate (FOR). It was hypothesized that i) the TRF16 group would exhibit higher FOR_{max} and that PA would enhance these effects, and ii) high-intensity interval training (HIIT) would result in greater effects on FORmax compared to low-moderate intensity steady state (LISS) PA.

Eighteen young adults (males = 8; females = 10) were recruited and participated in the supervised intervention. The discrete component open circuit spirometry system was used to measure oxygen consumption (VO_2), and Frayn's equation was used to determine the FOR plus

FOR_{max}. ANOVA was used to determine pre- and post-intervention differences in FOR_{max}. The FOR_{max} for the TRF16+HIIT intervention was significantly higher than the TRF12 and TRF16 fast alone (mean difference = 0.099, 0.093 g·min-1, p = 0.011, 0.002, respectively). The FOR_{max} for the TRF16+LISS PA intervention was significantly higher than that for TRF12 alone (mean difference = 0.099 g·min-1, p = 0.011). The FOR_{max} for TRF12+HIIT and TRF16+HIIT interventions were both significantly higher than the 12-hour fast alone (mean difference = 0.070 g·min^{-1}, 0.099 g·min^{-1}, p = 0.023, 0.011, respectively).

This study contributes to the body of literature on the acute effects of TRF and PA on young adult males and females. The findings suggest that the TRF16+HIIT PA intervention results in the highest FOR_{max}. Thus, the evidence supports combining TRF and PA interventions as an effective strategy for healthier weight management. Further investigations should examine the benefits of a prolonged combined intervention (TRF +PA).

MANUSCRIPT III: The Short-term Effects of Intermittent Fasting and Continuous Steady State Low-Moderate Intensity Exercise on Commonly Used Fatness Measurements and Fat-Oxidation Rates on Middle-aged Women

The World Health Organization estimates that within the next few years, non-communicable diseases will become the principal global causes of morbidity and mortality. While customarily employed techniques for weight loss have proven not to provide sustainable resolutions, intermittent fasting or time-restricted feeding (TRF) has gained popularity as a healthy lifestyle and weight management approach. The purpose of this investigation is to examine the chronic effects of TRF for 16 hours and manageable physical activity (PA), such as a continuous light-moderate intensity steady-state (LISS) intervention, as an effective strategy for weight management.

Fourteen middle-aged women were recruited and participated in the supervised intervention for three weeks. A subset of the participants (n = 3) was followed for an additional six weeks

(2 visits, once every three weeks), for a total of nine weeks, to assess the short-term effects of this intervention. An independent t-test was used to determine pre- and post-intervention differences for: anthropometrics, resting blood pressure (BP) and heart rate (HR), VO_2max, FOR_{max}, skinfold thickness, and percent body fat (%BF). Although the FOR_{max} values did not statistically significantly increase pre/post-3-week intervention, there were statistically significant differences ($p<0.05$) in body mass and various skinfold sites (iliac crest, medial calf) and total sum of five skinfolds (triceps, biceps, subscapularis, iliac crest, medial calf).

The statistically significant findings of this combined 3-week TRF and PA intervention showed improvements in subcutaneous and visceral adiposity, increases in VO_2max, reduction of body mass, and retention or improvement of estimated fat-free mass. This provides evidence to support the combined TRF and PA intervention as an effective and sustainable weight management strategy.

Manuscript IV: The importance of considering Body Mass Index in conjunction with VO_2max when evaluating the health and wellness of frontline fire suppression personnel.
While BMI has long been used in health screenings, the current approach to BMI as an evaluative and predictive diagnostic tool has come under clinical scrutiny (Flegal, 2023). BMI is a body composition metric quantified as weight in kilograms divided by the square of height in meters ($kg \cdot m^{-2}$). In contrast to other methods, BMI is a simple, inexpensive, and non-invasive estimate of total body fat and can be routinely measured and calculated (CDC, 2023). As BMI is used as an indicator of body fatness, it is widely used to describe population overweight and obesity; however, it should be noted that BMI measures excess body mass rather than excess fat (CDC, 2023). BMI is a crude index of adiposity, predominantly because it fails to differentiate body composition—fat mass versus not-fat mass versus lean or muscle mass (Nevill et al., 2010). The purpose of this investigation was to examine the Physical Employment Standards (PES) pass rates (PR) amongst different body mass indexes (BMI) and

job-related maximum oxygen consumption (VO_2max) categories (borderline/pass level I/pass level II). It was hypothesized that individuals with higher BMIs (≥ 25) within the same VO_2max category can carry out the critical physically demanding tasks more effectively (compared to BMI >25), thus observing greater PES PR.

VO_2 was measured via indirect calorimetry using the discrete-component open-circuit spirometry system for all male and female frontline fire suppression (FFS) candidates. The analysis was performed on 1,992 FFS candidates who completed the bona-fide Structural Firefighter Applicant Fitness Assessment (SFFA). The FFS candidates had a mean BMI of 25.6 ± 3.0 $kg \cdot m^{-2}$. The mean VO_2max was 50.0 ± 5.2 $mLO2 \cdot kg^{-1} \cdot min^{-1}$. The results of the binary logistic regression revealed no observed relationship between BMI (< 25.0, ≥ 25.0) alone and PR. The Chi-square analysis showed a statistically significant association between VO_2max and the overall SFFA PR between BMI refined by VO_2max and pass percentage ($x^2 = 17.759$, df = 2, $p < 0.001$).

The results of this investigation support our hypothesis that BMI should be refined by VO_2max when evaluating the health and wellness of FFS workers. The findings provide evidence to support that those with a BMI ≥ 25.0 who achieved the required job-related VO_2max were most likely to pass the PES successfully. Wellness and training programs for FFS workers should focus on cardiorespiratory and musculoskeletal fitness, and maintaining or improving lean mass rather than solely focusing on BMI. This would also be applicable to other emergency-related, physically demanding occupations where safe and effective job completion is critical to life and property.

Personal Statement on the COVID-19 Pandemic's Effects on Conducting In-Person Exercise Graduate Student Research

The COVID-19 pandemic has had a profound impact on the completion of my Ph.D. research, with many students experiencing significant loss of time and facing a range of challenges. The pandemic's disruption has lengthened the time required to undertake and finish research projects by delaying study participant recruitment, data collection, experimentation, and fieldwork. Additionally, due to travel limitations and social segregation policies, it was challenging for students to access research facilities and statistical support services and collaborate with peers.

The pandemic has substantially impacted in-person research; numerous studies have been put on hold or postponed because of travel restrictions, social isolation measures, and access restrictions to research institutions. To safeguard the safety of study participants and researchers, researchers have had to modify their procedures and investigate other approaches to data collection. Before the pandemic, the research team recruited and screened over 120 study participants who were lost during the pandemic. Throughout the pandemic, researchers were not permitted to invite any study participants into the laboratory, thus resulting in a complete data collection stall and a loss of critical time (~2 years).

The pandemic also highlighted the need for more adaptable and resilient research designs to cope with quickly changing situations. This researcher had initially planned to collect and analyze study participants' blood, saliva, and fecal samples to investigate the biochemical adaptations of the interventions. Given the loss of time and increased biosafety restrictions, this researcher was forced to adapt to the situation and remove this portion of the analysis. Furthermore, researchers had to re-focus and re-design some of their proposed studies.

Although the COVID-19 pandemic disrupted my in-person data collection and delayed the completion of my Ph.D. by ~2 years, the clinical and virtual teaching and mentoring experiences I was afforded during this period have been invaluable in strengthening my perseverance and professional and research capabilities.

CHAPTER 1: INTRODUCTION & REVIEW OF LITERATURE

FORWARD TO THE THESIS

This thesis comprises four separate manuscripts, preceded by an executive summary, an introduction, and a literature review. The four manuscripts are followed by the limitations and implications of the research findings sections. This thesis concludes with a detailed list of references.

This thesis consists of the following four manuscripts:

I. Validated Fat-Oxidation Rates at Rest and During Exercise in Postmenopausal Middle Eastern and Caucasian Women.
Yavelberg L.

II. The Acute Effect of Time-Restricted Feeding (12 & 16 hrs) and Varying Exercise Intensities on Fat-Oxidation Rate – a randomized control trial.
Yavelberg L.

III. The Short-term Effects of Intermittent Fasting and Continuous Steady State Low-Moderate Intensity Exercise on Commonly Used Fatness-measurements and Fat-Oxidation Rates on Middle-aged Women
Yavelberg L.

IV. The Importance of Considering Body Mass Index in Conjunction with VO_2max When Evaluating the Health and Wellness of Frontline Fire Suppression Personnel.
Yavelberg L.

INTRODUCTION

With the rising financial burden of healthcare costs linked to battling an obesity epidemic along with the associated co-morbidities, researchers must elucidate sustainable approaches to combat this global issue on an individual and population basis (James, 2008). The World Health Organization (WHO) estimates that non-communicable diseases kill 41 million people each year, equivalent to 71% of all deaths globally (WHO, 2018). Overweight and obesity are medically defined as excessive fat accumulation (both subcutaneous and visceral) that may impair health and increase mortality (World Health Organization). Living with overweight or obesity increases the risk of premature morbidity of several pathologies, including hypertension, dyslipidemia, type-II diabetes, coronary heart disease, stroke, non-alcoholic fatty liver disease, osteoarthritis, sleep apnea, and endometrial, breast, prostate, and colon cancers (Savini et al., 2013). According to the WHO, worldwide, there are around 2 billion adults living with overweight and more than 1 billion living with obesity—650 million adults, 340 million adolescents, and 39 million children. These estimates are primarily based on the body mass index (BMI = body mass (kg)/height (m^2)) metric. The prevalence of obesity, as determined by BMI, has doubled or even risen threefold in less than two decades, and in children, this is rising at a concerning rate in some regions of the world (James, 2008; WHO, 2018; Betts et al., 2014).

In the United States alone, total healthcare costs attributable to overweight and obesity will double every decade to $860.7–$956.9 billion by 2030, accounting for 16–18% of the total US healthcare costs (Wang et al., 2008). In Canada, in 2021, 53% of the population aged 18–34 self-reported their BMI as overweight or obese (30.8% overweight, 22.2% obese), while 69.4% of the population aged 35–49 self-reported their BMI as overweight or obese, with 36.6% reporting overweight and 32.8% reporting obese. These alarming percentages equate to roughly 18,300,00 out of 40,000,000 Canadians (Stats. Canada, 2021).

REVIEW OF LITERATURE:

A fundamental premise underlying overweight and obesity is the concept of energy imbalance, as seen in Figure 1. Assuming that an individual has no problem absorbing nutrients, stored energy will increase only if energy intake exceeds total body energy expenditure (TEE). Energy expenditure typically encompasses Physical Activity (PA), basal metabolism, and adaptive thermogenesis.

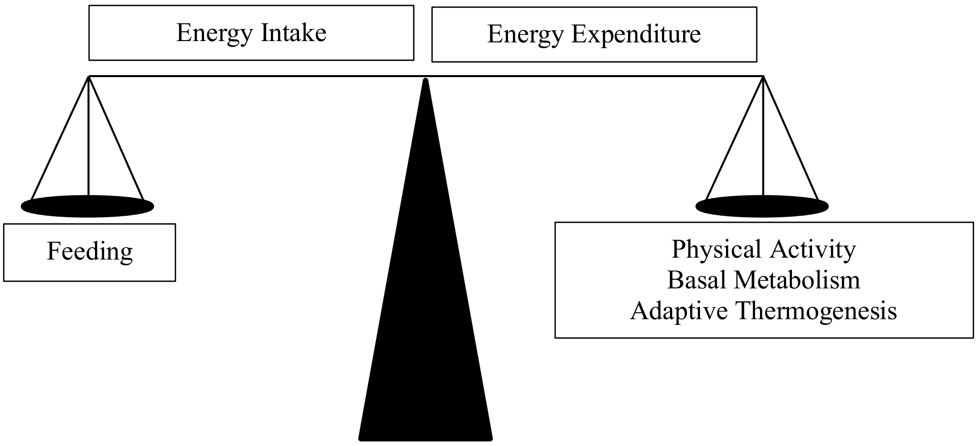


Figure 1. Key Components of the Energy Balance.

Overview of Physical Activity (PA)

PA is an umbrella term that encompasses all non-structured activities of daily living, leisure or recreational PA and structured exercise for the purposes of improving aspects of physical and physiological fitness (Bouchard, 1990). PA encompasses activities of daily living, active transport, occupation-related physical demands, structured exercise, specialized skilled movement, and sports participation (WHO, 2010). The inherent rate of energy demand imposed by PA participation aligns with global intensity spectrum descriptors such as very light, light, light-to-moderate, moderate, moderate-to-vigorous, vigorous, and vigorous-to-maximal and maximal (Gledhill & Jamnik, 2003; Norton et al., 2010; Jamnik & Gledhill, 2015). The body's ability to effectively respond to the varying intensities along the PA spectrum highly depends upon the continuous interplay between the aerobic and anaerobic metabolic systems (Gastin, 2001). Although both metabolic systems contribute to total metabolism, the greater or lesser shared reliance of the two metabolic systems in meeting the energy requirements is dictated by the PA intensity and duration. The aerobic metabolic system dominates at low tomoderate continuous energy demands. As the rate of energy demand progressively increases, there is a greater reliance on both the aerobic and anaerobic metabolic systems, regardless of whether the PA is continuous, interval, or intermittent (Astrand et al., 2003). In summary, the practice of stratifying PA as aerobic, aerobic-anaerobic, or anaerobic is intended to underscore the dominance of an energy system in resynthesizing the energy required to meet the imposed energy demands. It is necessary to underscore that using metabolic descriptors to classify PA and exercise intensities, while convenient, is overly simplistic and can be misleading.

Benefits of Physical Activity (PA)

The concept of habitual PA participation as a therapy for primary disease prevention and secondary disease management is far from novel and dates back to the 1950s with the work of Morris (Morris, 1953; Morris, 1953) and Paffenbarger in the 1970s (Paffenbarger 1975; Paffenbarger, 1996). As well, other studies assessed the relative risk of death resulting from physical inactivity and sedentarism (Berlin, 1990; Kohl, 2001; Lee, 2000; Oguma, 2002; Powel, 1987; Warburton, 2006). In addition, there has been undisputable evidence from more recent work discussing the benefits of habitual PA participation for primary disease prevention and secondary disease management. Such that, it has been proposed that there is a linear relationship between increases in PA participation and health status (Warburton, 2006).

The benefits of habitual PA and exercise participation positively impact many health outcomes and are not limited to improvements in FOR. These cited benefits are, but not limited to, improved body mass management, reduced risks for osteoporosis, reduced risks for cancer, increased quality of life, self-esteem (Warburton et al., 2006), improved blood pressure (Paffenbarger, 1996; Bouchard, 1990) and blood lipid profile (Campaigne et al., 1985;

Laaksonen et al., 2000). These benefits of regular PA not only directly benefit an individual's health but could also cause direct adaptations in the fat metabolism pathways and/or reduce fat mass (Dengel et al., 1998; Toth et al., 1995). Regular exercise involving cycling at 75% of maximum oxygen consumption (VO_2max) for 60 minutes, five days a week, has been shown to increase fatty acid turnover in healthy individuals (Friedlander et al., 1998 & 1999), as well as in persons living with obesity exercising at low and moderate intensity (40% of VO_2max) (Wagenmakers et al., 2015).

Characterizing Physical Activity (PA)

Typically, whole-body dynamic activity (popularly referred to as aerobic activity) is characterized as light-to-moderate and moderate-to-vigorous intensity PA, which may be performed continuously, at intervals, or intermittently but depends on an individual's functional capacity or VO_2max. An example of light-to-moderate intensity PA would be purposeful walking at a 15- to 20-minute mile pace of 3.5 – 3.7 mph (5.6–5.9 km/h) or light jogging at 5–6 mph (8–10 km/h), which would be associated with an intensity around 3–6 metabolic equivalents (METs), 50–75 percent of an individual's age-predicted maximum heart rate, 20 – 59% of heart rate reserve, or up to 50% of an individual's VO_2max, or 10–13 out of 20 on the original Borg subjective Rating of Perceived Exertion scale (RPE) (Astrand et al., 2003; Warburton et al., 2006; Warburton et al., 2011; Borg et al., 1982)

During continuous steady-state intensity exercise, carbohydrates (CHO) and fats are the two primary substrate sources of energy, and their relative utilization depends on the intensity of the exercise (Kelley et al., 1999). Briefly, absolute FOR increases from low to moderate exercise intensities and then markedly declines at high intensities. The intensity at which FOR begins to decline is used as an indication of maximal fat-oxidation rate (FOR_{max}) (Achten et al., 2002; Jeukendrup & Achten, 2001). Further, the findings of their investigation reveal exercise that elicits FOR_{max} does not appear to exceed moderate intensity. In an acute characterization study involving healthy young, 157 men and 143 women, whose average VO_2max was 46.3±0.7 $ml \cdot kg^{-1} \cdot min^{-1}$, Venables et al., 2004 reported an average FOR_{max} at 48% (range, 25%–77%) of VO_2max, on the other hand, others have measured FOR_{max} at an exercise intensity between 62% and 64% of VO_2max in moderately trained subjects (Venables et al., 2004; Achten & Jeukundrup, 2003; Nordby et al., 2006; Stisen et al., 2006).

<u>Aerobic-Anaerobic Physical Activity (PA)</u>

Aerobic-anaerobic exercise classically consists of interval moderate-to-vigorous PA interspersed with light-to-moderate intensity PA or intermittent vigorous-to-maximal intensity bouts of exercise such as sprints or maximal lifts, interspersed by a passive recovery period. The activity associated with moderate-to-vigorous intensities of 6–7 METs corresponds to 50–75 percent of an individual's VO_2max, and vigorous-to-maximal intensities correspond to upwards of 6–10+ METs and correspond to 75–100 percent of an individual's maximum heart rate (HRmax), or approximately 60% or more of an individual's VO_2max, or 16–20 out of 20 on the original Borg subjective RPE scale (Borg, 1982). The energy demand required upon initiating such activity is fulfilled by a combination of the anaerobic and aerobic metabolic systems, with a progressively increasing reliance on anaerobic glycolysis to meet the high-energy demands throughout the more intense bouts of exercise (Astrand et al., 2003; Tabata, 2019)

Several investigators (Timmons et al., 2009; Burgomaster et al., 2007 & 2008) have examined the efficacy of high-intensity interval training (HIIT; ≥85% VO_2max) to maintain or improve health as an alternative to longer-duration, continuous steady-state moderate-to-vigorous intensity PA approaches recommended by the WHO and ACSM. One of the primary advantages of HIIT, compared to lesser-intensity exercise, is that HIIT requires less time to exercise while providing similar or greater health-related benefits compared to published PA guideline recommendations (Ciolac, 2012; Gibala et al., 2012). As a result, it has been theorized that HIIT can mitigate the most commonly cited barrier to exercise, 'lack of time' (Godin et al., 1994; Reichert et al., 2007).

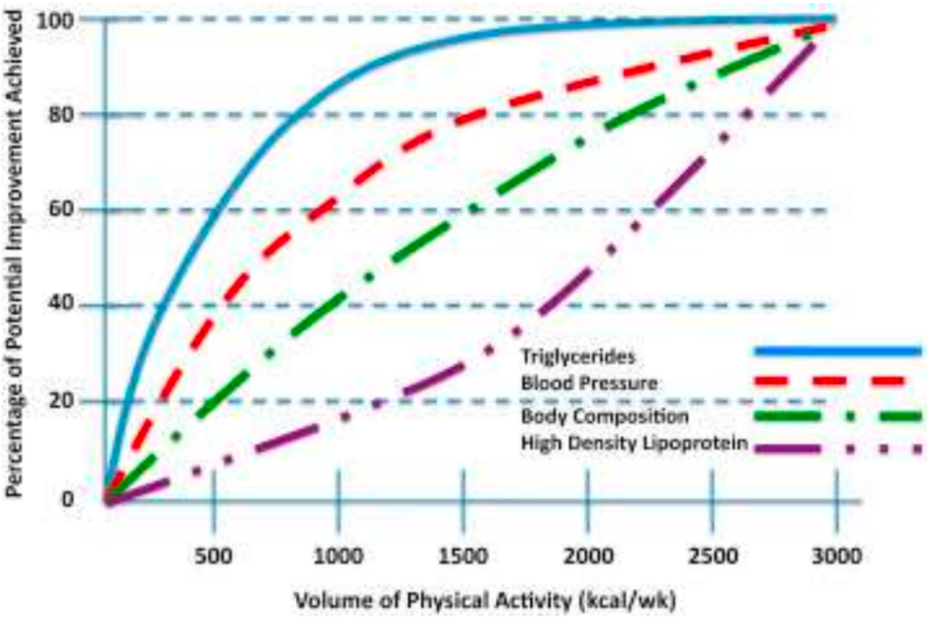
Interval training refers to exercise that involves alternating short bursts of higher-intensity activity with lower-intensity activity, whereas intermittent training implies a rest period. HIIT is an enhanced form of interval training involving brief, high-intensity anaerobic exercise (ranging from 85% to 200% VO_2max for 6 s to 4 min) separated by brief but slightly more prolonged bouts of low-intensity aerobic rest (ranging from 20% to 40% VO_2max for 10 s to 5 min) (Trapp et al., 2008).

Numerous studies have demonstrated greater health-related benefits from HIIT compared to traditional continuous steady-state moderate-intensity training. HIIT has been reported to more effectively increase VO_2max and reduce risk factors associated with metabolic syndrome, including blood pressure, insulin action, and lipogenesis, in various patient populations. Recent systematic reviews and meta-analyses have reported HIIT, compared to continuous steady-state moderate-intensity training, can significantly increase peak oxygen uptake in individuals with lifestyle-induced cardiometabolic diseases and stimulate improvements in VO_2max, compared to pretraining values in active non-athletic and sedentary individuals (Ciolac, 2012; Mohodt et al., 2009; Haram et al., 2008; Wisloff et al., 2007; Weston et al., 2014)

Dose-Response Relationship of Physical Activity (PA) & Health

The dose-response relationship between PA and health has been extensively studied over the years. Dose-response refers to the relationship between the amount of exposure to a particular factor (in this case, PA) and the resulting effect (in this case, health outcomes). The dose-response relationship between PA and health is generally positive, which means that as the amount of PA increases, the health benefits also increase. Several studies have found that PA has a dose-response relationship with health outcomes such as cardiovascular disease, diabetes, cholesterol levels, blood pressure, body mass, and all-cause mortality. For example, a study found that higher levels of PA were associated with a lower risk of cardiovascular disease and all-cause mortality and that the risk reduction was greater with higher levels of PA (Lee et al., 2012). Another study found that higher levels of PA were associated with a lower risk of type-2 diabetes and that the risk reduction was greater with higher levels of PA (Jefferis et al., 2016). There is a clear dose-response relationship between PA and chronic disease and premature mortality (Weston et al., 2014; Warburton et al., 2015), with diminishing returns in health benefits seen at higher volumes of PA and the greatest changes in health status seen when physically inactive individuals become more physically active. Notably, relatively minor increases in PA and fitness in previously inactive individuals will lead to marked reductions in the risk for chronic disease and premature mortality (Warburton et al., 2015). This appears to be particularly true for those living at the lower end of the fitness continuum, such as the frail elderly and those with chronic medical conditions. The dose-response relationship is also influenced by the level of PA (Warburton et al., 2016). It is known that with as little as 500 kcal/week, individuals can see improvements by as much as 20% in some physiological health markers, as illustrated in Figure 2.

Figure 2: Theoretical relationship between PA and various health status determinants, as Gledhill and Jamnik proposed.



kcal/week	500	1000	1500	2000	2500	3000
Minutes/day	15	30	45	60	75	90
Minutes/week	75	150	225	300	375	450
Hours/week	1 ¼ hr.	2 ½ hr.	3 ¾ hr.	5 hr.	6 ¼ hr.	7 ½ hr.

Reprinted with permission – PA & Lifestyle 'R' Medicine. Jamnik and Gledhill (2016) (Gledhill & Jamnik, 2003, Jamnik & Gledhill, 2015, Warburton et al., 2015)

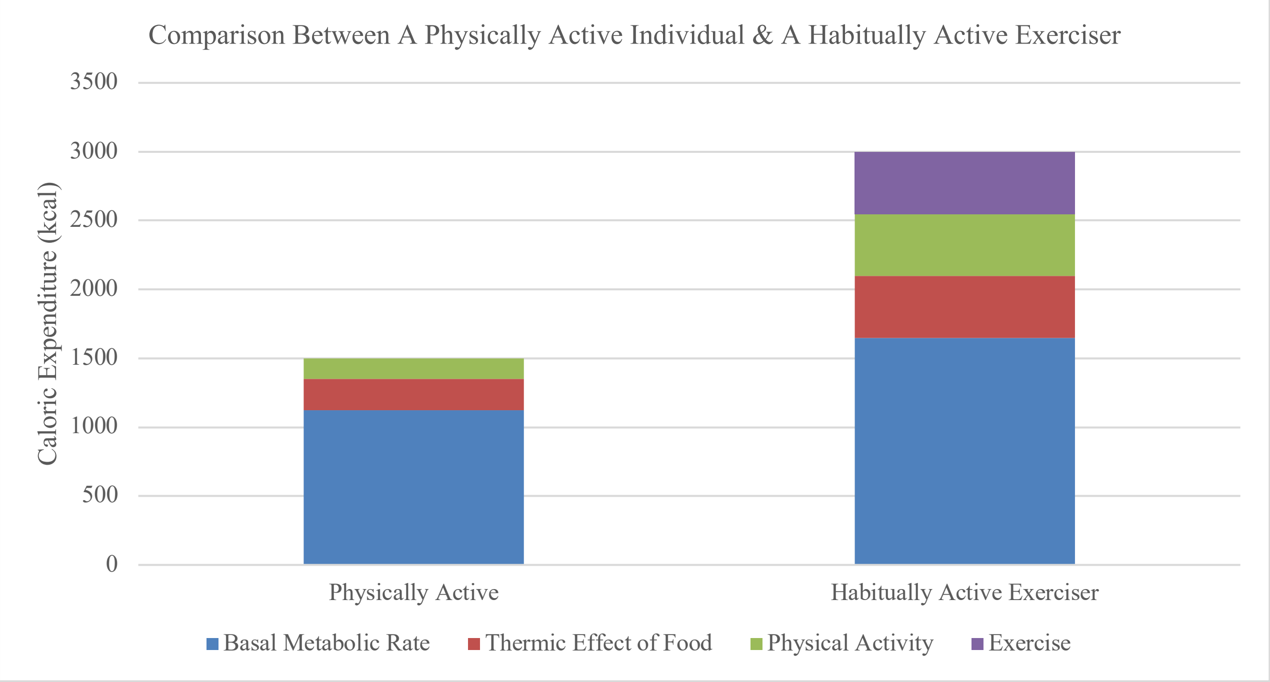
Figure 2 illustrates that much of the improvement in some health benefit indicators is achieved at lower volumes of PA participation (e.g., triglycerides and blood pressure), while much of the improvement in other health benefit indicators comes at higher volumes of participation (e.g., high-density lipoproteins). The 'volume' of PA is simply the sum of all bouts of PA, regardless of how short the duration is. Assuming a person expends 100 kcal/15 minutes, Figure 3 also illustrates how the volume of PA in kcal/per week relates to daily and weekly time commitments (over five days) (Gledhill & Jamnik, 2003; Jamnik & Gledhill, 2015).

<u>FITT Principle</u>

Although there are many acute and chronic benefits associated with PA participation, both the quantity and quality of the PA play integral roles in the benefits that can be realized. The exercise prescription must be mode- and load-dependent, including frequency, intensity, time, and type (FITT), commonly known as the FITT principle (Pollock et al., 1998). More importantly, the exercise should be specifically geared towards the individual's goals, include variations, and use periodized progressions to minimize desensitization and maximize training adaptations. All of the aforementioned elements must be considered when delivering a customized PA and/or exercise prescription protocol, as different conditions, diseases, and co-morbidities will require varying stimuli or dosages to maximize the benefits of the PA (Warburton et al., 2006).

PA refers to all voluntary movement, including structured exercise, while basal metabolism refers to the myriad of biochemical processes necessary to maintain homeostasis and sustain life. Adaptive thermogenesis refers to energy dissipated in the form of heat in response to environmental changes, such as exposure to cold and diet. Traditionally, the basal metabolism rate is defined as the energy expenditure of an individual relaxed and at rest, at thermo-neutrality, 8–12 hr after the last food ingestion (Spiegelman, 2001). Total daily energy expenditure (TEE) is a function of basal (resting) metabolic rate (BMR), dietary thermogenesis, non-exercise PA thermogenesis (standing, the basic body movements of daily living), and structured PA (including sports and exercise). Although the BMR composes a greater proportion of the TEE, it is a reasonably stable component that cannot be easily manipulated in the short term (Riddell et al., 2015). In contrast, the effect of non-structured and structured PA on TEE is quite variable, both between and within individuals, as seen in Figure 3. Compared to a physically active individual, as seen in Figure 3, a habitually active regular exerciser could expend up to 50% of their TEE by participating in structured physical activity.

Figure 3. Comparison of a physically active individual and habitually active exerciser and the daily caloric expenditure and its various subcomponents.



Fat-Oxidation

During exercise, skeletal muscle is the leading site for fat oxidation, and an increased capacity to utilize fats is often associated with health and exercise performance benefits (Achten & Jeukendrup, 2004. The heart and skeletal muscle are proficient in the handling of free fatty acids (FFA) for oxidation (energy) via the beta-oxidative pathway (Flatt, 1995). Skeletal muscle also has the ability to store small amounts of triglycerides. However, adipose tissue is the leading site for FFA storage (Flatt, 1995; Frayn, 2003). At rest, postprandial, and during periods of fasting or time-restricted feeding (TRF), energy is mainly derived from the hydrolysis (lipolysis) of adipose tissue triglyceride (ATGL) stores, subsequently increasing plasma FFA concentration for uptake into other tissues for oxidation. Thus, under resting conditions, especially in a fasted state, FFA are the predominant fuel the skeletal muscle uses (Romijn et al., 1993). At the onset of exercise, there is an increased utilization of FFA in skeletal muscle due to increased blood flow and energy demand of the contracting muscles. The available FFA oxidized by the skeletal muscle are derived from lipolysis of ATGLs, lipolysis of the skeletal muscles' triglyceride stores (intramuscular triglycerides; (IMTGs), and plasma FFA.

Using blood sampling and isotope tracers, Romijn et al. quantified fat and CHO oxidation rates during exercise performed at different intensities (Romijn et al., 1993). Five endurance-trained cyclists performed three exercise bouts on three consecutive days at 25%, 65%, and 85% of VO_2max. The authors observed that during the exercise bout performed at low intensity (~25% VO_2max), plasma FFA were the predominant energy source, and average FOR were ~27 μmol·kg·min^{-1}. During the moderate intensity exercise bout (~65% VO_2max), FOR increased to ~43 μmol·kg·min^{-1}. With further increases in exercise intensity (~85% VO_2max), FOR decreased (~30 μmol·kg·min^{-1}), and substrate use shifted towards predominately CHO sources (muscle glycogen and plasma glucose), despite maintaining high levels of whole-body lipolysis. This study by Romijn et al. is well-cited (> 2500) as it shows the change in substrate utilization with increased exercise intensity. However, the low sample size (N=5) is a major limitation (Romijn et al., 1993). In 2001, van Loon et al. (van Loon et al., 2001) confirmed these findings when taking muscle biopsies and isotopic tracers during three separate exercise bouts at 40%, 55%, and 75% maximal workload. Thus, it appears that when exercise intensity increases from low to moderate, substrate utilization shifts from predominately plasma FFA to greater utilization of FFA derived from IMTG lipolysis. However, with further increases in exercise intensity, FOR decreases, despite high rates of whole-body lipolysis, and CHO sources become the predominant energy substrate.

IMTG stores are an essential fuel source during exercise (van Loon et al., 2001 & 2004). As noted above, rates of FFA oxidation derived from IMTGs are increased during exercise performed at moderate intensity (van Loon et al., 2001 & 2004; Rice et al., 1999). The skeletal muscle of healthy individuals has the capacity to respond to metabolic and environmental stimuli, resulting in changes in substrate metabolism. For example, during fasting, FFA are the predominant substrate for skeletal muscle (Andres et al., 1965). In the postprandial state, a situation where plasma insulin is elevated, substrate selection shifts from fat-oxidation to predominately CHO substrate sources (in the form of glucose) (Kelley, 2005). The ability to alter substrate use is often referred to as skeletal muscle metabolic flexibility (Kelley, 1999 & 2005). Individuals living with obesity are less able to respond to environmental and metabolic changes, and therefore, metabolic flexibility is impaired (Kelley, 2005). For instance, under fasting conditions, CHO oxidation is higher in the skeletal muscle of persons living with obesity compared to the skeletal muscle of normal-weight persons despite comparable rates of skeletal muscle FFA uptake. Thus, FOR is lower, leading to the accretion of IMTGs. Furthermore, during periods of elevated plasma insulin (e.g., in a postprandial state), CHO uptake, oxidation, and storage are blunted. Thus, the dynamic metabolic flexibility of skeletal muscle is diminished, which may negatively impact health (Kelley, 1999).

Increased delivery of FFA to the skeletal muscle (a tissue not suited for fat storage) leads to the synthesis of long-chain acyl-CoAs and other FFA metabolites, such as diacylglycerols and ceramides (Schmitz-Peiffer, 2000). In brief, these named FFA metabolites are known to activate protein kinase C and ceramide-activated protein kinase, which phosphorylate and inactivate the insulin signaling pathway (Kim et al., 2002). This, in turn, reduces glucose uptake, resulting in skeletal muscle insulin resistance and, if untreated, may lead to type-II diabetes (Goodpaster, 2001).

Goodpaster et al. compared skeletal muscle insulin sensitivity and IMTG content in normal-weight, obese (with and without type 2 diabetes), and endurance-trained individuals (Goodpaster, 2001). As expected, histochemical analysis of muscle samples showed the highest IMTG content in the subjects living with obesity and type-II diabetes (Goodpaster, 2001).

These individuals also displayed the lowest insulin sensitivity. Therefore, interventions to increase FOR to reduce plasma FFA and IMTGs in obese populations have been the topic of investigation (Goodpaster, 2003; Solomon et al., 2008). Furthermore, low-moderate intensity steady state (LISS) exercise training has been found to elicit higher FOR in individuals living with obesity compared to HIIT (van Aggegel-Leijssen, 2001; Venables et al., 2008). This increase in FOR may aid in long-term weight management and, if coupled with a negative energy balance, could improve health (Rice et al., 1999).

Currently employed techniques for weight management consist of extreme caloric deprivation alone or in combination with exercise, exercise alone, or medically invasive procedures (gastric banding or bypass), all of which have proven not to provide sustainable resolutions due to relapse or lack of behaviour change (Brownell & Jeffery, 1987; Kramer et al., 1989). Due to the importance of combating a global obesity epidemic, the need for customized PA and exercise prescriptions to increase FOR is critical. In order to formulate a successful solution, researchers should examine the chronic effects of varying exercise intensities and modalities on FOR alone and in conjunction with healthier eating habits (time-restricted feeding with modest caloric deprivation). Studies primarily focus on examining the acute effects of training at a person's maximum FOR (Asano, 2014), while a limited number of studies examine the chronic effects. In order to successfully increase FOR in overweight and obese populations, exercise intensity, modality, and duration are essential.

Substrate oxidation is different during differing modes of exercise. Comparisons between running and cycling have generally shown higher FOR during running. VO_2 is also higher during running than during cycling (Achten et al., 2003; Carter et al., 2000; Houmard et al., 1991; Nieman et al., 1998); therefore, exercise at the same relative intensity results in greater energy expenditure during running. The respiratory exchange ratio (RER) is a unitless number used in calculations of non-protein substrate oxidation when estimated from VO_2 consumption and VCO_2 production. The RER value indicates which macronutrients are metabolized, as different energy pathways are used for fats and CHO (Vander et al., 2001). A value of 0.7 indicates that lipids are metabolized, 0.8 for a mixed diet, and 1.0 for carbohydrates. RER data indicates the proportion of fat and CHO used but does not provide a good reflection of the absolute amount of fat oxidized (because this is also dependent on energy expenditure). Substrate metabolism has been compared in running and cycling at the same VO_2 (Achten et al., 2003), relative intensity (Houmard et al., 1991; Nieman et al., 1998; Pascoe et al., 1990), intensity related to lactate threshold (Nikolopoulos et al., 2017), and over a wide range of intensities (Achten et al., 2003). Nieman et al. 1998, studied ten triathletes during 2.5 h of running and cycling at 75% of the respective VO_2max. No significant differences were observed in RER values between the two exercise modalities (0.85 versus 0.87 for running and cycling, respectively) and did not examine FOR. Whereas comparisons between walking and cycling examined by Achten et al., 2003 revealed absolute FOR was approximately 28% higher during walking than during cycling, but they did not report RER (Achten et al., 2003).

Maximal rates of Fat-Oxidation (FOR_{max})

Research from Achten & Jeukendrup reported that FOR increased from low to moderate intensities and decreased when the intensity became vigorous to maximal. Further, these authors documented that maximal rates of fat oxidation (FOR_{max}) were achieved at 47% and 52% of VO_2max in the general population and between 59% and 64% of VO_2max in trained individuals (Achten & Jeukendrup, 2004). Based on the literature, FOR_{max} is typically achieved at moderate exercise intensities (45% to 65% of VO_2max). The large variability of FOR_{max} between individuals could be attributed to, but not limited to, sex, training status, VO_2max, and dietary habits (Achten & Jeukendrup, 2004; Purdom et al., 2018; Venables et al., 2004).

The FOR protocol utilized in our investigation was a modified version of the Achten, Venables, and Jeukendrup treadmill protocol (Achten et al., 2002). The workloads were 3 minutes long, with consistent intensity increases at every stage. The researchers of this investigation modified the protocol to be walking in nature rather than running. At the start of the protocol, electronic chest-mounted heart rate monitors were strapped onto the study participants to measure HR. Indirect calorimetry was used to collect VO_2 and VCO_2 measurements. Frayn's equation for calculating FOR was used to calculate substrate oxidation at each workload (Frayn, 1983). The urinary nitrogen excretion rate was assumed to be negligible for the purposes of the calculations. The equation is as follows:

$$\text{Fat-oxidation rate } (g \cdot min^{-1}) = 1.67 * VO2 \ (L \cdot min^{-1}) - 1.67 * VCO2 \ (L \cdot min\text{-}1)$$

FOR and FOR_{max} were expressed relative to each participant's estimated fat-free mass (FFM) and total body mass at each workload. The FOR relative to FFM was used to create FOR curves for each participant and the analysis of resting and FOR_{max} (Frayn, 1983).

Since the development of the FOR_{max} protocol, it has been employed in many research studies (Achten et al., 2003; Achten & Jeukendrup 2003, Norby et al., 2006; Stisen et al., 2006; Venable et al., 2006; Riddell et al., 2008). Achten et al. recruited 55 endurance-trained individuals (average VO_2max ~65 $mL \cdot kg^{-1} \cdot min^{-1}$) who underwent a FOR_{max} test following an overnight fast. The average FOR_{max} in this cohort of study participants was 0.52 $g \cdot min^{-1}$ at an average of ~70% VO_2max (Achten & Jeukendrup, 2003). Despite the subjects being classified as endurance trained, the authors observed a wide spread of VO_2max values. Therefore, further analyses of these results were completed to establish if fitness level (according to VO_2max) altered FOR_{max}. The study participants were separated into two groups: those with a VO_2max above and below the mean. The authors found no difference in the exercise intensity at which FOR_{max} occurred (equalled ~63% VO_2max in both groups). However, the FOR_{max} rates were significantly higher in the high VO_2max group when compared to the low VO_2max group (0.56

and 0.48 g·min^{-1}, respectively). Additionally, the authors found a positive correlation (r=0.64) between FOR_{max} rates and VO_2max (Achten & Jeukendrup, 2003). However, only a small subgroup of subjects (moderately to highly trained athletes) were used in this study, meaning that the results could not be extrapolated to the general population. Using a similar study design, Nordby et al. 2006 examined 16 study participants who completed a FOR_{max} test. Study participants were classified as untrained or trained (average VO_2max ~47 and 57 mL·kg^{-1}·min^{-1} in the untrained and trained group, respectively). Once more, it was found that, on average, the trained individuals had higher rates of FOR_{max} compared to their untrained counterparts. In addition, the exercise intensity at which FOR_{max} occurred was also significantly higher in the trained group compared to the untrained (Nordby et al., 2006).

In order to elucidate what predicts FOR_{max}, a large-scale study was completed in 2004 (Venables et al., 2004). In this cross-sectional study, 300 volunteers differing in training status, age, body mass, BMI, and sex underwent a FOR_{max} test following a 4-hour fast. The authors found that, on average, the FOR_{max} was 0.46 ± 0.01 g·min^{-1} occurring at 48 ± 1% VO_2max. Interestingly, the authors also observed large inter-individual variations in both variables. FOR_{max} in these 300 volunteers ranged from 0.18-1.01 g·min^{-1}, occurring at exercise intensities as low as 22% VO_2max up to 77% VO_2max (Venables et al., 2004). Correlation analysis of these results showed that FFM, self-reported PA, VO_2max, sex, and FM were all significant predictors of FOR_{max}, accounting for 34% of the variance (Venables et al., 2004). However, the authors could not elucidate what accounted for the remaining 66% variance in the FOR_{max}. Riddell et al. examined the effects of age and sex on FOR_{max}. The researchers found that compared with men, pre-pubertal boys have higher FOR_{max} throughout a wide range of exercise intensities and that FOR_{max} drops as boys develop through puberty (Riddell et al., 2008). The pre-pubertal boys and men had similar levels of fitness according to VO_2peak (45.6 ± 6.5 mL·kg^{-1}·min^{-1}, 44.6 ± 9.0 mL·kg^{-1}·min^{-1} respectively). Thus, the differences in FOR_{max} are unrelated to the subjects' fitness levels. Other investigations also support these findings (Riddell et al., 2008; Martinez & Haynes, 1992; Timmons et al., 2003). Wade et al. found lower RER (indicative of higher FOR) during steady-state exercise in individuals who had a higher proportion of oxidative slow twitch muscle fibres (slow twitch are characterized as having high mitochondria content and capillary network) (Wade et al., 1990). Additionally, habitual diet may play a role in determining FOR. A low CHO diet, consumed for five days, has been found to significantly increase FOR compared to a one-day high-fat diet (Stepto et al., 2002). Thus, individuals who habitually consume a low CHO and/or high-fat diet may display higher FOR.

Fasting, Time Restricted Feeding (TRF) and Intermittent Fasting (IF)

Fasting is the voluntary abstinence from food intake for a specified period and is a well-known practice associated with many religious and spiritual traditions. Time-restricted feeding protocols (TRF) involve adhering to a daily routine requiring fasting for a certain number of hours and feeding for the remaining 24 hours (Rothschild et al., 2014). Fasting is distinct from caloric restriction, in which daily caloric intake is chronically reduced by up to 40%, but meal frequency is maintained (Longo & Mattson, 2014). In contrast to fasting, starvation is a chronic nutritional deficiency commonly incorrectly used as a substitute for fasting. Starvation may also refer to some extreme forms of fasting, which can result in an impaired metabolic state and/or death. Starvation typically implies chronic involuntary abstinence from food, which can lead to nutrient deficiencies and health impairment (Moro et al., 2016). While prolonged periods of fasting are difficult to perform for the normal population, TRF and intermittent fasting (IF) protocols have been shown to produce higher compliance (Moro et al., 2016). Typically, IF is defined by a complete or partial restriction in energy intake (between 50 and 100 % restriction of total daily energy intake) on 1–3 days per week or a complete restriction in energy intake for a defined period during the day that extends beyond the overnight fast (Moro et al., 2016). One particular form of IF that has recently grown in popularity through mainstream media is TRF. TRF allows subjects to consume ad libitum energy intake within a defined window of time (from 3–4 h to 10–12 h), which means a fasting window of 12–21 h per day is employed (typically 16 h). A key point concerning the TRF approach is that, generally, calorie intake is not controlled or restricted, but the feeding times are. A growing body of evidence suggests that, in general, TRF and IF could be valuable tools for improving health in the general population due to reports of improving blood lipids (Klempel et al., 2012 & 2013, Varady et al., 2011) and glycaemic control (Barnosky et al., 2014), reducing circulating insulin (Trepanowski & Bloomer, 2010), decreasing blood pressure (Trepanowski & Bloomer, 2010; Varady & Hellerstein, 2007; Tinsley & La Bounty, 2015; Varady & Bhutani, 2009), decreasing inflammatory markers (Farajeh et al., 2012) and reducing FM even during relatively short durations (8–12 weeks) (Varady & Bhutani, 2009). One key mechanism responsible for many of these beneficial effects appears to be the "flipping" of the metabolic switch. The metabolic switch typically occurs in the latter phase of fasting when glycogen stores in hepatocytes are depleted, and accelerated adipose tissue lipolysis produces increased fatty acids and glycerol (Cahill, 2005). The metabolic switch typically occurs between 12 to 36 hours after cessation of food consumption and can vary based on the liver glycogen content at the beginning of the fast and on the amount of the individual's energy expenditure/exercise during the fast. The lipids in adipocytes are then metabolized to FFAs and released into the blood. Simultaneously, other cells may also begin generating ketones, with astrocytes in the brain being one notable example. FFAs are transported into hepatocytes, where they are metabolized by β-oxidation to produce the ketones β-OHB and acetoacetate, which may induce mitochondrial biogenesis (Gano et al., 2014).

High concentrations of ketones are metabolized in muscle cells and neurons to acetyl coenzyme A, which then enters the tricarboxylic acid cycle to resynthesize ATP (Anton et al., 2018). Through these physiological processes, ketones can serve as an energy source to sustain the function of muscle and brain cells during extended fasting and/or sustained periods of physical exertion/exercise (Anton et al., 2018; Cahill, 2005; Puchalska et al., 2017). During IF, evidence suggests that a shift in the primary energy source from glucose to fatty acid-derived ketones may preserve muscle mass. In support of this, lean mass retention can be increased following TRF regimens for weight loss compared to continuous caloric restriction regimens in humans (Varady, 2011). Additionally, in mice, the decline in muscle mass that occurs during normal aging is prevented by time-restricted feeding (TRF) involving 40% caloric restriction (van Loon et al., 2015). Further, evidence suggests that TRF regimens can also optimize physiological function, enhance performance, and slow aging and disease processes (Anton et al., 2018). These reported effects are likely mediated through changes in metabolic pathways and cellular processes such as oxidative stress resistance (Ziegler et al., 2003), lipolysis (Barnosky et al., 2014; Farajeh et al., 2012; Paoli et al., 2013; Lodi et al., 2012; Mattson et al., 2003), and autophagy (Alirezaei et al., 2010; Mammucari et al., 2008). Thus, TRF regimens that induce the metabolic switch have the potential to improve body composition in individuals living with overweight or obesity.

Overview of Body Composition Assessment Techniques

Body composition can involve various methods of analysis: atomic, molecular, cellular, tissue–organ, and whole-body (Shen et al., 2005). Measuring body composition to predict individual health and wellness can be simplified into understanding a person's fat-free mass (FFM) in relation to total fat-mass (FM). The purpose of determining one's body composition is to gain a better understanding of adipose tissue (mass or thickness) in relation to all other tissues. Body composition assessment is essential for various reasons, including monitoring health and fitness levels, guiding weight loss and gain programs, and evaluating nutritional status. Furthermore, determining FM distribution within various parts of the body, including visceral, subcutaneous, intramuscular, and osseous deposits, provides even greater accuracy in gauging health risks. The most common body composition methods include dual-energy X-ray absorption (DXA), underwater weighing, air displacement, computed tomography, skinfold girth/thickness measurement, and bioelectrical impedance (BIA). DXA and BIA have become the instruments of choice for measuring percent body fat (%BF) in research and are considered commonly used tools for measuring fatness. DXA uses low-level X-rays to discern FM, %BF, and regional adipose deposition patterns. BIA measures the resistance to an electrical signal in muscle and fat tissue. BIA is also a valid method for determining %BF and regional FM. These technologies, however, can be expensive, cumbersome, time-consuming, labor-intensive, may not always be readily available, and typically require highly trained personnel. Many of these methods can also be difficult to standardize across observers or machines, complicating comparisons across study participants and periods.

Anthropometric body composition measurements provide a more cost-effective route for clinically accessible information. However, using these measures to predict health risks is the subject of much research and debate. These various measures aim to determine an individual's %BF, but fail to account for varying distribution patterns of fat tissue, and health risks associated with differing fat distribution patterns (gynoid vs android). For example, skinfold thickness measurements involve using calipers to measure the thickness of subcutaneous fat at various sites on the body. The measurements are then used to estimate body fat percentage using evidence-based mathematical equations, which can be age, race, and sex-dependant. Although this method can be relatively inexpensive, it requires trained personnel and may not be as accurate as other techniques (Zender, 2001).

Body mass index (BMI) is the default metric of body composition that has prevailed for the past 50 years. It was developed in the mid-1800s by a Belgian scientist, Adolphe Quetelet. BMI is defined as body mass divided by the square of one's height (BMI = body mass (kg)/height (m^2)). As mentioned above, BMI does not accurately assess obesity-related co-morbidity risks because it does not account for important factors such as frame size or type, varying body types, or varying proportions of bone, muscle, water, and fat mass (Zender, 2001). As a whole, BMI is a non-discriminatory metric that only provides general information on the proportion of body mass to height. The development of BMI was initially intended for use in large-scale population studies rather than as a diagnostic tool to determine the health risks of individuals. Although more accurate and valid measures of body composition are gaining in use, BMI remains the predominant evaluation tool of the Centers for Disease Control and Prevention (CDC) as a way of screening for potential health problems that could occur due to weight. Donini et al., 2013 found, however, that BMI performed similarly to a "coin flip" at estimating %BF when evaluated by predictive value analysis, confirming results that other anthropometric and biochemical measurements explained a greater amount of the variance in estimating FM when BMI was not included in the model.

An individual's body composition is strongly related to their level of health. Bjorndal et al., 2001 states that, "The distribution of fat between these depots seems to be more important than the total adipose tissue mass for the risk of developing obesity-related diseases." There are differences between the health hazards connected with the android and gynoid forms of fat accumulation (Bjorndal et al., 2011; Manolopouls et al., 2010). It is common to assume that the relationship between weight and health risk is linear, meaning that as weight rises, so do the associated hazards. However, several studies show that mild overweightness may not raise the risk of certain health conditions and may have protective effects (Elagizi et al., 2018). In addition to an increased risk of all-cause mortality, up to 40% of people with a normal BMI also exhibit some degree of metabolic or cardiovascular evidence of disease. These conditions include insulin resistance, high blood pressure, hyperlipidemia, prediabetes, or type-II diabetes (Flegal et al., 2013; Elagizi et al., 2018; Weiss et al., 2013; De Schutter et al., 2013). The obesity/overweight paradox is the name given to this conundrum (Kahn et al., 2012). This conundrum, also known as the fit but fat paradox, underscores that a physically active overweight individual is at a reduced risk for all-cause mortality compared to a normal-weight inactive individual (Lavie et al., 2015; Ortega et al., 2018).

Some aspects of this obesity/overweight paradox were elucidated by Lavie, De Schutter, and Milani in 2013 and 2015. Even after excluding underweight people from the analysis, they discovered that people with low BMI and poor percent %BF have the highest risks of CVD mortality. In addition, when %BF and FFM are considered, those with low %BF and low FFM have the greatest mortality rates, whereas people with high %BF and high FFM have the lowest mortality rates. A lower FFM had a greater impact on mortality than %BF values. The effect of cardiorespiratory fitness in connection to %BF and FFM on CVD prognosis and mortality risks has been identified by this group. Regardless of the mechanism used to define overweight/obesity, high cardiorespiratory fitness revealed lower death rates, suggesting that cardiorespiratory fitness modifies the effects of BMI on survival (Barry et al., 2014; Lee et al., 2010 & 2011).

Chapter 2: Study 1

Validated Fat Oxidation Rates at Rest and During Exercise in Postmenopausal Middle Eastern and Caucasian Women

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http://jscholaronline.org/full-text/JOMD/1_104/Validated-Fat-Oxidation.php

Abstract:

Background:

During menopause and throughout aging, women are at an increased risk for a plethora of chronic conditions, many of which are related to the interruption of estrogen. The primary and secondary prevention benefits of habitual unstructured and structured PA are well documented. Fat-oxidation rates (FOR) at rest and during exercise have been reported to decrease through the menopausal transition.

Methods:

Twenty-three middle-aged Middle Eastern (n=11) and Caucasian (n=12) women were recruited. An independent t-test was used to determine differences between the groups for: anthropometrics, menstrual characteristics, resting blood pressure (BP) and heart rate (HR), PA levels, blood lipid panel, blood hormone panel, Glucose, resting VO_2, and VO_2peak. To assess the protocol's reliability, a subset of participants had their VO_2 and maximum fat oxidation rate (FOR_{max}) determined on three separate occasions.

Results:

No significant differences were observed between FOR at rest, during exercise, and/or other physical and physiological parameters. There were no significant differences between the three separate trials for the VO_2 and FORmax values.

Conclusion:

This study contributed to the ever-growing body of literature on FOR and women's health by exploring an ethnic group that has not been previously studied. The findings of this investigation support the use of this protocol in further investigations examining FORmax.

Background:

During menopause and aging, with changing hormone levels, women are at an increased risk of chronic conditions such as cancer, type-II diabetes, autoimmunity, osteoporosis, and cardiovascular diseases (Lee et al., 2011; Stojanovska et al., 2014). The risks related to post-menopause are mainly due to the cessation of estrogen, which has indirect protective effects on lipid and glucose metabolism and direct effects on blood vessel function. Thus, post-menopause is commonly associated with hypertension, an increase in overall body mass, and altered adiposity distribution, the most frequently related factors to coronary artery disease (Carr, 2003). Hypertension is due to increased body mass index (BMI), insulin resistance, sodium retention, increased blood viscosity, and estrogen deficiency with increased smooth muscle cell proliferation, which causes an increase in systemic vascular resistance. Age and estrogen deficiency together are the most important causes of cardiovascular risk in post-menopause (Ferrara et al., 2002). Contrastingly, the benefits of unstructured PA have been well established, and promoting increased levels of PA to prevent and or treat several chronic diseases (obesity, diabetes, cardiovascular disease) dates back at least to the 1950s (Rossi et al., 2002; Morris et al., 1953; Morris et al., 1953; Paffenbarger et al., 1975 & 1978). Estrogen, progesterone, and testosterone levels have been reported to influence substrate metabolism and, more specifically, fat metabolism at both rest and during exercise (Bouchard et al., 1990 & 1994). As these hormone levels change during the menopausal transition, they may be contributing to the increase in overall body mass and visceral adiposity distribution observed post-menopause.

Fat-oxidation rates (FOR) at rest and during exercise have been reported to decrease throughout the menopausal transition, and therefore, the decrease in estrogen has been associated with decreases in FOR at rest and during PA (Bouchard et al., 1990; Santa Clara et al., 2006). In addition, differences in hormone levels (Hickner et al., 2001; Setiawan et al., 2006) and FOR

(Randolph et al., 2004) have been observed among White, African American, European, and South Asian ethnic groups. Further, differences in FOR have been previously observed between select ethnic groups, and the respective postmenopausal hormonal modifications have been speculated to influence these differences (Hall et al., 2010).

In health-oriented PA interventions, it is often reported that reaching FORmax may be associated with the most efficient weight reductions, although limited experimental evidence exists. Further insight into FORmax and its reliability would allow it to be used as a target within customized PA interventions. The purpose of this study was to i) validate the treadmill-based indirect calorimetry FOR procedures and ii) compare resting FOR, FOR during incremental exercise, and FORmax, hormone levels of Middle Eastern (ME) and Caucasian (C) postmenopausal women for further understanding of the menopausal transition and the effects on FOR. It was hypothesized that the ME women would exhibit lower FOR at rest and different sub-maximal exercise intensities and, therefore, have a lower FOR_{max}, lower estrogen levels, and possess higher cardiometabolic risk factors compared to the C women.

Study Participants and Requirements

Twenty-three middle-aged Middle Eastern (n=11) and Caucasian (n=12) women were recruited. The study participants' ages were 52.6 ± 2.8 and 57.1± 3.3, respectively. Study participants did not have any physical ailments that would contraindicate participation in the study (e.g., cardiomyopathies, neuropathy, other diabetes-related complications) and were screened by certified exercise physiologists using resting blood pressure in conjunction with the evidence-based screening tools, including the most current PAR-Q+ and, if required the ePARmed-X+ (www.eparmedx.com) for exercise contraindications and risk stratification. Eligibility was further confirmed once the data on the participant's BMI plus PA and

Sedentarism Score had been assessed. If the participants fulfilled the inclusion criteria, they were informed of the requirements of the study, and written informed consent was obtained.

Inclusion Criteria

The inclusion criteria indicated that participants must be postmenopausal and otherwise healthy, not on metabolic altering medications or hormone replacement therapy, and had not undergone surgically induced menopause. Menopausal status was based on the participant's self-report, having no menstrual cycles in the past 12 months, confirmed by their FSH level, >30 mIU/mL with the blood draw. Pre-exercise Heart Rate (HR) and blood pressure were measured using the BpTRU100 (Surgo Surgical Supplies, Toronto, Ontario) automated device to ensure participants were within an acceptable range prior to the initiation of the exercise protocols; blood pressure < 160/90 mmHg. Six measurements were taken consecutively with a 1-minute rest interval in between and averaged. Participants were grouped based on their ethnic origin, ME or C, determined by their birthplace as self-identified. Participants' BMI was assessed and had to be greater than 24.9 but no greater than 34.9 (overweight or obese class I according to BMI). Further, participants were absent of injuries that would diminish their ability to complete an exercise program, having a VO2max ≥ 20 $mL \cdot kg^{-1} \cdot min^{-1}$ and could not score greater than five on The PA and Lifestyle "R" Medicine PA Participation and Sedentarism Questionnaire (PAPSQ).

Exclusion Criteria

Subjects were only included in the trial if they met all inclusion criteria. Subjects classified as normal weight, overweight, or obese class I using BMI but were currently considered regular exercisers (active for the past three months, more than twice a week) corresponding to a score greater than five on the PAPSQ were not included for the trial.

Data Collection Methods and Instruments

All protocols were reviewed and approved by the Human Participants Review Sub-Committee at York University's Office of Research Ethics, and the experimental protocol conformed to the standards set by the Declaration of Helsinki. Participants reported to the York University Human Performance Laboratory, and the women provided written Informed Consent to their voluntary participation in the study prior to performing any study-specific procedures. A copy of the consent form was provided to the study participants, and another copy was added to the study master file. After completing the informed consent and the PAPSQ, study participants underwent a laboratory assessment to ensure they met the inclusion criteria. The pre-exercise screening took place on the first experimental day. The first visit consisted of pre-screening plus an incremental-to-maximal effort treadmill test for the determination of aerobic fitness or power (VO_2max) using the criterion open circuit spirometry discrete system. On the second experimental day, the study participants underwent the fat oxidation protocol following an 8-10 hour overnight fast and 500 mL of water. The FOR protocol was a modified version of the Achten, Venables, and Jeukendrup treadmill protocol (Achten et al., 2002). The workloads were the same duration in length, and the increase in intensity at each new stage was consistent with the protocol, but the current protocol was walking in nature rather than running. The third day was used to perform a second trial of the FOR_{max} protocol; the same starting speed and loading sequence were used, and duplication of the first trial was attempted. The FOR_{max} values of the two trials were used in the analysis and assisted with determining the reliability of the criterion open circuit spirometry system. A further description of the visits and the types of exercise performed are detailed below.

Visit 1

Anthropometric data, including height, body mass, body fat percentage, skin folds, and waist circumference, were collected using standardized laboratory protocols (Jamnik & Gledhill, 2015). The Seca Alpha Scale (Modell 770, Germany) measured body mass upon each visit. Body fat percentage was measured without shoes using bioelectrical impedance analysis (Tanita scale, model TBF-612, Arlington Heights, IL). Height was measured without footwear using a wall-mounted stadiometer. Waist circumference was measured following the standard National Institutes of Health protocol, with a tape measure around the waist, on the skin, and at the iliac crest level. Skinfolds (triceps, biceps, subscapularis, iliac crest, and medial calf) were measured using Harpenden fat calipers (Baty International, Burgess Hill, UK) according to the Physical Activity and Lifestyle "r" Medicine (PALM) protocol to determine body adiposity (Jamnik & Gledhill, 2015).

The incremental-to-maximal effort treadmill test for the determination of VO_2max followed the same loading sequence for all participants. The protocol included a 2-minute warm-up, and progressive exercise workloads increased every two minutes (treadmill speed and/or elevation). The participants were instructed to remain on the treadmill until their work tolerance was compromised, at which point they received a 2-minute low-intensity active recovery period. Following recovery, the participants completed another incremental workload followed by a 2-minute recovery. This discontinuous sequence was repeated until the VO_2 of the subsequent workload was equal to or lower than the previous, indicating attainment of VO_2max (Jamnik & Gledhill, 2015; Achten et al., 2003; Gledhill et al., 1994; Howley et al., 1995). The attainment of VO_2max was confirmed using a discontinuous protocol during which the participants exercised at higher workloads for 2 minutes, followed by another active recovery. This protocol sequence was repeated until the VO_2 of the subsequent workload was equal to or lower than the previous, indicating VO_2max. This could also be referred to as verification or supramaximal testing (Howley et al., 1995; Hancock et al., 2023). The VO_2 was determined from measurements obtained during the last 30 seconds of each workload via direct analysis of mixed expired gases. The VO_2max test was terminated if the study participant could no longer complete the workload due to volitional fatigue or if VO_2max criteria were met. This was determined by the qualified exercise physiologist present at the time.

The discrete component system consisted of; a 120L Tissot gasometer (Warren E Collins LTD, Braintree, MA), rapid response oxygen and carbon dioxide gas analyzers (Applied Electrochemistry, Model S-3A and CD-3S, Sunnyvale, CA), a flexible plastic hose, two-way y-valve (Ewald Koegal Co, San Antonio, TX), mouthpiece, and nose plugs. The mouthpiece was positioned between the participants' gums and teeth, and they were required to breathe in and out of the mouthpiece with their noses plugged throughout the VO_2 collection period. The Y-valve allowed the participants to inhale atmospheric air freely, then directly exhale air into the hose and tank, where the gases were collected and mixed. Once the expired gases were collected in the Tissot, they were analyzed using the gas analyzers. The collected variables, minute ventilation, and fractions of expired carbon dioxide and oxygen were then used to calculate the participants' VO2max (Hancock et al., 2023; Yavelberg et al., 2023). The criterion HR was measured throughout using a Polar HR chest monitor (Polar Electro, Kempele, Finland).

A separate cohort of participants (n = 9, five males and four females) had their VO_2, VO_2max, and FOR_{max} determined using the open circuit spirometry discrete system on three separate occasions to assess the reliability of the protocol and the measurement of FOR_{max}. The study participants characteristics can be found in Table 1b.

All study participants were asked to maintain the same lifestyle throughout the intervention, including no change in their diet and/or non-structured or structured PA, as dictated by a self-reported PA questionnaire PAPSQ (Appendix A). Study participants were also required to document their daily PA participation as well as their diet.

Visit 2

The study participants arrived at the laboratory following an 8-10 hour overnight fast. Blood samples were drawn from each participant at the beginning of the second visit while in a fasted state to characterize the blood lipid, sex hormone, and glucose levels. A certified phlebotomist performed the blood extractions. Once the blood was obtained from the participants, the vials rested for 30 minutes before being spun in a centrifuge for 15 minutes. After the samples were spun, the plasma was transferred to storage vials to be sent to an external laboratory (Canadian Life Labs). The blood lipid panel measured HDL-cholesterol, LDL-cholesterol, triglycerides, total cholesterol, and the HDL-cholesterol to total cholesterol ratio, which was calculated to ensure normal blood lipid levels for each participant. The blood sex hormone panel analyzed estradiol, estrone, progesterone, testosterone, SHBG, and androgen index, which was calculated using the testosterone and SHBG, FSH, LH, and insulin values. Urine samples were obtained to measure cortisol levels. The urine samples were taken on the same morning as the blood draws while in a fasted state. The sample was collected in sterile urine cups and transferred to vials to be sent to an external laboratory (Canadian Life Labs) along with the blood samples for analysis.

Following the blood and urine sample collections, the study participants underwent the modified Achten, Venables, and Jeukendrup walking FORmax protocol. Resting and exercise HR was measured via a Polar chest strap HR monitor (Polar Electro KP 4, Kemple, Finland). Resting VO_2 and FOR measurements were obtained with the participant seated. Expired gas was collected and analyzed in the same manner as during the GXT and then used in the formula to calculate FOR. The protocol began at 1.5-1.8 mph and 1% incline, depending on the comfort and height of the participant. Speed increased by 0.2 mph every 3 minutes until the participant walked briskly (3.4-3.6 mph). Once the maximum walking speed was attained, the incline increased by 2% every 3 minutes until a respiratory exchange ratio of 1.0 or greater was obtained.

In the workload's last 30-60 seconds, the expired gases were collected to calculate FOR. At the end of each workload, both participants' HR and the rating of perceived exertion score were obtained and were used to gauge the participants' work intensity. Using indirect calorimetry, Frayn's equation for calculating FOR was employed to measure substrate oxidation at each workload. The urinary nitrogen excretion rate was assumed to be negligible for the purpose of the calculations. The equation employed is as follows:

$$\text{Fat } (g\cdot min^{-1}) = 1.67 * VO_2 \ (L\cdot min^{-1}) - 1.67 * VCO_2 \ (L\cdot min^{-1})$$

FOR was expressed relative to each participant's fat-free mass and body mass at each workload. The FOR relative to fat-free mass was used to create the FOR curves for each participant and the analysis of resting and FORmax.

Visit 3

The third day was used to perform a second trial of the FOR protocol. The exact starting speed and loading sequence were used, and duplication of the first trial was attempted. The FORmax values of the two trials were used in the analysis and assisted with determining the reliability of the criterion open circuit spirometry discrete system.

Statistical Analysis:

The study participant characteristics were expressed as means and standard deviations (X±SD). A total of 24 study participants were recruited, 12 per group. One Middle Eastern woman was not able to continue with the experimental protocol. Thus, a total of n=12 C and n=11 ME were used for the statistical analysis. An independent t-test was used to determine differences between the ME and the C for the anthropometrics, menstrual characteristics, resting BP, resting HR, PA levels, blood lipid panel, blood hormone panel, glucose, resting VO_2, and VO_2max. A paired t-test was performed on the two trials of the FOR trials to determine any differences between the two occasions. Regression analysis was performed on each group's hormones and other measured variables against WC and FOR. Statistical analysis was conducted using a standard statistical software program, SPSS 28. The protocol's reliability was determined by testing for its coefficient of variation using repeated measures ANOVA and intra-class correlation coefficient (ICC) when it was reproduced on the same individual for the repeated FOR_{max} trials (three times for the sub-set). The ANOVA was calculated using the Excel two-factor without replication formula. The ICC was calculated using the IBM SPSS Statistics Data Editor Software. The two-way mixed model and the consistency type formula were used.

Applying a two-tailed t-test to the data suggests that 13 participants would be required to achieve 80% power when detecting a large effect size at an alpha level of 0.05 with a mean difference of 1 standard deviation effect type. The same holds true for the ANOVA analysis considering a medium-large effect size of 0.5. Collectively, this suggests that 13 participants will be required per group to establish within-treatment effects in the primary outcomes.

Results:

There were no significant differences between the separate trials for the VO_2 and FOR_{max} values in both study groups. The correlation between the two trials for the ME and C women was $r=0.97 \pm 0.03$ (Appendix C). For the subset group the ANOVA calculations revealed a significant difference between individuals regarding FOR_{max} ($p=0.000073$, $F=9.7$), which was expected given the individual variability. There was no significant difference within the same individual when the protocol was conducted on three different days ($p=0.60$, $F=0.52$). The ICC analysis on FOR_{max} ($r=0.893$) and $\%VO_2max$ ($r = 0.793$) indicated good reliability. This validated the application of the treadmill-based GXT protocol coupled with indirect calorimetry to be used as the criterion method during the remaining exercise sessions and comparisons.

Table 1 contains the anthropometric, physical plus physiological fitness profiles and menstrual plus age measures for all of the female study participants (12 C, 11 ME). Significant differences between the C and ME groups where observed for the following study participant characteristics; mean age of the ME was younger (p= 0.004), ME group observed their first period at an earlier age (p= 0.023) and had their last menstrual cycle early in life (p= 0.031), menstrual age (age of last cycle - age of first cycle) was shorter in the ME group (p= 0.007), ME had a higher body mass (p= 0.027), a higher BMI (p= 0.32) and a larger NIH waist circumference measurement (p= 0.005).

Table 1. Anthropometric, Physical plus Physiological Fitness Profiles and Menstrual Measures of the Study Participants.

Characteristics	**Caucasian** (n=12; X±SD)	**Middle Eastern** (n=11; X±SD)	**P-value**
Age (yrs.)	57.1± 3.3	52.6 ± 2.8	0.04
Age of First Cycle (yrs.)	12.2 ± 8.2	13.3 ± 1.1	0.023
Age of Last Cycle (yrs.)	51.1 ± 2.6	46.5 ± 5.7	0.031
Menstrual Age (yrs.)	39.0 ± 2.2	32.2 ± 5.6	0.007
Height (cm)	161.5 ± 4.6	162.2 ± 5.9	-
Body mass (kg)	71.0 ± 12.1	84.0 ± 16.7	0.027
BMI ($kg \cdot m^{-2}$)	27.0 ± 3.8	31.8 ± 5.9	0.032
NIH Waist Circumference (cm)	90. 9 ± 11.0	106.1 ± 11.2	0.05
Sum of 5 Skinfolds (mm)	107.5 ± 35.6	136.1 ± 49.3	-
Tanita Body Fat Scale (%)	37.0 ± 5.4	41.7 ± 6.4	-
Resting Blood Pressure (mmHg)	109/72 ± 12/11	114/72 ± 13/9	-
Resting Heart Rate (bpm)	67 ± 7.2	72 ± 12	-
Resting VO_2 Absolute ($LO_2 \cdot min^{-1}$)	0.26 ± 0.09	0.33 ± 0.05	-
VO_2max Absolute ($LO_2 \cdot min^{-1}$)	1.98 ± 0.3	1.78 ± 0.3	-
Peak Heart Rate (bpm)	164 ± 9	158 ± 10	-

-no significant differences

Table 1b contains the study participant characteristics for the subgroup reliability analysis.

Characteristics	N=9; X±SD
Age (yrs.)	25 ± 5
Height (cm)	170.8 ± 6.9
Body mass (kg)	71.7 ± 16.4
BMI ($kg \cdot m^{-2}$)	24.4 ± 4.7
Sum of 5 Skinfolds (mm)	62.1 ± 16.1
Tanita Body Fat Scale (%)	24.0 ± 4.5
VO_2max Relative ($mLO_2 \cdot min^{-1}$)	43.7 ± 7.2

Table 2 contains the sex hormone and blood lipid results of the C and ME participants with t-test for differences between groups. As well, it contains the normative values for postmenopausal women. No significant differences were not detected between the two groups, indicating that there are no hormonal variations between these two ethnicities.

Table 2. Blood Test Results of the Study Participants.

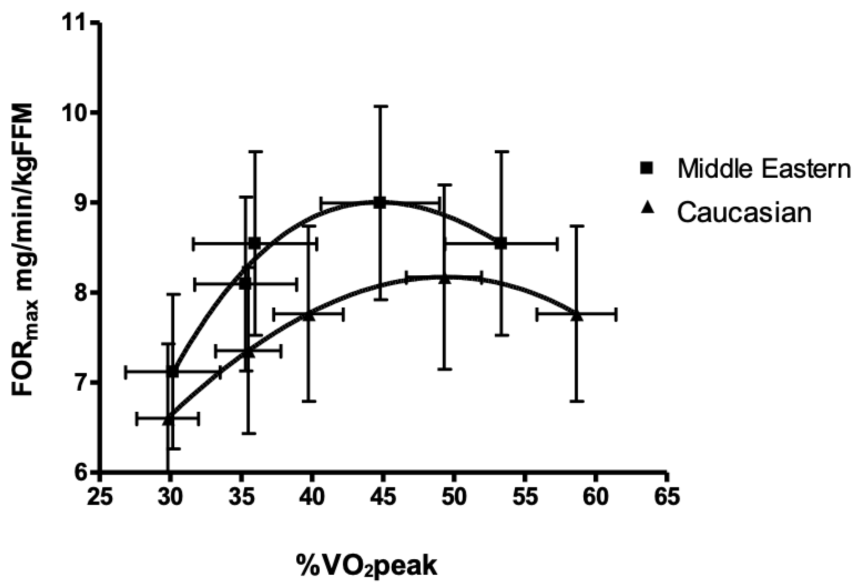
Characteristics	**Caucasian** (n=12; X±SD)	**Middle Eastern** (n=11; X±SD)
Estradiol (pmol/L)	84.93 ± 31.38	71.27 ± 4.55
Estrone (pmol/L)	138.25 ± 65.45	155.00 ± 52.74
Progesterone (nmol/L)	1.08 ± 0.29	1.36 ± 0.68
Testosterone (nmol/L)	1.33 ± 0.60	1.12 ± 0.63
Follicular Stimulating Hormone (IU/L)	85.0 ± 26.9	68.6 ± 28.9
Luteinizing Hormone (IU/L)	38.8 ± 12.3	33.4 ± 11.2
Sex Hormone-Binding Globulin (nmol/L)	45.04 ± 15.96	43.84 ± 21.91
Androgen Index	0.213 ± 0.131	0.146 ± 0.118
Cortisol (nmol/L)	215.58 ± 113.88	190.09 ± 100.50
Insulin (pmol/L)	46.08 ± 20.81	64.90 ± 50.98
Fasting Glucose (nmol/L)	5.33 ± 0.49	5.39 ± 0.80
Total Cholesterol (nmol/L)	5.53 ± 1.32	5.08 ± 1.21
LDL (nmol/L)	3.42 ± 1.15	3.12 ± 0.78
HDL (nmol/L)	1.57 ± 0.35	1.28 ± 0.57
CH/LDL (nmol/L)	3.69 ± 1.16	3.98 ± 1.03
Triglyceride (nmol/L)	1.21 ± 0.61	1.33 ± 0.64

No significant differences were detected between the two groups, indicating that there are no hormonal variations between these two ethnicities. A complete blood sample was not available for 1 participant in the ME group.

No significant differences were detected between the two groups' FOR_{max} characteristics, indicating no significant variations in FOR or the elicited intensity between these two ethnicities. FOR_{max} values and the respective $\%VO_2max$ for both trials of the protocol were statistically analyzed. A second trial of the FOR protocol for one participant in the ME group was not obtained due to the inability to complete the full protocol and, therefore, n = 22. The strength of the relationship between the two trials for FORmax is R^2=0.829 (p<0.00), and %VO_2max is R^2=0.333 (p=0.13). Since no significant differences were detected from one trial to the next, the two trials were compiled and fitted to a single curve for each participant to allow for more data points to create a best-fit third-order polynomial curve (Figure 1).

Figure 1 contains the best-fit third-order polynomial FOR curves for the C and ME participants at FORmax and 5%, 10%, and 20% below the FOR_{max}, along with the respective variance bars for both groups. The FOR is plotted with respect to %VO_2peak (GraphPad PRISM 9). These specific points provide a range of exercise intensities that elicit the highest FOR per group.

Figure 1. Fat-oxidation rate curves of both participant groups plotted at 5%, 10%, and 20% below the maximum Fat-oxidation rate.



Discussion:

This study aimed to compare FOR at rest and during incremental exercise, FOR_{max}, hormone levels, anthropometric characteristics, PA levels, and cardiometabolic risk factors between postmenopausal ME and C women. It was hypothesized that the ME women would exhibit lower FOR at rest and different sub-maximal exercise intensities and, therefore, have a lower FORmax, lower estrogen levels, and possess higher cardiometabolic risk factors compared to the C women. In contrast to the hypothesis, no statistically significant differences were observed between resting FOR, FOR during incremental exercise, FOR_{max}, hormone levels, height, body fat%, skinfold measurements, PA levels, resting BP, resting HR, resting VO_2, exercise HR max, fasting blood glucose and fasting blood lipid profile. The ME women did not exhibit lower FOR at rest, during incremental or maximum exercise. ME women did not have a lower estrogen level or more cardiometabolic risk factors than the C women. As a result of this research, new information was reported on FOR and hormonal characteristics for ME and C postmenopausal women. Further, data on FOR, FOR_{max}, and exercise intensity are expressed as a percentage of VO_2peak, at which maximal fat oxidation occurs, using a treadmill protocol and hormonal measurements for ME and W postmenopausal women.

The current study utilized a treadmill-based protocol to measure and calculate FOR over a wide range of sub-maximal exercise intensities and provide values on FOR and FOR_{max}. PA levels and anthropometrics were also obtained in this study, providing detailed data on the health and fitness characteristics of the study populations. Given the lack of statistically significant differences between the FOR for ME and C postmenopausal women, this study supports the use of the treadmill protocol for FOR-related investigations on diverse populations.

Limitations:

Although the subjects were instructed to maintain regular eating and beverage consumption habits throughout the experiment and to arrive in a fasted state, having only consumed 500ml of water the morning of the testing day, this study did not control for eating habits. Although some individuals demonstrated greater intra-variability, no significant differences were observed.

Nutrition plays a vital role in FOR, ingesting carbohydrates in the hours prior to testing decreases the FOR significantly when compared to fasted conditions. Contrary to this, conducting the testing in a fasted stated >6 hours increases FOR. Moreover, FOR has been demonstrated to decrease after consuming a high-fat diet, partially due to lower amounts of glycogen storage. When deciding about the rigor of controlling nutrition, there arises a dilemma between internal (as standardized as possible) and external validity (as closely resembling the "real" world as possible) (Hall et al., 2010). The present study aimed to employ control measures within the scope of restrictions that can be realistically applied to the general population. This gives an opportunity to define more rigorous procedures to improve reliability.

In addition, if one were to perform a power analysis to attain power at the 0.05 level for a two-tailed alpha with an effect size of 0.8, the number of participants in each group would have to be 60. The sample size was underpowered, which may have influenced the lack of statistical significance in the results.

Conclusion:

In summary, this study contributed to the growing body of literature on FOR and women's health by studying an ethnic group that has not been previously investigated. Significant differences were not observed between resting FOR, sub-maximal exercise FOR, FORmax, hormone levels, height, body fat%, skinfold measurements, resting BP, resting HR, resting VO_2, HR max, fasting blood glucose, and fasting blood lipid panel. In addition, this study is examined FOR_{max} and measure the hormones that may impact fat mobilization and oxidation during exercise in ME women. The current study is one of the few that utilized a treadmill-based FOR_{max} protocol to measure and calculate FOR over a wide range of sub-maximal exercise intensities and provide values on FOR_{max}. Furthermore, the statistical analysis of the acute day-to-day variability of the treadmill-based protocol for determining FOR_{max} revealed no significant differences. Given its reliability, the results of the investigation support the use of this modified Achten et al. treadmill-based FOR_{max} protocol. The findings of this investigation support the use of this protocol in further investigations examining FOR_{max}.

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Validated Fat-Oxidation Rates in Postmenopausal Women

Yavelberg Loren, Kaganovich Kristina, Abdullah Faiza, Riddell Michael, Gledhill Norman and Jamnik Veronica*

York University, 4700 Keele Street, Room 356, Bethune College, Toronto, Ontario M3J 1P3

***Corresponding author:** Jamnik Veronica, York University, 4700 Keele Street, Room 356, Bethune College, Toronto, Ontario M3J 1P3, Tel: 416-736-2100 ext.22995, E-mail: ronij@yorku.ca

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Abstract

Background: During menopause and throughout aging, women are at an increased risk for a plethora of chronic conditions many of which are related to the interruption of estrogen. The primary and secondary prevention benefits of habitual unstructured and structured physical activity (PA) are well documented. Fat oxidation rates (FOR) at rest and during exercise have been reported to decrease though the menopausal transition.

Methods: Twenty-three middle-aged Middle Eastern (n=11) and Caucasian (n=12) women were recruited. An independent t-test was used to determine differences between the groups for: anthropometrics, menstrual characteristics, resting blood pressure (BP) and heart rate (HR), PA levels, blood lipid panel, blood hormone panel, glucose, resting VO_2, and VO_{2peak}. A subset of participants had their VO_2 and maximum fat oxidation rate (FOR_{max}) determined on three separate occasions to assess the reliability of the protocol.

Results: No significant differences were observed between FOR at rest or during exercise, and/or other physical and physiological parameters. There were no significant differences between the three separate trials for the VO_2 and FOR_{max} values ($P = 0.565$).

Conclusions: This study contributed to the ever-growing body of literature on FOR and women's health by exploring an ethnic group that has not been previously studied.

Keywords: Cardio-Pulmonary Physiology; Fat Metabolism; Fat Oxidation; Weight Loss; Obesity Prevention; Menopause

Chapter 3: Study 2

The Acute Effect of Time-Restricted Feeding (12 & 16 hrs) and Varying Exercise Intensities on Fat-oxidation Rate – a randomized control trial

Abstract:

Background and Purpose:

Time-restricted feeding (TRF) is a dietary pattern alternating between fasting and feeding periods that has gained significant attention in recent years. The 16/8 approach consists of fasting for 16 hours and feeding for an 8-hour window, while the 12/12 method consists of fasting for 12 hours and a 12-hour feeding window. Limited research exists comparing the effects of these methods coupled with physical activity (PA). The aim of this investigation was to examine the acute effects of varying TRF durations (12 and 16 hours) and varying PA intensities on the Fat-oxidation rate (FOR). It was hypothesized that i) the TRF16 group would exhibit higher FOR_{max} and that PA would enhance these effects, and ii) High-Intensity Interval Training (HIIT) would result in greater effects on FOR_{max} compared to Low-Moderate Intensity Steady-State (LISS) PA.

Methods and Results:

Eighteen young adults (males=8, females=10) were recruited and participated in the supervised intervention. The discrete component open circuit spirometry system was used to measure oxygen consumption (VO_2), and Frayn's equation was used to determine the FOR plus FOR_{max}. ANOVA was used to determine pre- and post-intervention differences in FOR_{max}. The FOR_{max} for the TRF16+HIIT intervention was significantly higher than the TRF12 and TRF16 fast alone (mean difference = 0.099, 0.093 g·min-1, p = 0.011, 0.002, respectively). The FORmax for the TRF16+LISS PA intervention was significantly higher than that for TRF12 alone (mean difference = 0.099 g·min-1, p = 0.011). The FOR_{max} for TRF12+HIIT and TRF16+HIIT interventions were both significantly higher than the 12-hour fast alone (mean difference = 0.070 g·min-1, 0.099 g·min-1, p = 0.023, 0.011, respectively).

Conclusion:

This study contributes to the ever-growing body of literature on the acute effects of TRF and PA on young adult males and females. The findings suggest that the TRF16+HIIT PA intervention results in the highest FORmax. Thus, the evidence supports the combination of TRF and PA interventions as an effective strategy for healthier weight management.

Trial registration: Retrospective Registration ISRCTN # 10076373 (October 6, 2023)

Background:

Exercise and time-restricted feeding (TRF) are two lifestyle choices that have gained significant attention in recent years. TRF is a dietary pattern that alternates between periods of fasting and eating. The 16/8 approach consists of fasting for 16 hours and feeding for an 8-hour window, while the 12/12 method consists of fasting for 12 hours and feeding for a 12-hour window. The 16/8 method has been studied more extensively than the 12/12 method. Moro et al. (2016) found that the 16/8 method can significantly reduce body fat mass, insulin resistance, and blood pressure in resistance-trained men (Achten & Jeukendrup, 2004). Another randomized control trial by Gabel et al. (2018) found that the 16/8 method can significantly reduce body mass, waist circumference, and blood pressure in obese adults (Gabel et al., 2018; Moro et al., 2016). However, more research is needed to compare the effects of the 16/8 and 12/12 methods on health outcomes. A recent study by Wilkinson et al. (2020) investigated the effects of these two methods on weight loss and glycemic control in adults living with obesity and overweightness. The study found that both methods can significantly improve body mass and glycemic control, but there were no significant differences between the two fasting methods (Gabel et al., 2018). Another study by Hutchison et al. (2019) investigated the effects of the 16/8 and 12/12 methods on appetite and energy intake in overweight and obese men. These authors found that both methods can lead to significant reductions in appetite and energy intake, but there were no significant differences between the two methods (Wilkinson et al., 2020; Hutchison et al., 2019).

Further, a number of investigations, systematic reviews and meta-analyses on humans found that TRF can lead to significant improvements in body mass, blood pressure, insulin resistance, lipid profiles, oxidative stress markers, and reduced inflammation (Harris et al., 2018; Hutchinson et al., 2019; Moon et al., 2020; Pellegrini et al., 2020; Xie et al., 2020). These investigations were based on fasting windows per day ≥12 and <24 h, some of which included caloric reductions and others were ad libitum. Some studies also suggest that TRF may have potential benefits on cognitive function and longevity (De Cabo et al., 2019). Some studies also suggest that TRF may have potential benefits on cognitive function and longevity (De Cabo & Mattson et al., 2019). However, the acute effects of TRF on exercise performance and recovery have yet to be well known.

PA, including exercise, is an essential lifestyle factor that can have significant health benefits, including cardiovascular, metabolic, and mental health improvements. Various forms of exercise intensities exist; typically, low-moderate intensity steady-state exercise (LISS) and high-intensity interval (HIIT) or sprint-intensity intermittent training (SIT) are commonly cited. LISS involves performing exercise continuously at a low to moderate intensity for an extended period, such as jogging or cycling at a steady pace for 30 to 60 minutes. HIIT involves performing short bouts of high-intensity exercise followed by brief periods of low-intensity exercise, such as jogging or running for 30 seconds, followed by a 30-second walk period (i.e., a 1:1 ratio, but may vary). The SIT involves performing a maximum-effort activity bout, followed by a short period of rest/recovery.

A number of systematic reviews and meta-analyses, citing several studies, investigated the effects of LISS and HIIT on various health outcomes, including improvements in cardiorespiratory fitness, insulin sensitivity, glycemic control, lipid profiles and body composition (D'Alleva et al., 2023; Liu et al., 2020; Rugbeer et al., 2021; Wewege et al., 2017). Further, one of the studies determined that HIIT can improve these outcomes more than LISS (Matteson et al., 2018). Another meta-analysis indicated that HIIT may provide additional benefits, such as metabolic adaptations, in comparison to LISS (Costigan et al., 2015).

It is important to note that chronic exercise training can lead to more significant adaptations and improvements in health outcomes compared to acute exercise. A systematic review and meta-analysis found that chronic exercise training can improve cardiovascular fitness, glucose regulation, lipid metabolism, and inflammation (Lin et al., 2015). The type and intensity of exercise can also influence the magnitude and type of adaptations. A study by Ruffino et al. (2017) found that chronic HIIT can lead to greater improvements in cardiorespiratory fitness, insulin sensitivity, and muscle mitochondrial content compared to chronic LISS (Ruffino et al., 2017; Pedersen & Saltin, 2015; Wewege et al., 2017).

Despite the established benefits of TRF and exercise on health outcomes, limited research is available comparing the effects of different types of TRF and exercise on health outcomes, particularly in combination. Therefore, the aim of this study was to investigate the effects of TRF12 vs. TRF16, combined with either LISS or HIIT, on various health outcomes, including acute changes in cardiovascular fitness and the established maximum Fat-oxidation rate (FOR_{max}) in adults living with overweight and obesity. It was hypothesized that the TRF16 group would exhibit a higher FOR_{max} and that PA would further enhance these effects. Furthermore, it was hypothesized that HIIT would result in greater effects on FORmax compared to LISS PA.

Study Participants and Requirements

Eighteen young adult males and females aged 23 ± 2.0 years were recruited to participate in the study. The study participants' mean body mass index (BMI) was 23.5 ± 2.8 kg·m-2. Study participants did not have any physical ailments contraindicating participation in the study (e.g., cardiomyopathies, neuropathy, or other diabetes-related complications). Menstrual cycle status was not controlled for or documented by the researchers. Study participants were screened by certified exercise physiologists using resting blood pressure in conjunction with the evidence-based screening tools, including the current PAR-Q+ and, if needed, the ePARmed-X+ (www.eparmedx.com) for exercise contraindications and risk stratification. Eligibility was further confirmed once the data on participants' BMI plus PA and Sedentarism Score had been assessed. If the participants fulfilled the inclusion criteria and agreed to participate, they were randomized using Excel's simple randomization technique and informed of the requirements of the study and the TRF regime.

Inclusion Criteria

The inclusion criteria indicated that the study participants must be between the ages of 18 and 65 years old, from York University to ensure that the location of testing was convenient and prevent participants from dropping out, classified as normal weight (BMI = 18.5-24.9), overweight (BMI = 25.0-29.9), or obese class I (30.0–34.9), absent of injuries that would diminish their ability to complete an exercise session, having a $VO_2max \geq 30$ mL·kg-1·min-1, and resting blood pressure < 160/90 mmHg.

Exclusion Criteria

Study participants were only considered for the trials if they met all the inclusion criteria. Those classified as normal weight, overweight, or obese class I using BMI but who were currently considered regular exercisers (being active for the past three months, more than twice a week) were not considered for the trials.

Methods:

All protocols were reviewed and approved by the Human Participants Review Sub-Committee at York University's Office of Research Ethics (certificate # e2019-311), and the experimental protocol conformed to the standards set by the Declaration of Helsinki. The study adheres to CONSORT guidelines. Participants reported to the York University Human Performance Laboratory. All the study participants provided written informed consent for voluntary participation before performing any study-related procedures. A copy of the consent form was provided to the study participants, and another copy was added to the study master file.

Visit 1: Anthropometric, Physical, Physiological, and VO_2max Assessment

All study participants were asked to maintain the same lifestyle prior to each experimental day, including no change in their diet and/or nonstructured or structured PA. Anthropometric data, including height, body mass, BMI, and body fat percentage (%BF), were collected using standardized laboratory protocols (Jamnik & Gledhill, 2015). Pre-exercise blood pressure and heart rate (HR) measurements were determined in the seated position in a private room using an automated device (BpTRU Medical Devices Ltd. BC Canada). Following a five-minute seated rest period, the BpTRU™ recorded six sequential measurements, one minute apart. The BpTRU™ device generated an average value for the pre-exercise systolic plus diastolic blood pressures and pulse rate using the last five of the six measurements. Although not required, all hypertensive values were re-evaluated using the auscultatory blood pressure method. Body mass was measured upon each visit using the Seca Alpha Scale (Model 770, Germany). %BF was measured without shoes using bioelectrical impedance analysis (Tanita scale, model TBF-612, Arlington Heights, IL). Height was measured without footwear using a wall-mounted stadiometer.

Study participants were then outfitted with a chest-mounted heart rate monitor (Polar Electro, Kempele, Finland) and briefed on the VO_2max test. The incremental-to-maximal effort treadmill test for the determination of VO_2max followed the same loading sequence for all participants. The protocol included a 2-minute warm-up, and progressive exercise workloads increased every two minutes (treadmill speed and/or elevation). The participants were instructed to remain on the treadmill until their work tolerance was compromised, at which point they received a 2-minute low-intensity active recovery period. Following recovery, the participants completed another incremental workload followed by a 2-minute recovery. This discontinuous sequence was repeated until the VO_2 of the subsequent workload was equal to or lower than the previous, indicating attainment of VO_2max (Jamnik & Gledhill, 2015; Achten et al., 2003; Gledhill et al., 1994; Howley et al., 1995). The attainment of VO_2max was confirmed using a discontinuous protocol during which the participants exercised at higher workloads for 2 minutes, followed by another active recovery. This protocol sequence was repeated until the VO_2 of the subsequent workload was equal to or lower than the previous, indicating VO_2max. This could also be referred to as verification or supramaximal testing (Howley et al., 1995; Hancock et al., 2023). The VO_2 was determined from measurements obtained during the last 30 seconds of each workload via direct analysis of mixed expired gases. The VO_2max test was terminated if the study participant could no longer complete the workload due to volitional fatigue or if VO_2max criteria were met. This was determined by the qualified exercise physiologist present at the time.

The discrete component system consisted of; a 120L Tissot gasometer (Warren E Collins LTD, Braintree, MA), rapid response oxygen and carbon dioxide gas analyzers (Applied Electrochemistry, Model S-3A and CD-3S, Sunnyvale, CA), a flexible plastic hose, two-way y-valve (Ewald Koegal Co, San Antonio, TX), mouthpiece, and nose plugs. The mouthpiece was positioned between the participants' gums and teeth, and they were required to breathe in and out of the mouthpiece with their noses plugged throughout the VO_2 collection period. The Y-valve allowed the participants to inhale atmospheric air freely, then directly exhale air into the hose and tank, where the gases were collected and mixed. Once the expired gases were collected in the Tissot, they were analyzed using the gas analyzers. The collected variables, minute ventilation, and fractions of expired carbon dioxide and oxygen were then used to calculate the participants' VO2max (Hancock et al., 2023; Yavelberg et al., 2023). The criterion HR was measured throughout using a Polar HR chest monitor (Polar Electro, Kempele, Finland).

Visit 2: FOR_{max} assessment

Once the study participants met the preliminary inclusion criteria, they were then randomized into groups based on fasting durations (TRF12 (12-hour fast) or TRF16 (16-hour fast)) and exercise intensities (LISS or HITT). Following randomization, the study participants returned to the laboratory following a 12- or 16-hour overnight fast to complete the FOR_{max} test. This initial FOR_{max} test was used as the study participants' control for the purposes of statistical analysis.

The FOR_{max} test protocol was a validated version of the Achten, Venables, and Jeukendrup walking FOR treadmill protocol (Achten et al., 2002). The discrete open-circuit spirometry system was utilized for the determination of FOR_{max}. Resting and exercise HR were measured via a Polar chest strap HR monitor (Polar Electro KP 4, Kemple, Finland). Resting VO_2 and FOR measurements were obtained with the participants seated. Expired gases were collected and analyzed in the same manner as during the VO_2max and then used in Frayn's equation below to calculate FOR. The protocol began at 1.5–1.8 mph and a 1% incline, depending on the comfort and height of the participant. Speed increased by 0.2 mph every 3 minutes until the participant walked briskly (3.4–3.6 mph). Once the maximum walking speed was attained, the incline increased by 2% every 3 minutes thereafter until a respiratory exchange ratio of 1.0 or greater and/or a plateau in FOR were observed, indicating attainment of FOR_{max}. The expired gases were collected to calculate FOR in the workload's last 30–60 seconds. At the end of each workload, participants' HR was recorded. Indirect calorimetry and Frayn's equation were employed to measure substrate oxidation at each workload and calculate FOR. The urinary nitrogen excretion rate was assumed to be negligible for the purpose of the calculations. The equation employed is as follows:

$$\text{Fat (g·min-1)} = 1.67*\text{VO2 (L·min-1)} - 1.67*\text{VCO2 (L·min-1)}$$

FOR was expressed relative to each participant's fat-free body mass (Frayn, 1983).

Visits 3 to 8: Start of Acute Intervention TRF, PA & FOR_{max}

Based on their randomly selected exposure cohort, study participants arrived at the laboratory following a 12- or 16-hour overnight fast. A FOR_{max} test was conducted following either fasted PA session, LISS or HIIT. The continuous LISS PA intervention consisted of treadmill-based activity at a targeted heart rate equal to the heart rate corresponding to the study participants' FORmax for approximately 60 minutes (based on ~300 kcal per session expenditure). The HIIT protocol consisted of treadmill-based activity, starting with a LISS bout at ~50% HRmax for 60 seconds, followed by a 60-second maximal intensity bout (~100% HRmax) repeated ~10 times until 300 kcals were expended. Furthermore, both PA sessions were volume equivalent, meaning that study participants were required to expend 300 kcals during the PA session to complete the session successfully. Kcals were calculated during these visits by applying a conversion factor of 1 L of O2 = 4.86 kcal, assuming a mixed diet (Tarnopolsky, 2007).

The FOR_{max} test was repeated at the end of each acute intervention a total of 5 times throughout the study: baseline, TRF12 + LISS PA, TRF12 + HIIT PA, TRF16 + LISS PA, and TRF16+HIIT PA.

Statistical Analysis:

The study participant characteristics are expressed as the means ± standard deviations (X±SD). A total of n=18 study participants were recruited: 8 females and 10 males. Statistical analysis was conducted using a standard statistical software program, SPSS 28. Repeated-measures ANOVA (MANOVA) was used to test for significant differences between the intervention groups (varying PA intensities and fasting durations). The Wilks' Lambda post-hoc test was implemented to compare the means of several groups across multiple outcomes.

In addition, a power analysis calculator revealed that to achieve significance at the 0.05 level for a MANOVA, with a power of 0.8 and an effect size of 0.5 (medium-large effect), the number of participants in each group would have to be 18 (https://www.statskingdom.com). Thus, the sample size was sufficient.

Results:

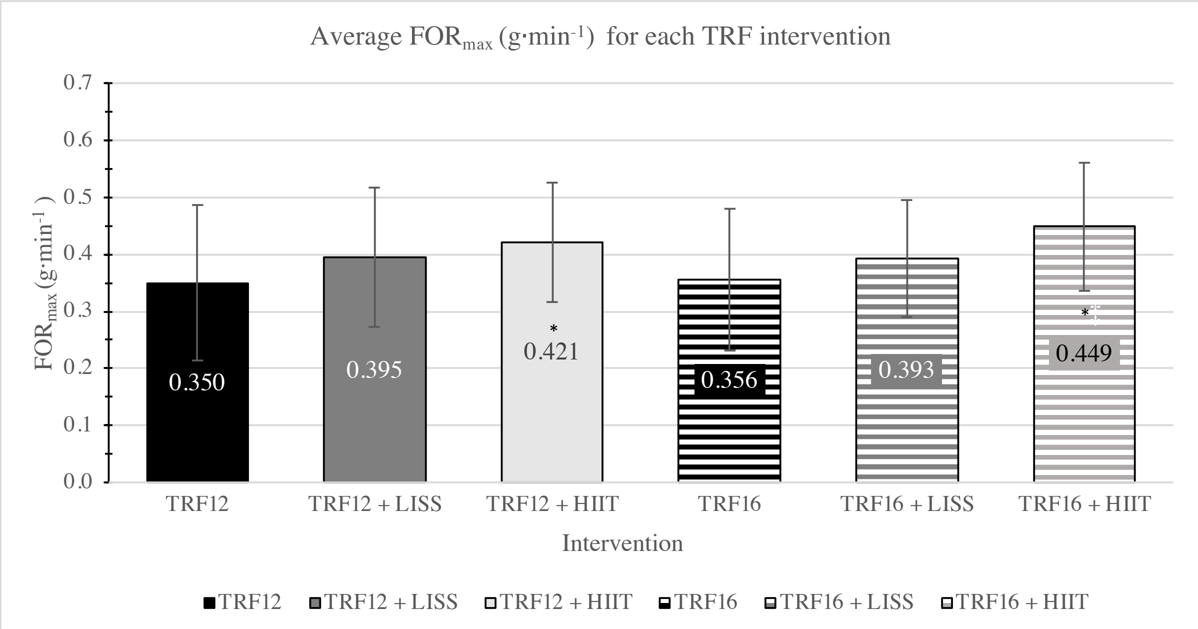
All subjects were able to complete all forms of the intervention. There were no significant differences in the FOR_{max} values between the two fasting-only interventions (12/16 hrs). The FOR_{max} for the TRF12 + HIIT and TRF16 + HIIT interventions was significantly higher than that for TRF12 alone (mean difference = 0.070, 0.099 g·min-1, p = 0.023, 0.011, respectively). The FOR_{max} for the TRF16 + HIIT intervention was significantly higher than that for TRF16 fast alone (mean difference = 0.093 g·min^{-1}, p = 0.002). The FOR_{max} for the TRF16 + LISS PA intervention was significantly higher than that for TRF12 fast alone (mean difference = 0.099 g·min^{-1}, p = 0.011). The FOR_{max} for the TRF16 + HIIT PA intervention was significantly higher than that for the TRF12 and TRF16 fast-only cohorts (mean difference = 0.099, 0.093 g·min^{-1}, p = 0.011, 0.002, respectively). The Wilks' Lambda post-hoc test was implemented (p=0.388, F=4.098, η^2=.612) with 0.826 observed power. Table 1 contains the anthropometric and physical plus physiological fitness profiles of all study participants (8 males, 10 females). As expected, statistical significance was observed between the sexes in height, body mass, and VO_2max. Given the normal expected sex differences and innate individual FOR variability, the males and females were combined for the analyses.

Table 1: All study participants' anthropometric, physical, and physiological fitness profiles.

Characteristic	**Combined** n=18 (X±SD)	**Males** n=8 (X±SD)	**Females** n= 10 (X±SD)	**P-value**
Age (yr.)	23.0 ± 2.0	23 ± 2.4	22 ± 1.8	-
Height (cm)	170.1 ± 9.8	176.9 ± 7.9	164.7 ± 7.6	0.05
Body mass (kg)	68.6 ± 13.2	76.5 ± 12.7	62.3 ± 10.2	0.018
BMI ($kg \cdot m^{-2}$)	23.5 ± 2.8	24.4 ± 2.8	22.9 ± 2.8	-
VO_2max ($mLO_2 \cdot kg^{-1} \cdot min^{-1}$)	41.2 ± 6.1	44.8 ± 7.3	38.2 ± 2.9	0.018

Figure 1 shows the group mean (X±SD) FOR_{max} ($g \cdot min^{-1}$) values for each of the acute interventions: TRF12, TRF12 + LISS, TRF12 + HIIT, TRF16, TRF16 + LISS and TRF16 + HIIT. A repeated-measures ANOVA was completed with SPSS 28.0. A statistically significant difference ($p<0.05$) was found when comparing the group mean FOR_{max} value between the 16-hour + HIIT and 12-hour fast-alone interventions. A statistically significant difference ($p<0.05$) was also found when comparing the group mean FOR_{max} value between the TRF12 + HIIT and TRF12 fast-only interventions. A statistically significant difference ($p<0.05$) was also found when comparing the group mean FORmax value between the TRF16 + HIIT and TRF16 fast-only interventions, as shown in Figure 1.

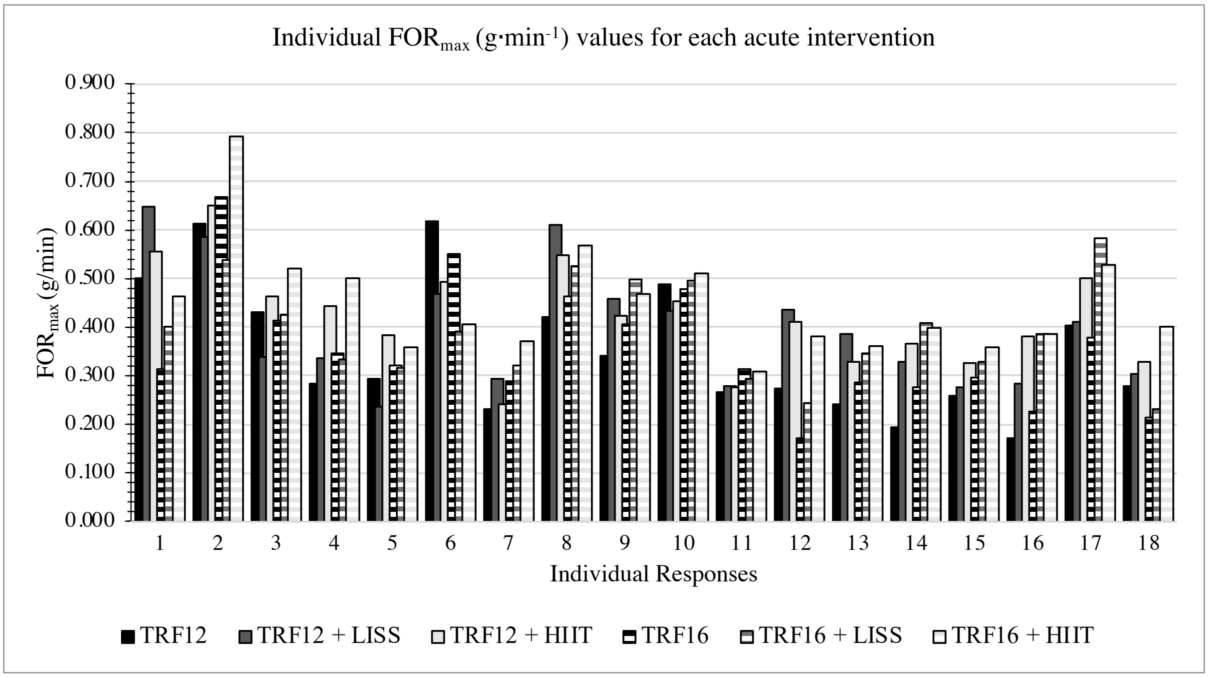
Figure 1: the group mean (X±SD) FOR_{max} ($g \cdot min^{-1}$) values for each of the acute interventions.



Light Intensity Steady State (LISS), High Intensity Interval Training (HIIT)
* $p<0.05$ compared to TRF12 hour fast alone
‡ $p<0.05$ compared to TRF16 hour fast alone

Given the variability in FOR_{max} ($g \cdot min^{-1}$) group responses above, examining the individual study participant's FORmax responses to each acute intervention is important. Figure 2 contains the study participants' individual FOR_{max} ($g \cdot min^{-1}$) responses and variability for each acute intervention: TRF12 only, TRF12 + LISS, TRF12 + HIIT, TRF16 only, TRF16 + LISS and TRF16 + HIIT. Based on the bar graph below, no clear trends were observed in regards to FOR_{max} as a result of the interventions, due to the individual variability of the study participants' responses. The literature suggests this is due to some combination of training status, VO_2max, dietary habits, & skeletal muscle metabolic flexibility (Achten & Jeukendrup, 2004; Kelley, 2005).

Figure 2: the individual acute responses in FOR_{max} ($g \cdot min^{-1}$) values for each acute intervention. Individual responses 1-8 are male study participants and responses 9-18 are female study participants.



Discussion:

The purpose of this study was to examine the effects of varying TRF durations and PA intensities on FOR_{max}. It was hypothesized that the TRF16 group would exhibit higher FORmax and that PA would further enhance these effects. Furthermore, it was hypothesized that HIIT would result in greater effects on FOR_{max} compared to LISS PA. In support of this hypothesis, statistically significant differences were observed in both TRF groups when coupled with HIIT. As hypothesized, TRF16 + HIIT resulted in the largest mean FOR_{max}. In slight contrast to the hypothesis, no significant differences were observed between the fasting durations without PA (fast alone), thus indicating the importance of coupling PA with TRF for acute physiological perturbations. The mechanisms for these results are likely attributable to some combination of physiological adaptations typically associated with high-intensity PA. Evidence suggests that combining low muscle glycogen from TRF with high-intensity PA may enhance metabolic and skeletal muscle adaptations (Gibala, 2012; Brown, 1995; Hulston et al., 2010).

As a result of this research, new information was reported on the effectiveness of TRF and acute physiological responses in FOR_{max} in young adult males and females. The current study utilized a treadmill-based protocol to measure and calculate FOR over a wide range of submaximal exercise intensities and provide values on FOR and FOR_{max}. Liepinsh et al. 2020 examined the effects of low-intensity exercise and found increases in FOR. Although the findings of our investigation did not reveal statistically significant improvements in FOR_{max} for the TRF+LISS PA, an increased FOR_{max} was observed compared to the fast-alone interventions. The researchers believe that this is partially attributable to the variable inter-individual response to the interventions. Low-intensity exercise, such as walking, has been shown to promote greater reliance on fat as a fuel source, leading to increases in FOR (Achten & Jeukendrup, 2004; Liepinsh et al., 2020). High-intensity exercise, such as sprinting or resistance training, has been associated with increased carbohydrate oxidation rates due to the higher energy demands (Romjin et al., 1993; Horowitz & Klein, 2000).

Interestingly, the combination of TRF16 + HIIT resulted in the highest FOR_{max}, indicating a potential synergistic effect when combining these interventions. Our findings suggest that combining TRF with PA may synergistically affect FOR and FOR_{max}, potentially enhancing fat metabolism, which could support weight management goals. However, future research is needed to confirm these results and investigate the chronic effects of this combination. Further studies are required to explore the potential interindividual variability in response to combining TRF and varying PA intensities on FOR/FOR_{max}.

Limitations:

Despite this study's comprehensive nature, some limitations must be acknowledged. First, the study duration was relatively short, and the long-term/chronic effects of TRF and PA were not evaluated. Future research should include more extended follow-up periods to investigate the sustainability and persistence of the observed effects. Second, the participant cohort consisted of healthy young adults, limiting the generalizability of the findings to other age groups and populations. Although both male and female study participants were observed, future studies should include a more diverse sample to understand the effects in different populations. This study was part of a series of studies that examined the immediate acute effects of exercise on FORmax post-TRF (12 vs 16 hours). Although some statistical significance was found, the differences between the TRF+PA strategies may have been more pronounced and significant with a larger sample size.

Furthermore, the study participants' meals prior to fasting were not rigidly controlled. It is known that a heavy fat/carbohydrate meal prior to fasting may influence FOR/FOR_{max}. Although the study participants may have consumed differing macronutrients prior to the fast, the TRF durations and PA intensities were carefully controlled. The menstrual cycle was not controlled for or documented. It is possible that hormonal fluctuations throughout the menstrual cycle could affect female FOR_{max}. Thus, the findings of this investigation can be cautiously generalized given the external and internal validity. In addition, this study will contribute to the gaps in the literature pertaining to varying TRF durations and PA intensities.

Conclusion:

This study contributed to the ever-growing body of literature on the acute effects of varying TRF durations + PA intensities on young adults, and the findings suggest that TRF16 + HIIT PA intervention results in the highest FOR_{max} in comparison to the other intervention arms. Thus, this evidence supports the combination of TRF16 + HIIT PA intervention as an effective strategy for healthier weight management.

Chapter 4: Study 3

The Short-term Effects of Intermittent Fasting and Continuous Steady State Low-Moderate Intensity Exercise on Commonly Used fatness-measurements and Fat-Oxidation Rates on Middle-aged Women

Abstract:

Background and Purpose:

The World Health Organization estimates that within the next few years, non-communicable diseases will become the principal global causes of morbidity and mortality. While customarily employed techniques for weight loss have proven not to provide sustainable resolutions, intermittent fasting/time-restricted feeding (TRF) has gained popularity as a healthy lifestyle and weight management approach. The purpose of this investigation is to examine the short-term effects of TRF for 16 hours and manageable Physical Activity (PA), such as a continuous light-moderate intensity steady-state (LISS) intervention, as an effective strategy for healthier weight management.

Methods and Results:

Fourteen middle-aged women were recruited and participated in the supervised intervention for three weeks. A subset of the participants (n = 3) was followed for an additional six weeks (2 visits, once every three weeks), for a total of nine weeks, to assess the short-term effects of this intervention. An independent t-test was used to determine pre- and post-intervention differences for: anthropometrics, resting blood pressure (BP) and heart rate (HR), VO_2max, FOR_{max}, skinfold thickness, and percent body fat (%BF). Although the FORmax values did not statistically significantly increase pre/post-3-week intervention, there were statistically significant differences ($p<0.05$) in body mass and select skinfold sites (iliac crest, medial calf, and SO5S).

Conclusion:

The statistically significant findings of this combined 3-week TRF and PA intervention showed changes in subcutaneous and visceral adiposity, improvements in peak FORmax, increases in VO2max, and retention or improvement of estimated fat-free mass. This provides evidence to

support the combined TRF and PA intervention as an effective and sustainable weight management strategy.

Background:

The World Health Organization estimates that within the next few years, non-communicable diseases will become the principal global causes of morbidity and mortality. The benefits of PA have been well established, and promoting increased levels of PA to prevent and/or treat several chronic diseases (obesity, diabetes, and cardiovascular disease) dates back at least to the 1950s (WHO, 2018; Savini et al., 2013; Betts et al., 2014; Wang et al., 2008; Stats. Canada, 2021; Spiegelman et al., 2001). While customarily employed techniques for weight loss have proven not to provide sustainable resolutions, intermittent fasting/time-restricted feeding (TRF) has gained popularity as a healthy lifestyle and weight management approach.

Fat-oxidation rate (FOR) is the difference between the rate of oxygen oxidation and carbohydrate synthesis. Frayn's equation considers both of these variables and is thus often used to determine the maximum FOR (FOR_{max}) (van Loon et al., 2004).

A systematic review by Horne et al. of randomized controlled clinical trials of fasting in humans evaluated the effects of fasting on surrogate outcomes. Improvements in weight and other risk-related outcomes were found in the three trials. Two observational clinical outcome studies in humans found that fasting was associated with a lower prevalence of CAD or diabetes diagnosis. No randomized controlled fasting trials for clinical outcomes were identified (Wewege et al., 2017).

A growing body of evidence suggests that TRF eating patterns could be a valuable tool for improving health in the general population due to reports of improved blood lipids (Moro et al., 2016; Klempel et al., 2012 & 2013), improved glucose metabolism (Horne et al., 2015; Harvie et al., 2013; Arguin et al., 2012; Halberg et al., 1985; Harvie et al., 2011), and glycaemic control (Varady et al., 2007), reduced circulating insulin (Trepanowski & Bloomer, 2010), reduced inflammation (Ziaee et al., 2006; Faris et al., 2012), reduced blood pressure (Barnosky et al., 2014; Trepanoski & Bloomer, 2010; Varady et al. 2007 & 2013, Tinsley et al. 2015; Johnson et al, 2007; Boutant et al., 2016), improved cardiovascular health (Hoddy et al. 2014, Horne et al. 2012, Klempel et al. 2012), increased resistance of cells to stress and disease in humans, decreased inflammatory markers (Varady et al., 2009) and reduced fat mass even during relatively short durations (8–12 weeks) (Tinsley & La Bounty, 2015). These effects have been established in animal studies as described above. However, only some of these adaptations to TRF have been investigated in humans, and then typically in overweight or obese subjects.

Moro et al. (2016) found that the TRF16 method can lead to significant reductions in body fat mass, insulin resistance, and blood pressure in resistance-trained men. Another randomized control trial by Gabel et al. (2018) found that the TRF16 method can lead to significant reductions in body mass, waist circumference, and blood pressure in obese adults. Further, a number of investigations, systematic reviews and meta-analyses on humans found that TRF can lead to significant improvements in body mass, blood pressure, insulin resistance, lipid profiles, oxidative stress markers, and reduced inflammation (Harris et al., 2018; Hutchinson et al., 2019; Moon et al., 2020; Pellegrini et al., 2020; Xie et al., 2020). These investigations were based on fasting windows per day ≥12 and <24 h, some of which included caloric reductions and others were ad libitum. Some studies also suggest that TRF may have potential benefits on cognitive function and longevity (De Cabo et al., 2019).

The purpose of this investigation is to examine the short-term effects of TRF for 16 hours and manageable Physical Activity (PA) such as a continuous light-moderate intensity steady-state (LISS) intervention as an effective strategy for healthier weight management. It was hypothesized that study participants would exhibit statistically significant differences in body mass and FORmax post-intervention as a result of this combined short-term intervention.

Study Participants and Requirements

Sixteen middle-aged female study participants with a BMI between 18.5 and 34.9 were recruited. The study participants were between the ages of 35 and 65. Study participants had no physical ailments that would contraindicate participation in the study (e.g., cardiomyopathies, neuropathy, or other diabetes-related complications). They were screened by certified exercise physiologists using resting blood pressure in conjunction with the evidence-based screening tools, including the 2019 PAR-Q+ and, if required, the ePARmed-X+ (www.eparmedx.com) for exercise contraindications and risk stratification. Eligibility was further confirmed once the participant's BMI, PA, and Sedentarism Score had been assessed. If the participant fulfilled the inclusion criteria, they were informed of the requirements of the study and their potential TRF regime. Written informed consent was obtained if the participant agreed to participate in the trial.

Inclusion Criteria

The inclusion criteria indicated that study participants must meet the following criteria: be between the ages of 35 and 65, from York University to ensure the location of testing is convenient for all subjects and avoid participant dropout, and classified as normal weight (BMI = 18.5-24.9), overweight (BMI=25.0-29.9) or obese class I (30.0-34.9) according to BMI, absent of injuries that would diminish their ability to complete an exercise program, having a $VO_2max \geq 25$ mL·kg^{-1}·min^{-1}, and cannot score greater than five on the PA and Lifestyle "R" Medicine PA Participation and Sedentarism Questionnaire (PAPSQ). Pre-exercise Heart Rate (HR) and blood pressure were measured using the BpTRU100 (Surgo Surgical Supplies, Toronto, Ontario) automated device to ensure participants were within an acceptable range prior to the initiation of the exercise protocols (blood pressure < 160/90 mmHg). Six measurements were taken consecutively, with a 1-minute rest interval in between, and averaged. Participants' BMI was assessed and had to be greater than 24.9 but no greater than

34.9 (overweight or obese class I according to BMI). Further, participants were absent of injuries that would diminish their ability to complete an exercise program. In addition, study participants were absent of any relevant chronic diseases that would impair their ability to exercise or confound the effects of the interventions.

Exclusion Criteria

Subjects were only included in the trial if they met all inclusion criteria. Subjects who were classified as normal weight, overweight, or obese class I using BMI but were currently considered regular exercisers (being active for the past three months, more than twice a week) corresponding to a score greater than five on the PAPSQ, were not included in the trial.

Data Collection Methods and Instruments

All protocols were reviewed and approved by the Human Participants Review Sub-Committee at York University's Office of Research Ethics, and the experimental protocol conformed to the standards set by the Declaration of Helsinki. Participants reported to the York University Human Performance Laboratory and provided written Informed Consent for voluntary participation in the study prior to performing any study-related procedures. A copy of the consent form was provided to the study participants, and another copy was added to the study master file. After completing the informed consent and the PAPSQ, study participants underwent a laboratory assessment to ensure they met the inclusion criteria. The pre-exercise screening took place on the first experimental day. The first visit consisted of pre-screening plus an incremental-to-maximal effort treadmill test to determine aerobic fitness or power (VO_2max) using the criterion discrete open circuit spirometry system. On the second experimental day, the study participants underwent the maximum fat-oxidation rate (FOR_{max}) protocol following a 16-hour overnight fast and 500 mL of water. The FORmax protocol in this investigation was a modified version of the Achten, Venables, and Jeukendrup treadmill protocol (Achten et al., 2002). All workloads were equivalent in duration and length, and the increase in intensity at each new stage was consistent with the Achten et al. protocol. A further description of the visits and the types of exercise performed are detailed below.

Visit 1: Anthropometric, Physical, Physiological, and VO_2max Assessment

All study participants were asked to maintain the same lifestyle prior to each experimental day, including no change in their diet and/or nonstructured or structured PA. Anthropometric data, including height, body mass, BMI, and body fat percentage (%BF), were collected using standardized laboratory protocols (Jamnik & Gledhill, 2015). Pre-exercise blood pressure and heart rate (HR) measurements were determined in the seated position in a private room using an automated device (BpTRU Medical Devices Ltd. BC Canada). Following a five-minute seated rest period, the BpTRU™ recorded six sequential measurements, one minute apart. The BpTRU™ device generated an average value for the pre-exercise systolic plus diastolic blood pressures and pulse rate using the last five of the six measurements. Although not required, all hypertensive values were re-evaluated using the auscultatory blood pressure method. Body mass was measured upon each visit using the Seca Alpha Scale (Model 770, Germany). %BF was measured without shoes using bioelectrical impedance analysis (Tanita scale, model TBF-612, Arlington Heights, IL). Height was measured without footwear using a wall-mounted stadiometer. Waist circumference was measured following the standard National Institutes of Health protocol, with a tape measure around the waist, on the skin, and at the iliac crest level. Skinfolds (triceps, biceps, subscapularis, iliac crest, and medial calf) were measured using Harpenden fat calipers (Baty International, Burgess Hill, UK) according to the Physical Activity and Lifestyle "R" Medicine (PALM) protocol to determine body adiposity (Jamnik & Gledhill, 2015). The composite body composition score was derived from the measurements of body mass index (BMI), sum of the five skinfolds (SO5S), and the NIH WC. In summary, the BMI and SO5S provided an indication of the overall amount of body fat and the WC provided information on visceral or central adiposity. The composite body composition score was used to estimate the health-risk attributable to body composition and this is accomplished by using graduated WC and SO5S within and across each BMI category (Jamnik & Gledill, 2015)

Study participants were then outfitted with a chest-mounted heart rate monitor (Polar Electro, Kempele, Finland) and briefed on the VO_2max test. The incremental-to-maximal effort treadmill test for the determination of VO_2max followed the same loading sequence for all participants. The protocol included a 2-minute warm-up, and progressive exercise workloads increased every two minutes (treadmill speed and/or elevation). The participants were instructed to remain on the treadmill until their work tolerance was compromised (they could no longer keep pace or requested to stop), at which point they received a 2-minute low-intensity active recovery period. Following recovery, the participants completed another incremental workload followed by a 2-minute recovery. This discontinuous sequence was repeated until the VO_2 of the subsequent workload was equal to or lower than the previous, indicating attainment of VO_2max (Jamnik & Gledhill, 2015; Achten et al., 2003; Gledhill et al., 1994; Howley et al., 1995). The attainment of VO_2max was confirmed using a discontinuous protocol during which the participants exercised at higher workloads for 2 minutes, followed by another active recovery. This protocol sequence was repeated until the VO_2 of the subsequent workload was equal to or lower than the previous, indicating VO_2max. This could also be referred to as verification or supramaximal testing (Howley et al., 1995; Hancock et al., 2023). The VO_2 was determined from measurements obtained during the last 30 seconds of each workload via direct analysis of mixed expired gases. The VO_2max test was terminated if the study participant could no longer complete the workload due to volitional fatigue or if VO_2max criteria were met. This was determined by the qualified exercise physiologist present at the time.

The discrete component system consisted of; a 120L Tissot gasometer (Warren E Collins LTD, Braintree, MA), rapid response oxygen and carbon dioxide gas analyzers (Applied Electrochemistry, Model S-3A and CD-3S, Sunnyvale, CA), a flexible plastic hose, two-way y-valve (Ewald Koegal Co, San Antonio, TX), mouthpiece, and nose plugs. The mouthpiece was positioned between the participants' gums and teeth, and they were required to breathe in and out of the mouthpiece with their noses plugged throughout the VO_2 collection period. The Y-valve allowed the participants to inhale atmospheric air freely, then directly exhale air into the hose and tank, where the gases were collected and mixed. Once the expired gases were collected in the Tissot, they were analyzed using the gas analyzers. The collected variables, minute ventilation, and fractions of expired carbon dioxide and oxygen were then used to calculate the participants' VO2max (Hancock et al., 2023; Yavelberg et al., 2023). The criterion HR was measured throughout using a Polar HR chest monitor (Polar Electro, Kempele, Finland).

All study participants were asked to maintain the same lifestyle throughout the intervention, including no change in their diet and/or non-structured or structured PA, as documented by a self-reported PA questionnaire PAPSQ (Appendix A). Study participants were also required to document their diets and daily PA participation.

<u>Visit 2: FORmax assessment</u>

Once the study participants had met the preliminary inclusion criteria, they were asked to return to the laboratory following a 16 hour overnight fast to complete the FOR_{max} test. This initial FOR_{max} test was used as the study participants' own control for the purposes of statistical analysis.

The FOR_{max} test protocol was a validated version of the Achten, Venables, and Jeukendrup walking FOR treadmill protocol (Achten et al., 2002). The discrete open-circuit spirometry system was utilized for the determination of FOR_{max}. Resting and exercise HR were measured via a Polar chest strap HR monitor (Polar Electro KP 4, Kemple, Finland). Resting VO2 and FOR measurements were obtained with the participants seated. Expired gases were collected and analyzed in the same manner as during the VO_2max and then used in Frayn's equation below to calculate FOR. The protocol began at 1.5–1.8 mph and a 1% incline, depending on the comfort and height of the participant. Speed increased by 0.2 mph every 3 minutes until the participant walked briskly (3.4–3.6 mph). Once the maximum walking speed was attained, the incline increased by 2% every 3 minutes thereafter until a respiratory exchange ratio of 1.0 or greater and/or a plateau in FOR were observed, indicating attainment of FOR_{max}. The expired gases were collected to calculate FOR in the workload's last 30–60 seconds. At the end of each workload, participants' HR was recorded. Indirect calorimetry and Frayn's equation were employed to measure substrate oxidation at each workload and calculate FOR. The urinary nitrogen excretion rate was assumed to be negligible for the purpose of the calculations. The equation employed is as follows:

$$\text{Fat (g·min-1)} = 1.67*\text{VO2 (L·min-1)} – 1.67*\text{VCO2 (L·min-1)}$$

FOR was expressed relative to each participant's fat-free body mass (Frayn, 1983).

Start of Intervention TRF16 + LISS PA

The PA intervention consisted of exercising on a treadmill at a specific heart rate percentage based on the study participants' individual results of the aerobic tests completed in the initial assessment. The continuous low-moderate intensity exercise (LISS) intervention consisted of treadmill-based activity at a targeted heart rate equal to the heart rate corresponding to the study participants' FORmax for approximately 60 minutes (based on ~300 kcal/session). The frequency of the supervised intervention was three times per week for a total of 3 weeks. A subset of the participants continued the intervention unsupervised for six weeks, returning to the lab every three weeks. A qualified exercise professional monitored all PA intervention sessions to ensure adherence and safety throughout the PA sessions. Study participants were asked to maintain the same lifestyle throughout the intervention, including no change in their diet and/or non-structured or structured PA, as documented by a self-reported PA questionnaire (PAPSQ).

In addition, every third week, one of the exercise sessions was replaced with a FOR_{max} to VO_2max test along with the following measurements: height, weight, %body fat, and skinfolds. The purpose of this was to re-assess the study participants' FOR_{max} to account for training adaptations. Study participants were also required to document their daily PA participation as well as their diet and fast duration.

Statistical Analysis:

The study participant characteristics were expressed as means and standard deviations (X±SD). A total of n=18 study participants were recruited. Four study participants could not continue with the experimental protocol and were excluded from the analysis. Fourteen middle-aged women participated in the supervised intervention for three weeks. A subset of the participants (n=3) was followed for an additional six weeks (total of nine weeks), reporting to the laboratory every three weeks. An independent t-test was used to determine pre- and post-intervention differences for: anthropometrics, resting blood pressure (BP) and heart rate (HR), VO_2peak, FORmax, skinfold thickness, and %BF. A paired t-test was performed on the two trials of the FOR trials to determine any differences between the two occasions. Statistical analysis was conducted using a standard statistical software program, SPSS 28.

Applying a two-tailed t-test to the data suggests that 13 participants would be required to achieve 80% power when detecting a medium-sized effect at an alpha level of 0.05. This suggests that 13 participants will be required per group to establish within-treatment effects in the primary outcomes.

Results:

A two-sided paired samples t-test was conducted on the data using SPSS 28.0. Although the FOR_{max} values did not statistically significantly increase pre/post-3-week intervention, there were statistically significant differences ($p<0.05$) in body mass, select skinfold sites (triceps, subscapularis, iliac crest, medial calf, and SO5S), NIH waist circumference, %BF with the Omron BIA device, and VO2peak values as seen in Table 1.

Table 1. The Study participants' anthropometric, Physical, and Physiological Fitness Profiles Pre/Post-3-week Fasting + Physical Activity Intervention.

Characteristics	Pre-Intervention (n=14; X±SD)	Post-Intervention (n=14; X±SD)	P-value
Age (years)	56 ± 6	-	-
Height (cm)	166.6 ± 5.5	166.6 ± 5.5	-
Body mass (kg)	83.3 ± 11.5	81.5 ± 10.9	<0.001
BMI	29.9 ± 3.4	29.3 ± 3.3	<0.001
NIH Waist Circumference (cm)	106.0 ± 13.1	102.1 ± 10.3	0.014
Sum of 5 Skinfolds (mm)	125.9 ± 29.5	116.4 ± 26.1	<0.001
Tanita Body Fat Scale (%)	41.2 ± 4.5	41.3 ± 5.11	-
Omron Body Fat Scale (%)	39.7 ± 5.0	38.2 ± 4.3	0.035
Resting Sys. Blood Pressure (mmHg)	122 ± 13	119 ± 15	-
Resting Dia. Blood Pressure (mmHg)	77 ± 8	76 ± 9	-
Resting Heart Rate (bpm)	70 ± 12	67 ± 7	-
VO_2max Absolute ($LO_2 \cdot min^{-1}$)	2.0 ± 0.5	2.1 ± 0.5	-
VO_2max ($mLO_2 \cdot kg^{-1} \cdot min^{-1}$)	24.1 ± 5.3	25.5 ± 4.6	0.032

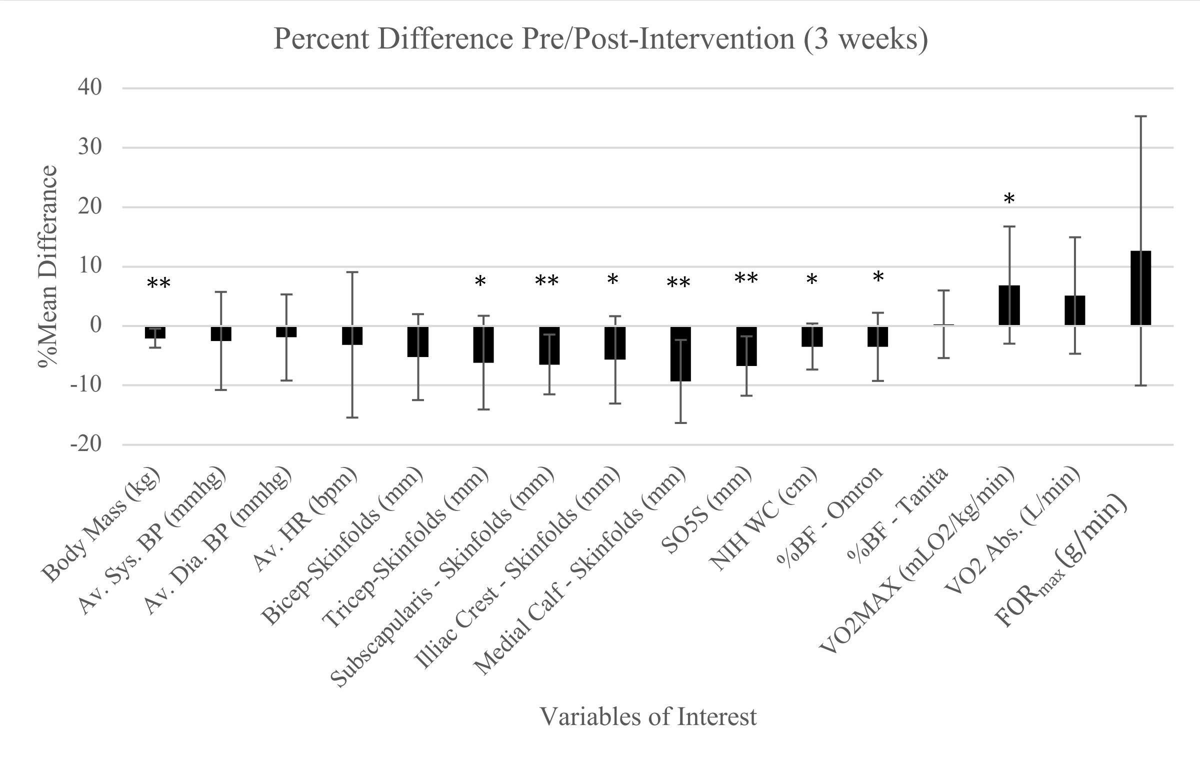
-no significant differences

The %mean difference data for the variables of interest pre/post-intervention (3 weeks) are depicted in Figure 1. The study participants' body mass had a statistically significant ($p<0.001$) mean difference of -1.8 kg ± 1.4 (-2.1% ± 1.6). The greatest body mass loss was 5.3 kg (5.8%).

The lowest body mass loss observed was 0.1 kg (0.1%). The study participants' triceps skinfold thickness had a statistically significant ($p=0.01$) mean difference of -1.9 ± 2.3 mm (-6.2% ± 7.9). The greatest loss of triceps skinfold thickness observed was 6.4 mm (23.8%). One study participant observed a 0.2 mm (1%) gain in triceps skinfold thickness. The study participants' subscapularis skinfold thickness had a statistically significant ($p<0.001$) mean difference of -1.9 ± 1.6 mm (-6.5% ± 5.0). The greatest loss of subscapularis skinfold thickness observed was 5.0 mm (11.3%). One study participant observed a 0.3 mm (1.2%) gain in subscapularis skinfold thickness. The study participants iliac crest skinfolds thickness had a statistically significant ($p<0.05$) mean difference of -1.8 ± 2.6 mm (-5.7% ± 7.4). The greatest loss of iliac crest skinfold thickness observed was 9.0 mm (24.4%). One study participant observed a 0.5 mm (1.6%) gain in iliac crest skinfold thickness. The study participants medial calf skinfolds thickness had a statistically significant ($p<0.001$) mean difference of -2.4 ± 1.9 mm (-9.3% ± 6.9). The greatest medial calf skinfold thickness loss observed was 6.7 mm (14.7%). One study participant observed no change in medial calf skinfold thickness. The study participants Sum of 5 Skinfolds (SO5S) had a statistically significant ($p<0.001$) mean difference of -8.8 ± 7.9 mm (-6.7% ± 5.0). The greatest loss of SO5S observed was 23.5 mm (12.3%). One study participant observed no change in SO5S. The study participants NIH WC had a statistically significant ($p=0.014$) mean difference of -4.0 ± 5.2 mm (-3.5% ± 3.9). The greatest loss of NIH WC observed was 21.0 mm (15.8%). One study participant observed no change in NIH WC. The study participants %BF with the Omron BIA device had a statistically significant ($p=0.035$) mean difference of -1.5 ± 2.4 mm (-3.5% ± 5.7). The greatest loss of %BF observed was 6.9% (16.4% difference). One study participant observed a + 0.7% in %BF. The study participants VO_2max had a statistically significant ($p=0.032$) mean difference of -1.4 ± 2.2 $mLO2 \cdot kg^{-1} \cdot min\text{-}^{1}$ (+6.9% ± 9.9). The greatest improvement of VO_2max observed was 4.24

mLO2·kg^{-1}·min^{-1} (17.4%). One study participant observed a 2.9 mLO2·kg^{-1}·min^{-1} (9.2%) decrease in VO_2max.

Figure 1 contains the percent mean difference (X±SD) for the variables of interest pre/post-intervention.

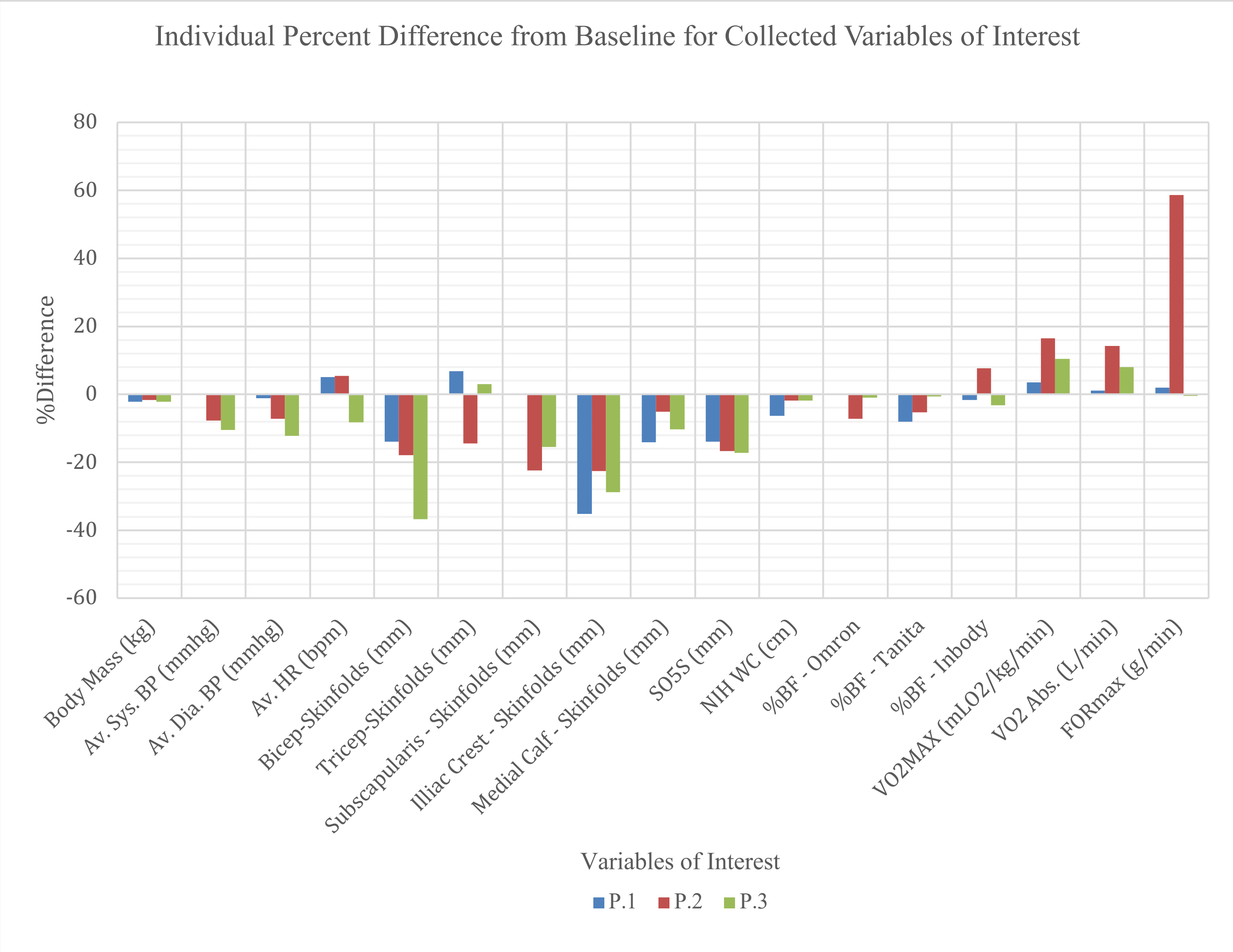


* $p<0.05$ statistically significant difference pre/post-intervention (3 weeks) with a two-sided paired samples t-test.
** $p<0.01$ statistically significant difference pre/post-intervention (3 weeks) with a two-sided paired samples t-test.

It is not uncommon for FOR_{max} to also be expressed in mg·min^{-1}·kgFFM^{-1}. An additional analysis in relation to FFM was completed. The results of the paired sample t-test analysis did not reveal any statistically significant differences. Therefore, the difference in FOR_{max} was not statistically different post-3 weeks of TRF + LISS intervention whether expressed in g·min^{-1} or mg·min^{-1}·kg FFM^{-1}.

As previously mentioned, a subset of the study participants (n=3) were followed for six additional weeks, for a total of 9 weeks. The %difference data for the variables of interest pre/post-intervention (weeks 3 to 9) are depicted in Figure 2. P.1 refers to study participant 1. P.2 refers to study participant 2. P.3 refers to study participant 3.

Figure 2 contains the percent difference (X±SD) for the variables of interest pre/post-intervention (weeks 3 to 9).



P.1 refers to study participant 1. P.2 refers to study participant 2. P.3 refers to study participant 3.

The study participants' body mass had a statistically significant ($p<0.05$) mean difference of -1.6 kg ± 0.29 (-2.0% ± 0.4). The greatest body mass loss was 1.9 kg (2.7%). The lowest body mass loss observed was 1.4 kg (1.6%). The study participants iliac crest skinfolds thickness had a statistically significant ($p<0.05$) mean difference of -8.0 mm ± 3.1 mm (-28.8 % ± 6.3). The greatest loss of iliac crest skinfold thickness observed was 9.8 mm (35.1%). The lowest loss of iliac crest skinfolds observed was 6.8 mm (28.8%). The study participants medial calf skinfolds thickness had a statistically significant ($p<0.05$) mean difference of -2.1 ± 0.5 mm (-9.9% ± 4.6). The greatest medial calf skinfold thickness loss observed was 2.4 mm (14.2%). The lowest loss of medial calf skinfold observed was 1.6 mm (5.1%). The study participants SO5S had a statistically significant ($p<0.05$) mean difference of -18.9 mm ± 6.8 (-16.0% ± 1.8). The greatest loss of SO5S observed was 25.9 mm (16.8%). The three BIA devices for %BF showed no statistically significant differences.

Discussion:

This study aimed to examine the short-term effects of varying TRF durations and LISS PA on FOR_{max}. It was hypothesized that study participants would exhibit statistically significant differences in body mass and FOR_{max} post-intervention. In support of the hypothesis, statistically significant differences were observed in the study participants' body mass during both parts of the intervention (supervised and unsupervised). In contrast to the hypothesis, no statistically significant differences were observed in FOR_{max}. It is important to note that statistical significance may have yet to be met due to the large variability in the study participants' responses to the intervention. In the first phase of the intervention, it was observed that the study participants had a mean difference of 12.6% in FOR_{max} but a standard deviation of 22.7%. One study participant's FOR_{max} improved by as much as 63.9%, while another one improved by 45.8%.

Contrary to this, 5 out of 14 study participants (35.7%) experienced a decrease in FOR_{max}, with the greatest loss being 15.4%. In the extended unsupervised investigation phase, the same study participant who experienced the greatest decrease in FOR_{max} earlier, improved their FORmax in this phase, resulting in a net improvement of 1.9%. In this small subset of study participants, 1 study participant exhibited an improvement of 58.6% in their FOR_{max}, while another study participant's FOR_{max} decreased by 0.5%.

The study participants' %BF was measured using three BIA devices (Tanita Scale, Omron hand-held, and Inbody 4-pole scale). Although some differences in study participants' %BF were observed, there were also some inconsistencies. For example, there were instances where a study participant experienced a reduction in body mass coupled with an increase in %BF. Furthermore, in another instance, one BIA device (Omron) reported a 3% decrease in %BF, while another device (Inbody) reported a 3% increase, and the Tanita scale reported no change. These observed discrepancies may explain the lack of statistical significance in the %BF. The mean %BF difference for each respective device (Omron, Tanita, Inbody) is as follows: -1.2% ± 1.8, -1.9% ± 1.4, 0.4% ± 2.3. Based on our findings, it appears the skinfold measurements (SO5S) appear to be more closely related to body composition and mass changes than BIA. Although skinfold measurements may be more intrusive than BIA devices, they accurately reflect anatomical site-specific changes. Kitano et al., found that skinfolds had the greatest correlation to %BF compared to DXA and BIA (Kitano et al, 2001). Another group of researchers found that compared to DXA, BIA, and skinfolds underestimate the training-induced positive changes in body composition. Further, the difference in %BF observed was smaller with the skinfold method vs. BIA compared to DXA **(**Sillanpää et al., 2013**)**. Thus, when measuring the success of a PA intervention, it is essential to consider the sensitivity and accuracy of commonly used fatness measurements such as skinfolds and BIA devices.

As a result of this research, new information was reported on the effectiveness of TRF and the short-term physiological adaptations in FOR_{max} in middle-aged women. The current study utilized a treadmill-based protocol to measure and calculate FOR over a wide range of sub-maximal exercise intensities and provide values on FOR_{max}. Liepinsh et al. examined the effects of low-intensity exercise and found increases in FOR (Liepinsh et al. 2020). Although the findings of our investigation did not reveal statistically significant improvements in FOR_{max} for the LISS PA, an increased FOR was generally observed. Low-intensity exercise, such as walking, has been shown to promote a greater reliance on fat as a fuel source, leading to increased FOR_{max} (Achten & Jeuknedrup, 2004; Liepinsh et al. 2020). Our findings suggest that combining TRF with PA may have synergistic effects on FOR_{max}, potentially enhancing metabolism and supporting weight management goals. However, future research is needed to confirm these results and investigate the chronic effects of this combination. Further studies are required to explore the potential inter-individual variability in response to TRF and LISS PA on FOR_{max}.

Limitations:

Although the subjects were instructed to maintain regular eating and beverage consumption habits throughout the experiment and to arrive fasted, having only consumed 500ml of water the morning of the testing day, this study did not control for eating habits. Nutrition plays a vital role in FOR, ingesting carbohydrates in the hours prior to testing decreases the FOR significantly when compared to fasted conditions. Moreover, FOR has been demonstrated to decrease after consuming a high-fat diet, partially due to lower amounts of glycogen storage. When deciding about the rigor of controlling nutrition, there arises a dilemma between internal (as standardized as possible) and external validity (as closely resembling the "real" world as possible) (Rice et al, 1999). The present study aimed to employ control measures within the scope of restrictions that can be realistically applied to the general population. This gives an opportunity to define more rigorous procedures to improve reliability. Furthermore, in the extended portion of the study, the subset of participants was underpowered. Thus, the small sample size and variability between participant results (standard deviation) prevented the attainment of statistical significance.

Conclusion:

The statistically significant findings of this combined 3-week TRF and PA intervention showed changes in subcutaneous and visceral adiposity, increases in VO_2max, and retention or improvement of estimated fat-free mass. Thus, there is evidence to support the combined TRF and PA intervention as an effective and sustainable weight management approach.

Chapter 5: Study 4

The importance of considering Body Mass Index in conjunction with VO_2max when evaluating the health and wellness of frontline fire suppression personnel.

Abstract:

Background and Purpose:

While BMI has long been used in health screenings, the current approach of BMI as an evaluative and predictive diagnostic tool has come under clinical scrutiny (Flegal, 2023). BMI is a body composition metric quantified as weight in kilograms divided by the square of height (meters) ($kg \cdot m^{-2}$). In contrast to other methods, BMI is a simple, inexpensive, and non-invasive estimate of total body fat and can be routinely measured and calculated (CDC, 2023). As BMI is used as an indicator of body fatness, it is widely used to describe population overweightness and obesity; however, it should be noted that BMI measures excess body mass rather than excess fat (CDC, 2023). BMI is a crude index of adiposity, predominantly because it fails to differentiate body composition, fat mass versus not-fat mass versus lean or muscle mass (Nevill et al., 2010). The purpose of this investigation was to examine the Physical Employment Standards (PES) Pass Rates (PR) amongst different body mass indexes (BMI) and job-related maximum oxygen consumption (VO_2max) categories. It was hypothesized that individuals with higher BMIs, within the same VO_2max, can carry out the critical physically demanding tasks more effectively, thus observing greater PES PR.

Methods and Results:

Based on male and female frontline fire suppression (FFS) candidates who completed the bona fide Structural Firefighter Applicant Fitness Assessment (SFFA). VO_2 was measured via indirect calorimetry using discrete component open circuit spirometry. N= 1,992 FFS candidates with a mean BMI of 25.6 ± 3.0 kg·m-2 were analyzed. The mean VO_2max was 50.0 ± 5.2 $mLO2 \cdot kg^{-1} \cdot min^{-1}$. There was no observed relationship between BMI (< 25.0, ≥ 25.0) alone and PR. A statistically significant relationship was observed between VO2max and overall SFFA PR% and between BMI refined by VO_2max and PR%.

Conclusion:

The results support the hypothesis that BMI should be refined by VO_2max when evaluating the health and wellness of FFS workers. The findings provide evidence to support that those with a BMI ≥ 25.0 who achieved the required job-related VO_2max were most likely to pass the PES successfully. Wellness and training programs for FFS workers should consider focusing on cardiorespiratory and musculoskeletal fitness and maintaining/improving lean mass rather than an unrefined BMI. This consideration applies to various emergency-related physically demanding occupations where safe and effective job completion is critical to life and property.

Background & Introduction:

The concept of body mass index (BMI) has been around since the early 19th century. However, it was not until the mid-1980s that doctors and scientists began using it to describe overweight and obesity patterns on a population basis, although many consider it flawed (Visaria, 2023). While BMI has long been used in health screenings, the current approach to BMI as an evaluative and predictive diagnostic tool has come under clinical scrutiny (Flegal, 2023). BMI is a body composition metric quantified as weight in kilograms divided by the square of height in meters ($kg \cdot m^{-2}$). In contrast to other methods, BMI is a simple, inexpensive, and non-invasive estimate of total body fat and can be routinely measured and calculated (CDC, 2023). As BMI is used as an indicator of body fatness, it is widely used to describe population overweightness and obesity; however, it should be noted that BMI measures excess body mass rather than excess fat (CDC, 2023). BMI is a crude index of adiposity, predominantly because it fails to differentiate body composition, fat mass versus not-fat mass versus lean or muscle mass (Nevill et al., 2010). Table 1 displays the commonly accepted BMI classifications.

Table 1. Commonly accepted BMI classifications.

BMI	Classification
< 18.5	Under Weight
18.5 – 24.9	Normal Weight
25.0 – 29.9	Over Weight
30.0 – 34.9	Obese Class 1
35.0 – 39.9	Obese Class 2
40.0 +	Obese Class 3 (Morbid)

The 2023 American Medical Association (AMA) Council on Science and Public Health Report addresses the problematic history of using BMI and explores alternatives. The report also outlined the harms and benefits of using BMI and pointed to BMI as an imperfect way to measure body fat in multiple groups, given that it does not account for differences across race/ethnic groups, sexes, genders, and age spans. Due to significant limitations associated with the widespread use of BMI in clinical settings, the AMA suggests that BMI be used in conjunction with other valid measures of risk. The AMA also recognizes that body shape and composition differences across race/ethnic groups, sexes, genders, and age span are essential to consider when applying BMI as a measure of adiposity and that BMI should not be used as a sole criterion to deny appropriate insurance reimbursement (AMA, 2023).

A study by Romero-Corral et al. compared the sensitivity and specificity of BMI-defined obesity (Class I: BMI $\geq$ 30 kg/m²) to body fat percent-defined obesity ($\geq$ 25% for men; $\geq$ 35% for women). The authors reported that the accuracy of BMI to diagnose obesity was limited, particularly for individuals in the Overweight (25-29.9 kg/m²) BMI group. Furthermore, those in the BMI Obese Class I category had a poor ability to detect body fat percent-defined obesity (Romeo-Corral et al., 2008). When BMI alone is applied as a diagnostic criterion, this may lead to the misclassification of persons (Hortobagyi et al., 1994; Romero-Corral et al., 2008). Also, multiple studies have found that persons living with overweightness (BMI > 25.0 kg/m²) have similar or better survival outcomes than normal-weight persons, highlighting how evaluating BMI alone may be flawed as a diagnostic tool (Franzosi, 2006; Romero-Corral et al., 2008).

Refining BMI by other metrics (musculoskeletal fitness, waist circumference, VO_2, etc.) may provide a better diagnostic understanding of an individual's health and fitness level. In the literature, BMI has been refined by waist circumference (WC), a useful surrogate measure of visceral adiposity, which reflects obesity-related health risks (WHO, 1998; Rankinen et al., 1999; Dogra et al., 2015). As recognized by the National Institute of Health (NIH), WC is measured at the level of the iliac crest using a tape measure at the end of an expiration (US

Dept. of Health and Human Serv., 1996). A study by Janssen et al. 2004 reported that BMI refined by WC did not predict health risk better than WC alone; conversely, WC refined by BMI was found to be a strong predictor of health risk compared to BMI alone. The authors suggested that WC, not BMI, explains obesity-related health risks. However, when WC was split into the normal and high-risk categories as advocated by the NIH, BMI remained a significant predictor of health risk. Janssen et al., 2004 suggested this was explained by absolute WC values being considerably greater in the study participants living with overweightness and obesity than the normal-weight study participants (Janssen et al.,2004). This evidence suggests that BMI alone does not fully explain obesity-related health risks despite being a surrogate measure of total adiposity. Visceral adiposity has been found to be more strongly associated with cardiovascular and metabolic disease risks; therefore, refining BMI by WC would create a more powerful diagnostic tool compared to using BMI alone (Rankinen et al., 1999; Savva et al., 2000; Jansen et al., 2004; Canoy et al., 2007). Furthermore, refining BMI with aerobic and/or musculoskeletal fitness may provide a better strategy for examining individuals' health risks.

Refining BMI is widely accepted in athletic populations but has not been extended to occupational/industrial athlete populations, including workers in emergency-related physically demanding occupations such as frontline fire suppression workers/candidates. Due to the strenuous nature of the job and the risks of loss of life/property, frontline fire suppression workers must demonstrate that they possess the physical and physiological capabilities to carry out the critical- job tasks safely and effectively (Gledhill & Jamnik, 1992). It has been reported that firefighting has an unusually high incidence of work-related injury and premature death among workers (Cady et al., 1979; Bahrke, 1982; Cady et al., 1985). However, when firefighters meet the established fitness standards, accidents and injuries are reduced, and job performance is enhanced (Mealey, 1979; Cady et al., 1985; Adams et al., 1986; Gledhill &

Jamnik, 1992). Typically, meeting the established Physical Employment Standards (PES) includes a maximal aerobic fitness assessment and a job-task simulation battery (Gledhill et al., 2001). Aerobic fitness is considered the most critical determinant in frontline fire suppression workers' capacity to work for extended periods, cope with physiological and environmental heat load, and provide information about heart disease risk (Gledhill & Jamnik, 1992). Additionally, an enhanced level of whole-body musculoskeletal fitness is necessary for this population to safely and effectively handle the weight of various equipment while wearing full turnout gear. In this cohort, it is not uncommon for the workers to have greater proportions of muscle mass, thus affecting their BMI. Given that BMI does not differentiate between lean and fat mass, the artificially inflated BMI can misclassify individuals as "overweight or obese," associating them with greater health risks. Thus, considering BMI in conjunction with aerobic and musculoskeletal fitness becomes vital in these industrial athletes. The purpose of this investigation was to examine the PES Pass Rates (PR) amongst different BMI and job-related aerobic fitness (VO_2max) categories. It was hypothesized that individuals with higher BMIs, within the same job-related VO2max level, can carry out the critical physically demanding tasks more effectively, thus observing greater PES PR.

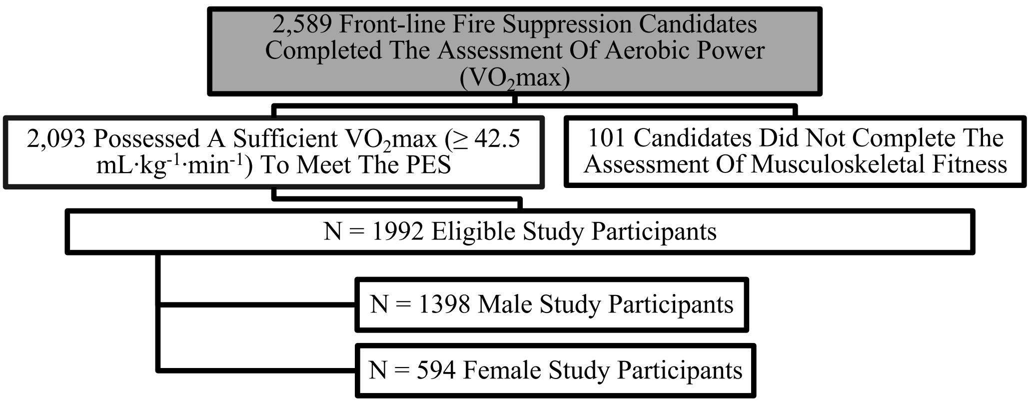
Methods:

All protocols were reviewed and approved by the Human Participants Review Sub-Committee at York University's Office of Research Ethics (certificate # E2019-236). The experimental protocol conformed to the standards set by the Declaration of Helsinki. All the study participants provided written Informed Consent to their voluntary participation in the study. Data was collected from n= 2,589 frontline fire suppression candidates who completed the bona-fide Structural Firefighter Applicant Fitness Assessment (SFFA). Participants were screened by a qualified exercise physiologist using the evidence-based tools PAR-Q+ and ePARmed-X+ (www.eparmedx.com) for contraindications and risk stratification (Warburton et al., 2011). Pre-exercise Heart Rate (HR) and blood pressure were measured using the automated BpTRU100 (Surgo Surgical Supplies, Toronto, Ontario) device to ensure participants were within an acceptable range of risk prior to the initiation of the exercise protocols; blood pressure < 160/90 mmHg. (Jamnik & Gledhill 2020). In a subset of the study population (n = 97), a PALM Health Physical Activity Participation and Sedentarism Questionnaire (which collected self-reported information regarding habitual physical activity) was completed (Tremblay et al., 2001; Jamnik & Gledhill, 2020). This subset of study participants also had additional anthropometric measurements; waist circumference was measured following the standard NIH protocol, with a tape measure around the torso, on the skin, and at the level of the iliac crest. Body fat percentage (%BF) was measured without shoes using bioelectrical impedance analysis (BIA) (Tanita scale, model TBF-612, Arlington Heights, IL; Omron handheld device, model HBF-306C; Inbody 270). The aim of recruiting a subset with additional measures was for the purposes of examining the relationship between %BF and pass rates. The incremental-to-maximal effort VO_2max treadmill test followed the same loading sequence for all participants. Study participants performed a brief 5-minute walking warm-up on the treadmill at 3.5 mph and 2.0% incline, during which they were given the test instructions and familiarized with the test equipment. The VO_2 was determined from measurements obtained during the last 30 seconds of each workload via analysis of mixed expired gases using the discrete open circuit spirometry system. Participants began the VO_2max test by running at 5.0 mph at an incline of 2.0% or 4.0% depending on their body mass (i.e., if their body mass was < 75.0 kg, an incline of 2.0% was used, and body mass > 75.0 kg, an incline of 4.0% was used) for 2 minutes. During each subsequent 2-minute workload, the incline was kept constant, and the treadmill's speed was progressively increased by 1.0 mph until a suitable running speed was achieved (i.e., between 6.0 and 7.0 mph). Once the maximum speed was achieved, the incline was progressively increased by 2% at every workload. Once the study participants could no longer work continuously, a discontinuous protocol was utilized, also referred to as verification or supramaximal testing (Hancock et al., 2023; Yavelberg et al., 2023). The VO_2max test was terminated if the study participant could no longer complete the workload or if the VO_2max plateau criteria were attained using verification workloads (Gledhill et al., 1994; Howley, 1995; Hancock et al., 2023). After attaining a VO_2max, the participants were given a 3–5-minute cool-down period during which they were instructed to walk on the treadmill at a speed of 3.0 mph and a grade of 1.0%. For full details of the equipment and protocol, refer to Hancock et al. 2023.

Inclusion and Exclusion Criteria

Figure 1 is a consort diagram depicting the sample size of study participants based on inclusion and exclusion criteria. 2,589 frontline fire suppression candidates completed the SFFA, 2093 possessed a sufficient VO2max (≥ 42.5 $mL \cdot kg^{-1} \cdot min^{-1}$) to meet the PES in accordance with The Supreme Court of Canada Meiron Decision. The 493 candidates who did not meet the job-related VO_2max standard were excluded from the study.

Figure 1: Consort Diagram of study participant enrollment based on inclusion/exclusion criteria.



Statistical Analyses:

Statistical analyses were performed using IBM SPSS version 28 for Windows (IBM Corp., Armonk, NY, USA). Univariate analyses were performed to provide descriptive statistics of the study population for Sex, BMI, and VO_2max. Binary logistic regression and Pearson's Chi-square analyses were performed to assess the relationship between Sex, BMI, and VO2max and the ability of study participants to successfully complete the critical job-related tasks. Values were considered statistically significant if $p < 0.05$. The covariates were sex, BMI, and VO_2max, and a pass of the job-related tasks was the dependent variable.

Conventional BMI categories (underweight: < 18.5 kg/m²; normal weight: 18.5 < 25.0 kg/m²; overweight: 25.0 < 30.0 kg/m²; obese class I: 30.0 < 35.0 kg/m²; obese class II: 35.0 < 40.0 kg/m²; and obese class III: ≥ 40.0 kg/m²) were collapsed into two categories: < 25.0 kg/m² and ≥ 25.0 kg/m² to allow for statistical analysis. The underweight: <18.5 kg/m² category was critically underpowered (n = 8); therefore, the underweight and normal weight categories were combined.

VO_2max categories were specific to frontline fire suppression applicant standards and were categorized into three categories: Borderline Acceptable (42.5 to 45 $ml \cdot kg^{-1} \cdot min\text{-}^{1}$), Pass Level I (45.0 to 47.99 $ml \cdot kg^{-1} \cdot min^{-1}$), and Pass Level II (≥ 48.0 $ml \cdot kg\text{-}^{1} \cdot min^{-1}$). These VO_2max categories represent thresholds at which incumbent firefighters could safely and efficiently perform the critical physically demanding job-related tasks.

Results:

1,992 frontline fire suppression candidates with a mean BMI of 25.6 kg/m² ± 3.0 were analyzed. The combined mean VO_2max was 50.0 $mLO_2 \cdot kg^{-1} \cdot min^{-1}$ ± 5.2. Table 2 shows the anthropometric, physical, and physiological fitness profiles for all study participants (1,398 males, 594 females), including the subset population who completed a body fat percentage (%BF) analysis (n=76, 69 males, 7 females). This subset of the study participants' (n = 76) data was analyzed in an attempt to explore a relationship between %BF, BMI, and VO_2max on PR.

Table 2. Anthropometric plus Physiological Fitness Profiles of all Study Participants.

Characteristic	**Combined** n=1992 (X±SD)	**Males** n=1398 (X±SD)	**Females** n=594 (X±SD)	**P-value**
Age (yr.)	28 ± 5.9	28 ± 5	27 ± 6	0.032
Height (cm)	176.5 ± 8.4	180.0 ± 6.5	168.3± 6.1	< 0.001
Body mass (kg)	80.0 ± 12.8	85.1 ± 10.8	67.9 ± 8.2	< 0.001
BMI ($kg \cdot m^2$)	25.6 ± 3.0	26.3 ± 2.9	24.0 ± 2.6	< 0.001
VO_2max ($LO_2 \cdot min^{-1}$)	4.0 ± 0.73	4.3 ± 0.5	3.2 ± 0.4	< 0.001
VO_2max ($mLO_2 \cdot kg^{-1} \cdot min^{-1}$)	50.0 ± 5.2	51.2 ± 5.3	47.1 ± 3.6	< 0.001

Table 3 shows the anthropometric profiles for the subset of study participants (n=76, 69 males, 7 females) for whom the additional %BF assessments NIH waist circumference (cm) was statistically significant between the Males and Females (p< 0.001). %BF using the Inbody 270 BIA device was not statistically significant between the sexes (p=0.012). %BF using the Tanita BIA device was statistically significant between the sexes (p=0.004). %BF using the Omron BIA device was statistically significant between the sexes (p=0.004). Fat-free mass percentage using the Inbody 270 BIA device was statistically significant between the sexes (p< 0.001). Given that the study participants of the subset experienced a 100% pass rate on the job-related musculoskeletal assessment, no further analysis could be completed examining the relationship between %BF and overall pass rates.

Table 3. Anthropometric Profiles of the Subset Study Participants.

Characteristic	Combined n=77 (X±SD)	Males n=69 (X±SD)	Females n=8 (X±SD)	P-value
NIH Waist Circum. (cm)	89.2 ± 8.7	90.5 ± 8.2	78.5 ± 4.5	< 0.001
Body Fat – Inbody (%)	18.0 ± 5.5	17.5 ± 5.3	22.6 ± 5.1	0.012
Body Fat – Tanita (%)	21.9 ± 5.3	21.3 ± 4.9	26.9 ± 5.8	0.004
Body Fat – Omron (%)	18.5 ± 5.5	17.9 ± 5.4	23.7 ± 3.0	0.004
Fat Free Mass – Inbody (%)	40.4 ± 8.6	41.7 ± 8.0	29.0 ± 1.9	< 0.001

BMI Alone & Pass Rate (PR):

Table 4 contains a summary of the relationship between BMI cut-points (< 25.0, ≥ 25.0) and PR for the male and female study participants. When examining the PR for female applicants who passed the job-related VO_2 standards (n = 594), there was no statistically significant difference observed in the PR between those who have a BMI < 25.0 or those who have a BMI ≥ 25.0 (x^2 = 2.234, df = 1, p = 0.135). For male applicants who passed the job-related VO_2 standards (n = 1,398), there were no statistically significant differences in PR between those who have a BMI < 25.0 or those who have a BMI ≥ 25.0 (x^2 = 1.458, df = 1, p = 0.227).

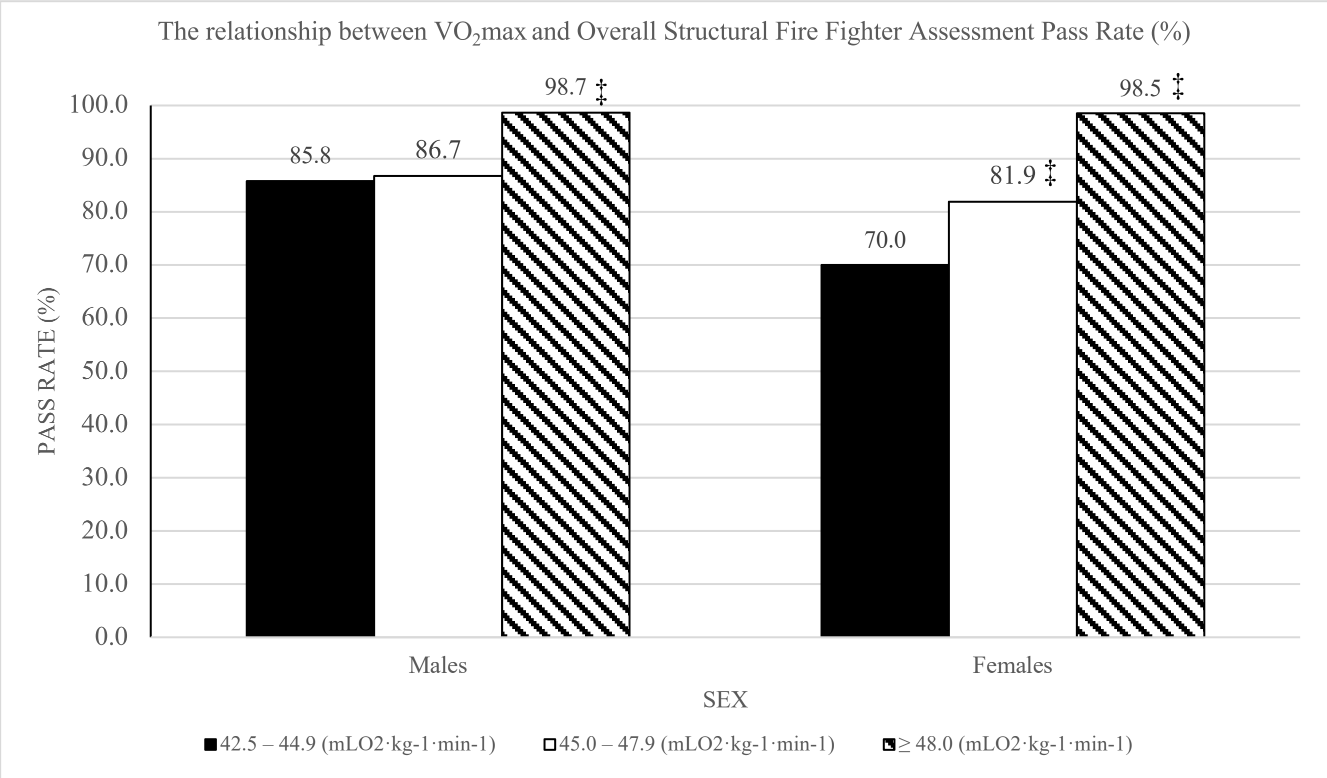
Table 4. Relationship between BMI cut-points & Structural Fire Fighter Assessment Pass Rates.

BMI	Males n=1398 (X±SD)		Females n=594 (X±SD)		P-value
	Pass	Fail	Pass	Fail	
< 25.0	460 (96.0%)	19 (4.0%)	342 (85.1%)	60 (14.9%)	-
≥ 25.0	869 (94.6%)	50 (5.4%)	154 (80.2%)	38 (19.8%)	-

VO_2 & Pass Rate (PR)

Figure 2 contains a bar graph examining the relationship between the VO_2max cut-points and SFFA Pass Rate Percentage (PR%) for the male and female study participants. When examining the SFFA pass rates for female applicants who passed the job-related VO_2max standards (n = 594), there is a statistically significant difference in pass rate between those who have a Borderline, Pass Level I, and Pass Level II VO_2max ($x^2 = 61.185$, df = 2, $p < 0.001$). There is a statistically significant difference in PR between those who have a Borderline (n = 207) and Pass Level I VO_2max (n = 182) ($x^2 = 7.331$, df = 1, p = 0.007); a statistically significant difference in pass rate between those who have a Borderline (n = 207) and Pass Level II VO_2max (n = 205) ($x^2 = 62.909$, df = 2, $p < 0.001$); and a statistically significant difference in PR between those who have a Pass Level I (n = 182) or Pass Level II VO_2max (n = 205) ($x^2 = 31.748$, df = 1, $p < 0.001$). For male applicants who passed the job-related VO_2max standards (n = 1,398), there is a statistically significant difference in PR between those who have a Borderline, Pass Level I, and Pass Level II VO_2max ($x^2 = 93.874$, df = 2, $p < 0.001$). There was no statistically significant difference in PR between those who have a Borderline (n = 162) and Pass Level I VO_2max (n = 249) ($x^2 = 0.074$, df = 1, p = 0.785). There was a statistically significant difference in pass rate between those who have a Borderline (n = 162) and Pass Level II VO_2max (n = 987) ($x^2 = 76.070$, df = 1, $p < 0.001$) and a statistically significant difference in PR between those who have a Pass Level I (n = 249) and Pass Level II VO_2max (n = 987) ($x^2 = 79.057$, df = 1, $p < 0.001$).

Figure 2. Relationship between VO2max cut-points & Pass Rates for Study Participants separated by sex.

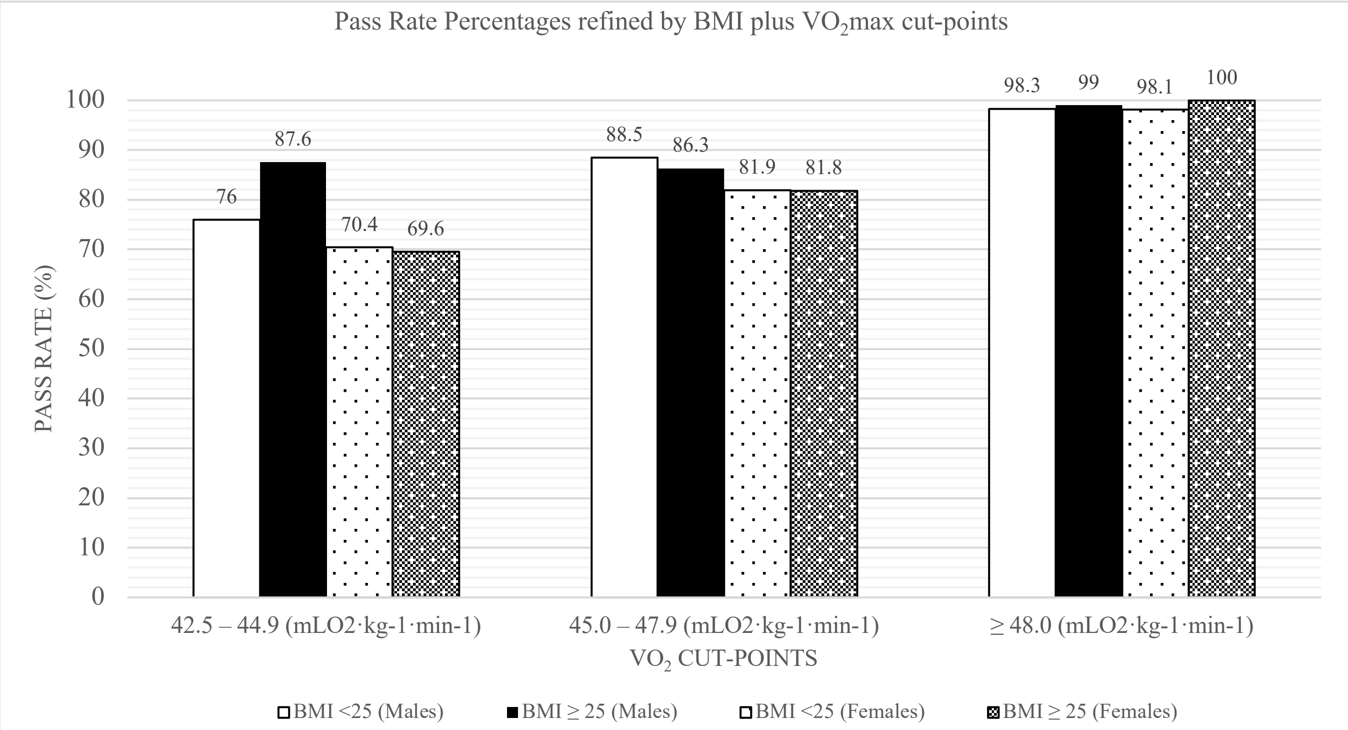


‡ $p < 0.001$ difference between pass rate percentage amongst the VO2max cut-points.

Pass Rates (PR) of BMI refined by VO_2max:

Figure 3 shows a bar graph examining the relationship between the VO2max cut-points and Pass Rate Percentage (PR%) refined by BMI (< 25.0, ≥ 25.0) for the male and female study participants. For all male applicants who had a BMI < 25.0 and achieved the job-related VO_2max standard (n = 479), there was a significant association between BMI refined by VO_2max and PR% ($x^2 = 39.392$, df = 2, $p < 0.001$). For all male applicants who had a BMI ≥ 25.0 and achieved the job-related VO_2max standard (n = 919), there was a significant association between BMI refined by VO_2max and PR% ($x^2 = 61.251$, df = 2, $p < 0.001$). For all female applicants who had a BMI < 25.0 and achieved the job-related VO_2max standard (n = 402), there was a significant association between BMI refined by VO_2max and PR% ($x^2 = 41.886$, df = 2, $p < 0.001$). For all female applicants who had a BMI ≥ 25.0 and achieved the job-related VO_2max standard (n = 192), there was a significant association between BMI refined by VO_2max and PR% ($x^2 = 17.759$, df = 2, $p < 0.001$).

Figure 3. Relationship between BMI + VO_2max & Pass Rates for Study Participants separated by Sex.



Discussion:

This investigation aimed to examine the PES PR amongst different BMI and job-related VO_2max categories. It was hypothesized that individuals with higher BMIs, within the same job-related VO_2max level, can carry out the critical physically demanding tasks more effectively, thus observing greater PES PR. Our investigation demonstrates that VO_2max is the driving factor for successful, safe, and effective job performance. Rhea et al., 2004 observed higher job performance measures with increased aerobic fitness, upper-body strength, upper-body endurance, squat endurance, and decreased 400-m sprint time (Rhea et al., 2004). Task-specific training programs can increase the effectiveness of job-specific tasks and provide firefighters with the general health benefits associated with regular exercise. The general goals of health and fitness programs tailored to firefighters should include thorough baseline testing and exercise programming with aerobic fitness training and general strength and conditioning in mind (Bjerke, 2011).

It is important to highlight the limitations of utilizing BMI alone in wellness initiatives for frontline fire suppression workers. Current wellness initiatives for candidates, such as the International Association of Firefighters Wellness-Fitness Initiative, utilize BMI in their programming, largely focusing on weight loss and achieving BMI targets (von Haehling, 2019; Wills, 2022). It would be less suitable to solely target BMI within these initiatives, as the results of this investigation imply that having a higher BMI was advantageous for applicants with lower but passable VO_2max scores. For example, in males who achieved a Borderline VO_2max score. An 11.6% lower PR was observed between men with a BMI <25 and ≥ 25 in the Borderline VO_2max category. From this, it is understood that body mass can be integral in successfully carrying out critical job tasks in this subgroup. Therefore, it is suggested that wellness programs, which solely focus on reducing BMI, may result in reductions in both VO_2max and MSK fitness, which ultimately contributes to the individual's inability to meet the PES requirements. Though the workforce is diverse in physical and physiological attributes, it should be acknowledged that when looking at the general characteristics of frontline fire suppression candidates and the specific demands of the job, their overall body mass and BMI are generally greater than that in the general population (Gledhill & Jamnik, 1992). As the job-related tasks simulate the critical job demands, the results of this investigation demonstrate that having a higher BMI plus VO_2max is advantageous for the performance of the critical job-related demands. It is time to look beyond the arbitrary and questionable BMI categories and evaluate other approaches to promote health and well-being (Flegal, 2023). A paradigm has been suggested, according to which overweight and moderate obesity may be beneficial for patients with a broad spectrum of chronic diseases (von Haehling, 2019). Evidence suggests that PA and fitness may be more important for health than adiposity (Ahmadi et al., 2022; Lavie et al., 2022; Wills, 2022).

Limitations:

Although this investigation had a large sample size (n=1992), the analysis of the sub-set population was limited. Given that the male study participants (n=69) in the sub-group experienced 100% PR, no statistical analysis could be completed on the effects of %BF and PR. Further, the female study participants in the sub-group consisted of only 8, limiting this analysis's power and accuracy. Thus, no statistical analysis on the effects of %BF and overall SFFA pass rate could be completed. Additionally, for statistical analysis, study participants were separated into cohorts based on their VO_2max. In some instances, it is possible that study participants elected to prematurely conclude the assessment of VO_2max, resulting in a VO_2peak rather than a true VO_2max. This could explain the lack of statistical significance in the male study participants in the lower VO_2max cohort.

Conclusion:

In conclusion, the results of this study support the hypothesis that BMI should be considered in conjunction with VO_2max when evaluating the health and wellness of frontline fire suppression workers. This paper demonstrates that the driving factor for the likelihood of frontline fire suppression candidates meeting the required PES is a higher-than-average VO_2max. The findings provide evidence to support that those individuals with a BMI >25 who achieved the required job-related VO_2max were most likely to successfully pass the overall PES.

When developing training programs and wellness initiatives for frontline fire suppression workers should focus on cardiorespiratory fitness, musculoskeletal fitness, and maintaining/improving less mass rather than evaluating participants using an unrefined BMI, which alone is limited in its diagnostic power. This would also apply to all frontline workers in various emergency-related physically demanding occupations (i.e., Wildland firefighting, Policing, Nuclear Power Emergency Personnel, etc.) where safe and effective job completion is critical to life and property.

CHAPTER 6: LIMITATIONS & IMPLICATIONS OF FINDINGS

Limitations:

This research project was subject to a number of unexpected challenges. The COVID-19 pandemic has had a profound impact on the completion of my Ph.D. research, as mentioned earlier.

As mentioned before, the pandemic also brought attention to the need for more adaptable and resilient research designs that can cope with situations that change quickly. This researcher had initially planned to collect and analyze study participants' blood, saliva, and fecal samples to investigate the biochemical adaptations of the interventions. Given the loss of time and increased bio-safety restrictions, the researchers were forced to adapt to the situation and remove this portion of the biochemical analysis. Furthermore, researchers had to re-focus and re-design some parts of their proposed studies.

Manuscript I was limited in sample power and could have had better fasting control. Although the subjects were instructed to maintain regular eating and beverage consumption habits throughout the experiment and to arrive fasted, having only consumed 500ml of water the morning of testing day, this study did not control for eating habits. Even though some individuals demonstrated greater intra-variability, no significant differences were observed.

Nutrition plays a vital role in FOR, and ingesting carbohydrates in the hours prior to testing decreases the FOR significantly when compared to fasted conditions. Moreover, FOR has been demonstrated to decrease after consuming a high-fat diet, partially due to lower amounts of glycogen storage. When deciding about the rigor of controlling nutrition, there arises a dilemma between internal (as standardized as possible) and external validity (as closely resembling the "real" world as possible) (Hall et al., 2010). It was the aim of the present study to employ control measures within the scope of restrictions that can be realistically applied to the general population. It may be possible to improve reliability with more rigorous dietary control procedures put in place.

In addition, a power analysis calculator revealed that to achieve significance at the 0.05 level for a two-tailed alpha, with a power of 0.8 and an effect size of 0.5 (medium-large effect), the number of participants in each group would have to be 64 (https://www.statskingdom.com). Thus, the sample size was underpowered, which may have influenced the lack of statistical significance in the results.

Manuscript II was limited in study duration (although an acute investigation) and potential generalizability. First, the study duration was relatively short, and TRF and PA's long-term/chronic effects were not evaluated. Future research should include more extended follow-up periods to investigate the sustainability and persistence of the observed effects. Second, the participant cohort consisted of healthy young adults, limiting the generalizability of the findings to other age groups and populations. Although both male and female study participants were observed, future studies should include a more diverse sample to understand the effects in different populations. This study was part of a series of studies that examined the immediate acute effects of exercise on FORmax post-TRF (12 vs 16 hours). Although some statistical significance was found, the researchers believe that the differences between the TRF+PA strategies may have been more pronounced and significant with a larger sample size.

Furthermore, the study participants' meals prior to fasting were not rigidly controlled. It is known that a heavy fat/carbohydrate meal prior to fasting may influence FOR/FOR_{max}. Although the study participants may have consumed differing macronutrients prior to the fast, the TRF durations and PA intensities were carefully controlled. The menstrual cycle was not controlled for or documented. It is possible that hormonal fluctuations throughout the menstrual cycle could affect female FOR_{max}. Thus, the findings of this investigation can be cautiously generalized given the external and internal validity. In addition, this study will contribute to the gaps in the literature pertaining to varying TRF durations and PA intensities.

Manuscript III had limitations similar to those of the previous fasting studies. Although the subjects were instructed to maintain regular eating and beverage consumption habits throughout the experiment and to arrive fasted, having only consumed 500ml of water the morning of testing day, this study did not control for eating habits. Nutrition plays a vital role in FOR, ingesting carbohydrates in the hours prior to testing decreases the FOR significantly when compared to fasted conditions. When deciding about the rigor of controlling nutrition, there arises a dilemma between internal (as standardized as possible) and external validity (as closely resembling the "real" world as possible) (Rice et al., 1999). It was the aim of the present study to employ control measures within the scope of restrictions that can be realistically applied to the general population. Furthermore, in the extended portion of the study, the subset of participants was underpowered (https://www.statskingdom.com). Thus, the small sample size and variability between participant results (standard deviation) prevented the attainment of statistical significance.

Manuscript IV experienced power limitations in the sub-set population. Although this investigation was well-powered (n=1,992), the analysis of the sub-set population was limited. Given that the male study participants (n=69) in the sub-group experienced a 100% PR, no statistical analysis could be completed on the effects of %BF and PR. Further, the female study participants in the sub-group consisted of only 8, limiting this analysis's power and accuracy. Thus, no statistical analysis on the effects of %BF and overall SFFA pass rate could be completed.

Additionally, for statistical analysis purposes, study participants were separated into cohorts based on their VO_2max. In some instances, it is possible that study participants elected to prematurely conclude the assessment of VO_2max, resulting in a VO_2peak rather than a true VO_2max. This could explain the lack of statistical significance in the male study participants in the lower VO_2max cohort.

Study Implications:

Through these investigations, the researchers were able to share their newly found knowledge with the scientific community and those interested in exercise as a primary disease prevention and secondary disease management strategy. This study was precipitated by the need to elucidate effective and sustainable weight management strategies and reframe our current perspectives on weight loss, FOR_{max}, VO_2max, and commonly used fat measurements. These findings may play an integral part in customizing primary disease prevention and secondary disease prevention PA prescriptions and illuminate the synergistic effects of TRF and PA. The results of this investigation will aid in the understanding of PA prescriptions with respect to FOR and commonly used fatness measures. Given that lack of time and motivation are often cited as a justification for sedentarism, individuals living with overweight or obesity may be able to efficiently exercise with TRF to manage their weight. The simplicity of this weight management strategy may aid in bridging this gap of immediate gratification and feeling of accomplishment from exercise. With further research, the effects of TRF and varying exercise intensities on FOR and commonly used fatness measurements will be confidently advocated as a successful strategy for effective and sustainable weight management.

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Appendix A: Study pre-screen tools (2019 PAR-Q+, Informed consent, PAPSQ)

2019 PAR-Q+

The Physical Activity Readiness Questionnaire for Everyone

The health benefits of regular physical activity are clear; more people should engage in physical activity every day of the week. Participating in physical activity is very safe for MOST people. This questionnaire will tell you whether it is necessary for you to seek further advice from your doctor OR a qualified exercise professional before becoming more physically active.

GENERAL HEALTH QUESTIONS

Please read the 7 questions below carefully and answer each one honestly: check YES or NO.	YES	NO
1) Has your doctor ever said that you have a heart condition ☐ OR high blood pressure ☐?	☐	☐
2) Do you feel pain in your chest at rest, during your daily activities of living, **OR** when you do physical activity?	☐	☐
3) Do you lose balance because of dizziness **OR** have you lost consciousness in the last 12 months? Please answer **NO** if your dizziness was associated with over-breathing (including during vigorous exercise).	☐	☐
4) Have you ever been diagnosed with another chronic medical condition (other than heart disease or high blood pressure)? **PLEASE LIST CONDITION(S) HERE:** ______	☐	☐
5) Are you currently taking prescribed medications for a chronic medical condition? **PLEASE LIST CONDITION(S) AND MEDICATIONS HERE:** ______	☐	☐
6) Do you currently have (or have had within the past 12 months) a bone, joint, or soft tissue (muscle, ligament, or tendon) problem that could be made worse by becoming more physically active? Please answer **NO** if you had a problem in the past, but it **does not limit your current ability** to be physically active. **PLEASE LIST CONDITION(S) HERE:** ______	☐	☐
7) Has your doctor ever said that you should only do medically supervised physical activity?	☐	☐

If you answered NO to all of the questions above, you are cleared for physical activity.
Please sign the PARTICIPANT DECLARATION. You do not need to complete Pages 2 and 3.

- Start becoming much more physically active – start slowly and build up gradually.
- Follow International Physical Activity Guidelines for your age (www.who.int/dietphysicalactivity/en/).
- You may take part in a health and fitness appraisal.
- If you are over the age of 45 yr and NOT accustomed to regular vigorous to maximal effort exercise, consult a qualified exercise professional before engaging in this intensity of exercise.
- If you have any further questions, contact a qualified exercise professional.

PARTICIPANT DECLARATION

If you are less than the legal age required for consent or require the assent of a care provider, your parent, guardian or care provider must also sign this form.

I, the undersigned, have read, understood to my full satisfaction and completed this questionnaire. I acknowledge that this physical activity clearance is valid for a maximum of 12 months from the date it is completed and becomes invalid if my condition changes. I also acknowledge that the community/fitness center may retain a copy of this form for its records. In these instances, it will maintain the confidentiality of the same, complying with applicable law.

NAME ______ DATE ______

SIGNATURE ______ WITNESS ______

SIGNATURE OF PARENT/GUARDIAN/CARE PROVIDER ______

If you answered YES to one or more of the questions above, COMPLETE PAGES 2 AND 3.

Delay becoming more active if:

- You have a temporary illness such as a cold or fever; it is best to wait until you feel better.
- You are pregnant - talk to your health care practitioner, your physician, a qualified exercise professional, and/or complete the ePARmed-X+ at **www.eparmedx.com** before becoming more physically active.
- Your health changes - answer the questions on Pages 2 and 3 of this document and/or talk to your doctor or a qualified exercise professional before continuing with any physical activity program.

2019 PAR-Q+

FOLLOW-UP QUESTIONS ABOUT YOUR MEDICAL CONDITION(S)

1. Do you have Arthritis, Osteoporosis, or Back Problems?

If the above condition(s) is/are present, answer questions 1a-1c — If **NO** ☐ go to question 2

1a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments)	YES ☐ NO ☐
1b.	Do you have joint problems causing pain, a recent fracture or fracture caused by osteoporosis or cancer, displaced vertebra (e.g., spondylolisthesis), and/or spondylolysis/pars defect (a crack in the bony ring on the back of the spinal column)?	YES ☐ NO ☐
1c.	Have you had steroid injections or taken steroid tablets regularly for more than 3 months?	YES ☐ NO ☐

2. Do you currently have Cancer of any kind?

If the above condition(s) is/are present, answer questions 2a-2b — If **NO** ☐ go to question 3

2a.	Does your cancer diagnosis include any of the following types: lung/bronchogenic, multiple myeloma (cancer of plasma cells), head, and/or neck?	YES ☐ NO ☐
2b.	Are you currently receiving cancer therapy (such as chemotheraphy or radiotherapy)?	YES ☐ NO ☐

3. Do you have a Heart or Cardiovascular Condition? This includes Coronary Artery Disease, Heart Failure, Diagnosed Abnormality of Heart Rhythm

If the above condition(s) is/are present, answer questions 3a-3d — If **NO** ☐ go to question 4

3a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments)	YES ☐ NO ☐
3b.	Do you have an irregular heart beat that requires medical management? (e.g., atrial fibrillation, premature ventricular contraction)	YES ☐ NO ☐
3c.	Do you have chronic heart failure?	YES ☐ NO ☐
3d.	Do you have diagnosed coronary artery (cardiovascular) disease and have not participated in regular physical activity in the last 2 months?	YES ☐ NO ☐

4. Do you have High Blood Pressure?

If the above condition(s) is/are present, answer questions 4a-4b — If **NO** ☐ go to question 5

4a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments)	YES ☐ NO ☐
4b.	Do you have a resting blood pressure equal to or greater than 160/90 mmHg with or without medication? (Answer **YES** if you do not know your resting blood pressure)	YES ☐ NO ☐

5. Do you have any Metabolic Conditions? This includes Type 1 Diabetes, Type 2 Diabetes, Pre-Diabetes

If the above condition(s) is/are present, answer questions 5a-5e — If **NO** ☐ go to question 6

5a.	Do you often have difficulty controlling your blood sugar levels with foods, medications, or other physician-prescribed therapies?	YES ☐ NO ☐
5b.	Do you often suffer from signs and symptoms of low blood sugar (hypoglycemia) following exercise and/or during activities of daily living? Signs of hypoglycemia may include shakiness, nervousness, unusual irritability, abnormal sweating, dizziness or light-headedness, mental confusion, difficulty speaking, weakness, or sleepiness.	YES ☐ NO ☐
5c.	Do you have any signs or symptoms of diabetes complications such as heart or vascular disease and/or complications affecting your eyes, kidneys, **OR** the sensation in your toes and feet?	YES ☐ NO ☐
5d.	Do you have other metabolic conditions (such as current pregnancy-related diabetes, chronic kidney disease, or liver problems)?	YES ☐ NO ☐
5e.	Are you planning to engage in what for you is unusually high (or vigorous) intensity exercise in the near future?	YES ☐ NO ☐

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6.	**Do you have any Mental Health Problems or Learning Difficulties?** This includes Alzheimer's, Dementia, Depression, Anxiety Disorder, Eating Disorder, Psychotic Disorder, Intellectual Disability, Down Syndrome If the above condition(s) is/are present, answer questions 6a-6b — If **NO** ☐ go to question 7	
6a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments)	YES ☐ NO ☐
6b.	Do you have Down Syndrome **AND** back problems affecting nerves or muscles?	YES ☐ NO ☐
7.	**Do you have a Respiratory Disease?** This includes Chronic Obstructive Pulmonary Disease, Asthma, Pulmonary High Blood Pressure If the above condition(s) is/are present, answer questions 7a-7d — If **NO** ☐ go to question 8	
7a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments)	YES ☐ NO ☐
7b.	Has your doctor ever said your blood oxygen level is low at rest or during exercise and/or that you require supplemental oxygen therapy?	YES ☐ NO ☐
7c.	If asthmatic, do you currently have symptoms of chest tightness, wheezing, laboured breathing, consistent cough (more than 2 days/week), or have you used your rescue medication more than twice in the last week?	YES ☐ NO ☐
7d.	Has your doctor ever said you have high blood pressure in the blood vessels of your lungs?	YES ☐ NO ☐
8.	**Do you have a Spinal Cord Injury?** This includes Tetraplegia and Paraplegia If the above condition(s) is/are present, answer questions 8a-8c — If **NO** ☐ go to question 9	
8a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments)	YES ☐ NO ☐
8b.	Do you commonly exhibit low resting blood pressure significant enough to cause dizziness, light-headedness, and/or fainting?	YES ☐ NO ☐
8c.	Has your physician indicated that you exhibit sudden bouts of high blood pressure (known as Autonomic Dysreflexia)?	YES ☐ NO ☐
9.	**Have you had a Stroke?** This includes Transient Ischemic Attack (TIA) or Cerebrovascular Event If the above condition(s) is/are present, answer questions 9a-9c — If **NO** ☐ go to question 10	
9a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer NO if you are not currently taking medications or other treatments)	YES ☐ NO ☐
9b.	Do you have any impairment in walking or mobility?	YES ☐ NO ☐
9c.	Have you experienced a stroke or impairment in nerves or muscles in the past 6 months?	YES ☐ NO ☐
10.	**Do you have any other medical condition not listed above or do you have two or more medical conditions?** If you have other medical conditions, answer questions 10a-10c — If **NO** ☐ read the Page 4 recommendations	
10a.	Have you experienced a blackout, fainted, or lost consciousness as a result of a head injury within the last 12 months **OR** have you had a diagnosed concussion within the last 12 months?	YES ☐ NO ☐
10b.	Do you have a medical condition that is not listed (such as epilepsy, neurological conditions, kidney problems)?	YES ☐ NO ☐
10c.	Do you currently live with two or more medical conditions?	YES ☐ NO ☐

PLEASE LIST YOUR MEDICAL CONDITION(S) AND ANY RELATED MEDICATIONS HERE: ______________________

GO to Page 4 for recommendations about your current medical condition(s) and sign the PARTICIPANT DECLARATION.

2019 PAR-Q+

If you answered NO to all of the FOLLOW-UP questions (pgs. 2-3) about your medical condition, you are ready to become more physically active - sign the PARTICIPANT DECLARATION below:

- It is advised that you consult a qualified exercise professional to help you develop a safe and effective physical activity plan to meet your health needs.
- You are encouraged to start slowly and build up gradually - 20 to 60 minutes of low to moderate intensity exercise, 3-5 days per week including aerobic and muscle strengthening exercises.
- As you progress, you should aim to accumulate 150 minutes or more of moderate intensity physical activity per week.
- If you are over the age of 45 yr and **NOT** accustomed to regular vigorous to maximal effort exercise, consult a qualified exercise professional before engaging in this intensity of exercise.

If you answered **YES** to **one or more of the follow-up questions** about your medical condition:

You should seek further information before becoming more physically active or engaging in a fitness appraisal. You should complete the specially designed online screening and exercise recommendations program - the **ePARmed-X+ at www.eparmedx.com** and/or visit a qualified exercise professional to work through the ePARmed-X+ and for further information.

Delay becoming more active if:

- You have a temporary illness such as a cold or fever; it is best to wait until you feel better.
- You are pregnant - talk to your health care practitioner, your physician, a qualified exercise professional, and/or complete the ePARmed-X+ **at www.eparmedx.com** before becoming more physically active.
- Your health changes - talk to your doctor or qualified exercise professional before continuing with any physical activity program.

- You are encouraged to photocopy the PAR-Q+. You must use the entire questionnaire and NO changes are permitted.
- The authors, the PAR-Q+ Collaboration, partner organizations, and their agents assume no liability for persons who undertake physical activity and/or make use of the PAR-Q+ or ePARmed-X+. If in doubt after completing the questionnaire, consult your doctor prior to physical activity.

PARTICIPANT DECLARATION

- All persons who have completed the PAR-Q+ please read and sign the declaration below.
- If you are less than the legal age required for consent or require the assent of a care provider, your parent, guardian or care provider must also sign this form.

I, the undersigned, have read, understood to my full satisfaction and completed this questionnaire. I acknowledge that this physical activity clearance is valid for a maximum of 12 months from the date it is completed and becomes invalid if my condition changes. I also acknowledge that the community/fitness center may retain a copy of this form for records. In these instances, it will maintain the confidentiality of the same, complying with applicable law.

NAME ______________________________ DATE ______________________________

SIGNATURE ______________________________ WITNESS ______________________________

SIGNATURE OF PARENT/GUARDIAN/CARE PROVIDER ______________________________

For more information, please contact
www.eparmedx.com
Email: eparmedx@gmail.com

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The PAR-Q+ was created using the evidence-based AGREE process (1) by the PAR-Q+ Collaboration chaired by Dr. Darren E. R. Warburton with Dr. Norman Gledhill, Dr. Veronica Jamnik, and Dr. Donald C. McKenzie (2). Production of this document has been made possible through financial contributions from the Public Health Agency of Canada and the BC Ministry of Health Services. The views expressed herein do not necessarily represent the views of the Public Health Agency of Canada or the BC Ministry of Health Services.

Key References

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Informed Consent Study 1 & 2

Informed Consent Form

Study name: The effect of varying time restricted feeding durations on commonly used fatness-measurements and maximum fat oxidation rate.

Researchers:

Researcher name: Loren Yavelberg, PhD Candidate, Graduate Program in Kinesiology and Health Science, Email address loreny@yorku.ca, Office phone 416-736-2100 ext. 77236

Researcher name: Dr. Veronica Jamnik, Room 357 Norman Bethune College, York University, Email address ronij@yorku.ca, Office phone 416-736-5794

Purpose of the research:

The purpose of this project is to examine the effect of varying time restricted feeding durations (12h and 16h) on fat oxidation rate (FOR) as reflected in commonly used practices to measure fatness (%Body Fat, Waist Circumference, Skinfolds).

What you will be asked to do in the research:

There will be a maximum of 6 visits to the laboratory. On the initial and fifth test day you will undergo an incremental-to-maximal effort treadmill test for the determination of your aerobic fitness (VO2max). Additionaly, the following measurments will also be carried out: height, body mass, resting blood pressure plus pulse rate, sum of 5 skinfolds, waist circumference and percent body fat using a bioelectric impedance device (eg. Tanita Scale).

Following the initial test day, you will return to the lab for secondary screening which includes a light-to-moderate intensity FOR_{max} test. The light-to-moderate intensity FOR_{max} test will repeated on the final (sixth) visit, this is to examine any effects of varying time restricted feeding (TRF) durations on FOR and commonly used practices to measure fatness.

Upon completion of the assessment, study participants will be randomized and directed to adhere to the TRF guidelines of maintaining a daily 16 or 12 hour fast, for a duration 12 weeks. In addition, study participants will be required to report to the lab every 3 weeks for the duration of the study to undergo the following measurements: height, weight, %body fat, skinfolds, and a FOR_{max} to VO_2max test. Study participants will also be required to document their daily PA participation as well as their diet and fast duration.

All measurements and aerobic tests will be performed in the Human Performance Laboratory at York University and will be supervised by qualified exercise professionals (Certified Exercise Physiologists)

Risks and Discomforts:

As with any strenuous physical activity, there some known risks of participation which include, but are not limited to: dizziness, fatigue, nausea, lightheadedness, loss of consciousness, hypoglycemia, abnormal blood pressure, increased breathing, increased heart rate, increased blood pressure, chest pain, leg cramps, and extremely rare cases – death. Every possible precaution will be taken to avoid such instances, including the use of pre-participation medical risk assessments. All exercise will be supervised by a Certified Exercise Physiologist who is trained in emergency interventions to deal will any problems which may arise.

Benefits of the Research and Benefits to You:

By participating, you will provide the researchers with valuable information pertaining to the effects of TRF on FOR. The benefits to you include the opportunity to experience unique fitness testing as well as the exposure to various forms of exercise intensity plus modalities. The benefits of exercise include possible weight management, improved blood glucose control, improved cardiovascular and musculoskeletal health, improved self-appearance and elevated self-confidence.

Voluntary Participation: Your participation in the study is completely voluntary and you may choose to stop participating at any time. Your decision not to volunteer will not influence the relationship you may have with the researchers or study staff or the nature of your relationship with York University either now, or in the future.

Withdrawal from the study: You can stop participating in the study at any time, for any reason, if you so decide. Your decision to stop participating, or to refuse to answer particular questions, will not affect your relationship with the researchers, York University, or any other group associated with this project. In the event you withdraw from the study, all associated data collected will be immediately destroyed wherever possible.

Confidentiality: All the information that you supply during the research will be held in confidence in a password protected manner and your name will not appear in any report or publication. All archived data will be removed of any personal identifiers. The paper data will be filed and electronic data will be archived on password protected computers for at least 7 years after publication. The data will be safely stored in Dr. Jamnik's laboratory which has restricted access and only select research staff will have access to this information. Confidentiality will be provided to the fullest extent possible by law.

Questions about the research? If you have any questions about the research in general or about your role in the study, please feel free to contact the researchers by telephone or by email. This research has been reviewed and approved by the Human Participants Review Sub-Committee, York University's Ethics Review Board and conforms to the standards of the Canadian Tri-Council Research Ethics guidelines. If you have any questions about this process, or about your rights as a participant in the study, your may contact the Senior Manager and Policy Advisor for the Office of Research Ethics, 5th Floor, York Research Tower, York University, telephone 416-736-5914 or e-mail ore@yorku.ca or the Graduate Program in Kinesiology and Health Science, 341 Norman Bethune College, York University, Telephone: 416-736-5728, Fax: 416-736-5774, Email: kahs@yorku.ca

Legal rights and signatures:

I ________________________________ consent to participate in the study conducted by Loren Yavelberg. I have understood the nature of this project and wish to participate. I am not waiving any of my legal rights by signing this form. My signature below indicates my consent.

Signature ________________ **Date**___________________
Participant

Signature ________________ **Date**___________________
Principal Investigator

Informed Consent Study 3

Informed Consent Form

Study name: The effect of intermittent fasting and continuous steady state low-moderate intensity exercise on commonly used fatness-measurements and fat oxidation rate.

Researchers:

Researcher name: Loren Yavelberg, PhD Candidate, Graduate Program in Kinesiology and Health Science, Email address loreny@yorku.ca, Office phone 416-736-2100 ext. 77236

Researcher name: Dr. Veronica Jamnik, Room 357 Norman Bethune College, York University, Email address ronij@yorku.ca, Office phone 416-736-5794

Purpose of the research:

The purpose of this project is to examine the effect of time restricted feeding (16h) plus continuous steady state low-moderate intensity exercise on fat oxidation rate (FOR) as reflected in commonly used practices to measure fatness (%Body Fat, Waist Circumference, Skinfolds).

What you will be asked to do in the research:

There will be a maximum of 40 visits to the laboratory. On the initial and final test days you will undergo an incremental-to-maximal effort treadmill test for the determination of your aerobic fitness (VO2max). Additionaly, the following measurments will also be carried out: height, body mass, resting blood pressure plus pulse rate, sum of 5 skinfolds, waist circumference and percent body fat using a bioelectric impedance device (eg. Tanita Scale).

Following the initial test day, you will return to the lab for secondary screening which includes a light-to-moderate intensity FOR_{max} test. The light-to-moderate intensity FOR_{max} test will repeated on the final (sixth) visit, this is to examine any effects of varying time restricted feeding (TRF) durations on FOR and commonly used practices to measure fatness.

Upon completion of the assessment, study participants will be randomized and directed to adhere to the TRF guidelines of maintaining a daily 16 hour fast, for a duration 12 weeks. In addition, study participants may be randomized to an exercise intervention group and will be required to report to the lab 3 times per week, every week for the duration of the study to participate in continuous low-moderate intensity exercise. This exercise intervention group will be required to exercise at a targeted heart rate percentage ≤65% HRmax for a duration of approximately forty minutes (based on total kcal/session). Study participants will also be required to document their daily PA participation as well as their diet and fast duration.

All measurements and aerobic tests will be performed in the Human Performance Laboratory at York University and will be supervised by qualified exercise professionals (Certified Exercise Physiologists)

Risks and Discomforts:

As with any strenuous physical activity, there some known risks of participation which include, but are not limited to: dizziness, fatigue, nausea, lightheadedness, loss of consciousness, hypoglycemia, abnormal blood pressure, increased breathing, increased heart rate, increased blood pressure, chest pain, leg cramps, and extremely rare cases – death. Every possible precaution will be taken to avoid such instances, including the use of pre-participation medical risk assessments. All exercise will be supervised by a Certified Exercise Physiologist who is trained in emergency interventions to deal will any problems which may arise.

Benefits of the Research and Benefits to You:

By participating, you will provide the researchers with valuable information pertaining to the effects of TRF on FOR. The benefits to you include the opportunity to experience unique fitness testing as well as the exposure to various forms of exercise intensity plus modalities. The benefits of exercise include possible weight management, improved blood glucose control, improved cardiovascular and musculoskeletal health, improved self-appearance and elevated self-confidence.

Voluntary Participation: Your participation in the study is completely voluntary and you may choose to stop participating at any time. Your decision not to volunteer will not influence the relationship you may have with the researchers or study staff or the nature of your relationship with York University either now, or in the future.

Withdrawal from the study: You can stop participating in the study at any time, for any reason, if you so decide. Your decision to stop participating, or to refuse to answer particular questions, will not affect your relationship with the researchers, York University, or any other group associated with this project. In the event you withdraw from the study, all associated data collected will be immediately destroyed wherever possible.

Confidentiality: All the information that you supply during the research will be held in confidence in a password protected manner and your name will not appear in any report or publication. All archived data will be removed of any personal identifiers. The paper data will be filed and electronic data will be archived on password protected computers for at least 7 years after publication. The data will be safely stored in Dr. Jamnik's laboratory which has restricted access and only select research staff will have access to this information. Confidentiality will be provided to the fullest extent possible by law.

Questions about the research? If you have any questions about the research in general or about your role in the study, please feel free to contact the researchers by telephone or by email. This research has been reviewed and approved by the Human Participants Review Sub-Committee, York University's Ethics Review Board and conforms to the standards of the Canadian Tri-Council Research Ethics guidelines. If you have any questions about this process, or about your rights as a participant in the study, your may contact the Senior Manager and Policy Advisor for the Office of Research Ethics, 5th Floor, York Research Tower, York University, telephone 416-736-5914 or e-mail ore@yorku.ca or the Graduate Program in Kinesiology and Health Science, 341 Norman Bethune College, York University, Telephone: 416-736-5728, Fax: 416-736-5774, Email: kahs@yorku.ca

Legal rights and signatures:

I ________________________________ consent to participate in the study conducted by Loren Yavelberg. I have understood the nature of this project and wish to participate. I am not waiving any of my legal rights by signing this form. My signature below indicates my consent.

Signature ________________ **Date**___________________
Participant

Signature ________________ **Date**___________________
Principal Investigator

Participation and Sedentarism Questionnaire (PAPSQ)

The Physical Activity and Lifestyle "R" Medicine Physical Activity Participation and Sedentarism Questionnaire

Client's Name: ________________________________ **Date:** ______________________

A. Answer the following questions:

#1 Frequency

Over a typical seven-day period (one week), how many times do you engage in structured physical activity or exercise session that is sufficiently prolonged and intense to cause sweating and a rapid heartbeat?

- ☐ At least three times
- ☐ Normally once or twice
- ☐ Rarely or never

#2 Intensity

When you engage in structured physical activity or an exercise session, do you have the impression that you:

- ☐ Make a vigorous effort (e.g. jogging)
- ☐ Make a moderate effort (e.g. brisk walking)
- ☐ Make a light effort (e.g. standing, light house work, shopping, light gardening)

#3 Perceived Fitness

In a general fashion, would you say that you current physical fitness is:

- ☐ Very Good
- ☐ Good
- ☐ Average
- ☐ Poor
- ☐ Very Poor

B. Circle you score for each answer and total your score.

Item	**Male**	**Female**	**Male**	**Female**	**Male**	**Female**
#1 Frequency	Rarely or never		Normally once or twice		At least three times	
	0	0	2	3	3	5
#2 Intensity	Light effort		Moderate effort		Intense effort	
	0	0	1	2	3	3
#3 Perceived Fitness	Very Poor or Poor		Average		Good or Very Good	
	0	0	3	1	5	3

Total Score = _________

Scoring

C. Step 1 Add 1 points to your total score from B for each of the following that apply:

- You engage in Active Transport on a daily basis where you walk or cycle to your job, school, shopping, social events, take stairs wherever possible, etc.
- You engage in Daily Activities of Living such as house cleaning, mowing the lawn, cooking, doing laundry, ironing, light gardening for more than 2 hours a day at least 3 times each week.
- You have an active job where you are standing, walking for most of your work shift

Step 2 Subtract 2 points for each of the following that apply:

- You Drive everywhere, use elevators and escalators regularly
- You have a sedentary occupation where you sit for the majority of your work day or more than 2 hours at a time

D. Final PALM PAPS Score = Total Score + Step 1- Step 2 [Note: Assign 0 to any negative Final Scores]

Final PALM Score = ___________________

Use Tables 4-1 and Table 4-2 to determine and interpret your health benefit zone rating based on your Final PALM Physical Activity Participation and Sedentarism Score (PALM PAPSS) from the calculation in D.

Table 4-1 Health-Related Physical Activity Participation and Sedentarim Score– Determination of Health Benefit Zones

Health Benefit Zone	**FINAL HRPAPS Score**
Excellent	≥ 9
Very Good	6-8
Good	4-5
Fair	1-3
Needs improvement	0

Table 4-2 Interpret the Derived Health Benefit Zone Rating

Health Benefit Zone		
Excellent	↑	Your physical activity participation falls within a range that is generally associated with maximizing health benefits.
Very Good	↑	Your physical activity participation falls within a range that is generally associated with considerable health benefits.
Good	↑	Your physical activity participation falls within a range that is generally associated with many health benefits
Fair	⇧	Your physical activity participation falls within a range that is generally associated with some health benefits but also with some health risks. Progressing from here into the GOOD zone is a very significant step to increasing the health benefits from your physical activity participation.
Needs improvement	↑	Your physical activity participation falls within a range that is generally associated with considerable health risks. Try to reduce your sedentary time for at least 10 minutes per waking hour PLUS work towards accumulating at 150 minutes of moderate to vigorous intensity of physical activity/ week.