The Use of a Verification Phase in Determination of VO_{2max} in Older Adults

by

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ABSTRACT

Maximal oxygen uptake (VO_{2max}) declines with age and is a predictor of morbidity and mortality risks. Due to these implications, accurate assessment and determination of VO_{2max} are important for the older population. Without the presence of a VO_2 plateau, secondary criteria are used to determine whether the test resulted in a maximal value. However, inconsistent secondary criteria do not account for intersubject variability. To circumvent this issue, a verification phase following a traditional ramp assessment may be utilized. The purpose of this study was to compare verification phase strategies in older adults. A secondary purpose of this study was to examine the repeatability of the ramp assessment performed during each visit. Twenty-two older adults between 60 and 80 years of age were recruited to participate in the study. Each subject completed two experimental trials in a randomized, counterbalanced cross-over design. Both trials consisted of a ramp test and verification phase at either 85% (VP85) or 110% (VP110) of the peak work rate achieved during the ramp (Ramp85 and Ramp110, respectively). Expired gases and heart rate (HR) were monitored continuously and measured every ten seconds. VO_{2peak} was determined by the highest 30-second averages for the ramp and verification phases. No significant differences were observed for absolute (L/min) VO_{2peak} between VP85 ($P = 0.679$) or VP110 ($P = 0.200$) and the associated ramp. There was also no significant difference in maximal HR between VP85 ($P = 0.243$) or VP110 ($P = 0.085$) and the associated ramp. However, individual data shows that 36% of individuals achieved a 2% greater VO_2 (L/min) during the VP85 compared to the Ramp85, while only 15% of subjects achieved a 2% greater VO_2 (L/min) during the VP110 compared to Ramp110. No significant differences ($P < 0.05$) were found for most variables between Ramp1 and Ramp2. These data suggest that if a verification phase is employed for VO_{2max} assessment in otherwise healthy older adults, a power slightly below peak work rate may provide a more accurate assessment compared to a power slightly above peak work rate.

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CHAPTER ONE

INTRODUCTION

Maximal oxygen consumption (VO_{2max}) and the measurement of VO_{2max} have been of interest over the last century due to its use as an indicator of health and aerobic performance (1-4). Traditionally, VO_{2max} is often assessed through the use of a graded exercise test, employing either a ramp or incremental-step test until volitional exhaustion of the participant. More specifically, an incremental step test uses a constant load for a designated period of time (e.g., ~2-3 minutes) before increasing the work rate, while a progressive ramp frequently increases the load at a set amount throughout the duration of the test (e.g., 30W/min using frequent changes in work rate every few seconds). By definition, VO_{2max} is achieved when a plateau is VO_2 is observed (3, 5-7), for instance, no change in VO_2 (≤ 150 ml/min) with an increase in exercise intensity (8). However, a plateau in VO_2 has been found to only occur in 17% of assessments (7), which has produced queries as to the validity of these tests for accurately assessing VO_{2max} (7, 9, 10). Given the importance of VO_{2max} as a predictor of cardiovascular disease risk (1, 2), particularly in at risk populations, identifying strategies to accurately assess VO_{2max} may provide an avenue to better identify individuals at risk for cardiovascular disease as well as those with increased risk of morbidity and mortality.

Currently, a lack of accepted standards makes it difficult to determine whether a “true max” has been attained during an exercise test (7, 9, 11). In the situation where a plateau in VO_2 does not occur, researchers use secondary criteria to distinguish between a VO_{2peak} and a true VO_{2max}. The most commonly used secondary criteria include a mixture of a respiratory exchange ratio (RER) ≥ 1.00, 1.10, or 1.15, a maximal heart rate (HR) within 10 bpm of the subject’s age-predicted maximum, a rating of perceived exertion (RPE) ≥ 18, and blood lactate concentrations ≥ 8mmol/L (5, 11, 12). Despite the acceptance of these secondary criteria, there is a lack of standard

thresholds for these criteria. For example, Midgley et al. found eight different cut points that have been used for respiratory exchange ratio (RER) that would indicate a maximal test (11). Further, these secondary criteria thresholds also do not account for inter-subject variability that occurs with exercise testing (11). To circumvent this issue, the use of a verification phase has been implemented as a strategy to assess VO_{2max} (9, 10). Specifically, a verification phase is a constant-load exercise bout that is performed following a graded exercise test. Verification phase tests have been performed at either submaximal (7, 13-15), maximal (16), or supramaximal (9, 10, 13-15, 17-25) work rates relative to the peak exercise work rate achieved during the preceding graded exercise test. For example, most previous studies have employed verification phase test between 85-115% of peak power output achieved (9, 10, 13-27). In addition, time/rest periods between the ramp and the verification phase have ranged between 3 min to 1 week (9, 10, 13-27). Verification phase tests have been shown to result in similar (7, 9, 10, 14-19, 22, 23, 25-27), or higher (25), VO_2 values relative to that achieved during a ramp test. To our knowledge, no studies have reported a lower VO_{2peak} during the verification phase compared to the ramp test. This discrepancy in findings may be the result of various strategies employed, including the work rate at which the verification phase is performed (24, 28). To what extent the work rate of the verification phase impact measures of VO_2 and other variables is relatively unexplored.

It is known that VO_{2max} decreases with advancing age (1, 2). Moreover, a reduced VO_{2max} in older adults is associated with functional limitations such as difficulty walking, climbing stairs, and performing daily activities (29). These functional limitations are associated with increased dependency and rising healthcare costs (29). The age-related decline in VO_{2max} is attributed to various components of the Fick equation, which states VO_2 is equal to the product of cardiac output [HR x stroke volume (SV)] and arteriovenous oxygen difference (a-vO_2-difference). In particular, it is well described that maximal HR decreases with age such that maximal HR is approximately 20-25% or 20-30 bpm lower in older adults (~80 years old) when compared to younger individuals (30-

32). On the other hand, SV has been reported to decrease (32-35), increase (36-39), or not be affected by advancing age (30, 31, 39, 40), however, these discrepancies in the findings may be attributed to methodological differences between studies (41). Moreover, while researchers have found that maximal a-vO_2 difference is not affected by age (39), half of the reduction in VO_{2max} with aging may be related to the loss of skeletal muscle mass (42). Given that VO_2 is a strong predictor of morbidity and mortality and it is known to be reduced with advancing age, an accurate assessment of VO_{2max} in older adults has clinical relevance, particularly in older adults with a relatively low VO_{2max}. Consequently, identifying the variability and improving the accuracy for assessment of VO_{2max} in older adults could enhance the ability to identify individuals who are at risk for cardiovascular disease, functional limitations, difficulty with activities of daily living, and increased risk of morbidity and mortality.

SPECIFIC AIMS AND HYPOTHESES

The primary purpose of this study is to assess the utility of a verification phase test performed at different work rates for the determination of maximal oxygen consumption (VO_{2max}) and maximal heart rate in healthy older adults. Secondarily, this study will also examine to what extent similar maximal VO_{2max} and maximal HR values are obtained when performing a ramp test on two separate occasions. This study will pursue the following specific aims:

Specific Aim #1: To determine the extent to which verification phase work rate impacts values obtained for VO_{2max} and maximal HR.

Hypothesis #1: A verification phase performed slightly below (85%) peak work rate will elicit higher values for VO_{2max} and maximal HR compared to a ramp test whereas a verification phase performed slightly above (110%) peak work rate will elicit similar values VO_{2max} and maximal HR compared to a ramp test.

Specific Aim #2: To determine the repeatability for values obtained for VO_{2max} and maximal HR during two identical ramp tests completed on different days.

Hypothesis #2: There will be no difference in the values obtained for VO_{2max} and maximal HR during two ramp tests completed on different days.

CHAPTER TWO

REVIEW OF LITERATURE

I. INTRODUCTION TO REVIEW OF LITERATURE

This review of literature is largely focused on exercise physiology, with an emphasis on the metabolic processes through which adenosine triphosphate (ATP) is resynthesized using aerobic processes. Emphasis is also placed on the measurement of VO_2max/VO_2peak. In particular, this Thesis is focused on the measurement of VO_{2peak} in older adults, and therefore, the literature review will include discussion of the physiological factors contributing to VO_{2max} and how those are impacted with advancing age. The historical perspectives behind VO_{2max} testing will also be discussed and how testing has evolved over time. Special attention will be given to the use of a verification phase to measure VO_{2max}, including the demographics it has been studied in and why it is a useful additional step during VO_{2max} testing.

II. OVERVIEW OF METABOLIC PROCESSES RELATED TO ATP RESYNTHESIS AND OXYGEN CONSUMPTION

Bioenergetics is the process of converting the energy contained in the substrates we ingest (i.e., the food we eat), namely carbohydrates or fatty acids, into usable energy in the form of ATP. The primary focus of this section will be the complete oxidation of substrates. Glycolysis is the initial process for converting glucose (free or derived from glycogen) into acetyl-CoA whereas beta oxidation is the process of preparing acetyl-CoA from fatty acids. The aerobic metabolism system consists of the Krebs cycle, electron transport chain, and beta oxidation. Glycolysis yields NADH+H while the Krebs cycle yields NADH+H and $FADH_2$. These electron carriers transport electrons obtained from each of these systems to the electron transport chain that serves as an important step for ATP resynthesis. These systems are discussed in more detail below.

Glycolysis is a metabolic process that takes place in the cytosol and begins with free glucose or glucose derived from glycogen (storage form of glucose in the cell). This process consists of ten to twelve different reactions and ultimately yields a net gain of two ATP when originating with glucose or three ATP when originating with glycogen. To prepare the glucose molecule to undergo glycolysis, two ATP are initially used. Glycolysis is largely controlled at the rate-limiting step, a reaction catalyzed by the enzyme phosphofructokinase (PFK). At this step the cell commits to the resynthesizing ATP through glycolysis and the activity of PFK is allosterically regulated by several factors that activate its activity (i.e., increases in AMP or excess phosphate) or inhibit its activity (i.e., a high ratio of ATP to ADP or reductions in pH). The 6-carbon glucose molecule is split into 2, 3-carbon molecules that will then undergo identical reactions. Of note, during the conversion of glyceraldehyde-3-phosphate to 1.3 bisphosphoglycerate, an NADH+H is produced. An ATP will be yielded during the conversion of 1.3 bisphosphoglyerates to 3-bisphosphoglyercates. The final reaction of glycolysis, the conversion of phosphoenol pyruvate to pyruvate will produce another ATP. Each of the above reactions occur twice from a given glucose molecule. Thus, in addition to a net gain of 2-3 ATP, glycolysis yields 2 NADH+H, and 2, 3-carbon pyruvate molecules. Pyruvate can be converted to lactate, acetyl-CoA, or oxaloacetate. Fates of lactate include diffusion into circulation, conversion back to pyruvate where it can be oxidized by other muscles or muscle fibers, or conversion to glucose in the liver.

Complete oxidation of glucose requires entry of the carbons into the Krebs cycle. There is a preparatory step prior to the Krebs cycle in which the 3-carbon pyruvate is converted to a 2-carbon acetyl-CoA in the mitochondria through the pyruvate dehydrogenase complex. This reaction produces a CO_2 and also reduces an NAD to form NADH+H. The primary function of the Krebs cycle, which takes place in the mitochondria, is to produce electron carriers (NADH+H and $FADH_2$). Each “turn” of the Krebs cycle (i.e., for each pyruvate that enters the Krebs cycle) yields 3 NADH+H, 2 CO_2, 1 $FADH_2$ and 1 ATP (GTP). Given that each 6-carbon glucose molecule results in two, 3-

carbon pyruvate molecules from glycolysis, each glucose molecule will yield two “turns” of the Krebs cycle, thus producing a total of: 6 $NADH+H^+$, 4 CO_2, 2 $FADH_2$ and 2 ATP. The first step in the Krebs cycle produces citrate from Acetyl-CoA and oxaloacetate, a reaction catalyzed by citrate synthase. Through a series of 8 reactions, oxaloacetate is reformed, completing the cycle.

The electron carriers ultimately deliver their electrons to the electron transport chain to take part in oxidative phosphorylation. The electron transport chain consists of four complexes used to pass electrons and produce a proton (H+) gradient across the inner mitochondrial membrane, which is necessary to provide the energy to resynthesize ATP. Electrons carried by NADH+H are first delivered to complex I, NADH Dehydrogenase, where NADH+H is oxidized to NAD^+. Two electrons are released into complex I where they will pass through the Flavin mononucleotide (FMN) and the iron centers. The electrons bind to Ubiquinone creating Ubiquinol and are transferred to complex III. This transfer of electrons results in 4 protons pumped from the mitochondrial matrix into the intermembrane space. At Complex III, or Cytochrome-C oxidoreductase, Cytochrome-C will oxidize Ubiquinol and pass the electrons to Cytochrome-C. During this process, 4 more protons will be pumped into the intermembrane space. Cytochrome-C will transport the electrons from complex III to complex IV. In complex IV, or Cytochrome oxidase, oxygen serves as the final electron acceptor and is reduced to water. During this process another 2 protons are pumped into the intermembrane space. The hydrogen ions pass from the intermembrane space through Complex V, or ATP synthase. In general, for every 4 hydrogen ions that pass through Complex V, an ATP is resynthesized. Each NADH+H that passes it electrons through the ETC will thus lead to the resynthesis of 2.5 ATP (10 total protons pumped out, 4 protons required for ATP resynthesis).

The major difference between electrons carried by NADH+H and $FADH_2$ is that electrons carried by $FADH_2$ are not delivered to complex I, but rather are first delivered to complex II, succinate dehydrogenase. Electrons transfer from complex II to complex III ensuing processes as

described above. Bypassing complex I, electrons carried by $FADH_2$ results in a total of six protons pumped to the intermembrane space. As a result, each $FADH_2$ generated results in the resynthesis of 1.5 ATP.

The ability to resynthesize ATP through aerobic metabolism relies on the amount of oxygen within the cell. Adaptations to an aerobic exercise regimen occur that result in the cells being able to utilize more oxygen. This includes the improvements in transporting oxygen through the vascular system and the ability to extract more oxygen at the tissue level. Specificity, as noted above oxygen serves as the final electron accepter in the ETC. When more electrons are delivered to the ETC, as occurs with training and increased mitochondrial content (43), more oxygen is needed to accept those electrons.

III. PHYSIOLOGICAL FACTORS CONTRIBUTING TO VO_{2MAX}

VO_{2max} is dependent on the ability to efficiently transport oxygen to the mitochondria at the exercising tissue and the ability to extract the oxygen from the blood as it moves through the vascular system. The physiological factors that can influence VO_2 are cardiac output (Q), heart rate (HR), stroke volume SV), and a-vO_2 difference. These factors make up the Fick equation, $VO_2 = Q$ (SVxHR) x a-vO_2 difference. The product of SV and HR is cardiac output. Below, various factors that may influence VO_2 will be discussed and how each of these variables are impacted by advancing age.

A. Heart Rate

The heart serves as the pump to continuously circulate blood throughout the body. Measured in beats per minute (bpm), HR can be assessed through palpation or various HR monitors. The Sinoatrial (SA) node controls when the heart beats through the autonomic nervous systems (ANS). Without stimulation from the ANS, the intrinsic HR is approximately 100-110 bpm

(44). The parasympathetic nervous system slows down HR and the sympathetic nervous system will increase HR. At rest, the parasympathetic nervous system suppresses the HR to ~60-80 bpm, however, this value is reduced by fitness/exercise training (45). The endocrine system also regulates HR. For example, the hormones norepinephrine and epinephrine increase HR.

As discussed briefly above, a lower resting heart rate can be used as an indicator of cardiovascular fitness. During exercise parasympathetic activity is suppressed to increase HR closer to the intrinsic rate and then activity of the sympathetic nervous system will increase HR as work rate increases. In untrained individuals, resting HR values will be greater and rise at a steeper slope as exercise work rate increases in comparison to trained individuals (46), who have lower resting value and will take a longer period of time at a higher absolute work rate to reach HR_{max}.

1. Impact of Aging

Maximal HR has typically been estimated by the equation HR_{max} = 220 – age (5). However, this equation has been found to underestimate the HR_{max} of older individuals. Tanaka et al. determined that the equation HR_{max} = 208 - 0.7 x age may be a more appropriate equation for a healthy population over 40 years of age (47). HR_{max} in older individuals ~80 years of age has been found to decline by ~20-25% or about 20-30 bpm, which may begin as early as 30 years of age (30-32). While it is not completely understood why maximal HR decreases with age, it may be attributed to a reduction in the intrinsic activity of the heart (48), meaning the sinoatrial node causes a contraction at a lower rate. These decreases contributes to a decline in maximal cardiac output and therefore a reduced VO_{2max} with advancing age.

B. Stroke Volume

Stroke Volume (SV) is defined as the amount of blood ejected from a specified ventricle during each beat of the heart. SV is described using the equation SV = End Diastolic Volume (EDV)

– End Systolic Volume (ESV), where EDV is the amount of blood in the ventricle prior to contraction, and ESV is the remaining volume of blood after ejection (49). Normal resting SV values for healthy adults range from ~70-100 ml. During exercise, SV is largely regulated through venous return and contractility (see below) and will increase until it plateaus at ~40% of VO_{2max} in a non-competitive population. However, in elite endurance athletes, SV will increase up to VO_{2max} (50).

Valves within the veins ensures that blood can only go towards the heart. Thus, when muscle around the veins contract, blood is "milked" back toward the heart, a process referred to as the muscle pump. In addition, the respiratory pump will also assist in returning blood to the heart by creating a pressure gradient between the chest cavity and the veins during inhalation to draw blood into the vena cava. Collectively, the muscle pump and respiratory pump increase venous return, allowing more blood to enter the heart. Thus, during exercise, the amount of blood returned to the heart will increase as a result of these "pumps". When there is more blood in the ventricle, the length-tension relationship of the cardiac muscles will be at an optimal alignment. The heart will respond to this optimal alignment by contracting more forcefully through the Frank-Starling mechanism (49). Exercise training will increase both resting and maximal exercise SV. This adaptation will increase VO_2 assuming HR does not change at maximal exercise (49).

1. Impact of Aging:

There has been conflict in the literature on how SV responds to maximal exercise and this conflict is present in older individuals as well. During exercise, maximal SV has been reported to decrease (32-35), increase (36-39), or not be affected by aging (30, 31, 39, 40). These differences may be attributed to methodological difference between studies (41). Carrick-Ranson et al. state that SV_{max} does not decline with age when normalized to total body mass, but it increases when normalized to LBM (39). Shibata et al. (51) found that it may be a decrease in the function of the Frank-Starling mechanism and a greater instance arterial stiffening may account for a decrease in

SV_{max}. Arterial stiffening will reduce the ability for the heart to contract forcefully. These effects of advancing age on stroke volume and heart rate will in turn influence cardiac output.

C. Cardiac Output

Cardiac output is the amount of blood that cycles through the heart during a given period of time, typically measured in liters per minute (L/min). Cardiac output is the product HR and SV and is mainly regulated by the need for oxygenated blood throughout the body. It is influenced by the same factors as HR and SV. Cardiac index is the amount of blood cycled through the heart normalized to the subject's size. At rest, cardiac output is ~5 L/min in an adult, depending on body size. As the work rate of exercise increases, so will the need for more oxygenated blood throughout the body increasing cardiac output ~4-7x the resting values. These maximal exercise values can be influenced by training. For instance, the maximal cardiac output of a trained individual can be increased to about 30 L/min, however, the resting cardiac output will be unchanged (49).

1. Impact of Aging

Maximal cardiac output will decrease with age partially due to a decrease in maximal HR, as described above. However, Ogawa et al. determined that decreases in HR_{max} only accounts for ~28% of decreases in cardiac output (33). Decreases in HR may also increase filling time causing an increase in SV. The declines in maximal cardiac output with age may also be associated with a decrease in SV during maximal exercise (32-35, 52). This decrease in cardiac output will cause a reduction in VO_{2max} due to reduced oxygen delivery. Therefore, this decline in cardiac output is directly linked to the decrease in VO_2 and increases in morbidity and mortality risks with advancing age.

D. Arteriovenous Oxygen Difference

The arteriovenous oxygen difference (a-vO_2 difference) is the difference in oxygen content in the arterial blood and the venous blood. It is used to estimate how much oxygen is extracted by the mitochondria. a-vO_2 difference can be assessed non-invasively by back calculation with the use of a Physioflow (Manatec Biomedical, Petit Ebersviller, France) which estimates cardiac output, or a similar device (CN systems, Graz, Austria). Using the Fick equation, the known VO_2 and cardiac output allow for the calculation of a-vO_2 difference. a-vO_2 difference can also be assessed by the use of a fiberoptic catheter that can continually monitor a-vO_2 difference. Resting values for a-vO_2 difference are ~5mlO_2 per 100ml of blood. These values will increase to 17-18mlO_2/100ml blood with the increased demand for oxygen in the muscle cell during intense exercise. a-vO_2 difference can be influenced by the amount of blood flow to the exercising muscles. Exercise training can improve a-vO_2 difference slightly at rest and at maximal exercise (53). This improvement will lead to an improvement in VO_{2peak}.

1. Impact of Aging:

a-vO_2 difference has been shown to decline with age (33, 39, 54). However, these reductions in a-vO_2 difference may be attributed to detraining opposed to the aging process as aerobic exercise training can improve a-vO_2 difference in adults over the age of 60 (39). Similar to younger subjects these adaptations are due to increases in mitochondrial density and enzymatic activity (55), increased vasodilator response and redistribution of blood flow to exercising muscle mass (56).

E. Slow Component

Another factor that can influence the measurement of VO_2 is the VO_2 slow component. The slow component of VO_2 can be described as the continued rise in VO_2 beyond the third minute of

constant-load exercise (57) and can account for ≥ 25% of the increases from baseline VO_2 (58). Examples of the slow component have been seen as far back as a study performed by August Krogh in 1913 (59) and again in 1923 during a study by A.V. Hill (3). In both cases, the resulting VO_2 was explained by other circumstances. This is most likely because it did not fit known VO_2 models at the time. More recently, Gaesser and Poole state that there is a distinct difference between slow component and oxygen drift (57). Typically, during prolonged moderate exercise VO_2 may increase < 200 ml of O_2 without an increase in blood lactate concentration. This is commonly known as O_2 drift (57). On the other hand the VO_2 slow component can increase VO_2 slightly during intense exercise above the lactate threshold lasting ~3 minutes (57).

While there are a plethora of possible causes, the origin of the VO_2 slow component originates from the exercising muscle mass (57). It has been hypothesized that the accumulation of lactate could be the main cause of the increases in VO_2 (57). Ryan et al. found that by injecting sodium lactate into the blood, they were able to raise VO_2 by 129 ml/min (60). Other researchers also hypothesized that it is not the increase in lactate itself, but the decrease in blood pH that is the reason for increases in VO_2 (61, 62). Other hypothesized causes are increased core temperatures, (63, 64), recruitment of type II muscle fibers (65-67), and reduced chemical-mechanical coupling efficiency (63, 68, 69). The slow component of VO_2 has primarily been identified during constant-load submaximal exercise on a cycle ergometer and may result in a VO_{2max} at these work rates (57). This notion that a maximal VO_2 can be attained during submaximal exercise is the rationale behind using a verification phase below 100% of peak work rate, which will be discussed later.

F. Lean Body Mass

Lean body Mass percentage (LBM%) is the amount of non-fat tissue in the body. Lean body mass can be assessed a number of different ways, such as the use of skinfold calipers or a Dual Energy X-ray Absorptiometry (DEXA) scan. Knowing LBM is crucial because during aerobic

exercise ~95% of oxygen is consumed in the exercising muscle mass (70). Muscle mass is also known to decrease throughout the aging process starting at 30 years of age (70). Moreover, Jackson et al. determined that this decline to be at about 2.8 kg per decade (71). These declines influence VO_2 ability at the cellular level.

VO_{2max} can be expressed in absolute measures (mL/min or L/min) or in relative to body mass. Relative VO_{2max} (ml/kg/min) may be a better representation than absolute measures as it is based on body mass. This makes it easier to generalize across demographics. A study by Maciejczyk et al. identified that regardless of cause, a higher body mass will decrease relative VO_{2max} (72). This is due to the mass component. When oxygen consumption is divided by mass, an increase in body mass will decrease overall VO_2. Relative VO_2 (ml/kg/min) may not be the best way to represent VO_{2max} due to 95% of the oxygen is being used in the exercising muscle (70). Therefore, VO_{2max} normalized to LBM may be a more accurate representation (70). For instance, Ogawa et al. determined that normalizing VO_{2max} values to LBM instead of overall body weight decreases the difference between young and older subjects (33). Similarly, Proctor et al. determined that relative VO_2 (ml/kg/min) values were 24-34% lower in older subjects when compared to younger subjects (33, 73), however, when normalizing for LBM, VO_{2max} values in older subjects were found to be 16-17% lower than in the younger subjects (74). These differences indicate that comparing the different measures of VO_2 may be more ideal so that the research can determine an accurate measurement.

Normalizing measurements to lean body mass is not just restricted to VO_2 measures. Normalizing to LBM can help differentiate other variables between the young and old populations. When normalized to LBM, cardiac output differences between old and young subjects decreased from 26% to 17%. (33). Ogawa et al. normalized SV to weight and they found older subjects differed from young individuals by 19% (33). When SV was normalized to LBM the relative difference

decreased to 9-13% in trained older individuals (33). These findings show that normalizing variables to LBM influences comparisons across the age demographics.

1. Impact of Aging:

Throughout the aging process, many physiological changes occur and the loss of muscle strength and VO_{2max} are among the most important and clinically relevant . Loss of muscle mass and strength with age can partially be associated with a decline in physical activity (2). Fleg et al. found that ~50% of reductions in VO_{2max} with advancing age may be due to decreases in lean body mass (42). These declines in LBM may be associated with a decrease in physical activity with age. Reductions in physical activity will lead to decreases in mitochondria, which will decrease the ability to extract oxygen. This will in turn lead to a decline in VO_{2max} and an increased risk of morbidity and mortality (1, 2).

IV. HISTORICAL PERSPECTIVES OF THE MEASUREMENT OF VO_{2max}

Over the last century the study of exercise physiology, metabolism, and VO_{2max}, has advanced greatly with numerous discoveries and contributions to the field. This includes; the grandfather of exercise physiology, August Krogh; Otto Meyerhof, the discoverer of glycolysis; the influence of the Harvard fatigue lab and some of its contributors; John Scott Haldane, who determined that oxygenated blood will carry less carbon dioxide; and Henry Longstreet Taylor, who was the first to implement “grade” in maximal exercise testing.

A. August Krogh

August Krogh was a Danish professor at the University of Copenhagen in the department of zoophysiology. He believed that “For many problems there is an animal on which it can be most conveniently studied” (75). Krogh used animal models as one of the first steps of the scientific

process. This process follows today as many research questions are initially pursued using animal studies. He studied oxygen deficit and diet as well as respiratory quotient during exercise. Krogh was one of the first pioneers of exercise testing and oxygen consumption during exercise (59). Exercise was performed on a stationary bicycle while the subject breathed into a mouthpiece connected to a spirometer. They found that at rest, the subject consumed 300 mL of O_2, and at higher work rates, the subject utilized ~2 liters of O_2 (59). Later, in 1920 he won the Nobel Prize in for his work on capillary diffusion. He determined the partial pressures needed to facilitate oxygen transportation to the muscles (76).

B. Otto Meyerhof

Otto Meyerhof was a German professor who won a share of the Nobel Prize for Medicine and Science in 1922 (with Archibald Vivian Hill) for determining the fixed relationship between lactate metabolism and VO_2 at the muscle level. Meyerhof is known for the discovery of glycolysis, which is also referred to as the Embden-Meyerhof pathway. He determined that in the presence of oxygen, lactate will be reconverted into pyruvate to be used as an energy source for ATP production (77).

C. Archibald Vivian Hill

Archibald Vivian (AV) Hill was an English professor who won a share of the Nobel Prize for Physiology or Medicine in 1922 (shared with Otto Meyerhof). Along with his work in muscle metabolism, he also formulated the length-tension relationship and the force-velocity relationship (78). AV Hill's work is relevant because he was one of the first exercise physiologists to study VO_2 and paved the way for current exercise testing.

In his experiments he examined the amount of oxygen that is needed during both resting and severe exercise domains (3, 79). Hill determined that during rest, the oxygen requirements are

lower than while running. Hill had his subjects run along a track while connecting a mouthpiece to a bag that was strapped to their back (3). The air samples were then analyzed for composition of carbon dioxide and oxygen. In addition, AV Hill also studied oxygen debt, when the amount of required oxygen cannot be met by the “income” of oxygen through ventilation (79). When oxygen intake matches oxygen requirements, it is considered steady-state, and typically occurs 2-3 minutes after exercise intensity changes (5).

D. Harvard Fatigue Lab

Opened by Lawrence Joseph Henderson in 1927, the Harvard Fatigue Lab was established to study the industrial workers. The idea was to study the “normal man” and the physical and mental effects of work. The lab studied fatigue by observing humans on a treadmill or a cycle ergometer and by measuring variables before, during, and after exercise. The lab produced articles on blood and oxygen transportation throughout the vascular system (80).

David B. Dill arrived in 1925 and served as the research director at the Fatigue Lab until it closed in 1947. His primary role at the lab was first to set up the lab and coordinate the various research projects. Along with Henderson, Dill studied the gas exchange differences during exercise (81). The lab itself was initially comprised of two rooms in the Harvard business building and later grew to add a third room. The Harvard Fatigue lab expanded to include a lab at Wright Air Force Base. While these were two of the main facilities, multiple field labs were set up to conduct experiments in differing environments.

During the ~20 years the fatigue lab was open, two PhD students graduated. Sid Robinson and Steven Horvath. Robinson, started his career as a middle distance runner and competed in the 1928 Olympics. He began his PhD in 1936 at Harvard Fatigue lab and graduated in 1938. The following year, he join the faculty at Indiana University and became the chair of the Department of Anatomy and Physiology. Horvath, who was both one of Dill’s students and his son-in-law, worked

at the various labs during his career, including time at Fort Knox, the south pacific, and the Arctic during WWII. In 1961 He moved on to the University of California, opening the Institute of Environmental Stress.

Throughout World War II, the Harvard Fatigue Lab performed experiments to test metabolic costs of extreme heat and cold on soldiers. This included cold weather clothing, sleeping bags, and tents in a chamber that could be set to -40 degrees Fahrenheit. Heated flight suits were also tested in the laboratory before being field tested and issued to high-altitude flight crews.

E. John Scott Haldane

John Scott Haldane was a Scottish physiologist born in the 1860's. His work on the pulmonary system, sometimes on himself, led to the invention of the first gas mask in WWI. He also discovered what is now known as the Haldane effect. The Haldane effect states that deoxygenated blood can carry more amounts of carbon dioxide while oxygenated blood will not be able to carry as much carbon dioxide (82). Haldane first created a decompression chamber in 1907 and experimented on mice to prove carbon monoxide binds to hemoglobin in red blood cells (83). In humans, Haldane studied the influences of various concentrations on the human body. This crucial finding shows that with an increased affinity for carbon monoxide, the red blood cells will not be able to perform its role in oxygen transportation (83).

F. Henry Longstreet Taylor

Born in Minnesota, Henry Longstreet Taylor worked and trained at the Harvard Fatigue Lab while attending Harvard Medical School. Taylor returned to University of Minnesota to he complete his Ph.D. in physiology in 1941. After graduation he accepted a position at the Laboratory of Physiological Hygiene. He studied cardiovascular disease and physical activity while working with firefighters and railroad workers. Through his work, Henry Longstreet Taylor became

instrumental in establishing VO_{2max} exercise testing as the standard for aerobic capacity. While exercise testing, Taylor also implemented “grade” while treadmill testing (8). This implementation elicits a VO_2 plateau when subjects may not be able to physically run fast enough to keep up with the treadmill (8).

V. METHODOLOGICAL CONSIDERATIONS FOR MEASURING OF PEAK OXYGEN CONSUMPTION

Over the last 100 years it has been determined that VO_{2max} is an important physiological measure related to both health and performance. Thus, assessment techniques have been modified to improve the accuracy of these tests. Today, VO_{2max} can be assessed via submaximal exercise tests and maximal exercise tests. Maximal exercise tests utilize indirect calorimetry to determine VO_2, while submaximal exercise tests often estimate VO_{2max} through submaximal exercise HR and using prediction equations or nomograms to predict VO_{2max}.

A. Submaximal Protocols

Submaximal exercise tests to estimate VO_{2max} are used on the basis that HR response and VO_2 are linearly related. As HR increases, VO_{2max} will also increase. Submaximal tests are either single stage or multistage tests that are used to increase HR and to estimate a VO_{2max}. A single stage test uses one continuous work load for the duration of the test, while multistage tests will increase the resistance after a given period of time (5). Some tests, like the Astrand-Ryhming cycle ergometer test, use nomograms and known values of HR, work rate and watts to estimate VO_{2max} (84). As it was originally published, the Astrand-Ryhming nomogram underestimated VO_{2max} and has been modified by other researchers (85). Submaximal VO_2 tests can be more practical due to not needing specialized equipment such as a metabolic cart and multiple people can be assessed at one time. However, submaximal exercise protocols may underestimate VO_{2max} compared to a

traditional maximal exercise test. For instance Grant et al. determined that some submaximal running assessments underestimate VO_{2max} by 8-24% depending on the submaximal protocol when compared to a maximal treadmill VO_{2max} test (86). On the other hand, submaximal exercise assessments on a cycle ergometer have been found to overpredict VO_{2max} in untrained individuals and underestimate VO_{2max} in trained individuals (87). Submaximal exercise assessments may be used to estimate VO_{2max}, however, it is difficult to determine without a true VO_{2max} assessment.

B. Maximal Protocols

Maximal exercise tests are used to determine VO_{2max} by measuring expired air through the use of Douglas bags or real time analysis such as metabolic carts (i.e., Parvomedics). Douglas bags are large rubberized bags that can be used to collect expired air samples as a participant exercises. The air samples are analyzed to determine the percentage of carbon dioxide and oxygen. Air samples are also assessed to determine the volume of expired air over the time in which it was collected. These analyses are generally performed after the exercise is completed making it difficult for researchers to track progress during the test.

Real time analysis can be used to help eliminate human error that may be present with the use of Douglas bags. Real time analysis is done by attaching a hose or mask to the device and it measures the percentage of carbon dioxide and oxygen in the expired air as well as the volume of air expired (or inspired). This also allows researchers to determine any discrepancies real time during the test. Maximal exercise tests are either performed using a ramp stage or an incremental stage until volitional exhaustion. Relative to submaximal tests, maximal tests are more strenuous as the subject is pushed to its maximal performance and are dependent on the subject pushing to volitional exhaustion.

C. Treadmill Exercise Testing

Treadmill maximal exercise testing is typically performed as a progressive ramp or incremental stages. Incremental exercise tests increase speed and or percent grade at given intervals of ~2-3 minutes depending on protocol. Progressive ramp tests increase difficulty at a gradual rate set by the researcher. There are specific protocols that have been come standards. For example, the Bruce protocol is an incrementally staged test (88). It begins the first stage with the speed at 1.7 mph and the grade at 10%. As the test continues, the grade increases by 2% and the speed increases at different rates until volitional exhaustion. The Bruce protocol can also be modified for a less athletic population such as elderly or sedentary subjects. The Modified Bruce protocol begins at 1.7mph and 0% grade and a second stage continues at 1.7mph and 5% grade. From this point on, the Modified Bruce protocol is the same as the original Bruce protocol.

The Balke protocol (89) is similar to the Modified Bruce test as it is typically used for the less athletic population. The Balke protocol maintains a constant speed throughout the test while the gradient is increased to 2% after the first minute and then 1% every minute after until volitional exhaustion. The increased recruitment of whole body muscle mass during exercise leads to more accurate VO_{2max} assessments in most populations. In a review by Beltz et al. they found this VO_2 to be up to 20% higher during treadmill testing (90).

D. Cycle Ergometer

Cycle ergometer maximal exercise tests are performed as a ramp test or an incremental stage test. Like the treadmill protocols, cycle ergometer testing protocols can be adjusted to meet the needs of the individual. The elite level subjects would require a greater number of watts at the beginning of the test and require a larger increase at each interval. Figueira et al. began at 75W and increased work rate by 35W every 3 minutes for elite cyclists while Roffey et al. started recreationally active subjects at 50W and increased at 30W every 3 minutes (91, 92). Cycle

ergometers may also be easier to assess other measures such as exercising blood pressure due to less artifact being produced during exercise (93). This mode of exercise may be considered safer in certain populations because the subjects can stop pedaling when they reach exhaustion (5). While safety of the participant is always important, there are some drawbacks to cycle ergometry testing. Compared to treadmill VO_{2max} assessments, cycle ergometer VO_{2max} may be underestimated by ~10% due the difference in the exercising muscle of extremely overweight children and by as much as 20% in a normal population (5, 90, 94). This underestimation can be attributed to the amount of exercising muscle during this mode of exercise (90).

E. Other Modes of Exercise

Elliptical ergometers have become of a popular mode of exercise in the various health and fitness settings due it being weight bearing, but not as stressful on the joints. Mays et al. (95) studied the results of estimated VO_{2max} test from a cycle ergometer, treadmill, and an elliptical ergometer in young female subjects. It was found that the cycle ergometer estimated significantly lower VO_{2peak} results than both the treadmill and elliptical ergometer. Treadmill and elliptical ergometers require a larger exercising muscle mass compared to a cycle ergometer and will require a higher VO_2 to perform these activities (94).

It is possible to determine VO_{2max} in almost any mode of exercise, but the mode of exercise may present difficulties in collecting data. An example of this would be swimming. Swimming VO_2 can be assessed in either a flume or in a standard pool. The flume is a specialize pool in which the swimmer remains in place while water speeds can be adjusted to increase or decrease swim speeds. Compared to running, swimming in a flume will produce a VO_{2peak} ~6% lower than during a treadmill test (96, 97). This difference can be seen across all aerobic exercise modalities. Cross-country skiers have been found to have some the highest VO_{2max} measurements ever recorded for both males (94 ml/kg/min) and females (77 ml/kg/min) (98).

VI. CURRENT VO_{2MAX} CRITERIA

Determining whether a true VO_{2max} has been achieved is evaluated by the use of several criteria. The primary criteria that is used is the occurrence of a VO_2 plateau (no increase) with an increase in work rate. However, Day et al. found that a large majority (~83%) of traditional ramp protocols do not elicit a plateau in VO_2 , so researchers use secondary criteria to determine whether a true max was achieved (7). These secondary criteria include RPE, HR_{max}, RER, and blood lactate concentration (BLa). These criteria are discussed below.

A. VO_2 Plateau

VO_2 plateau is defined as a small or no increase in VO_2 in response to an increase in work rate (8). This is used to show that oxygen consumption is at its maximal rate. However, if there are still small increases in VO_2 (<50ml/min) (99), this is not an absolute plateau and the rate of oxygen utilization has slowed but has not yet plateaued. In the mid-2000s, Midgley et al. (11) found that a majority of the studies they reviewed did not specify what criteria was used to determine VO_{2max}, and there were seven different criteria used for determination of a VO_2 plateau. While this criterion would be the most useful to determine VO_{2max}, one study found that a plateau occurred in only 17% of the ramp protocols (7). The lack of plateau in VO_2 observed using modern testing techniques may be due to the evolution of real time gas analysis coupled with the use continuous ramp protocols vs. discontinuous protocols to assess VO_{2max}. In particular, discontinuous protocols employed when using Douglas bag techniques to assess VO_2 utilized longer stages at the same work rate allowing for a plateau to occur when the subject moved on to the next stage. In fact, the use of a discontinuous ramp may elicit a plateau in VO_2 approximately 80% of the time (100) compared to 17% using modern techniques (7).

B. Rating of Perceived Exertion (RPE)

Rating of Perceived Exertion (RPE) is based on either Borg's 15-point scale (6-20), or a 1-10 fatigue scale. Borg's RPE scale can be associated with HR, but a 1-10 scale is more familiar to most individuals. To determine whether a VO_{2max} was achieved, Midgley et al. (11) found 3 different thresholds for RPE with a minimum value of 17, 18 or 19 on the 20-point scale. The inclusion of this criteria has been found to be questionable to some researchers as the RPE scale lacks objectivity (24). This requires the subject to understand how to interpret the scale and that they are able to accurately quantify their efforts. When trying to determine whether a true VO_{2max} was achieved, a subjective measure such as RPE may not be reliable.

C. Blood Lactate Concentration, Respiratory Exchange Ratio (RER), & Heart Rate (HR)

Blood lactate concentration (BLa), respiratory exchange ratio, and HR are all used as secondary criteria for achieving a VO_{2max}. These three measures have a large between-subjects' variation, meaning that subjects may be able to achieve these thresholds prior to a "maximal" exercise. BLa typically has a threshold of either 8 or 10mmol/L. Midgley et al. (11) found eight different RER thresholds that have been used, ranging between 1.00 and 1.20. Almost everyone has a different HR_{max} based on age, training, environment, and during a maximal exercise test all of these can contribute to different values. There are a number of different "standard" values used for each of these secondary criteria so it can be difficult to determine whether a true max was achieved or not. The distinction between a peak and a max (discussed below) is important as different VO_2 can mean a higher or lower risk of mortality.

D. "Peak" vs. "Max" Values

Accurate assessment of VO_2 is essential in all populations due to the health and performance indications. This necessity leads to researchers being able to differentiate between a

VO_{2peak} and the presence of a plateau indicating VO_{2max}. In the instance where a VO_2 plateau does not occur, secondary criteria are used to determine whether a VO_{2max} has been achieved. However, as discussed above there is a wide variation of the norms of the secondary criteria and the utilization of these criteria may be underestimate true VO_{2max} by as much as 30-40% (28). In an attempt to circumvent this issue, researchers have resorted to using the term VO_{2peak} to distinguish the highest maximal VO_2 for that test, while VO_{2max} is the overall VO_{2max} for that individual. To help distinguish this difference researchers have called for a new technique to differentiate between a VO_{2peak} and a VO_{2max} (9, 11, 28). One technique is the addition of a verification phase to the traditional ramp test.

VII. OVERVIEW OF RESEARCH INVOLVING THE VERIFICATION PHASE

First studied by Thoden et al. in 1982 (101), the then called exhaustive phase is used to confirm whether a VO_{2max} was achieved during the ramp phase of the test. This additional phase would be required when a VO_2 plateau does not occur during the ramp phase. A verification phase typically consists of a constant work rate at a given percentage of peak work rate during the ramp test until volitional exhaustion. A verification phase of ~10% higher than the peak work rate during the ramp test has been proven effective for confirmation of VO_{2max} in individuals across all activity levels in young to middle aged subjects < 60 years of age (28).

While Thoden et al. receives credit as the first to study the use of a verification phase, a study by Niemelä et al. was completed in 1980 that also studied the use of a verification phase during VO_{2max} testing (27). Since then, the verification phase has been studied across various demographics and has several different variations to the test. The verification phase has been administered anywhere between one-minute post ramp and a week following a ramp test (20, 27). The verification phase includes a change in work rate equal to a given amount of the ramp test depending on the protocol. Some have determined that if a VO_2 plateau is not reached then the

additional phase should be administered (10). Below, various data related to the use of the verification phase are discussed. Results of these studies are outlined in Table 1.

A. Demographics

Eighteen studies that used a verification phase are listed in Table 1. Twelve of these studies used a cycle ergometer (7, 10, 13-19, 26-28) and eight studies used a treadmill (10, 19-25). The studies varied on how they defined subject activity levels and the activity levels that they studied. Sedentary individuals were used in three studies (16, 17, 27), eight studies used active individuals (10, 18, 19, 21-23, 26, 27), two studies examined the use of recreationally active subjects (15, 28, 69), three studies used competitive athletes at various levels (19, 24, 25).

The age of the subjects varied between nine (18) and seventy-three years of age (13). One study examined the use of a verification phase in children (18). A majority of the studies examined the use of a verification phase in young adults (7, 13-17, 19, 21, 23-25, 27, 28), or middle aged subjects (7, 10, 16, 22, 27), and three studies examined the use of a verification phase in older individuals (13, 26, 27). One study did not state the age ranges (20). Across the different demographics only one of the eighteen studies found a significant different between the ramp phase and verification phase (25), which was performed in elite young male endurance athletes. This shows there is validity to verification testing. The results show that there may not be a need for a verification phase in VO_{2max} testing. However, while most studies found no significant differences in the group data, it should be noted that VO_{2max} assessments have intersubject variability, and some subjects may achieve a significant increase of VO_2 during a verification phase. Researchers have noted the importance of measuring individual responses during these VO_{2max} assessments opposed to solely analyzing group mean data (10, 24, 25, 102).

B. Timing of Verification Phase

The authors do not provide rationale for their rest periods, however, the thought may be that if the subject has a longer rest period, they may be able to recover from any muscle fatigue and have a better test. The rest period between the end of the ramp stage and the initiation of the verification phase varies greatly in the literature. The longest rest period found is in the study by Niemelä et al. in which the rest period was a minimum of one week (27). Several studies stated their rest periods were on a separate day or more than twenty-four hours later (9, 17, 20). Two studies used a rest period of one hour (23, 26). Weatherwax et al. and Nolan et al. used 20 minutes for their rest periods (23, 25). Three studies used ten minutes for their rest period, two of them used ten minutes of active rest (18, 22), and one of them used ten minutes of passive rest (10). Barker et al. followed his active recovery with five minutes of passive rest. Sawyer et al. had a flexible rest period with a minimum of five minutes and a maximum of ten (16). Murias et al. (13) and Rossiter et al. (14) used a five-minute rest period. Leicht et al. used a combination of two minutes passive and five minutes of active recovery (21). Two studies used three-minute recovery periods (15, 19), and one study used sixty seconds between the ramp and the verification phase (19).

C. Work Rates

There have been many different protocols used for the change in work rate for the verification phase. After reviewing the literature, it has been determined there are two different rationales when determining a work rate for the verification phase. The first is to have a work rate that is below the achieved maximal work rate. This will allow for a longer verification phase which will allow for the slow component to be fully utilized. A drawback to this protocol is that the individual may have been able to achieve a higher work rate, which in theory would elicit a higher VO_2. The second rationale is to have an increased work rate for the verification phase. This protocol allows the examiners to determine if the subject is capable of achieving an increased work rate which will

elicit an increased VO_2 compared to the ramp protocol. The drawback of this protocol is that the individual may not be able to continue at this work rate for an extended period of time and may not be ideal for certain populations (28).

Eight studies were found that used a verification phase lower than the work rate achieved during the ramp phase. Rossiter et al. used a verification phase of 95% of achieved peak power during the ramp phase (14). Day et al. used a verification phase ~90% of the ramp phase (7). One study used 85% of the ramp phase (13). Sedgeman et al. used the work rate from two stages before volitional exhaustion (15). Some of the studies did not use a percentage of the ramp phase. They instead used a predetermined amount to increase the work rate. Foster et al. used a 25 W increase on a cycle ergometer test while on the treadmill they increased the speed 0.45 m/s for both genders while increasing the grade 4% for males and 3% for females (19). Midgley et al. increased the speed 0.5 km/hr on the treadmill for the verification phase (22). One study used a 0.64 km/hr increase for males and a 0.48 km/hr increase for females (25). Leicht et al. studied wheelchair athletes using an increase of 0.3% grade for tetraplegic athletes and a 0.6% increase for paraplegics and individuals without spinal cord injuries (21). A single study kept the verification phase at the same work rate as the end of the ramp (16). This may be to see if the individual is able to continue at that work rate for an extended period of time opposed to at the end of a ramp phase.

Nine studies were found that used a higher work rate than achieved during the ramp phase. Several studies increased the work rate to 105% of the end of ramp max (9, 13, 14, 17, 18, 23, 26). Scharhag-Rosenberger et al. used a two-part verification phase. The first verification phase uses an increase of 110% of the amount achieved during the ramp. If the VO_2 increased during this stage, the subject would come back a day later to complete a verification phase at 115% (24). One study used 115% of the ramp phase for the verification phase (23). Hawkins et al. used a verification phase work rate requiring greater than 130% of VO_{2peak} (20). Midgley at al used an incremental

verification phase. The subject spent two minutes at 50% of their achieved work rate, one minute at 70%, and then the final stage was at one stage higher than the maximally achieved work rate (10).

Table 2-1 Summary of Verification Phase Studies Including Study Protocol and Outcome

Study	N	Activity Level	Mode	Age (Years)	Rest period	VP Change	Ramp Stage	Verification Phase
Astorino et al. (17)	15	Sedentary	Cycle	22.4±3.9	>24hrs	105%	2.67±0.60 L/min 2.77±0.69 L/min	2.75±0.76 2.71±0.67
Barker et al. (18)	13	Active	Cycle	9-10	10m active 5m passive	105%	1.69 L/min	1.62 L/min
Dalleck et al. (26)	18	Active	Cycle	59.7±6.3	1hr	105%	2.33±.78 L/min	2.31±.76 L/min
Day et al. (7)	71	N/A	Cycle	19-61	N/A	~90%	3.64±.7 L/min	3.64±.71 L/min
Foster et al. (19)	20	Active	Cycle	M: 31.5±14.5 F: 28.0±12.4	60s	25W Increase	3.95±.75 L/min	4.06±.75 L/min
Foster et al. (19)	20	Competitive	Treadmill	M: 21.6±3.0 F: 21.0±4.5	3m	Grade: M 4% Speed .45m/s Grade: F 3% Speed .45m/s	4.09±.97 L/min	4.03±1.16 L/min
Hawkins et al. (20)	52	Trained	Treadmill	N/A	Separate Day	WR Requiring ≥ 130% of VO2max	63.3 ml/kg/min	62.9 ml/kg/min**
Leicht et al. (21)	24	Active	Treadmill	Tetra: 28.1±5.2 Para:31.7±8.7 Non-Sci: 24.0±6.2	2min passive 5min active	.3% grade .6% grade .6% grade		
Midgley et al. 2009 (10)	10	Active	Treadmill	39.3±6.9	10m passive	2m @50%	3.86 L/min	3.92 L/min
	10		Cycle	36.0±5.8		1m @70%	4.05 L/min	3.96 L/min
Midgley et al. 2006 (22)	16	Active	Treadmill	38.7±7.5	10m active	1 stage higher than Wrmax .5km/hr	4.04 L/min	3.99 L/min
Murias et al. (13)	31	N/A	Cycle	68 ± 5	5m active	Young 85%	3.73±1.22 L/min	3.76±1.24 L/min
	30			25 ± 4		Young 105%	3.90±1.28 L/min	3.89±1.28 L/min
						Old 85%	2.18±.28 L/min	2.18±.28 L/min
						Old 105%	2.52±.32 L/min	2.57±.36 L/min

Table. 2-1 (Continued)

Study	N	Activity Level	Mode	Age (Years)	Rest period	VP Change	Ramp Stage	Verification Phase
Niemelä et al (27)	115	34 Sedentary 61 Moderate 17 Very 3 Heavily	Cycle	25-62	1 Week	N/A	2.95 L/min 3.14 L/min	3.05 L/min
Nolan et al. (23)	12	Active	Treadmill	23.0±2.9	A: 20m B: 60m C: 20m D: 60m	A: 105% B: 105% C: 115% D: 115%	3.64±1.06 L/min 3.60±1.05 L/min 3.68±1.06 L/min 3.65±1.07 L/min	3.66±1.06 L/min 3.60±1.05 L/min 3.64±1.06 L/min 3.58±1.04 L/min
Poole et al. (28)	8	Recreationally	Cycle	27 ± 4	Separate Day	105%	4.03 L/min	3.95 L/min
Rossiter et al. (14)	12	N/A	Cycle	26 ± 10	5m active	95% Peak Power 105% Peak Power	4.11±.48 L/min 4.15±.50 L/min 4.33±.52 L/min	4.12±.53 L/min 4.09±.45 L/min 4.30±.51 L/min
Sawyer et al. (16)	19	Sedentary	Cycle	35.8 ± 8.6	5-10m active	100%	2.29±.71 L/min	2.34±.67 L/min
Scharhag-Rosenberger et al. (24)	40	24 untrained 4 trained 12 National-level	Treadmill	18-35	10m if increased 24hr	110% if increased 115%	3.82±.99 L/min	3.77±.99 L/min 3.75±1.00 L/min
Sedgeman et al. (15)	13	Recreationally	Cycle	29 ± 9	3m active	End Max minus 2 stages 105%	3.69±1.49 L/min 3.71±1.5 L/min	3.69±1.49 L/min 3.64±1.47 L/min
Weatherwax et al. (25)	24	Elite Endurance	Treadmill	21.9 ± 3.6 20.2 ± 2.0	20m	.64 km/hr for males .48km/hr for females	3.98±.36 L/min 2.68±.13 L/min	3.94±324 L/min * 2.67±.10 L/min

N= Number of participants *Notes a significant difference from ramp **Notes data presented in ml/kg/min

D. Known Data

The data found on verification phase studies are listed in Table 2-1. 17 of the 18 studies show there is no statistical difference ($P < 0.05$) in VO_{2peak} between the ramp phase and the verification phase. This would mean the subjects achieved their VO_{2max} during the ramp phase of the study. Weatherwax et al. found a statistical difference between the ramp phase and the verification phase (25). The significant difference was found in the male group subjects as well as the overall group mean data, however the female group data was found to not be significantly different. The significant difference in the males was not present when individual subject data was analyzed. While most of the studies did not note individual differences, Astorino et al. noted a significant difference in individuals between the ramp phase and the verification phase, but the group means were not significantly different (17). This may show the importance of analyzing data of individual subjects over the use of a means across the group.

VIII. SUMMARY

This literature review discussed the history of VO_{2max} as well as the physiological factors that influence VO_2 and how each of them can be affected by age. Cardiac output, a-VO_2 difference, HR, lean-body mass, stroke volume all may change with age and can decrease VO_{2max}. It is important to be able to accurately assess VO_{2max} because of the association with mortality risks and a low VO_{2max}. Differences between modes of exercise were discussed and how they can affect the results of a VO_{2max} assessment. A cycle ergometer test will typically elicit lower results than a treadmill or elliptical ergometer test but, will produce less artifact when performing other measurements.

The commonly used secondary criteria such as RER, BLa, HR, and the prevalence of a plateau in VO_2 were explained and that they may not be enough to determine whether a true VO_{2max} was achieved. There are many different standard values meaning an individual may reach max according to one set of standards but not according to another set. This has led to the call for an additional step in some VO_{2max} assessments. The use of a verification phase, with a few exceptions,

has mostly been studied in younger individuals. The current data shows that the work rate during the verification phase is valid at 85-130% of the work rate during the ramp phase. There is a gap in the literature on whether a verification phase testing in older adults and if it is, what work rates should be used for it.

CHAPTER THREE

METHODS

Participants

Twenty-four otherwise healthy adults from the greater Phoenix, AZ metropolitan area volunteered to participate in this study. All participants were between the ages of 60-80 years. Subjects were recruited by advertisement, locally posted flyers, and word of mouth. Subjects completed a brief online pre-screening questionnaire (Qualtrics®) which was reviewed by the researchers. Following the pre-screener, qualified subjects were invited to the laboratory for a formal informed consent process. Additional screening included a medical history and the Physical Activity Readiness Questionnaire for Everyone (PARQ+) and assessment of blood pressure. A pregnancy test was also completed for females prior to undergoing a DXA scan unless menses has not been for > 5 years. Inclusion criteria and exclusion criteria are listed below in Table 3-1. Prior to any study activities, subjects read and provided written informed consent. This study was approved by the Arizona State University Institutional Review Board (in compliance with the Declaration of Helsinki, as revised in 1983).

Table 3-1. Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
• Ability to communicate in English • Are competent to provide written informed consent	• Uncontrolled hypertension • Any self-reported acute or chronic illness, medical/orthopedic conditions precluding exercise • Currently training for an endurance event (i.e. marathon, triathlon • Self-reported significant heart, liver, kidney, blood, or respiratory disease • Peripheral vascular disease • Diabetes or endocrine disease • Active cancer • Use of tobacco • If they are pregnant

Study Design and Procedures

Subjects were studied during two separate experimental trials, both of which took place at the Exercise Physiology Laboratory in the Arizona Biomedical Collaborative building at the Arizona State University Downtown Campus. The experimental trials were separated by approximately 1 week and were performed in a randomized, counterbalanced cross-over design. Each experimental trial consisted of a ramp test to determine VO_{2peak} and a verification phase test performed 10 minutes following completion the ramp test. The ramps tests were identical for each experimental trials, however, the visits differed in the work rate at which the verification phase was performed.

During each experimental trial, and prior to any metabolic testing, the subject's height and weight were measured on a calibrated stadiometer and resting blood pressure measures were obtained. Subsequently, the subjects were equipped with a mouthpiece attached to a hose, and a chest worn Polar HR monitor (Lake Success, NY) to continuously monitor HR. Prior to performing the metabolic testing, resting measures were collected for two minutes and then the subjects performed a warm-up in which the subjects pedaled on a stationary cycle ergometer (Ergoline Viasprint 150, Bitz, Germany) to the cadence of their choice at 50 Watts for males and 40 Watts for females for five-minutes. Expired gases at rest and during the ramp test and verification phase tests were analyzed for ventilation, O_2 and CO_2 using a Truemax 2400TM metabolic cart (Parvomedics, Sandy Utah).

Ramp Test

During both experimental trials, subjects performed an identical ramp test on a cycle ergometer (Ergoline Viasprint 150, Bitz, Germany). Immediately following the warm-up phase (described above), the work rate on the cycle ergometer was increased in a ramp fashion corresponding to 20 Watts/min for males (1 Watt every 3 seconds) and 15 Watts/min for females (1 Watt every 4 seconds) until the subject reached volitional exhaustion. Subjects were allowed to pedal at a cadence of their choice, although subjects were encouraged to maintain a cadence of ~50-60 rpm. Expired gases were assessed (see above) in 10-second averages and HR was

continuously monitored throughout the duration of the ramp test. Ratings of Perceived Exertion (RPE) was assessed every 60 seconds throughout the duration of the ramp test. The test was terminated at volitional exhaustion (i.e., the subject requesting to stop) or if the subject was unable to maintain RPM.

Verification Phase

The verification phase was completed following the ramp test, specifically after a ten-minute active recovery period. The recovery period consisted of light pedaling at approximately the warm-up load. The verification phase for each visit was performed at a work rate equivalent to either 85% or 110% of the peak work rate (Watts) reached during the preceding ramp test. Subjects were randomized to perform either the 85% or 110% verification phase during the first visit, whereas during the second visit, the subject completed the verification phase at the other work rate. Both verification phase tests were performed at a constant work rate until volitional exhaustion. Expired gases were assessed (see above) in 10-second averages and HR was continuously monitored throughout the duration of the verification phase test. RPE was assessed at the end of the verification phase. The test was terminated at volitional exhaustion (i.e., the subject requesting to stop) or if the subject was unable to maintain RPM.

Assessment of Body Composition

During the second visit, subjects underwent a Dual-energy X-ray Absorptiometry (DEXA) scan (Lunar iDXA, GE Healthcare, Madison, WI). The DEXA was performed prior to any testing and after voiding the bladder. The subject laid down on the DEXA for 15 minutes prior to the DXA to avoid any influence of fluid shifts. A trained and certified radiologist administered the DEXA scan.

Physiological Outcomes

VO_{2peak} values for the ramp tests and verification phase tests were taken as the highest three consecutive 10-second measurements, which were averaged to yield a peak 30-second value. VO_{2peak} measures are presented as absolute (L/min) values and relative to body weight (ml/kg/min) and to DEXA-derived lean body mass (ml/kgLBM/min). Peak RER values were taken as an average of the three 10-second measurements at the same time point as VO_{2peak}. Peak RPE was assessed immediately following the termination of the ramp and verification phase tests. Peak HR for the ramp tests and verification phases were taken as the highest recorded HR. Individual data was calculated to determine the percent change of physiological outcomes between verification phase and the associated ramp, as well as between the ramp during the first visit (Ramp1) compared to the ramp during the second visit (Ramp2). A cutoff of 2% increase was used for estimated error margins to remain consistent with other studies (11, 16).

Statistical Analysis

All data were tested for normality using Shapiro-Wilks test for normality. A one way repeated measures analysis of variance (ANOVA) was used to assess differences between the ramp tests and verification phase tests for all outcomes. Pairwise comparisons were performed following the ANOVA using an least significant difference (LSD) post hoc analyses adjusted for the following two comparisons: verification phase at 85% of peak work load (VP85) vs. the associated ramp (Ramp85); verification phase at 110% of peak work load (VP110) vs. the associated ramp (Ramp110). Outcome variables obtained from the first (Ramp1) and second ramp test (Ramp2) were compared using a dependent t-test for equivalence. Pearson's correlations were used to determine the relationships between variables for the verification phase vs. ramp and for Ramp1 vs. Ramp2. Bland-Altmans and coefficients of variation were used to compare the agreement for all variables between the verification phase and corresponding ramp test and between Ramp1 and Ramp2. All comparisons including a verification phase were made to the ramp performed during the same visit. Pearson's correlations were also used to examine the following relationships within

each experimental trial: 1) Difference in VO_2 (L/min) between VP85 and Ramp85 and time to exhaustion of VP85, 2) Difference in VO_2 (L/min) between VP110 and Ramp110 and time to exhaustion of VP110, and 3) Time to exhaustion vs. VO_{2peak} (L/min) during Ramp85 and Ramp110. All data were analyzed using SPSS Software (SPSS v24) and significance was set at $P \leq 0.05$. All are presented as means ± standard deviations.

CHAPTER FOUR

RESULTS

Of the twenty-four subject that enrolled in the study, two subjects were excluded during the screening process. Two additional subjects dropped out of the study after completing the first visit due to circumstances unrelated to the study. Thus, 20 total subjects (age 67 ± 6), 8 men and 12 women completed the entire study. The subjects who only completed one visit were included in the analysis for ramp vs. verification phase (both subjects only completed the trial in which the verification phase work rate was 85%), but these subjects were not included in the comparisons between Ramp1 and Ramp2. Subject characteristics are listed below in Table 4-1.

Table 4-1. Subject Characteristics

	Men (n=9)	Women (n=13)	Total (n=22)
Age, yr	69 ± 6	65 ± 6	67 ± 6
Height, cm	171.6 ± 8.5	160.6 ± 5.1	165.2 ± 8.6
Weight, kg	77.4 ± 17.8	68.7 ± 16.1	72.3 ± 17.0
BMI, kg/m^2	26.0 ± 4.1	26.56 ± 5.8	26.3 ± 5.1
Body fat, %	28.1 ± 6.0	37.8 ± 10.5	34.0 ± 10.0
Lean Body Mass, kg	52.8 ± 11.78	38.5 ± 3.2	44.2 ± 10.4

Data are presented as mean ± SD.

Ramp vs. Verification Phase (Group Data)

Absolute VO_{2peak} (L/min) did not differ (P = 0.679) between Ramp85 (1.85 ± 0.73 L/min) and VP85 (1.86 ± 0.72 L/min) (Table 4-2, Table 4-3, Figure 4-1A, Figure 4-7A, Figure 4-8A). Similarly, absolute VO_{2peak} was not significantly different (P = 0.200) between Ramp110 (1.85 ± 0.57 L/min) and VP110 (1.79 ± 0.73 L/min) (Table 4-2, Table 4-3, Figure 4-1B, Figure 4-7B, Figure 4-8B). Intraclass correlations showed agreement in VO_{2peak} (L/min) between ramp and verification

phase for both VP85 (ICC = 0.997) and VP110 (ICC = 0.979) (Table 4-2, Table 4-3). VO_{2peak} relative to body mass (ml/kg/min) did not differ (*P* = 0.373) between ramp (26.46 ± 10.56) and VP85 (26.48 ± 10.27) (Table 4-2, Table 4-3, Figure 4-2A, Figure 4-7C, Figure 4-8C) or between ramp (27.26 ± 6.38 ml/kg/min) and VP110 (25.86 ± 9.40 ml/kg/min) (*P* = 0.088) (Table 4-2, Table 4-3, Figure 4-2B, Figure 4-7D, Figure 4-8D). Intraclass correlations for VO_{2peak} relative to body mass showed agreement between ramp and verification phase for both VP85 (ICC = 0.993) and VP110 (ICC = 0.976) (Table 4-3, Table 4-4). VO_{2peak} normalized to LBM (ml/kgLBM/min) did not differ (*P* = 0.664) between the ramp (41.24 ± 11.88) and VP85 (41.39 ± 11.82) (Table 4-2, Figure 4-3A, Figure 4-7E, Figure 4-8E) or between ramp (41.29 ± 12.55 ml/kgLBM/min) and VP110 (40.06 ± 10.88 ml/kgLBM/min) (*P* = 0.213) (Table 4-2, Table 4-3, Figure 4-3B, Figure 4-7F, Figure 4-8F). Intraclass correlations for VO_{2peak} normalized to LBM showed agreement between ramp and verification phase for both VP85 (ICC = 0.992) and VP110 (ICC = 0.954) (Table 4-3, Table 4-4).

Time to exhaustion during the ramp or verification phase were examined to determine whether they influenced differences in VO_{2peak} (L/min) between the ramp and corresponding verification phase. Time to exhaustion on VP85 was not significantly correlated with the difference in VO_{2peak} (L/min) between Ramp85 and VP85 (R^2=0.330; *P* = 0.134), and nor was time to exhaustion on Ramp85 (R^2= -.0117; P=0.606). Time to exhaustion was also not significantly correlated (R^2 = 0.270; *P* = 0.224) between Ramp85 (388.1 ± 113.7) and VP85 (175.6 ± 81.1). Time to exhaustion on VP110 was not significantly correlated with the difference in VO_{2peak} (L/min) between Ramp110 and VP110 (R^2 = 0.203; *P* = 0.392). However, there was a weak negative correlation with the difference in VO_{2peak} (L/min) and , time to exhaustion on Ramp110 (R^2 = -0.473; *P* = 0.035). Time to exhaustion had a weak positive correlation between (R^2 = 0.473; *P* = 0.035) between Ramp110 (372.7 ± 132.7) and VP110 (81.9 ± 62.3).

HR_{max} did not differ (*P* = 0.243) between Ramp85 (150 ± 17 BPM) and VP85 (153 ± 17 bpm) (Table 4-2, Table 4-3, Figure 4-9A, Figure 4-10A). Similarly, HR_{max} did not differ (*P* = 0.085) between Ramp110 (149 ± 16 bpm) and VP110 (146 ± 16 bpm) (Table 4-2, Figure 4-9B, Figure 4-10B). Intraclass correlations showed agreement in HR_{max} between ramp and verification phase for

both VP85 (ICC = 0.950) and VP110 (ICC = 0.906) (Table 4-3, Table 4-4). RER at maximal exercise was significantly different ($P < 0.01$) between Ramp85 (1.17 ± 0.09) and VP85 (1.07 ± 0.08) (Table 4-2, Table 4-3). Similarly, RER at maximal exercise was significantly different ($P < 0.01$) between Ramp110 (1.16 ± 0.08) and VP110 (1.03 ± 1.0) (Table 4-2, Table 4-3, Table 4-4). Intraclass correlations showed moderate positive agreement in RER between ramp and verification phase for both VP85 (ICC = 0.595) and VP110 (ICC = 0.548) (Table 4-4). RPE at maximal exercise did not differ ($P = 0.602$) between Ramp85 (18.5 ± 1.3) and VP85 (18.3 ± 1.7) (Figure 4-6A, Figure 4-9E, Figure 4-10F). RPE was not strongly correlated between Ramp85 and VP85 ($R^2 = 0.513$) (Figure 4-9E). Similarly, RPE at maximal exercise did not differ ($P = 0.629$) between Ramp110 (18.7 ± 1.0) and VP110 (18.6 ± 1.1) (Figure 4-6B, Figure 4-9F, Figure 4-10F). RPE between Ramp110 and VP110 was also not correlated ($R^2 = 0.361$) (Figure 4-9F).

Ramp1 vs. Ramp2 (Group Data)

Absolute VO_{2peak} (L/min) during Ramp1 (1.82 ± 0.72) was not significantly different ($P = 0.100$) from Ramp2 (1.86 ± 0.81) (Table 4) (CV = 2.90 ± 1.89) (Table 4-2, Table 4-3, Figure 4-11A, Figure 4-12B). Absolute VO_{2peak} was also in strong agreement ($R^2 = 0.987$) between Ramp1 and Ramp2 (Figure 4-12A). VO_{2peak} relative to body mass (ml/kg/min) during Ramp1 (25.86 ± 10.01) was significantly lower ($P = 0.002$) from Ramp2 (27.92 ± 11.58) (Table 4) (CV = 4.10 ± 2.74) (Table 4-2, Table 4-3, Figure 4-11B, Figure 4-12D). VO_{2peak} relative to body mass was in strong agreement ($R^2 = 0.985$) between Ramp1 and Ramp2 (Figure 12C). VO_{2peak} normalized to LBM (ml/kgLBM/min) during Ramp1 (40.83 ± 11.61) was not significantly different ($P = 0.082$) from Ramp2 (41.70 ± 12.78) (Table 4-3) (CV = 2.90 ± 1.89) (Table 4-2, Figure 4-11C, Figure 4-12F). VO_{2peak} normalized to LBM was in strong agreement between tests ($R^2 = 0.979$) (Figure 4-12E).

HR_{max} did not differ ($P = 0.115$) between Ramp1 (150 ± 17) (Table 4-2) and Ramp2 (149 ± 15) (Table 4-2) (CV = 2.30 ± 2.06) (Table 4-3) and values were in strong agreement between Ramp1 and Ramp2 ($R^2 = 0.876$) ($P < 0.01$) (Table 4-4, Figure 4-16A). RER did not differ ($P = 0.348$) between Ramp1 (1.16 ± 0.09) and Ramp2 (1.16 ± 0.08) (Table 4-2) (CV = 3.20 ± 2.05) (Table 4-3)

and values were in agreement between Ramp1 and Ramp2 (R^2 = 0.529) (P < 0.01) (Table 4-2, Table 4-4, Figure 4-16B). Peak power output (Watts) did not differ between Ramp1 (156 ± 53) and Ramp2 (158 ± 53) (Table 4-2) (CV = 5.3 ± 5.40) (Table 4-3, Table 4-4) and values were in strong agreement between Ramp1 and Ramp2 (R^2 = 0.905) (P < 0.01) (Figure 4-16C). Time to exhaustion did not differ (P = 0.663) between Ramp1 (374 ± 108) and Ramp2 (388 ± 136) (Table 4-2) (CV = 8.0 ± 8.04) (Table 4-3, Table 4-4) and values were strongly correlated between Ramp1 and Ramp2 (R^2 = 0.912) (P < 0.01) (Figure 4-16D). RPE did not differ (P = 0.481) between Ramp1 (18.5 ± 1.1) and Ramp2 (18.6 ± 1.3) (Table 4-2, Table 4-3) and RPE was not significantly correlated with Ramp1 and Ramp2 (R^2 = 0.480) (P < 0.01) (Figure 4-16C).

Individual Data

We observed that 36% of subjects (8 of 22) achieved an absolute VO_{2peak} (L/min) during VP85 that was at least 2% (range: 2.0-10.6%) higher than that achieved during Ramp85 (Table 4-2). During VP110, only 15% of subjects (3 of 20) achieved a value that was at least 2% (range: 3.5-9.7%) higher than Ramp110 (Table 4-2). The trend of a decreased percentage of individuals achieving a 2% increase during VP110 compared to VP85 is fairly consistent across all physiological data (Table 4-2). Further, 45% of subjects (9 of 20) achieved a 2% higher absolute VO_{2peak} (L/min) during Ramp2 compared to Ramp1 (Table 4-2). The number of subjects achieving 2% increase during Ramp2 compared to Ramp1 is displayed in Table 4-2 for other physiological data.

Table 4-2. Outcome Variables in Ramp and Verification Tests

	VO_{2peak} (L/min)	VO_{2peak} (ml/kg/min)	VO_{2peak} (ml/kgLBM/min)	HR Peak (bpm)	RER Peak	Power (Watts)	Time to exhaustion (seconds)
			Comparison of Ramp 1 vs. Ramp 2				
Ramp 1	1.82 ± 0.72	25.9 ± 10.0	40.8 ± 11.6	150 ± 17	1.16 ± 0.09	156 ± 53	374 ± 108
Ramp 2	1.86 ± 0.81	27.9 ± 11.6*	41.7 ± 12.8	149 ± 15	1.16 ± 0.08	158 ± 53	388 ± 136
Ind. Data	(9/20)	(13/20)	(8/20)	(4/19)	(6/20)	(9/20)	(9/20)
			Comparison of Ramp vs. Verification Phase at 85%				
Ramp	1.85 ± 0.73	26.5 ± 10.6	41.2 ± 11.9	150 ± 17	1.17 ± 0.09	158 ± 52	388 ± 114
VP 85	1.86 ± 0.72	26.5 ± 10.3	41.4 ± 11.8	153 ± 17	1.07 ± 0.08*	133 ± 45	176 ± 81
Ind. Data	(8/22)	(4/22)	(6/22)	(7/21)	(1/22)		
			Comparison of Ramp vs. Verification Phase at 110%				
Ramp	1.85 ± 0.57	27.3 ± 6.4	41.3 ± 12.6	149 ± 16	1.16 ± 0.08	156 ± 54	373 ± 133
VP 110	1.79 ± 0.73	25.9 ± 9.4	40.1 ± 10.9	146 ± 16	1.03 ± 0.10*	170 ± 60	82 ± 62
Ind. Data	(3/20)	(1/20)	(4/20)	(3/19)	(0/20)		

Data are mean ± SD. HR, Heart Rate; RER, Respiratory Exchange; Ind. Data represents number of subjects that achieved a 2% increase during the verification phase vs. ramp or during Ramp 2 vs. Ramp 1.
*P<0.05 Ramp 1 vs Ramp 2.

Table 4-3. Coefficients of Variation

	VO_{2peak} (L/min)	VO_{2peak} (ml/kg/min)	VO_{2peak} (ml/kgLBM/min)	HR Peak (bpm)	RER Peak	Power (Watts)	Time to exhaustion (seconds)
Ramp 1 & Ramp 2	2.90 ± 1.89	4.10 ± 2.74	2.90 ± 1.89	2.30 ± 2.06	3.20 ± 2.05	5.30 ± 5.40	8.00 ± 8.04
Ramp & VP 85	2.10 ± 2.14	2.90 ± 3.33	2.00 ± 2.03	2.60 ± 2.45	6.90 ± 4.54	12.00 ± 0.88	53.40 ± 25.27
Ramp & VP 110	3.60 ± 4.47	4.00 ± 4.86	3.60 ± 4.47	2.70 ± 2.54	8.60 ± 5.79	6.60 ± 0.69	95.60 ± 17.82

Data represent coefficients of variation as percent (%) and are displayed as mean ± SD. HR Peak, Heart Rate; RER, HR Peak, Heart Rate; RER, Respiratory Exchange Ratio.

Table 4-4. Intraclass Correlation Coefficients

	VO_{2peak} (L/min)	VO_{2peak} (ml/kg/min)	VO_{2peak} (ml/kgLBM/min)	HR Peak (bpm)	RER Peak	Power (Watts)	Time to exhaustion (seconds)
Ramp 1 & Ramp 2	0.994	0.992	0.989	0.936	0.727	0.951	0.912
Ramp & VP 85	0.997	0.993	0.992	0.950	0.575	1.000	0.387
Ramp & VP 110	0.979	0.976	0.954	0.906	0.548	1.000	0.473

HR Peak, Heart Rate; RER, Respiratory Exchange Ratio.

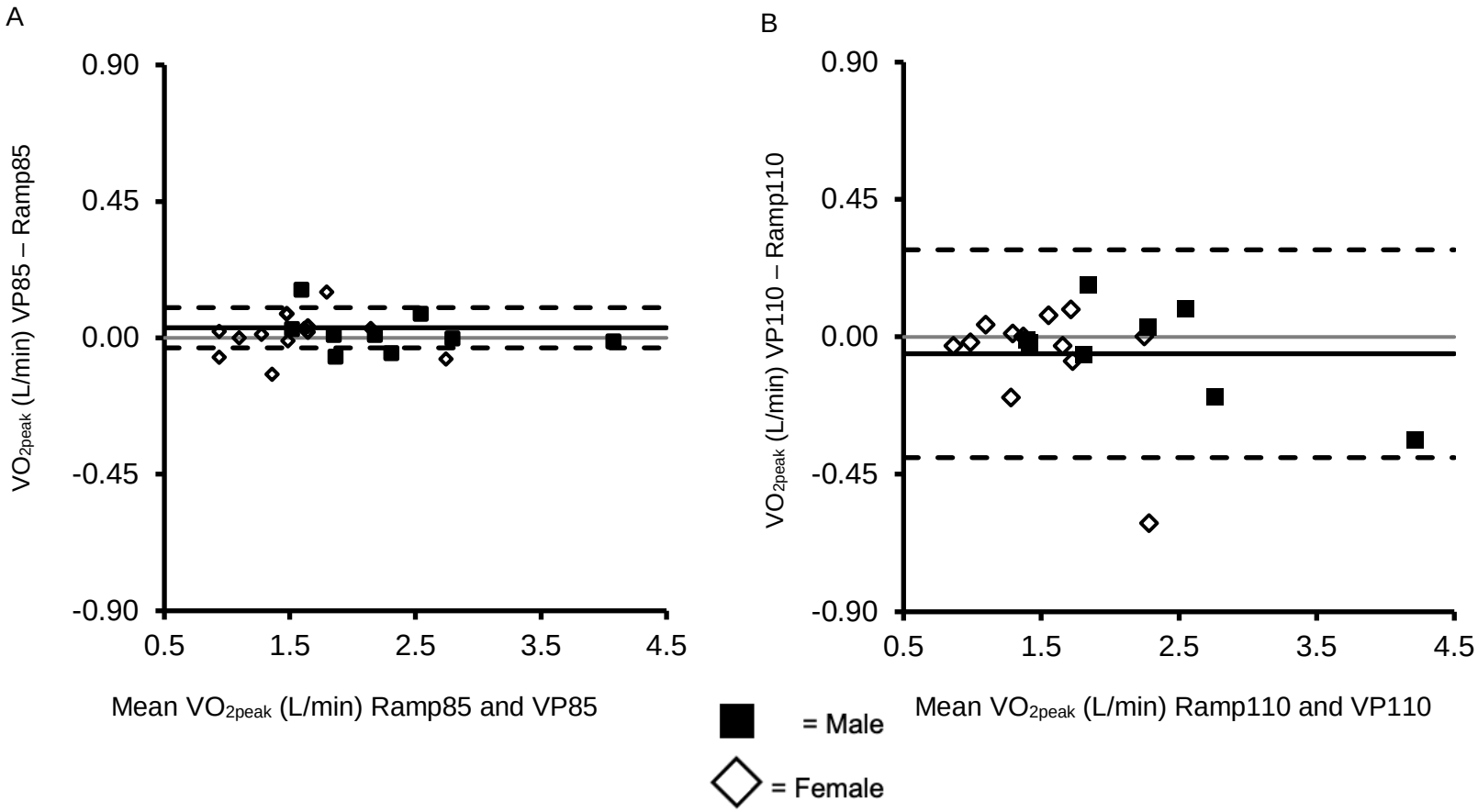

Figure 4-1. Bland-Altman plots for absolute (L/min) oxygen uptake (VO_2) for verification phase performed at 85% peak work rate (VP85; A) and verification phase performed at 110% peak work rate (VP110; B) relative to the ramp test. Y-axis = verification-ramp; x-axis = mean of ramp and verification phase; bold dotted lines = mean ± 1.96 × SD; light solid lines = 0 on the y-axis; dark solid lines = mean of verification phase-ramp.

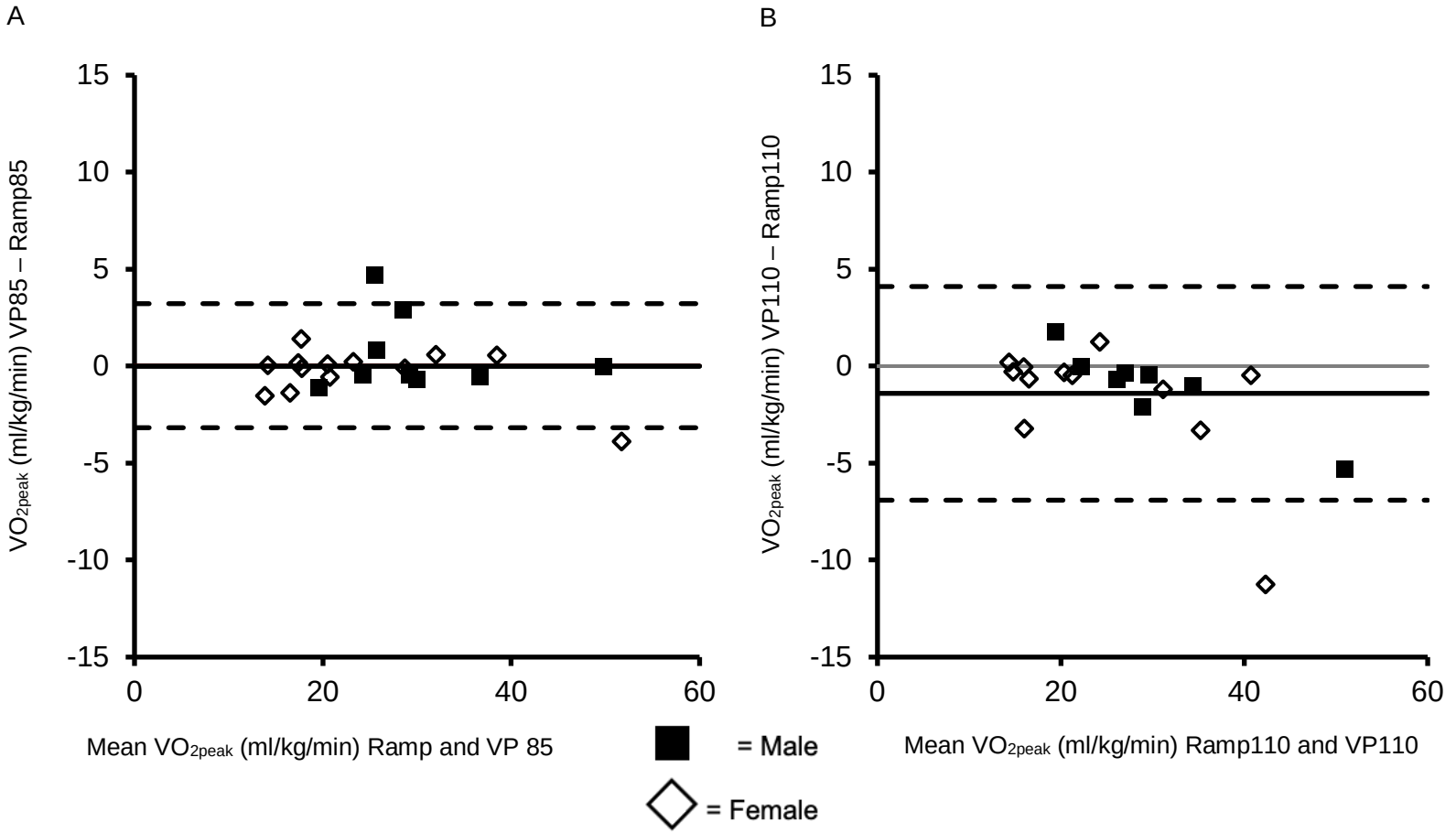

Figure 4-2. Bland-Altman plots for relative (ml/kg/min) oxygen uptake (VO_2) verification phase performed at 85% peak work rate (VP85; A) and verification phase performed at 110% peak work rate (VP110; B) relative to the ramp test. Y-axis = verification-ramp; x-axis = mean of ramp and verification phase; bold dotted lines = mean ± 1.96 x SD; light solid lines = 0 on the y-axis; dark solid lines = mean of verification phase-ramp.

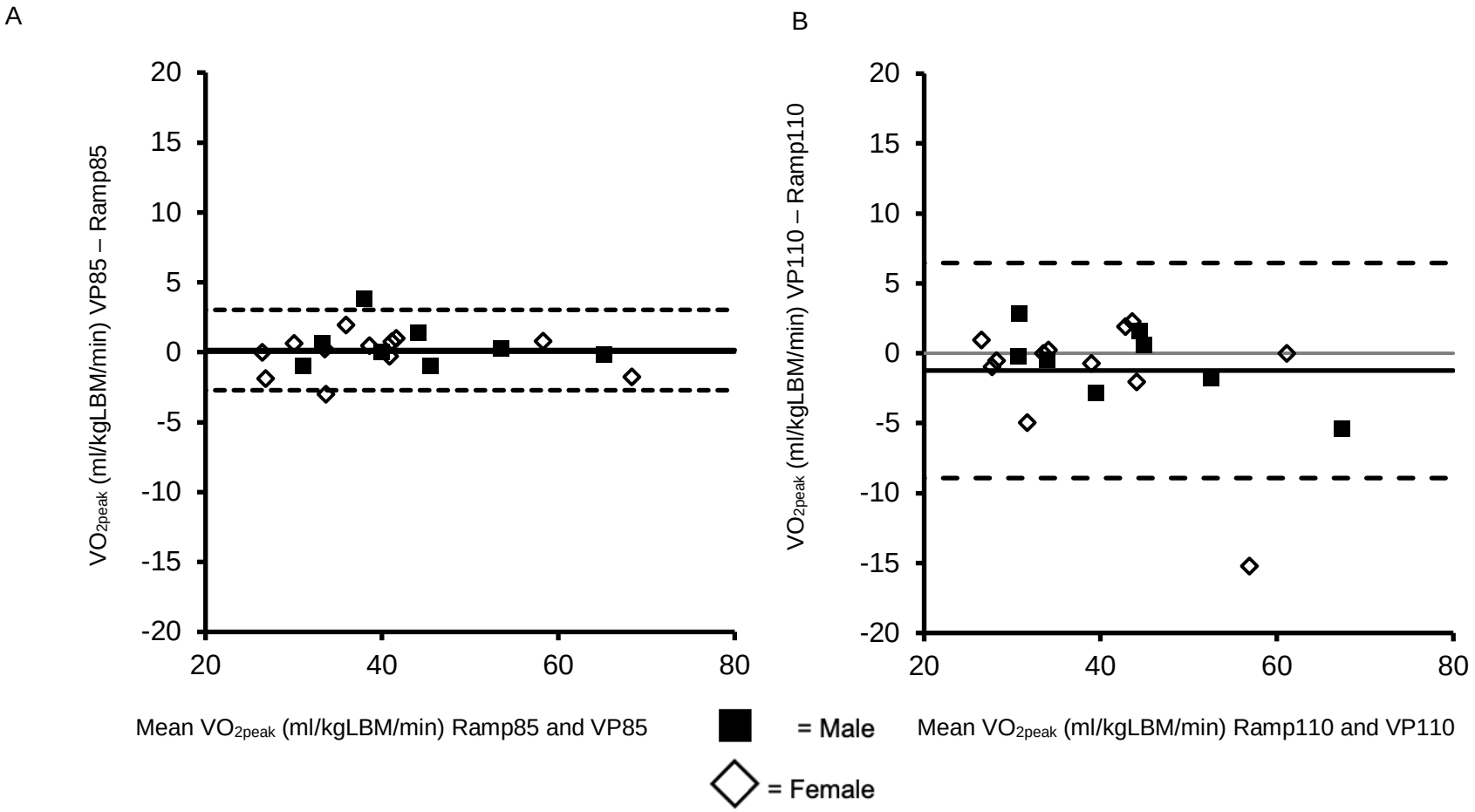

Figure 4-3. Bland-Altman plots for maximal oxygen uptake (VO_2) normalized to LBM (ml/kgLBM/min) verification phase performed at 85% peak work rate (VP85; A) and verification phase performed at 110% peak work rate (VP110; B) relative to the ramp test. Y-axis = verification-ramp; x-axis = mean of ramp and verification phase; bold dotted lines = mean ± 1.96 x SD; light solid lines = 0 on the y-axis; dark solid lines = mean of verification phase-ramp.

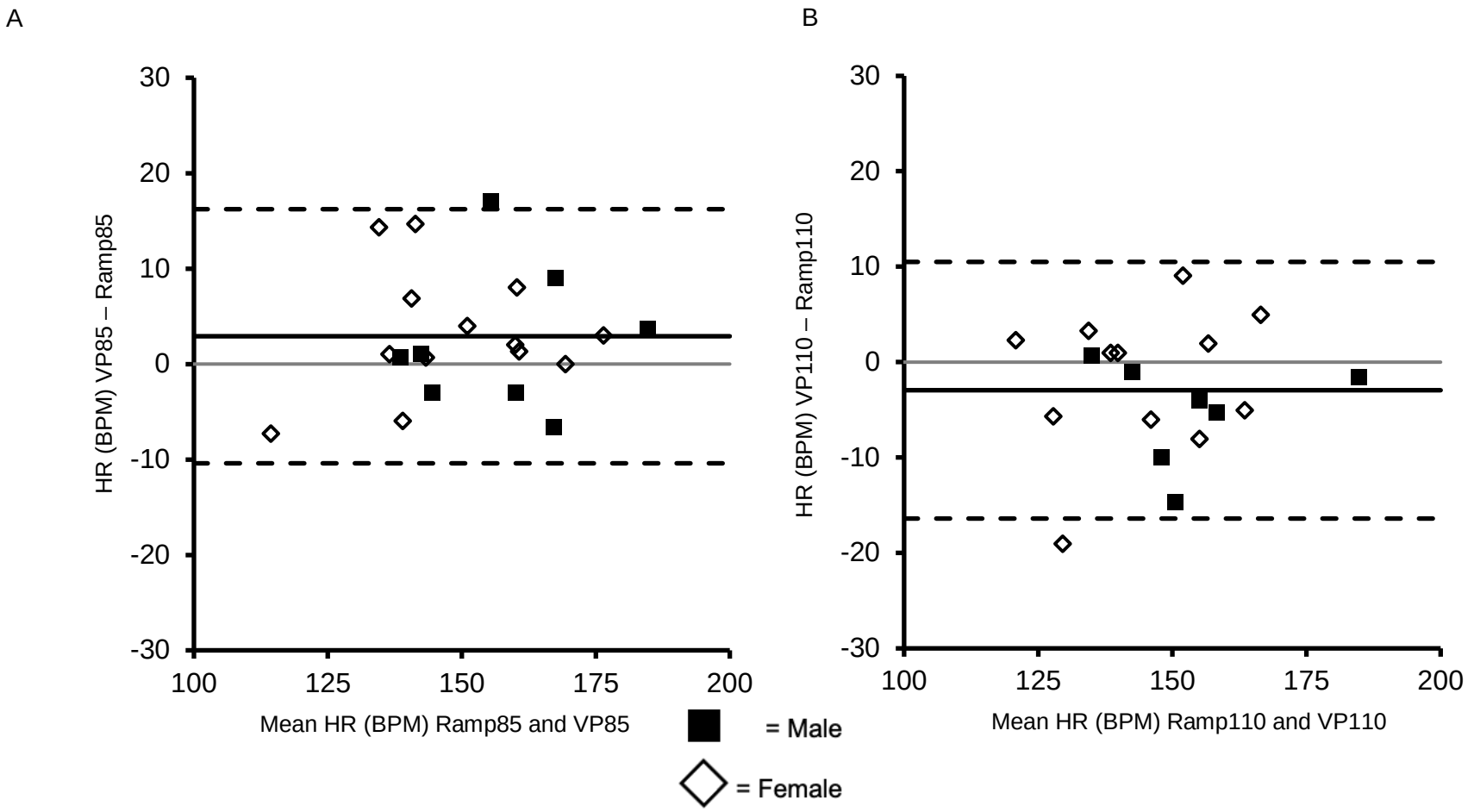

Figure 4-4. Bland-Altman plots for heart rate (HR) for verification phase performed at 85% peak work rate (VP85; A) and verification phase performed at 110% peak work rate (VP110; B) relative to the ramp test. Y-axis = verification-ramp; x-axis = mean of ramp and verification phase; bold dotted lines = mean ± 1.96 x SD; light solid lines = 0 on the y-axis; dark solid lines = mean of verification phase-ramp.

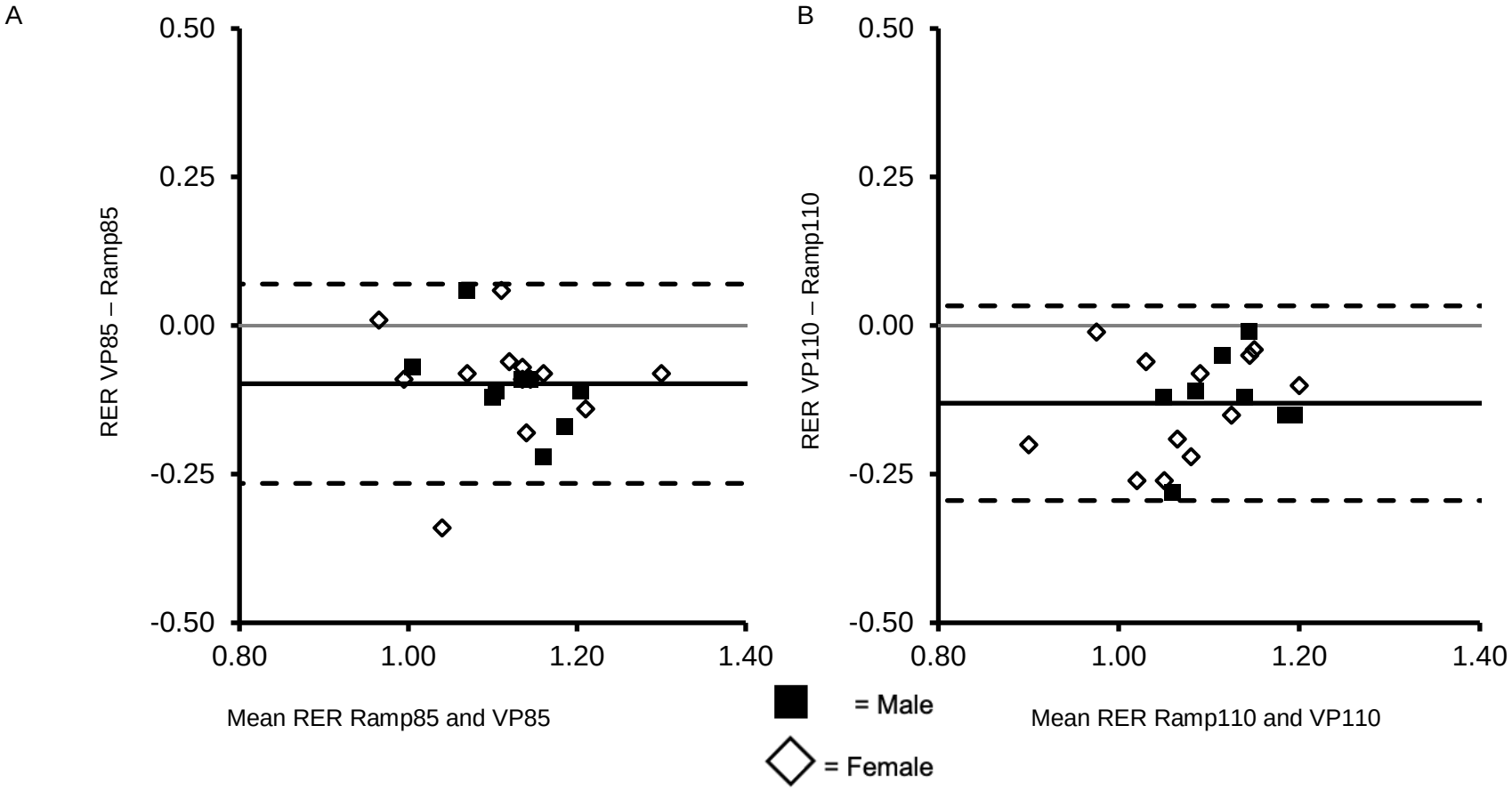

Figure 4-5. Bland-Altman plots for respiratory exchange ratio (RER) for verification phase performed at 85% peak work rate (VP85; A) and verification phase performed at 110% peak work rate (VP110; B) relative to the ramp test. Y-axis = verification-ramp; x-axis = mean of ramp and verification phase; bold dotted lines = mean ± SD; light solid lines = 0 on the y-axis; dark solid lines = mean of verification phase-ramp.

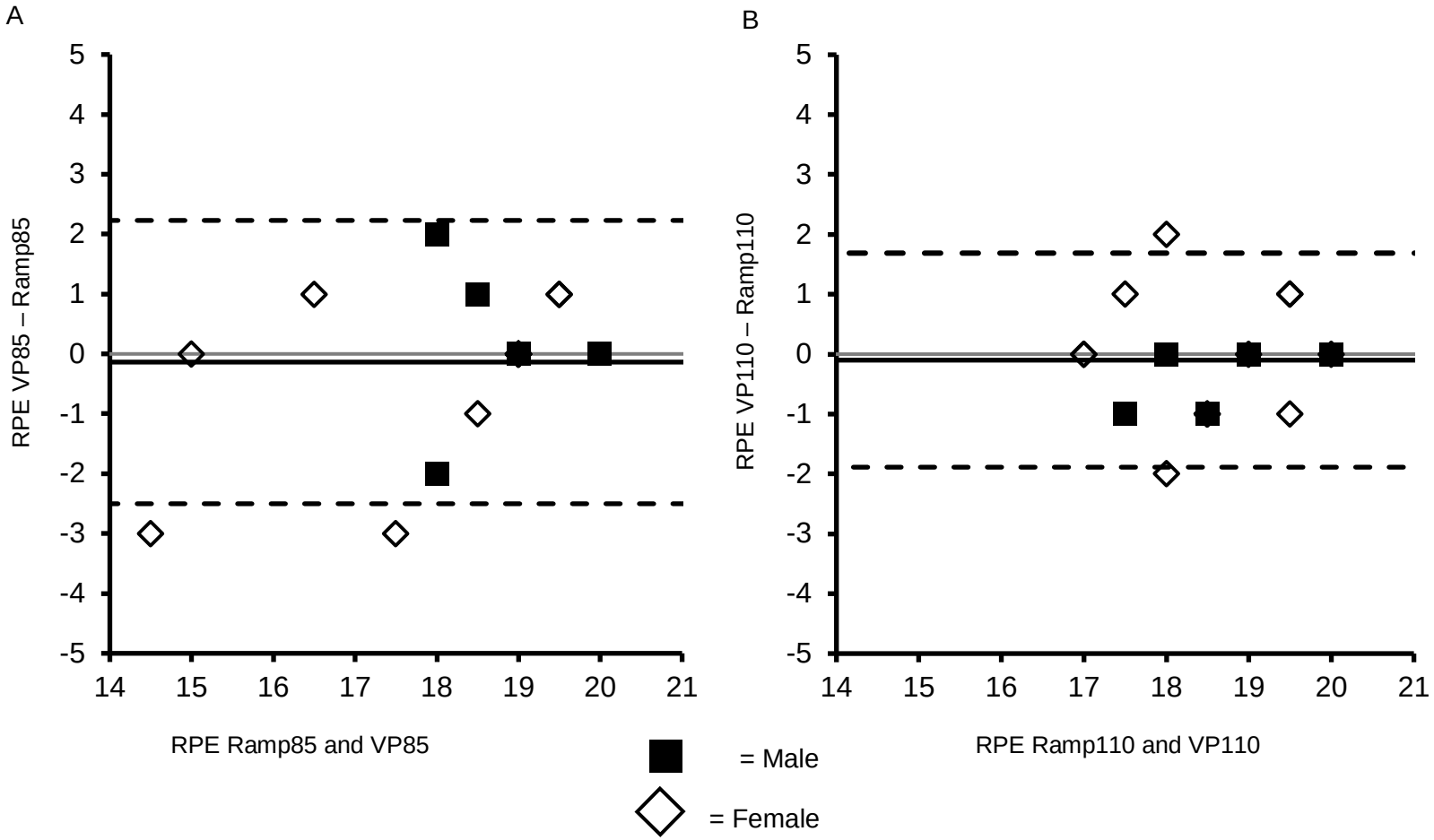

Figure 4-6. Bland-Altman plots for rating of perceived exertion (RPE) for verification phase performed at 85% peak work rate (VP85; A) and verification phase performed at 110% peak work rate (VP110; B) relative to the ramp test. Y-axis = verification-ramp; x-axis = mean of ramp and verification phase; bold dotted lines = mean ± 1.96 x SD; light solid lines = 0 on the y-axis; dark solid lines = mean of verification phase-ramp.

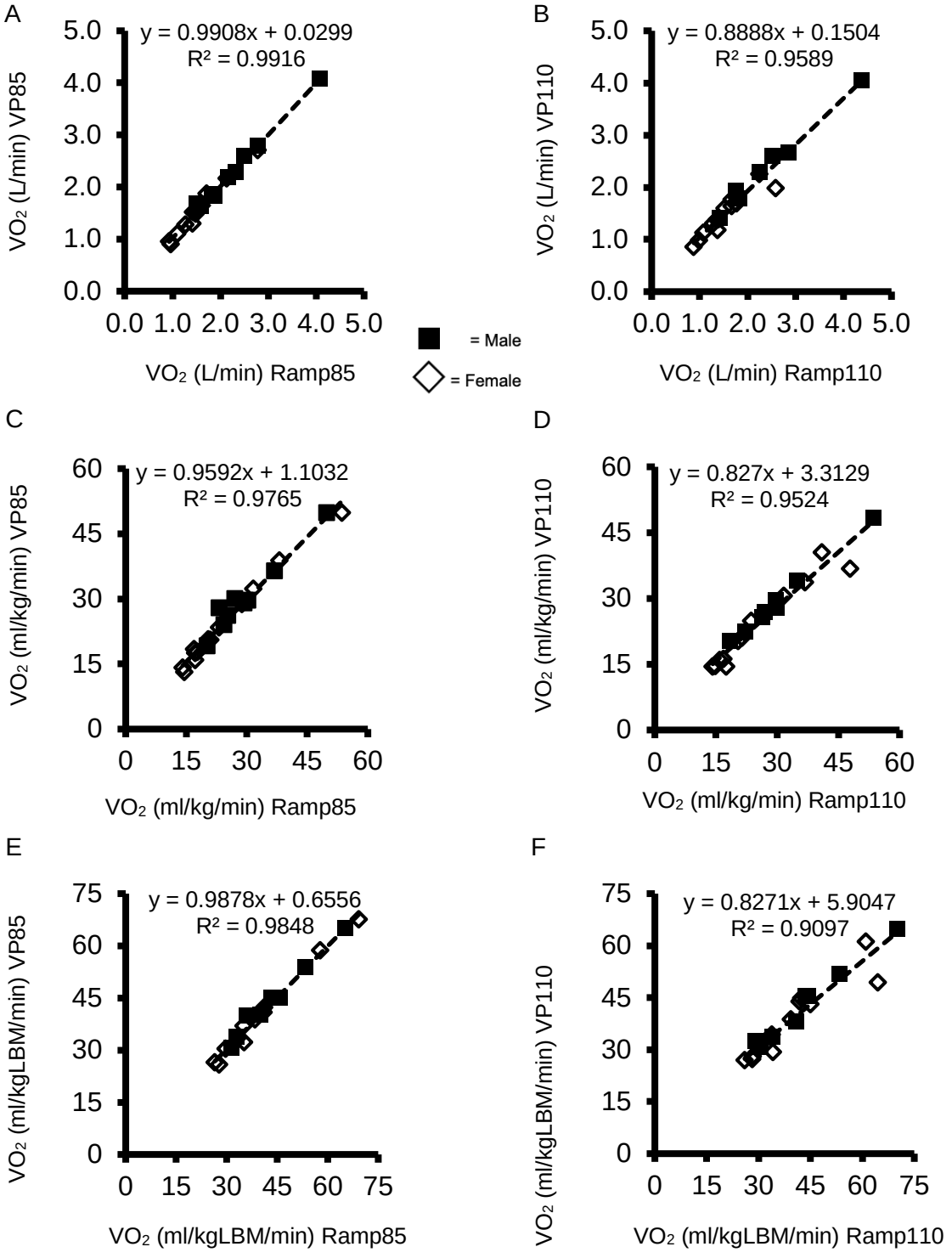

Figure 4-7. Pearson Correlation's for VO_{2peak} achieved on the ramp (x-axis) and verification (y-axis) phase for each subject. Data presented as absolute measures (L/min) for VP85 (A) and VP110 (B). Data presented as relative to body mass (ml/kg/min) for VP85 (C) and VP110 (D). Data presented for VO_2 normalized to LBM (ml/kgLBM/min) for VP85 (E) and VP110 (F).

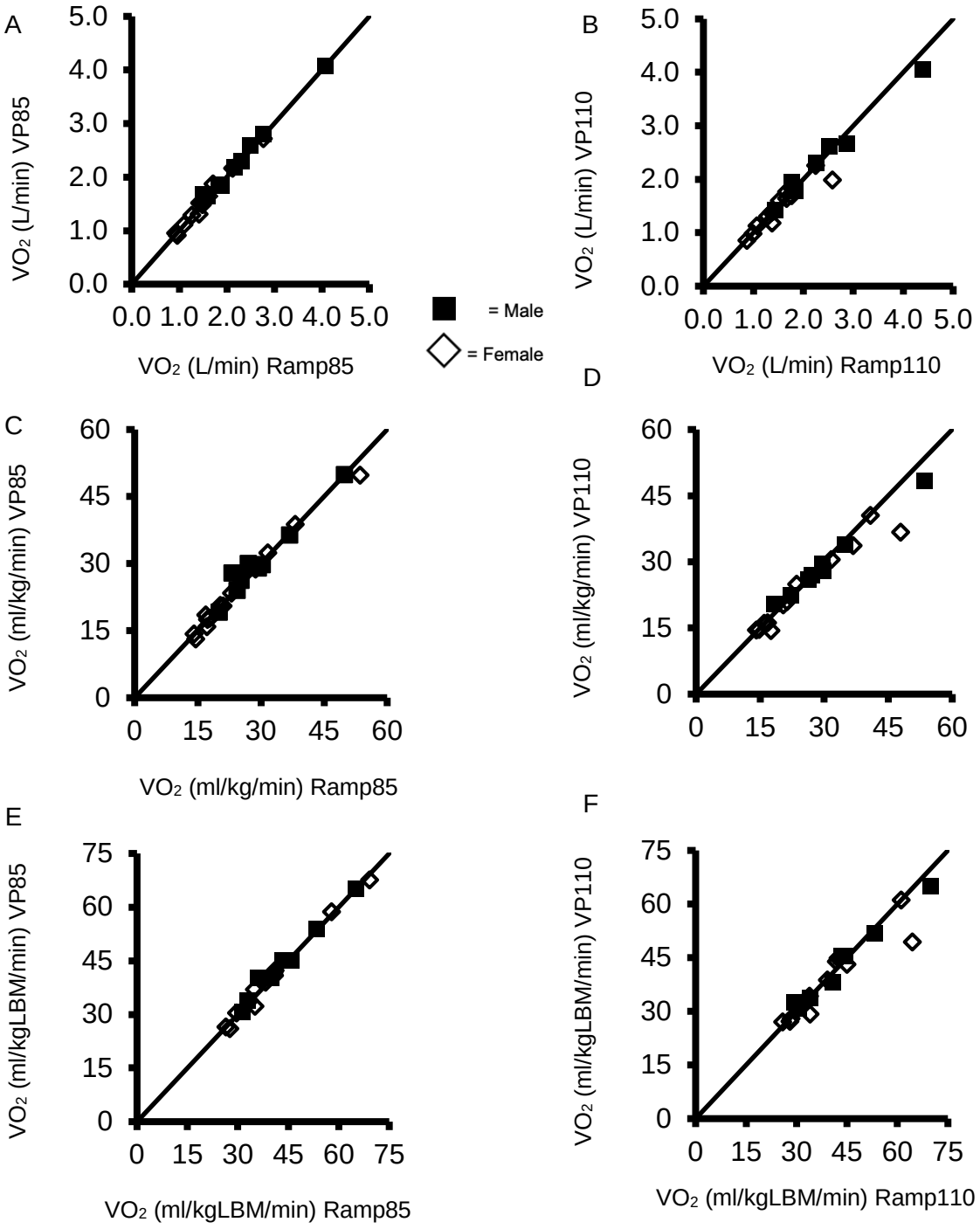

Figure 4-8. Maximal oxygen uptake (VO_{2max}) achieved on the ramp (x-axis) and verification (y-axis) phase for each subject. The line represents the line of identity (y=x). Data presented as absolute measures (L/min) for verification phase at 85% (VP85) of peak power attained on the associated ramp (Ramp85) (A) and the verification phase at VP110% (VP110) of peak power attained on the associated ramp (Ramp110) (B). Data presented as relative to body mass (ml/kg/min) for VP85 (C) and VP110 (D). Data presented for VO_2 normalized to LBM (ml/kgLBM/min) for VP85 (E) and VP110 (F).

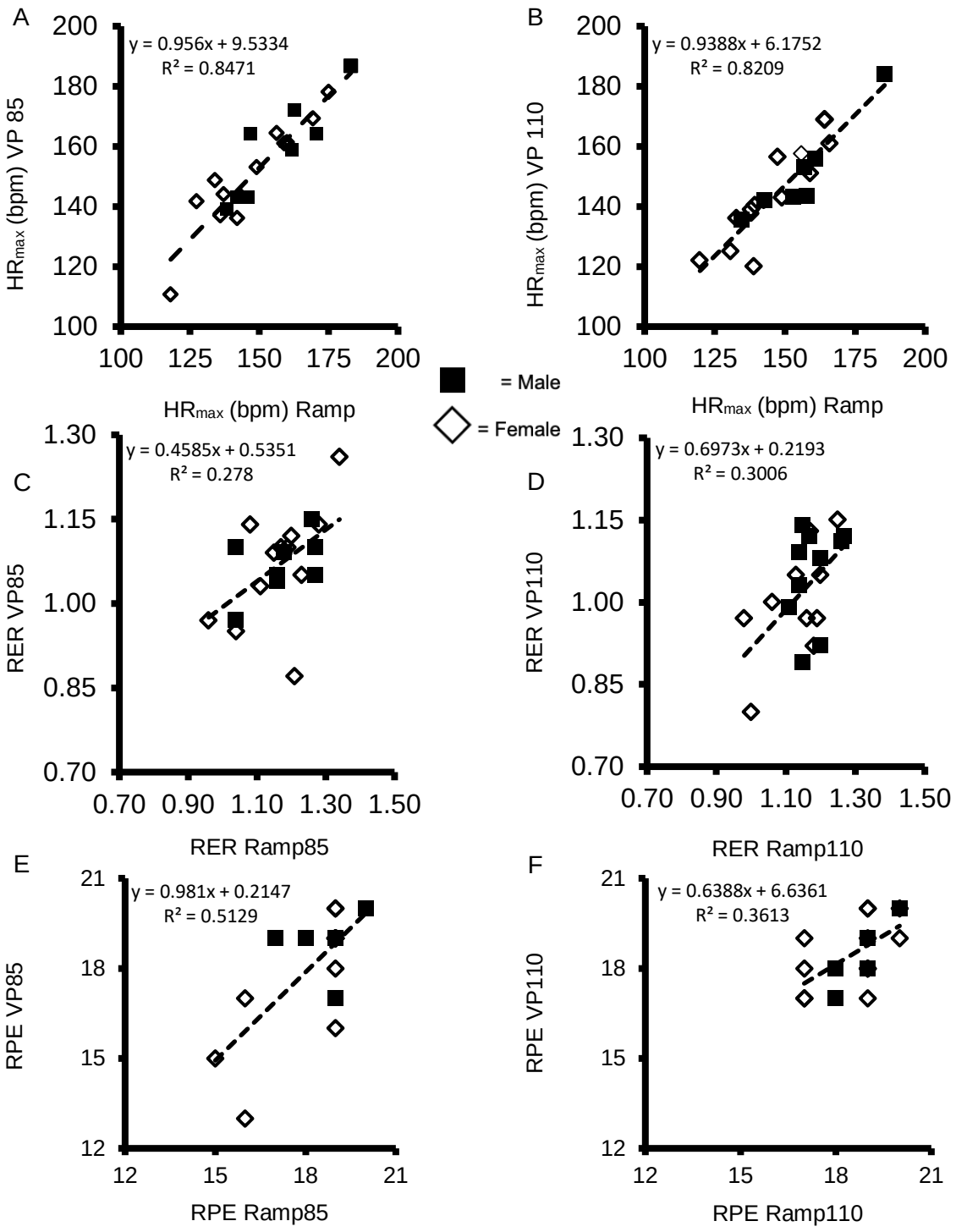

Figure 4-9. Pearson's Correlations for heart rate (HR), respiratory exchange ratio (RER), and ratings of perceived exertion (RPE) achieved on the ramp (x-axis) (Ramp85 & Ramp110) and the associated verification phase (y-axis) (VP85 & VP110) for each subject. HR data is presented for VP 85 (A) and VP110 (B). RER data is presented for VP85 (C) and VP110 (D). RPE is presented for VP85 (E) and VP110 (F).

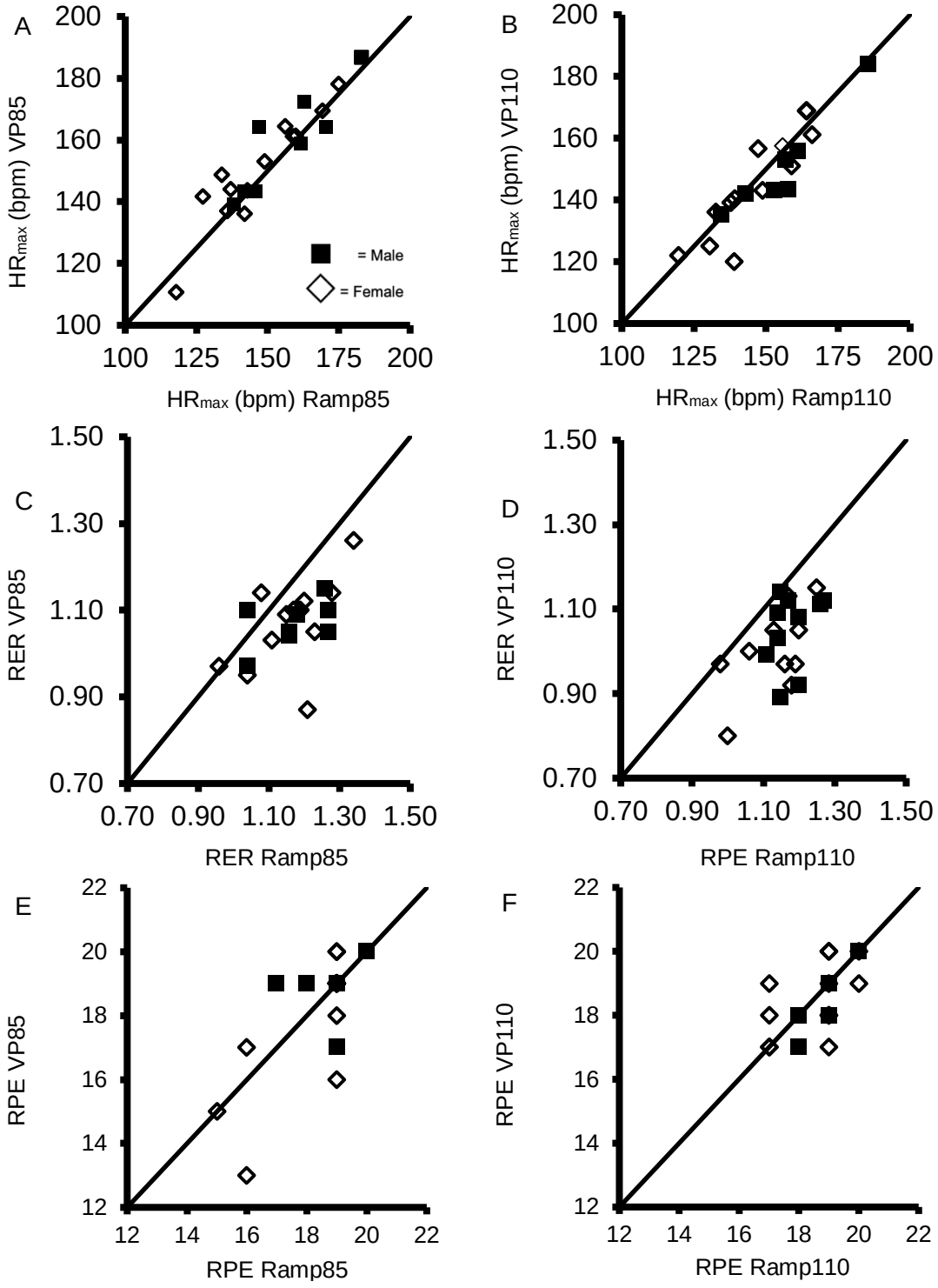

Figure 4-10. Heart rate (HR), respiratory exchange ratio (RER), and ratings of perceived exertion (RPE) achieved on the ramp (x-axis) (ramp85 & ramp110) and verification phase (y-axis) (VP85 & VP110) for each subject. The line represents the line of identity (y=x). HR data is presented for VP 85 (A) and VP110 (B). RER data is presented for VP85 (C) and VP110 (D). RPE is presented for VP85 (E) and VP110 (F).

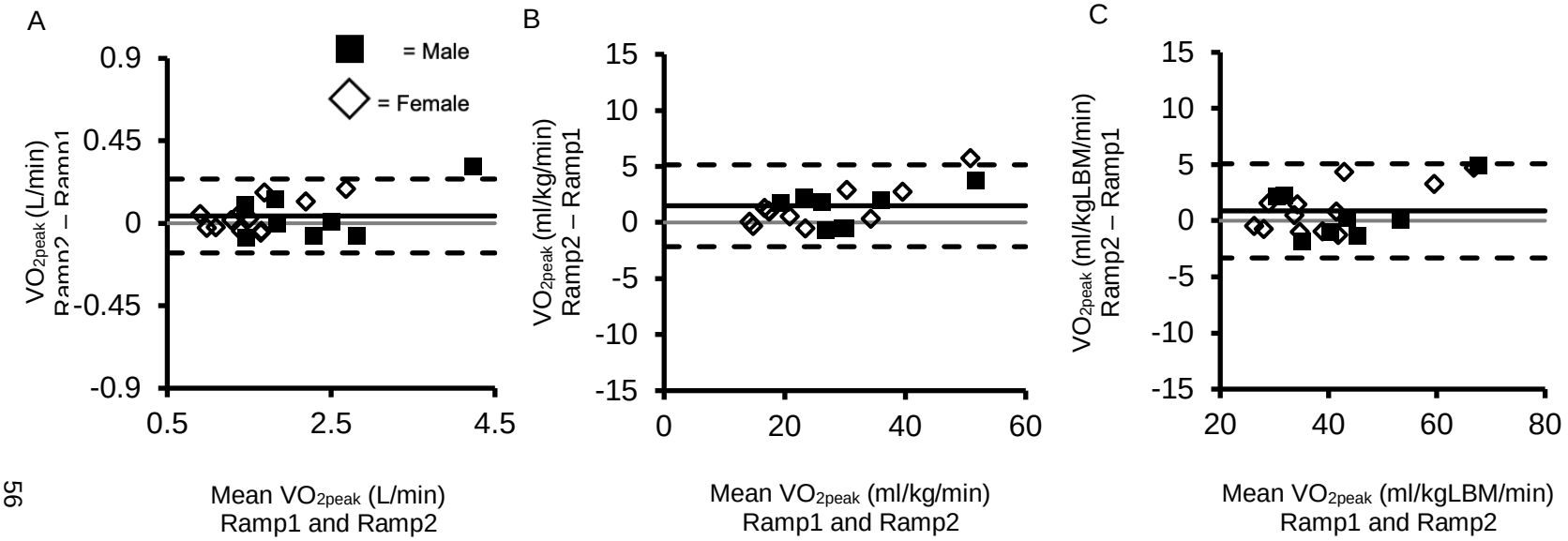

Figure 4-11. Bland-Altman plots for VO_{2peak} during the ramp on the first visit (Ramp1) and the ramp on the second visit (Ramp2). (A) Maximal oxygen uptake (VO_{2peak}) in absolute measures (L/min). (B) VO_{2peak} relative to body mass (ml/kg/min). C) VO_{2peak} normalized to lean body mass (ml/kgLBM/min). Y-axis = verification-ramp; x-axis = mean of ramp and verification phase; bold dotted lines = mean ± 1.96 x SD; light solid lines = 0 on the y-axis; dark solid lines = mean of verification phase-ramp

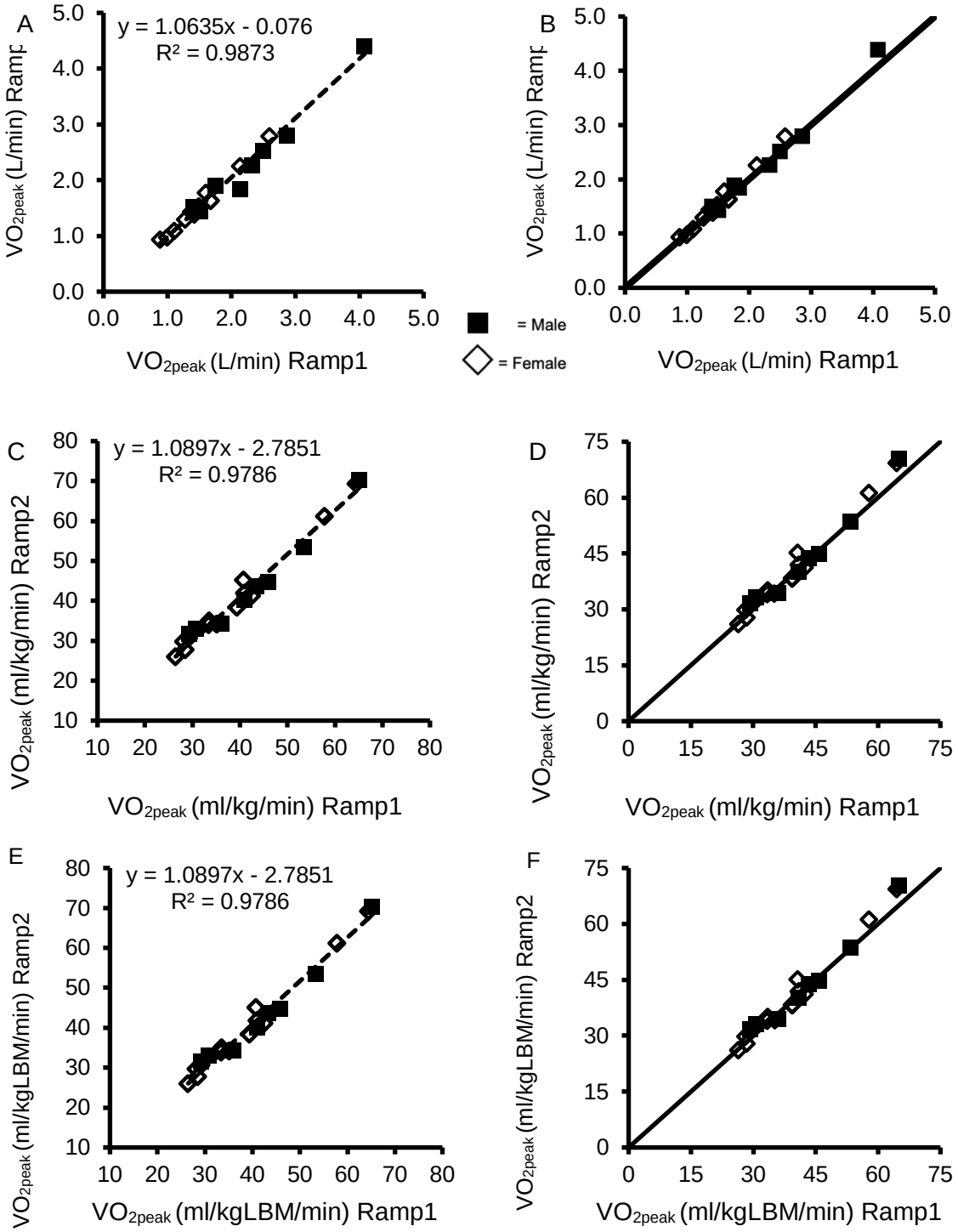

Figure 4-12. VO_{2peak} Comparisons between the ramp performed on the first visit (Ramp1) and second visit (Ramp2). Maximal oxygen uptake (VO_{2peak}) achieved on Ramp1 (x-axis) and Ramp2 (y-axis) phase for each subject. Line of Identity where (x=y) for absolute VO_2 (L/min) (B), relative to body mass (ml/kg/min) (D), and normalized to lean body mass (ml/kgLBM/min) (F). Pearson's Correlations are presented for absolute (L/min) (A), relative to body mass (C), and normalized to LBM (E).

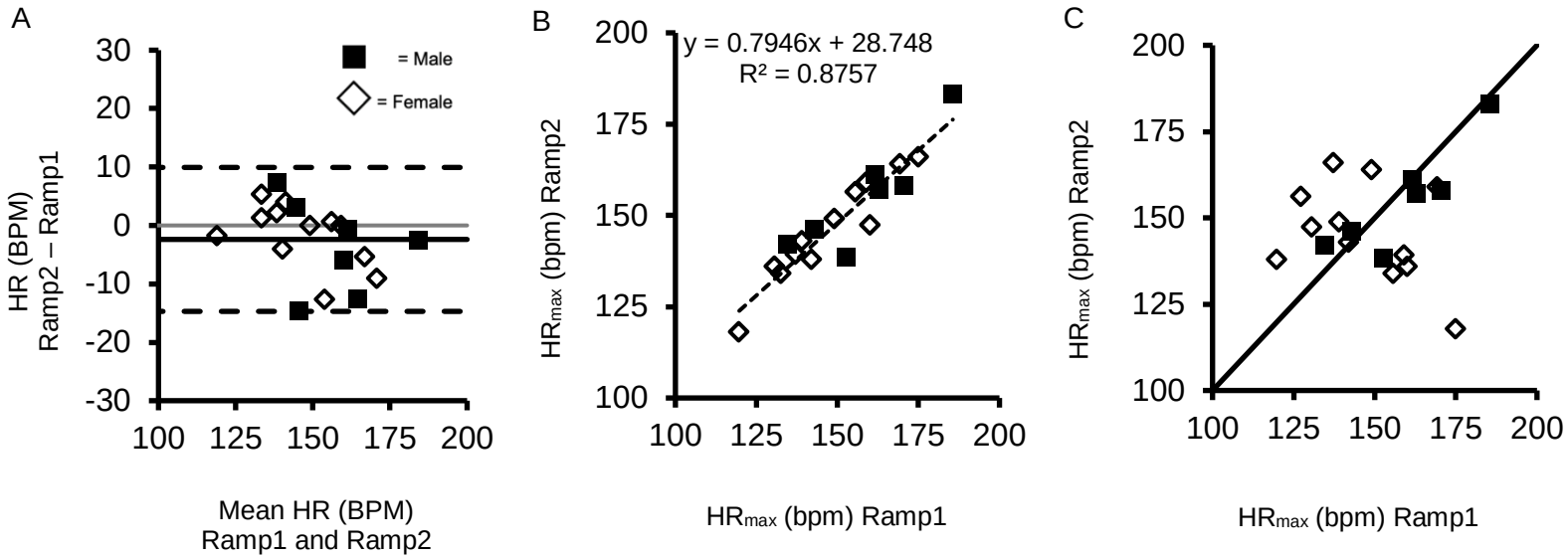

Figure 4-13. Heart rate (HR) comparisons between the ramp performed on the first visit (Ramp1) and the ramp performed on the second visit (Ramp2). Bland-Altman plot for HR. Y-axis = Ramp2 – Ramp1; x-axis = Mean HR for Ramp1 and Ramp2; bold dotted lines = mean ± 1.96 x SD; light solid lines = 0 on the y-axis; dark solid lines = mean of Ramp2 – Ramp1 (A). Pearson's Correlations of maximal heart rate (HR_{max}) between Ramp1 (x-axis) and Ramp2 (y-axis) (B). Line of Identity (y = x), Ramp1 (x-axis) and Ramp2 (y-

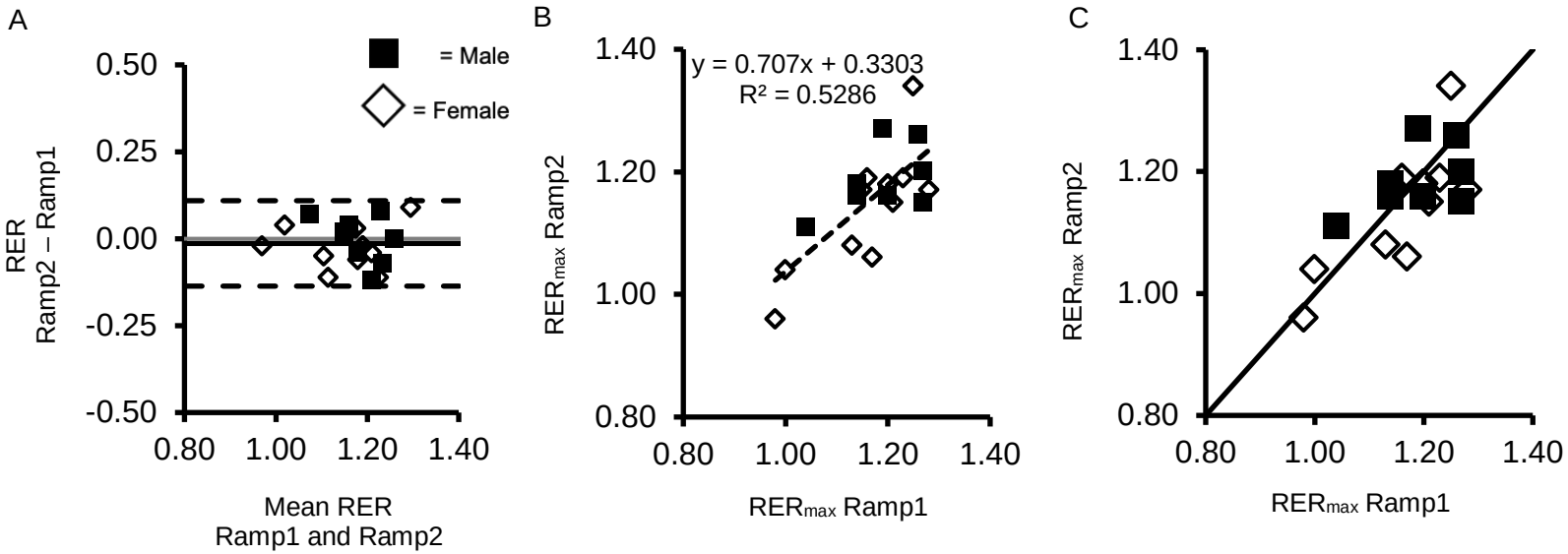

Figure 4-14. Respiratory exchange ratio (RER) comparisons between the ramp performed on the first visit (Ramp1) and the second visit (Ramp2). Bland-Altman plot for RER. Y-axis = Ramp2 – Ramp1; x-axis = Mean RER for Ramp1 and Ramp2; bold dotted lines = mean ± 1.96 x SD; light solid lines = 0 on the y-axis; dark solid lines = mean of Ramp2 – Ramp1 (A). Pearson's Correlations between Ramp 1 (x-axis) and Ramp 2 (y-axis) (B). Line of Identity (y = x), RER at maximal exercise (RER_{max}) Ramp1 (x-axis) and Ramp2 (y-axis) (C)

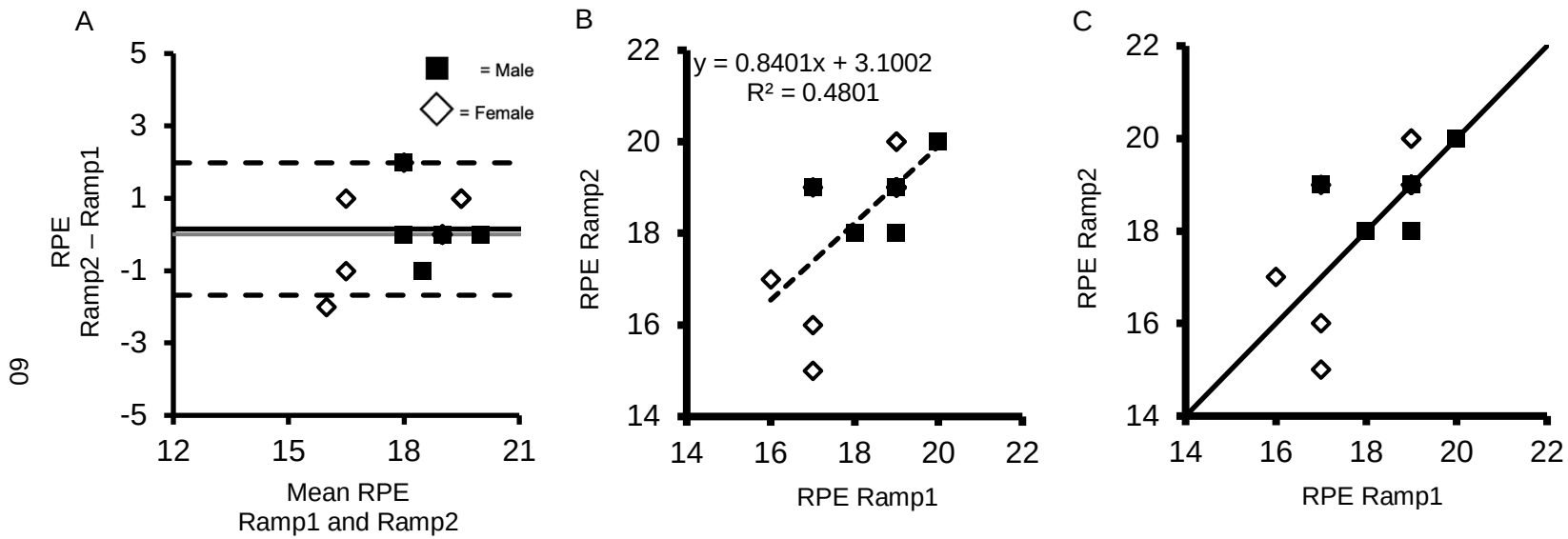

Figure 4-15. Ratings of perceived exertion (RPE) comparisons between the ramp performed on the visit (Ramp1) and second visit (Ramp2). Bland-Altman plot for RPE. Y-axis = Ramp2 – Ramp1; x-axis = Mean RPE for Ramp1 and Ramp2; bold dotted lines = mean ± 1.96 x SD; light solid lines = 0 on the y-axis; dark solid lines = mean of Ramp2 – Ramp1 (A). Person's Correlations between Ramp1 (x-axis) and Ramp2 (y-axis) (B). Line of Identity (y = x), Ramp1 (x-axis) and Ramp2 (y-axis) (C)

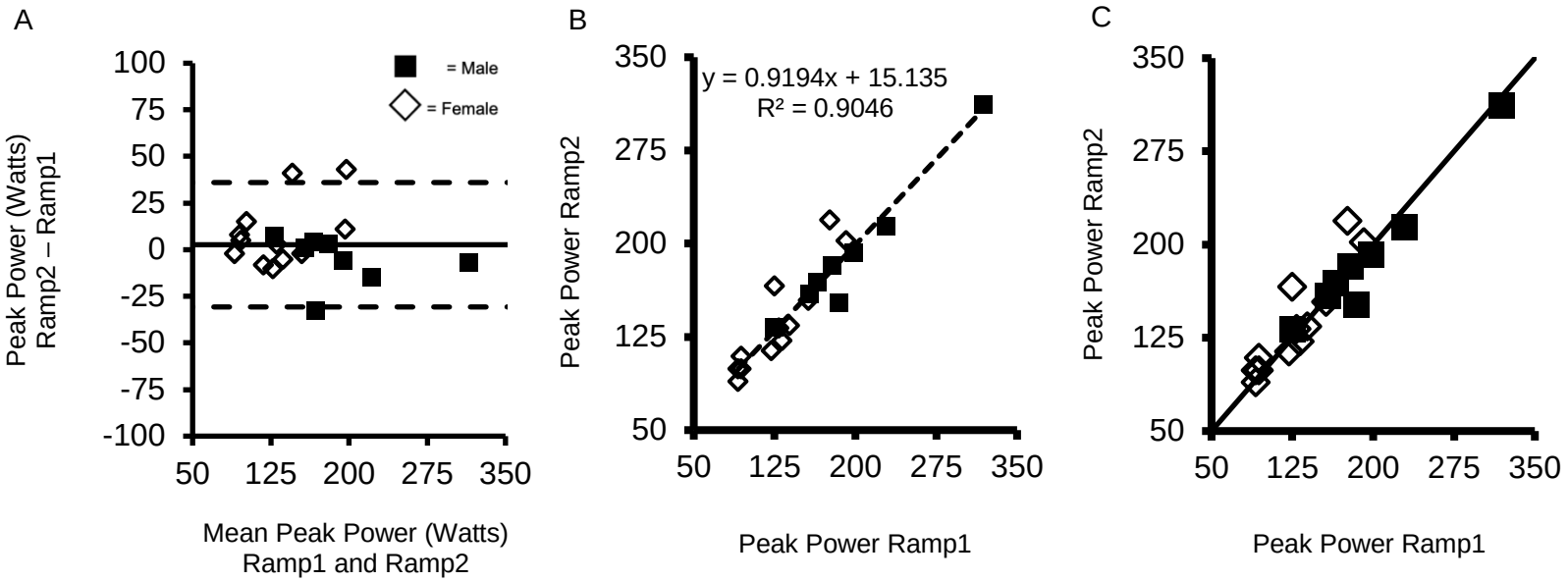

Figure 4-16. Peak Power (Watts) comparisons between the ramp performed during the first visit (Ramp1) and the second visit (Ramp2). Bland-Altman plot for Peak Power. Y-axis = Ramp2 – Ramp1; x-axis = Mean Peak Power for Ramp1 and Ramp2; bold dotted lines = mean ± 1.96 x SD; light solid lines = 0 on the y-axis; dark solid lines = mean of Ramp2 – Ramp1 (A). Pearson's Correlations between Ramp1 (x-axis) and Ramp2 (y-axis) (B). Line of Identity (y = x), Ramp1 (x-axis) and Ramp2 (y-axis) (C)

CHAPTER FIVE

DISCUSSION

This study was designed to evaluate various strategies to accurately assess VO_{2max} in older adults. The need to accurately determine VO_{2max} in older adults is related to the declining VO_{2max} present in the older population and the increased health risks associated with a low VO_{2max}. In particular, one of the difficulties of VO_2 assessments is determining whether the test resulted in a true VO_{2max}. To help differentiate between a VO_{2peak} and a VO_{2max}, some researchers have called for the use of a verification phase (11, 28). Previous research has recommended the analysis of individual data opposed to group means due to the intersubject variability that may present the necessity of a verification phase from some subjects while a traditional ramp assessment may elicit accurate results on its own. The goal of the study was to determine whether a verification phase was necessary for otherwise healthy individuals between 60-80 years of age, and if so, whether a higher (110%) or lower (85%) verification phase work rate would elicit more accurate results. The novel findings from this study are 1) an otherwise healthy older adult is capable of performing a traditional ramp assessment with the addition of a verification phase, 2) a verification phase may not be necessary for attainment of VO_{2max}, and 3) a submaximal verification phase may elicit a more accurate measurement of VO_{2peak} than a supramaximal verification phase. Collectively, these findings indicate that in most older healthy adults a single traditional ramp test can be used to accurately assess VO_{2peak}, however, if a verification phase test is employed for the assessment of VO_{2max} in otherwise health older adults, a work rate slightly below peak may provide a more accurate assessment compared to a work rate slightly above peak.

Previous studies have utilized verification phases between 85% and 115% of peak work rate achieved on a cycle ergometer to assess VO_2 (7, 9, 10, 13-19, 26, 27). Thus, we selected work rates at the high and low end of the spectrum to compare whether a work rate above or below peak work rate would elicited higher VO_2 values. Specifically, we hypothesized that the submaximal verification phase would yield higher values given these individuals were not accustomed to

performing high intensity exercise. In contrast, however, both the supramaximal and submaximal work rates yielded similar physiological data as the corresponding ramp, at least when comparing group means. These findings are consistent with other reports in the literature in older adults in which no difference between the verification phase and the ramp was found (13, 26). Interestingly, however, the individual data shows that a greater number of individuals achieved a higher VO_{2peak} during VP85 compared to Ramp85 (8 of 22) than during VP110 compared to Ramp110 (3 of 20). Moreover, examination of the Bland-Altman Plots demonstrate no systematic bias of the use of either verification phase work rate along the range of VO_{2max} values assessed in the current study. However, the Bland-Altman plots do demonstrate greater variation for VP110 vs. VP85. Collectively, these data would suggest that a verification phase may not be needed in a majority of the older adult population, but instead may be needed depending on the individual. The individual findings of this study indicate that if a verification phase were to be conducted, the submaximal verification phase may elicit more accurate results than a supramaximal verification phase in otherwise older adults.

The present study found that the supramaximal verification phase elicited a shorter exercise duration (~82 seconds) compared to the longer duration of the submaximal verification phase (~180 seconds). Previous research in otherwise healthy older adults utilized a verification phase at 105% of peak work load achieved verification phase durations of ~102 seconds (13) and ~150 seconds (26). The decrease in duration may be due to the 5% difference in verification phase work rate in subjects approximately the same age (13, 26). The short duration of VP110 may also result in lower values for VO_{2peak} due to a decreased utilization of the slow component of VO_2 (57). In contrast, the longer duration of VP85 may take an advantage of the slow component. Specifically, it has been previous reported that an exercise duration of 3-minutes is necessary to observe changes in O_2 kinetics that are due to the VO_2 slow component (57). While we did not observe a correlation between exercise duration of the VP85 and the difference if VO_{2peak} between Ramp85 and VP85, the greater number of individuals that achieved a higher VO_{2peak} compared to the ramp test during VP85 could be due to the longer exercise duration compared to VP110.

HR is commonly used for exercise prescription in various settings (5). An accurate measure of maximal HR is important is essential for adequate estimation of exertion levels for a subject. The present study found no statistical differences between maximal HR between Ramp85 and VP85 or between Ramp110 and VP110. This data contradicts a previous study that found a significantly different HR_{max} between a supramaximal verification phase and the associated ramp as well as between the submaximal verification phase and the associated ramp in subjects ~68 years of age (13). The differences in results could be due to methodological considerations as to how HR was assessed during exercise. Murias et al. assessed HR through the use of a three-lead electrocardiogram, while we used a polar HR monitor and Physioflow device to assess HR (13). Similar to VO_{2peak} measures, individual data indicate that some subjects had a higher HR_{max} from ramp to verification phase during VP85 (7 of 21) and VP110 (3 of 19). These individual data may indicate that a supramaximal verification phase until volitional exhaustion is a more accurate assessment of HR_{max} compared to a submaximal verification phase.

In addition to comparison of different work rates for a verification phase, the present study also examined the repeatability of a traditional ramp assessment in older individuals. In our study, subjects completed two identical traditional ramp assessments approximately a week apart. We chose this time frame so the subject should have adequate time to recover from the first visit (5), but not enough time for change in VO_{2max} to occur due to any training or detraining (5). Our results show there is no significant differences between the ramp performed on the first visit (Ramp1) and the ramp performed on the second visit (Ramp2) in the absolute measures of VO_{2peak} and HR. Moreover, compared to the ramp vs. verification phase comparisons, a slightly greater number of subjects achieved a higher VO_{2peak} during Ramp2 compared to Ramp1 (45%; 9 of 20). However, we did find a significant difference between Ramp1 and Ramp2 in VO_{2peak} relative to body weight (ml/kg/min). At this time, we cannot fully explain this difference, but it may be due to slight increases in VO_2 and slight decreases in body weight. While no significant differences in the time to exhaustion and peak power outputs between Ramp1 and Ramp2 were detected, the higher VO_{2peak} in 8 of the 9 subjects corresponded to increased time to exhaustion during Ramp2 compared to

Ramp1. These data indicate an accurate assessment of VO_{2peak} may be obtained during a single ramp test for most subjects, however, some subjects may not be accustomed to the maximal intensity of exercise, mode of exercise or the breathing apparatus (103). Moreover, the results of the present study indicate that a familiarization trial or second ramp could increase the accuracy of VO_{2peak} assessments in older adults, perhaps for a greater number of individual as compared to the use of a verification phase,

There are some limitations to this study. First, we utilized stationary cycle ergometer testing. It is known that testing on a cycle ergometer produces ~10% lower values for VO_{2peak} compared to treadmill testing, and consequently, whether similar results would be obtained on a treadmill require further investigation. However, we chose to perform the tests on a cycle ergometer as a safety measure for older participants. This study also utilized a 10-minute active rest period between the end of the ramp test and the initiation of the verification phase. Previous studies have utilized rest periods as low as 3-minutes and up to a full week between tests (7, 9, 10, 13-27). Consequently, whether similar results would be obtained using longer rest periods is unknown. However, from a practical standpoint a recovery time of ~10 minutes may be more efficient for both research and clinical practice as the subject would not be required to come back at a later time or date. On the other hand, a considerable strength of this study is that we employed a randomized, counterbalanced cross over design in which each subject completed both a supramaximal and a submaximal verification phase. In fact, previous verification phase studies using older adults have had subjects complete either the supramaximal verification phase or the submaximal verification phase (13). Lastly, our results are also limited to otherwise healthy older adults. Therefore, further research is needed to determine whether a verification phase would be beneficial to use in the older clinical populations, and at what work rate.

In conclusion, this study found that maximal oxygen uptake can be accurately assessed in most otherwise healthy individuals 60-80 years of age during a single traditional ramp test without a verification phase. These results are in line with current studies using similar protocols (13, 26). However, based on the individual data, if a verification phase is to be used, a submaximal work

rate may be a more accurate assessment than a supramaximal work rate, at least in otherwise healthy older adults. Moreover, the results of this study suggest that a second ramp assessment may be beneficial as 45% of subjects achieved a high VO_2 during the second ramp compared to the first. Given the role of VO_2 as an indicator for cardiovascular disease, functional limitations, and increased risk of morbidity and mortality, the results of this study may assist risk assessment in otherwise healthy older individuals. Additional research should be employed in clinical populations to identify at risk individuals to assist with exercise protocols decrease these risks.

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APPENDIX A

HUMAN SUBJECTS

CONSENT FORM

Title of research study: Use of a Verification Phase for Determination of VO_2Max in Older Adults

Investigator: Jared M. Dickinson, PhD
College of Health Solutions
Arizona State University

Ian R. Villanueva, BS
College of Health Solutions
Arizona State University

Why am I being invited to take part in a research study?

We invite you to take part in a research study because:

- You are between 60 and 80 years of age
- You are healthy, and do not have any major health problems such as heart trouble, lung, kidney or liver problems, active cancer, or existing muscle/bone injuries

Why is this research being done?

The study being done to identify the best practices for determining maximal oxygen uptake (VO_2) in older adults. This is important because maximal VO_2 is the most amount of oxygen your body can utilize in a given time and is very relevant to determining general health risk.

How long will the research last?

We expect that individuals will visit our laboratory for two (2) visits. The first visit will last about 90 minutes and the second visit will last about one (1) hour.

How many people will be studied?

We expect up to 40 people from the Phoenix area to participate in this research study.

What happens if I say yes, I want to be in this research?

It is up to you to decide whether or not to participate. Your participation will involve coming to the test site where the study will be explained to you, we will answer any questions you may have and you will be asked to sign this consent. When the consent is signed you will go through the following tests (a study timeline is presented later in this consent form):

Screening (Visit #1 only):

1. Fill out and sign a questionnaire called the PAR-Q+ to acknowledge that you are suitable to perform exercise. If you answer "Yes" to any of the questions on the PAR-Q+ you may need to obtain permission from a physician to participate in this study.
2. Measurement of your height, weight and blood pressure to ensure that you meet the criteria of participation.
3. We will ask you to complete a medical history and exercise questionnaire.

Body Composition (Visit #2 only):

4. You will be asked to undergo a DXA scan (similar to a low-dose x-ray). You will be escorted to the second floor of the ABC building and positioned on a padded, examination table lying face up. The DXA scan will last no more than five (5) minutes and will consist of a scanning head that will travel over top of the body. A licensed radiology technician will perform the DXA scan. If you are a female of child-bearing age, before you receive the DXA scan we will ask you to perform a pregnancy test that we provide and use this test to determine that you are not pregnant prior to performing the DXA scan.

Maximal Exercise Testing (Both Visit #1 and Visit #2):

5. We will fit the cycle ergometer to your comfort.
6. Maximal Exercise Test: We will ask you to perform a maximal exercise test (similar to a stress test at a doctor's office) on a stationary cycle. You will be asked to cycle with increasing intensity (resistance) until you decide you can no longer exercise, at which point you the intensity will be lowered for a cool down. After a 10-minute rest period you will perform an "all-out" bout of exercise at resistance either slightly below or slightly above the end of the previous test. Again, you will push yourself as hard as you feel comfortable with until you are exhausted.
    a. During this test you will be equipped with a mouthpiece attached to a hose that collects your expired breath.
    b. We monitor your heart rate with a wireless strap that is worn on your chest.
    c. You will also have 6 (six) electrodes placed around your chest to monitor the activity of your heart during exercise.
7. Upon completion of the Maximal Exercise Test, you will enter another cool-down period of light cycling.
8. We will have you recover in the lab to ensure you do not have any adverse post-test side effects.

SUMMARIZED SCHEDULE AND TIME COMMITMENT

Visit #1

- Review of study
- Screening
- Maximal exercise testing

Time Commitment: 90 minutes

Visit #2 (Familiarization)

- Body composition assessment
- Blood pressure measurement
- Maximal exercise testing

Time Commitment: 60 minutes

What happens if I say yes, but I change my mind later?

You can leave the research at any time, it will not be held against you. If you stop being in the research project, data collected up to the point of your withdrawal from the study will remain with the research team to ensure the integrity of the research project. These data will be handled the same as research data. If you decide to stop the research project, no explanation is required.

Is there any way being in this study could be bad for me?

1) **Screening Tests**. In the case that one or more of the screening test results do not allow you to participate in the study, a member of the research team will inform you. These tests include your blood pressure as well as your answers to the PAR-Q+ and medical history questionnaire. Not being able to participate or being informed of abnormal blood pressure may upset you.
2) **DXA Scan.** This procedure will expose you to a very small amount of radiation, much less than most X-ray procedures, and less than the amount of radiation you would be exposed to in a 2-hour plane flight. Exposure to radiation can increase the risk of getting cancer and birth defects. The amount of radiation to which you will be exposed during the DXA scan is so small that the exact risk is unknown. The exposure of radiation via X-ray during DXA scans is especially risky for women who are pregnant or have a risk of being pregnant.
3) **Exercise Testing**. Muscle soreness or cramps may occur. These are the most likely side effects of exercise, and can be reduced with an adequate warm-up. Exercise may also expose you to a low risk of cardiovascular events, such as a heart attack, especially if you have a predisposing condition. However, a cardiovascular event such as a heart attack is a very rare potential risk in individuals without a predisposing condition. Our screening procedures are specifically designed to minimize your risks.
4) **Confidentiality**. There is a general risk of disclosure of personal sensitive data in a clinical investigation. To minimize this risk only the investigators and the laboratory personnel will have access to your personal information. All research data containing your name will be locked in the Principal Investigator's office. To preserve confidentiality, immediately after enrollment you will be assigned a code by which all research material will be identified, thus avoiding identification by technicians or non-qualified individuals.
5) **Other unforeseen or unknown risks may occur**. As with any research, there is some a possibility that you be subject to risks that have not yet been identified. You will be closely monitored for any unforeseen risks. You should not be pregnant while in this research study.

Will being in this study help me in any way?

We cannot promise any benefits to you or others from your taking part in this research. You will receive a copy of your exercise testing results if you so choose. However, the knowledge gained from this study could have a benefit to society by providing new data regarding the how best to identify VO2max, which could improve our ability to identify people with general health risks. After your participation in the study is complete, selected results will be available to you if the Research Results Acknowledgement Statement is signed.

What happens to the information collected for the research?

Efforts will be made to limit the use and disclosure of your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise complete secrecy. Organizations that may inspect and copy your information include the IRB and other representatives of this organization.

What else do I need to know?

If you agree to take part in this research study, we will pay you for your time and effort. All study-related costs associated with your participation will be paid by funds allocated to the research team. If you drop out or are excluded, we will pay you a prorated basis for your participation up to the point of termination:

- $5 for showing up for screening but not completing any tests
- $15 total for the completion of all tests described under visit #1
- $30 total for completion of all tests for visit #1 and visit #2

There will be no cost to you, the subject, during your participation in this study other than the cost of travel to and from the Arizona Biomedical Collaborative Building. If you agree to participate in the study, then consent does not waive any of your legal rights. However, no funds have been set aside to compensate you in the event of injury. However, if any injury occurs due to the experimental procedures, first aid will be provided. If there is a situation that the research team believes needs attention by a primary care practitioner, you will be referred to the Nurse Practitioner Clinic on the Downtown Arizona State University campus (approximately two (2) blocks from the lab). If any injury occurs after the Nurse Practitioner Clinic is closed, you should seek attention at an urgent care facility. If a medical emergency were to occur during this study, we will call "911" to bring emergency medical personnel to the lab. You will be responsible for any costs incurred. Your participation may be stopped by the research team without your consent if

1) You do not meet the inclusion/exclusion criteria of this study.
2) You experience adverse events such as extreme muscle soreness or inability to complete the measurements during the visit
3) The study physician determines that your participation in this study will interfere with your safety and well-being.

Who can I talk to?

If you have questions, concerns, or complaints, or think the research has hurt you, talk to the research team at 602-827-2492 (business hours), ian.villanueva@asu.edu (any time) or 602-827-2269 (business hours), jared.dickinson@asu.edu (any time).

This research has been reviewed and approved by the Bioscience IRB ("IRB"). You may talk to them at (480) 965-6788 or research.integrity@asu.edu if:

- Your questions, concerns, or complaints are not being answered by the research team.
  - You cannot reach the research team.
  - You want to talk to someone besides the research team.
  - You have questions about your rights as a research participant.
  - You want to get information or provide input about this research.

Written Informed Consent

- Your participation in this study is completely voluntary and you have been told that you may refuse to participate or stop your participation in this project at any time without penalty or loss of benefits and without jeopardizing any relationships with Arizona State University. If you decide to stop your participation in this project and revoke your authorization for the use and disclosure of your health information, Arizona State University may continue to use and disclose your health information in some instances. This would include any health information that was used or disclosed prior to your decision to stop participation and needed in order to maintain the integrity of the research study. If we get any information that might change your mind about participating, we will give you the information and allow you to reconsider whether or not to continue.
- The purpose of this research study, procedures to be followed, risks and benefits have been explained to you. You have been allowed to ask questions and your questions have been answered to your satisfaction. You have been told who to contact if you have additional questions. You have read this consent form and voluntarily agree to participate as a subject in this study. You are free to withdraw your consent, including your authorization for the use and disclosure of your health information, at any time. You may withdraw your consent by notifying Ian Villanueva, BS at (ian.villanueva@asu.edu or 602-827-2492). You will be given a copy of the consent for which you have signed.

Informed consent is required of all persons in this project. Whether or not you provide an informed consent for this research study will have no effect on your current or future relationship with Arizona State University.

Your signature documents your permission to take part in this research.

Signature of participant	Date
Printed name of participant	
Signature of person obtaining consent	Date
Printed name of person obtaining consent	

APPENDIX B

SCREENING FORMS

CSEP approved Sept 12 2011 version

PAR-Q+

The Physical Activity Readiness Questionnaire for Everyone

Regular physical activity is fun and healthy, and more people should become more physically active every day of the week. Being more physically active 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.

SECTION 1 - GENERAL HEALTH

	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)?	☐	☐
5.	Are you currently taking prescribed medications for a chronic medical condition?	☐	☐
6.	Do you have a bone or joint problem that could be made worse by becoming more physically active? Please answer NO if you had a joint problem in the past, but it does not limit your current ability to be physically active. For example, knee, ankle, shoulder or other.	☐	☐
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.

Go to Section 3 to sign the form. You do not need to complete Section 2.

- Start becoming much more physically active – start slowly and build up gradually.
- Follow the Canadian Physical Activity Guidelines for your age (www.csep.ca/guidelines).
- You may take part in a health and fitness appraisal.
- If you have any further questions, contact a qualified exercise professional such as a CSEP Certified Exercise Physiologist® (CSEP-CEP) or CSEP Certified Personal Trainer® (CSEP-CPT).
- If you are over the age of 45 yrs. and NOT accustomed to regular vigorous physical activity, please consult a qualified exercise professional (CSEP-CEP) before engaging in maximal effort exercise.

If you answered YES to one or more of the questions above, please GO TO SECTION 2.

Delay becoming more active if:

- You are not feeling well because of a temporary illness such as a cold or fever – wait until you feel better
- You are pregnant – talk to your health care practitioner, your physician, a qualified exercise professional, and/or complete the PARmed-X for Pregnancy before becoming more physically active OR
- Your health changes – please answer the questions on Section 2 of this document and/or talk to your doctor or qualified exercise professional (CSEP-CEP or CSEP-CPT) before continuing with any physical activity programme.

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SECTION 2 - CHRONIC MEDICAL CONDITIONS

Please read the questions below carefully and answer each one honestly: check YES or NO.			YES	NO
1.	Do you have Arthritis, Osteoporosis, or Back Problems?		☐ If yes, 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)	☐	☐
	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)?	☐	☐
	1c.	Have you had steroid injections or taken steroid tablets regularly for more than 3 months?	☐	☐
2.	Do you have Cancer of any kind?		☐ If yes, 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 neck?	☐	☐
	2b.	Are you currently receiving cancer therapy (such as chemotherapy or radiotherapy)?	☐	☐
3.	Do you have Heart Disease or Cardiovascular Disease? This includes Coronary Artery Disease, High Blood Pressure, Heart Failure, Diagnosed Abnormality of Heart Rhythm		☐ If yes, answer questions 3a-3e	☐ 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)	☐	☐
	3b.	Do you have an irregular heart beat that requires medical management? (e.g. atrial fibrillation, premature ventricular contraction)	☐	☐
	3c.	Do you have chronic heart failure?	☐	☐
	3d.	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)	☐	☐
	3e.	Do you have diagnosed coronary artery (cardiovascular) disease and have not participated in regular physical activity in the last 2 months?	☐	☐
4.	Do you have any Metabolic Conditions? This includes Type 1 Diabetes, Type 2 Diabetes, Pre-Diabetes		☐ If yes, answer questions 4a-4c	☐ If no, go to question 5
	4a.	Is your blood sugar often above 13.0 mmol/L? (Answer YES if you are not sure)	☐	☐
	4b.	Do you have any signs or symptoms of diabetes complications such as heart or vascular disease and/or complications affecting your eyes, kidneys, and the sensation in your toes and feet?	☐	☐
	4c.	Do you have other metabolic conditions (such as thyroid disorders, pregnancy-related diabetes, chronic kidney disease, liver problems)?	☐	☐
5.	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 yes, answer questions 5a-5b	☐ If no, go to question 6
	5a.	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)	☐	☐
	5b.	Do you also have back problems affecting nerves or muscles?	☐	☐

Please read the questions below carefully and answer each one honestly: check YES or NO.			YES	NO
6.	Do you have a Respiratory Disease? This includes Chronic Obstructive Pulmonary Disease, Asthma, Pulmonary High Blood Pressure		☐ If yes, answer questions 6a-6d	☐ 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)	☐	☐
	6b.	Has your doctor ever said your blood oxygen level is low at rest or during exercise and/or that you require supplemental oxygen therapy?	☐	☐
	6c.	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?	☐	☐
	6d.	Has your doctor ever said you have high blood pressure in the blood vessels of your lungs?	☐	☐
7.	Do you have a Spinal Cord Injury? This includes Tetraplegia and Paraplegia		☐ If yes, answer questions 7a-7c	☐ 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)	☐	☐
	7b.	Do you commonly exhibit low resting blood pressure significant enough to cause dizziness, light-headedness, and/or fainting?	☐	☐
	7c.	Has your physician indicated that you exhibit sudden bouts of high blood pressure (known as Autonomic Dysreflexia)?	☐	☐
8.	Have you had a Stroke? This includes Transient Ischemic Attack (TIA) or Cerebrovascular Event		☐ If yes, answer questions 8a-c	☐ 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)	☐	☐
	8b.	Do you have any impairment in walking or mobility?	☐	☐
	8c.	Have you experienced a stroke or impairment in nerves or muscles in the past 6 months?	☐	☐
9.	Do you have any other medical condition not listed above or do you live with two chronic conditions?		☐ If yes, answer questions 9a-c	☐ If no, read the advice on page 4
	9a.	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?	☐	☐
	9b.	Do you have a medical condition that is not listed (such as epilepsy, neurological conditions, kidney problems)?	☐	☐
	9c.	Do you currently live with two chronic conditions?	☐	☐

Please proceed to Page 4 for recommendations for your current medical condition and sign this document.

PAR-Q+

If you answered NO to all of the follow-up questions about your medical condition, you are ready to become more physically active:

- It is advised that you consult a qualified exercise professional (e.g., a CSEP-CEP or CSEP-CPT) 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 – 20-60 min. 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 yrs. and NOT accustomed to regular vigorous physical activity, please consult a qualified exercise professional (CSEP-CEP) before engaging in maximal effort exercise.

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

- You should seek further information from a licensed health care professional before becoming more physically active or engaging in a fitness appraisal and/or visit a or qualified exercise professional (CSEP-CEP) for further information.

Delay becoming more active if:

- You are not feeling well because of a temporary illness such as a cold or fever – wait until you feel better
- You are pregnant - talk to your health care practitioner, your physician, a qualified exercise profesional, and/or complete the PARmed-X for Pregnancy before becoming more physically active OR
- Your health changes - please talk to your doctor or qualified exercise professional (CSEP-CEP) before continuing with any physical activity programme.

SECTION 3 - DECLARATION

- You are encouraged to photocopy the PAR-Q+. You must use the entire questionnaire and NO changes are permitted.
- The Canadian Society for Exercise Physiology, the PAR-Q+ Collaboration, and their agents assume no liability for persons who undertake physical activity. If in doubt after completing the questionnaire, consult your doctor prior to physical activity.
- 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.
- Please read and sign the declaration below:

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 a Trustee (such as my employer, community/fitness centre, health care provider, or other designate) may retain a copy of this form for their records. In these instances, the Trustee will be required to adhere to local, national, and international guidelines regarding the storage of personal health information ensuring that they maintain the privacy of the information and do not misuse or wrongfully disclose such information.

NAME _____ DATE _____

SIGNATURE _____ WITNESS _____

SIGNATURE OF PARENT/GUARDIAN/CARE PROVIDER _____

For more information, please contact:
Canadian Society for Exercise Physiology
www.csep.ca

KEY REFERENCES
1. Jamnik VJ, Warburton DER, Makarski J, McKenzie DC, Shephard RJ, Stone J, and Gledhill N. Enhancing the eectiveness of clearance for physical activity participation; background and overall process. APNM 36(S1):S3-S13, 2011.
2. Warburton DER, Gledhill N, Jamnik VK, Bredin SSD, McKenzie DC, Stone J, Charlesworth S, and Shephard RJ. Evidence-based risk assessment and recommendations for physical activity clearance; Consensus Document. APNM 36(S1):S266-s298, 2011.

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 BC Ministry of Health Services.

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MEDICAL HISTORY QUESTIONNAIRE

The following questions are designed to obtain a thorough medical history. The information you provide will help us to make the best determination about your eligibility for a particular study. Please answer all questions and provide as much information as you possibly can. This questionnaire, as well as any other medical information you provide, will be kept confidential and will not be shared with any unauthorized person or organization unless you specifically request us to do so.

Subject ID: _____

Date Completed: _____

Personal Physician's Name: _____Phone_____

Address:_____

_____

Height: estimated _____ in

Weight: estimated _____ lb

Personal Health History

Have you ever been hospitalized or had surgery? Yes _____ No _____

Please list all hospitalizations and surgeries to the best of your recollection

Hospitalized for Disease/Operation	Duration	Age when Hospitalized

List any disease or illness you have had not listed above (e.g., hepatitis, severe infection, broken bones, blood clotting / bleeding issues, etc.)

_____

_____

_____

_____

Are you allergic, sensitive, or intolerant of any foods or nutritional supplements, products, or substitutes? Yes___ No___

If yes, please describe: _____

Are you allergic, sensitive, or intolerant of any medications? Yes___ No___

If yes, please describe:_____

Are you allergic, sensitive, or intolerant of latex? Yes___ No___

Are you allergic, sensitive, or intolerant of any kind of tape or adhesive? Yes___ No___
Are you currently seeing a doctor or other health care provider for any reason?

Yes _____ No _____

If yes, please explain:

_____

_____

_____

Have you ever been diagnosed with osteoporosis or other bone disorder?

Yes ____ No____

If yes, please explain:

_____

_____

_____

Do you have, or have you ever had any of the following conditions?

Memory problems or confusion	Yes _____	No _____
Recurring headaches	Yes _____	No _____
Recent changes in your vision	Yes _____	No _____
Numbness of an arm or leg	Yes _____	No _____
Weakness of an arm or leg	Yes _____	No _____
Difficulty in speaking or slurred speech	Yes _____	No _____
Fainting or dizziness	Yes _____	No _____
Difficulty in walking (staggering)	Yes _____	No _____
Shortness of breath	Yes _____	No _____
Lung or Respiratory Disease	Yes _____	No _____
Rheumatism or arthritis	Yes _____	No _____
Heart disease	Yes _____	No _____
Epilepsy	Yes _____	No _____
Tumors	Yes _____	No _____

Mental illness Yes _____ No _____

Bleeding or blood clotting disorders Yes _____ No _____

Risk for infectious diseases Yes _____ No _____
(AIDS, IV drug use, blood transfusions, hemophilia, hepatitis)

Skin: rashes, lumps, moles, itching, eczema Yes _____ No _____

Nose, sinuses: frequent colds, sinus trouble Yes _____ No _____
nose-bleeds, deviated septum

Neck lumps, swollen glands, pain or stiffness Yes _____ No _____

Breasts: lumps, nipple discharge, pain or discomfort Yes _____ No _____

High blood cholesterol Yes _____ No _____
Date of last reading _____ Value _____

Stomach: chronic indigestion, ulcer, hiatal hernia, Yes _____ No _____
heartburn, trouble swallowing, vomiting.

Intestine: constipation, diarrhea, change in bowel Yes _____ No _____
habits, irritable bowel disorder, colitis, polyps.

Rectum: hemorrhoids, bleeding, polyps Yes _____ No _____

Liver, gallblader: hepatitis, gallstones Yes _____ No _____

Urinary: frequent urination, urgency, burning, Yes _____ No _____
pain, blood in urine, infection, kidney stones

Incontinence: Loss of bladder or rectal control Yes _____ No _____

Have you ever had any form of cancer, skin or other? Yes _____ No _____

If yes, what kind: _____

Do you have diabetes mellitus (high blood sugar)? Yes _____ No _____

If yes, when and what kind of treatment did/do you receive:

Insulin _____ Diet _____ Pills _____ No treatment _____

Have you ever had or been told that you had high blood pressure?

Yes _____ No _____

If yes, when and what kind of treatment or medicine did/do you receive:

_____

Do you have any chronic illnesses or medical conditions? Yes _____ No _____

If yes, please explain:

_____

_____

_____

_____

List all the prescribed medications you are currently taking:

Medicine	Reason for Medication

List all the over-the-counter medications you are currently taking:

Medicine	Reason for Medication	Is it doctor recommended

Specifically, are you currently taking any pain medications, such as Tylenol or Advil, on a regular basis? Yes _____ No _____ If yes, how much and how often do you consume these medications?

_____

_____

Dietary Information

Are you currently taking any vitamins, minerals or health food supplements (e.g., fish oil, ginko biloba) at least once per week on a regular basis? Yes _____ No _____

If yes, please describe:

Supplement	Amount	How often	How long	Doctor Recommended

Have you had a weight loss or gain in the last 6 months? Yes _____ No _____

If yes, how much? _____lbs. Gain _____ Loss _____ (check one)

How do you describe your appetite? Poor _____ Fair _____ Good _____

Do you have any food allergies/intolerance (e.g., shellfish/iodine)? Yes _____ No _____

If so, please explain:

_____

_____

_____

Do you drink caffeinated beverages? (coffee, tea, soda) Yes _____ No _____

If yes, how many caffeinated beverages do you drink in an average day? _____/day

If required during a study, would giving up caffeine cause any problems for you?

Yes _____ No _____

Do you drink alcoholic beverages? Yes _____ No _____

If yes, how many alcoholic beverages do you consume in an average week? _____/wk

Would you be willing to forego drinking alcoholic beverages for the duration of a research study?

Yes _____ No _____

Smoking History

Do you currently use any products containing nicotine, for example cigarettes, electronic cigarettes, nicotine patches, cigars, pipe, chew, smokeless tobacco at present?

Yes _____ No _____

Did you use any of the above products in the past and quit permanently? Yes _____ No _____

When did you quit? (check one)
less than 1 year _____
1 to 5 years _____
more than 5 years _____

Exercise History

Do you participate in a regular exercise program? Yes _____ No _____

If yes, please describe the exercise that you usually participate in (e.g., walking, running, weightlifting).

_____

_____

_____

_____

If you are not currently participating in a regular exercise program, have you participated in one in the past? Yes _____ No _____

If yes, when was the last time you participated in the exercise on a regular basis?

Could you please describe the type of activity that you performed (e.g., walking, running, weightlifting).

_____

_____

_____

_____

How often did you exercise (days/week)? _____

At what intensity did you exercise? Light _____
Moderate _____
Hard _____

On days that you did exercise, how long did you usually exercise for (hours)?_____

APPENDIX C

DATA COLLECTION FORMS

Age Verification Study: Visit #1: VO_2peak Test

Subject #: _____ Date: _____ Time: _____

Prior to Exercise:

- *Complete informed consent, PAR-Q, HHQ*
- *Void bladder*
- *Obtain height and weightBlood pressure measurement*
- *Physioflow*
- *Attach HR strap*

Subject Characteristics:

Body weight: _____ kg Height: _____ cm Age: _____ yrs

Blood Pressure (sys./dia.): _____ mmHg Resting HR: _____ bpm

Mouthpiece size: _____

Seat Height:_____ Handlebar Height:_____

Maximal Exercise Test:

- *Position subject on bike and attach metabolic mask*
- *Collect Resting VO_2 for 2 minutes*
- *Initiate 5 min warm-up @ 25 W*
- *Begin test (15 W per minute)*
- *Initiate 10 min cool-down @ 25 W*

Ramp Test Duration (mm:ss): _____

W_{max}: _____ HR_{max}: _____ bpm

Highest 30-sec VO_2 (L/min): _____

2nd Highest 30-sec VO_2 (L/min): _____ VO_2peak (L/min): _____

Verification Phase Percentage: 85%

110%

Verification W_x: _____ HR_{max}: _____ bpm

Verification Test Duration (mm:ss): _____

Highest 30-sec VO_2 (L/min): _____

2nd Highest 30-sec VO_2 (L/min): _____ VO_2peak (L/min): _____

**** Print metabolic data sheets ****

Age Verification Study: Visit #1: VO_2peak Test

AVS Study- Graded Exercise Test				
Time	VO_2	HR	RPE	Watts
Rest			-	
Min3				25
Min5			-	25
Min1				
Min2				
Min3				
Min4				
Min5				
Min6				
Min7				
Min8				
Min9				
Min10				
Min11				
Min12				
Min13				
Min14				
Min15				
Min16				
Min17				
Min18				
Min19				
Min20				

Age Verification Study: Visit #2: VO_2peak Test

Subject #: _____ Date: _____ Time: _____

Prior to Exercise:

- *Obtain height and weight*
- *Void bladder*
- *Blood pressure measurement*
- *DXA*
- *Physioflow*
- *Attach HR strap*

Subject Characteristics:

Body weight: _____ kg Height: _____ cm Age: _____ yrs

Blood Pressure (sys./dia.): _____ mmHg Resting HR: _____ bpm

Mouthpiece size: _____

Maximal Exercise Test:

- *Position subject on bike and attach metabolic mask*
- *Collect Resting VO_2 for 2 minutes*
- *Initiate 5 min warm-up @ 25 W*
- *Begin test (15 W per minute)*
- *Initiate 10 min cool-down @ 25 W*

Ramp Test Duration (mm:ss): _____

W_{max}: _____ HR_{max}: _____ bpm

Highest 30-sec VO_2 (L/min): _____

2nd Highest 30-sec VO_2 (L/min): _____ VO_2peak (L/min): _____

Verification Phase Percentage: 85%

110%

Verification W: _____ HR_{max}: _____ bpm

Verification Test Duration (mm:ss): _____

Highest 30-sec VO_2 (L/min): _____

2nd Highest 30-sec VO_2 (L/min): _____ VO_2peak (L/min): _____

Age Verification Study: Visit #2: VO_2peak Test

**** Print metabolic data sheets ****

AVS Study- Graded Exercise Test				
Time	VO_2	HR	RPE	Watts
Rest			-	
Min3				25
Min5			-	25
Min1				
Min2				
Min3				
Min4				
Min5				
Min6				
Min7				
Min8				
Min9				
Min10				
Min11				
Min12				
Min13				
Min14				
Min15				
Min16				
Min17				
Min18				
Min19				
Min20				

APPENDIX D

RAW DATA WITH COEFFICIENTS OF VARIATION

Using Coefficients of Variations from Ramp1 to Ramp2 to identify individuals with a higher VO_{2peak} during the verification phase vs. the Ramp.

	VO_{2peak} (L/min)	VO_{2peak} (ml/kg/min)	VO_{2peak} (ml/kgLBM/min)	HR Peak (bpm)	RER Peak	Power (Watts)	Time to exhaustion (seconds)
CV[A]	**2.9**	**4.1**	**2.9**	**2.3**	**3.2**	**5.3**	**8.0**
			Comparison of Ramp 1 vs. Ramp 2				
Ramp1	1.82 ± 0.72	25.9 ± 10.0	40.8 ± 11.6	150 ± 17	1.16 ± 0.09	156 ± 53	374 ± 108
Ramp2	1.86 ± 0.81	27.9 ± 11.6*	41.7 ± 12.8	149 ± 15	1.16 ± 0.08	158 ± 53	388 ± 136
Ind. Data	(8/20)	(11/20)	(8/20)	(4/19)	(5/20)	(5/20)	(6/20)
			Comparison of Ramp vs. Verification Phase at 85%				
Ramp	1.85 ± 0.73	26.5 ± 10.6	41.2 ± 11.9	150 ± 17	1.17 ± 0.09	158 ± 52	388 ± 114
VP 85	1.86 ± 0.72	26.5 ± 10.3	41.4 ± 11.8	153 ± 17	1.07 ± 0.08*	133 ± 45	176 ± 81
Ind. Data	(8/22)	(3/22)	(3/22)	(6/21)	(1/22)		
			Comparison of Ramp vs. Verification Phase at 110%				
Ramp	1.85 ± 0.57	27.3 ± 6.4	41.3 ± 12.6	149 ± 16	1.16 ± 0.08	156 ± 54	373 ± 133
VP 110	1.79 ± 0.73	25.9 ± 9.4	40.1 ± 10.9	146 ± 16	1.03 ± 0.10*	170 ± 60	82 ± 62
Ind. Data	(5/20)	(2/20)	(5/20)	(2/19)	(0/20)		

Data are mean ± SD. [A]mean coefficient of variation (CV) from Ramp1 to Ramp2. HR, Heart Rate; RER, Respiratory Exchange; CV; Coefficient of Variation; Ind. Data represents number of subjects that achieved a higher VO_{2peak} value during the verification phase vs. the associate ramp. The criteria for a higher VO_{2peak} was that the value had to be greater than the CV for Ramp1 to Ramp2.

*P<0.05 Ramp 1 vs Ramp 2.

APPENDIX E

RAW DATA

Raw Data for Subject Characteristics

Subject	Sex	Age (y)	Height (cm)	Weight (kg)	BMI (kg/m^2)	% Body Fat	LBM (kg)	Leg LM (kg)
1	M	62	170.8	84.4	28.79	23.0	62.54	22.47
2	F	66	157.1	54.4	22.04	24.2	40.16	13.70
3	F	67	166.1	52.0	18.85	27.9	36.32	18.66
4	F	75	159.5	66.9	26.28	46.1	34.936	11.25
5	F	60	158.4	55.4	22.08	29.8	36.812	12.28
6	M	67	159.2	50.8	20.04	28.6	34.417	10.37
7	F	61	162.2	80.6	30.64	45.5	42.467	14.96
8	F	69	170.2	77.7	26.82	44.6	41.549	14.46
10	F	60	154.9	86.5	36.05	50.8	40.88	13.80
11	M	77	161.4	54.6	20.96	20.0	41.82	14.56
12	F	65	167.9	101.6	36.43			
13	F	76	152.4	53.5	23.03	39.4	31.26	9.79
14	M	77	172.5	62.9	21.12	25.1	45.47	15.02
15	F	60	162.0	71.3	27.17	42.3	39.35	13.41
16	M	67	183.8	96.2	28.48	24.7	69.77	24.28
17	M	76	177.4	95.0	30.19	34.9	59.90	21.84
18	M	68	172.6	78.1	26.22			
19	M	65	181.3	97.0	29.51	37.0	57.50	19.50
20	F	67	156.4	50.3	20.56	18.8	39.26	12.32
21	M	60	165.2	78.0	28.58	32.1	50.65	16.57
22	F	60	159.6	82.2	32.27	49.2	40.40	13.27
23	F	60	163.2	60.9	22.87	35.4	37.99	12.29
All Subjects								
Mean		67	165.2	72.3	26.32	34.0	44.17	15.24
SD		6	8.5	17.0	5.05	10.0	10.43	4.09
Men								
Mean		69	171.6	77.4	25.99	28.2	52.76	18.08
SD		6	8.5	17.8	4.11	6.0	11.79	4.74
Women								
Mean		65	160.7	68.7	26.55	37.8	38.45	13.35
SD		6	5.1	16.1	5.77	10.5	3.18	2.19

Raw Data for VO_{2peak} (L/min)

Subject	Ramp1	Ramp2	Ramp85	VP85	Ramp110	VP110
1	4.08	4.39	4.08	4.07	4.39	4.05
2	2.59	2.78	2.78	2.71	2.59	1.98
3	1.49	1.52	1.49	1.48	1.52	1.59
4	0.99	0.97	0.97	0.90	0.99	0.98
5	2.13	2.25	2.13	2.16	2.25	2.25
6	1.84	1.84	1.84	1.85	1.84	1.78
7	1.67	1.63	1.63	1.65	1.67	1.64
8	1.10	1.08	1.10	1.10	1.08	1.12
10	1.37	1.43	1.43	1.51	1.37	1.37
11	1.51	1.43	1.51	1.67	1.43	1.41
12	1.72		1.72	1.87		
13	0.88	0.93	0.93	0.95	0.88	0.85
14	1.40	1.50	1.50	1.53	1.40	1.39
15	1.67	1.62	1.62	1.66	1.67	1.76
16	2.86	2.79	2.79	2.79	2.86	2.66
17	1.76	1.89	1.89	1.83	1.76	1.93
18	1.81		2.17	2.18		
19	2.50	2.51	2.50	2.58	2.51	2.60
20	1.60	1.77	1.60	1.63	1.77	1.69
21	2.33	2.26	2.33	2.28	2.26	2.29
22	1.42	1.38	1.42	1.30	1.38	1.18
23	1.27	1.29	1.27	1.28	1.29	1.30
All Subjects						
Mean	1.82	1.86	1.85	1.86	1.85	1.79
SD	0.72	0.81	0.72	0.72	0.81	0.73
Max	4.08	4.39	4.08	4.07	4.39	4.05
Min	0.88	0.93	0.93	0.90	0.88	0.85
Males						
Mean	2.23	2.33	2.29	2.31	2.31	2.26
SD	0.84	0.96	0.80	0.78	0.99	0.87
Max	4.08	4.39	4.08	4.07	4.39	4.05
Min	1.40	1.43	1.50	1.53	1.40	1.39
Females						
Mean	1.53	1.55	1.55	1.55	1.54	1.48
SD	0.46	0.53	0.49	0.50	0.50	0.42
Max	2.59	2.78	2.78	2.71	2.59	2.25
Min	0.88	0.93	0.93	0.90	0.88	0.85

Raw Data for VO_{2peak} (ml/kg/min)

Subject	Ramp1	Ramp2	Ramp85	VP85	Ramp110	VP110
1	49.9	53.6	49.9	49.8	53.6	48.3
2	47.9	53.7	53.7	49.8	47.9	36.7
3	28.8	31.7	28.8	28.7	31.7	30.5
4	14.9	14.6	14.6	13.1	14.9	14.6
5	38.2	41.0	38.2	38.7	41.0	40.5
6	35.0	36.9	36.9	36.4	35.0	33.9
7	20.5	21.1	21.1	20.5	20.5	20.2
8	14.1	14.2	14.1	14.2	14.2	14.4
10	16.0	17.3	17.3	17.5	16.0	15.9
11	27.1	26.4	27.1	30.0	26.4	25.7
12	17.0		17.0	18.4		
13	16.8	17.8	17.8	17.7	16.8	16.2
14	22.2	24.6	24.5	24.0	22.2	22.2
15	23.6	23.1	23.1	23.3	23.6	24.9
16	30.0	29.5	29.5	29.0	30.0	27.8
17	18.5	20.2	20.2	19.1	18.5	20.3
18	23.2		23.2	27.9		
19	25.4	27.2	25.4	26.2	27.2	26.8
20	31.7	36.9	31.7	32.3	36.9	33.6
21	30.4	29.8	30.4	29.7	29.8	29.4
22	17.2	17.6	17.2	15.9	17.6	14.4
23	20.5	21.5	20.5	20.6	21.5	21.0
All Subjects						
Mean	25.9	27.9	26.5	26.5	27.3	25.9
SD	10.0	11.6	10.6	10.3	11.1	9.4
Max	49.9	53.7	53.7	49.8	53.6	48.3
Min	14.1	14.2	14.1	13.1	14.2	14.4
Males						
Mean	29.1	31.0	29.7	30.2	30.3	29.3
SD	9.2	10.3	9.0	8.7	10.6	8.7
Max	49.9	53.6	49.9	49.8	53.6	48.3
Min	18.5	20.2	20.2	19.1	18.5	20.3
Females						
Mean	23.6	25.9	24.3	23.9	25.2	23.6
SD	10.3	12.3	11.4	10.8	11.4	9.5
Max	47.9	53.7	53.7	49.8	47.9	40.5
Min	14.1	14.2	14.1	13.1	14.2	14.4

Raw Data for VO_{2peak} (ml/kgLBM/min)

Subject	Ramp1	Ramp2	Ramp85	VP85	Ramp110	VP110
1	65.2	70.2	65.2	65.1	70.2	64.8
2	64.5	69.2	69.2	67.5	64.5	49.3
3	41.0	41.9	41.0	40.8	41.9	43.8
4	28.5	27.7	27.7	25.9	28.5	27.9
5	57.9	61.1	57.9	58.7	61.1	61.1
6	53.5	53.5	53.5	53.8	53.5	51.7
7	39.3	38.4	38.4	38.9	39.3	38.6
8	26.5	26.0	26.5	26.5	26.0	27.0
10	33.5	35.0	35.0	36.9	33.5	33.5
11	36.1	34.2	36.1	39.9	34.2	33.7
12						
13	28.2	29.8	29.8	30.4	28.2	27.2
14	30.8	33.0	33.0	33.7	30.8	30.6
15	42.4	41.2	41.2	42.2	42.4	44.7
16	41.0	40.0	40.0	40.0	41.0	38.1
17	29.4	31.6	31.6	30.6	29.4	32.2
18						
19	43.5	43.7	43.5	44.9	43.7	45.2
20	40.8	45.1	40.8	41.5	45.1	43.1
21	46.0	44.6	46.0	45.0	44.6	45.2
22	35.2	34.2	35.2	32.2	34.2	29.2
23	33.4	34.0	33.4	33.7	34.0	34.2
All Subjects						
Mean	40.8	41.7	41.2	41.4	41.3	40.1
SD	11.6	12.8	11.9	11.8	12.6	10.9
Max	65.2	70.2	69.2	67.5	70.2	64.8
Min	26.5	26.0	26.5	25.9	26.0	27.0
Males						
Mean	43.2	43.8	43.6	44.1	43.4	42.7
SD	12.0	12.9	11.3	11.1	13.5	11.6
Max	65.2	70.2	65.2	65.1	70.2	64.8
Min	29.4	31.6	31.6	30.6	29.4	30.6
Females						
Mean	39.3	40.3	39.7	39.6	39.9	38.3
SD	11.6	13.1	12.5	12.4	12.3	10.5
Max	64.5	69.2	69.2	67.5	64.5	61.1
Min	26.5	26.0	26.5	25.9	26.0	27.0

Raw Data for Heart Rate (BPM)

Subject	Ramp1	Ramp2	Ramp85	VP85	Ramp110	VP110
1	162	161	162	159	161	156
2	139	143	143	144	139	120
3	137	139	137	144	139	140
4	120	118	118	111	120	122
5	169	164	169	169	164	169
6	186	183	183	187	186	184
7	156	156	156	164	156	158
8	160	147	160	161	147	157
10	133	134	134	149	133	136
11	171	158	171	164	158	143
12	127		127	142		
13	131	136	136	137	131	125
14	135	142	142	143	135	135
15	149	149	149	153	149	143
16	153	138	138	139	153	143
17	143	146	146	143	143	142
18	147		147	164		
19	163	157	163	172	157	153
20	175	166	175	178	166	161
21						
22	142	138	142	136	138	139
23	159	159	159	161	159	151
All Subjects						
Mean	150	149	150	153	149	146
SD	17	15	17	17	15	16
Max	186	183	183	187	186	184
Min	120	118	118	111	120	120
Males						
Mean	157	155	156	159	156	151
SD	16	15	16	16	16	16
Max	186	183	183	187	186	184
Min	135	138	138	139	135	135
Females						
Mean	146	146	147	150	145	143
SD	17	14	17	18	14	16
Max	175	166	175	178	166	169
Min	120	118	118	111	120	120

Raw Data for Respiratory Exchange Ratio (RER)

Subject	Ramp1	Ramp2	Ramp85	VP85	Ramp110	VP110
1	1.04	1.11	1.04	0.97	1.11	0.99
2	1.00	1.04	1.04	0.95	1.00	0.80
3	1.15	1.17	1.15	1.09	1.17	1.12
4	0.98	0.96	0.96	0.97	0.98	0.97
5	1.17	1.06	1.17	1.10	1.06	1.00
6	1.26	1.26	1.26	1.15	1.26	1.11
7	1.13	1.08	1.08	1.14	1.13	1.05
8	1.28	1.17	1.28	1.14	1.17	1.13
10	1.25	1.34	1.34	1.26	1.25	1.15
11	1.27	1.20	1.27	1.05	1.20	0.92
12	1.11		1.11	1.03		
13	1.16	1.19	1.19	1.10	1.16	0.97
14	1.14	1.18	1.18	1.09	1.14	1.03
15	1.20	1.18	1.18	1.09	1.20	1.05
16	1.20	1.16	1.16	1.05	1.20	1.08
17	1.14	1.16	1.16	1.04	1.14	1.09
18	1.04		1.04	1.10		
19	1.19	1.27	1.19	1.10	1.27	1.12
20	1.20	1.18	1.20	1.12	1.18	0.92
21	1.27	1.15	1.27	1.10	1.15	1.14
22	1.21	1.15	1.21	0.87	1.15	0.89
23	1.23	1.19	1.23	1.05	1.19	0.97
All Subjects						
Mean	1.16	1.16	1.17	1.07	1.16	1.03
SD	0.09	0.08	0.09	0.08	0.08	0.10
Max	1.28	1.34	1.34	1.26	1.27	1.15
Min	0.98	0.96	0.96	0.87	0.98	0.80
Males						
Mean	1.17	1.19	1.17	1.07	1.18	1.06
SD	0.09	0.06	0.09	0.05	0.06	0.07
Max	1.27	1.27	1.27	1.15	1.27	1.14
Min	1.04	1.11	1.04	0.97	1.11	0.92
Females						
Mean	1.16	1.14	1.16	1.07	1.14	1.00
SD	0.09	0.10	0.10	0.10	0.08	0.10
Max	1.28	1.34	1.34	1.26	1.25	1.15
Min	0.98	0.96	0.96	0.87	0.98	0.80

Raw Data for Ratings of Perceived Exertion

Subject	Ramp1	Ramp2	Ramp85	VP85	Ramp110	VP110
1	17	19	17	19	19	19
2	17	19	19	19	17	19
3	19	19	19	19	19	20
4	19	19	19	19	19	18
5	19	20	19	20	20	20
6	19	19	19	19	19	19
7	17	16	16	17	17	18
8	19	20	19	19	20	19
10	19	19	19	19	19	18
11	19	18	19	17	18	17
12	19		19	18		
13	17	15	15	15	17	17
14	18	18	18	19	18	18
15	19	19	19	19	19	19
16	19	19	19	19	19	18
17	20	20	20	20	20	20
18	19		19	19		
19	19	19	19	19	19	19
20	19	19	19	20	19	20
21	19	19	19	19	19	19
22	19	19	19	16	19	17
23	16	17	16	13	17	17
All Subjects						
Mean	19	19	18	18	19	19
SD	1	1	1	2	1	1
Max	20	20	20	20	20	20
Min	16	15	15	13	17	17
Males						
Mean	19	19	19	19	19	19
SD	1	1	1	1	1	1
Max	20	20	20	20	20	20
Min	17	18	17	17	18	17
Females						
Mean	18	18	18	18	19	19
SD	1	2	1	2	1	1
Max	19	20	19	20	20	20
Min	16	15	15	13	17	17

Raw Data for Peak Work Rate Achieved (Watts)

Subject	Ramp1	Ramp2	Ramp85	VP85	Ramp110	VP110
1	319	312	319	269	312	343
2	191	202	201	171	191	210
3	129	132	129	109	132	145
4	125	166	166	141	125	138
5	176	219	176	151	219	240
6	158	159	159	134	158	174
7	132	122	122	103	132	145
8	94	99	94	77	99	108
10	91	99	99	83	91	100
11	185	152	186	156	152	167
12	136		136	116		
13	91	89	89	74	91	100
14	125	132	132	108	135	125
15	139	134	134	112	139	150
16	229	214	214	180	229	250
17	165	169	169	142	165	179
18	200		200	170		
19	198	192	198	169	192	215
20	156	154	156	133	154	173
21	179	182	178	152	182	199
22	122	114	122	104	114	126
23	94	109	94	79	109	120
All Subjects						
Mean	156	158	158	133	156	170
SD	53	53	52	45	54	60
Max	319	312	319	269	312	343
Min	91	89	89	74	91	100
Males						
Mean	195	189	195	164	191	207
SD	55	56	53	45	57	66
Max	319	312	319	269	312	343
Min	125	132	132	108	135	125
Females						
Mean	129	137	132	112	133	146
SD	32	41	35	30	39	43
Max	191	219	201	171	219	240
Min	91	89	89	74	91	100

Raw Data for Time to Exhaustion (Seconds)

Subject	Ramp1	Ramp2	Ramp85	VP85	Ramp110	VP110
1	810	791	810	170	791	70
2	570	610	610	378	570	30
3	360	377	360	200	377	60
4	350	480	350	169	480	90
5	550	720	550	199	720	330
6	330	331	331	109	330	80
7	370	331	331	151	370	70
8	220	240	220	190	240	60
10	210	241	241	180	210	80
11	410	261	410	160	261	40
12	390		390	457		
13	220	201	201	109	220	71
14	230	252	252	170	230	50
15	400	380	380	190	400	60
16	588	531	531	119	588	69
17	380	391	391	128	380	80
18	431		431	210		
19	481	460	481	220	460	100
20	510	500	510	180	500	89
21	420	410	420	229	410	69
22	370	340	370	50	340	40
23	260	322	260	91	322	48

All Subjects						
Mean	403	408	401	185	410	79
SD	144	160	142	88	162	62
Max	810	791	810	457	791	330
Min	210	201	201	50	210	30
Males						
Mean	453	428	451	168	431	70
SD	166	175	157	44	184	19
Max	810	791	810	229	791	100
Min	230	252	252	109	230	40
Females						
Mean	368	395	367	196	396	86
SD	121	156	126	110	152	79
Max	570	720	610	457	720	330
Min	210	201	201	50	210	30

Raw Data for Ventilation (L/min)

Subject	Ramp1	Ramp2	Ramp85	VP85	Ramp110	VP110
1	144.75	154.09	144.75	143.84	154.09	139.33
2	78.69	94.57	94.57	81.42	78.69	57.21
3	93.57	88.14	93.57	92.61	88.14	95.52
4	43.84	44.76	44.76	48.50	43.84	47.11
5	90.99	93.21	90.99	94.78	93.21	97.39
6	84.60	81.84	81.84	99.21	84.60	90.01
7	62.41	58.24	58.24	66.93	62.41	59.45
8	60.47	50.80	60.47	59.57	50.80	55.53
10	66.23	71.50	71.50	82.24	66.23	65.42
11	77.15	62.38	77.15	69.77	62.38	50.01
12	60.03		60.03	71.75		
13	43.03	45.28	45.28	45.66	43.03	42.28
14	47.55	53.85	53.85	53.98	47.55	44.92
15	62.88	59.19	59.19	59.28	62.88	60.49
16	155.74	142.17	142.17	140.44	155.74	156.87
17	65.95	80.15	80.15	70.26	65.95	71.92
18	52.16		52.16	76.02		
19	118.34	123.68	118.34	131.92	123.68	121.94
20	60.43	70.44	60.43	72.38	70.44	53.45
21	117.37	105.69	117.37	114.51	105.69	118.81
22	57.70	59.47	57.70	42.62	59.47	44.26
23	48.12	46.81	48.12	45.61	46.81	44.77
All Subjects						
Mean	76.91	79.31	77.85	80.15	78.28	75.83
SD	31.69	31.84	30.01	30.20	33.63	34.83
Max	155.74	154.09	144.75	143.84	155.74	156.87
Min	43.03	44.76	44.76	42.62	43.03	42.28
Males						
Mean	95.96	100.48	96.42	99.99	99.96	99.23
SD	39.62	36.96	35.30	34.06	41.73	41.46
Max	155.74	154.09	144.75	143.84	155.74	156.87
Min	47.55	53.85	52.16	53.98	47.55	44.92
Females						
Mean	63.72	65.20	64.99	66.41	63.83	60.24
SD	15.83	18.39	17.54	17.98	16.62	18.39
Max	93.57	94.57	94.57	94.78	93.21	97.39
Min	43.03	44.76	44.76	42.62	43.03	42.28