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AGE-RELATED CHANGES IN MUSCULAR STRENGTH, POWER, ENDURANCE, AND QUALITY IN RECREATIONALLY ACTIVE WOMEN AGED 20 TO 89 YEARS

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AGE-RELATED CHANGES IN MUSCULAR STRENGTH, POWER, ENDURANCE, AND QUALITY IN RECREATIONALLY ACTIVE WOMEN AGED 20 TO 89 YEARS

A DISSERTATION APPROVED FOR THE
DEPARTMENT OF HEALTH AND EXERCISE SCIENCE

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To my dearest Hannah,

and to Mom, Dad, Kaley, Anthony, Kobi, Max, and Sloane.

Thank you for your constant love and support.

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Abstract

The purpose of this study was to investigate the influence of chronological age on muscular strength, power, endurance, and quality in recreationally active women 20 to 89 years of age. One hundred and fifty-two female volunteers completed the study requirements and were divided into five-year age intervals (20 to 24, 25 to 29, 30 to 34, etc.) to 75 to 79 years, with an additional group of 80 to 89 years. Apart from the two oldest groups, each five-year interval contained at least 10 female volunteers. The participants completed physical function assessments (grip strength and vertical jump) as well as comprehensive muscle function testing of the elbow extensors and flexors, the knee extensors and flexors, and the plantar and dorsiflexors. Muscle function testing consisted of measures of maximal isometric strength and isometric rate of torque development; maximal dynamic strength and the time to achieve peak output at 60 and 240 deg/s; components of maximal muscular power such as peak power, peak velocity, and time to peak power, and time to peak velocity during isotonic contractions at 1 Nm and 20, 40, and 60% of maximal isometric strength; dynamic muscular endurance testing at a slow and fast contraction velocity (60 and 240 deg/s); and muscle quality and specific power indices were determined among the isometric, isokinetic, and isotonic assessments made relative to body composition measures. Body composition was assessed using dual energy x-ray absorptiometry (DXA), in addition to site specific measures of muscle cross-sectional area and muscle density of the upper and lower leg via peripheral computed tomography (pQCT). Age-related changes in serum levels of myostatin and interleukin 6 (IL-6) and their relationships with the included muscle characteristics were assessed. Significant age group differences were observed among many of the parameters, with

some of these observations being removed when accounting for muscle mass (muscle quality/specific power). Across the force output parameters, critical ages for the onset of rate of decline occurred in the following order: dynamic strength and muscular power, muscular endurance during 240 deg/s, isometric strength/muscle quality/specific power, and latest during the muscular endurance task at 60 deg/s. Further, critical ages were detected within younger age groups for the lower body parameters when compared to the upper body parameters. Muscle groups representing different fiber type composition did not appear to influence the onset of critical changes. Location of the muscle group tended to influence the magnitude of decline since groups located distally and groups located anteriorly displayed greater decreases with increasing age. Contraction velocity also influenced age-related changes with larger declines being observed during the faster contraction conditions. Myostatin and IL-6 were positively associated with age (both $p<0.05$), however their relationships with muscle mass and performance were diminished when controlling for age. In summary, the influence of age on muscle function is a question that must be further qualified as many factors, namely the muscle group, contraction type, and contraction velocity/intensity each play a role. Although serum myostatin and IL-6 displayed significant relationships with age, their limited relationships with muscle characteristics hinders their ability to serve as age- and muscle-related biomarkers.

Chapter I: Introduction

Recent projections indicate that by 2050 one in five Americans will be 65 years of age or older, increasing the number of older individuals from 43 to 87 million, and this growth will be accompanied by an increase in life expectancy (Iwamura and Kanauchi, 2017; Papa, Dong and Hassan, 2017). Increased longevity has been regarded as one of society's greatest achievements; however, such increases in longevity are often accompanied by a loss of independence and a diminished quality of life. For example, the mean life expectancy for women is 84 years but by age 63 women begin to develop physical limitations resulting in up to 21 years spent with a decreased quality of life (Rechel *et al.*, 2013). Increasing life expectancy is a current global health goal, thus preserving the capacities to live independently and maintain quality of life during the extended years is of paramount significance. Therefore, preserving individuals' independence and quality of life during aging as well as improving our understanding of the factors contributing to this maintenance represents a primary global objective (Cruz-Jentoft *et al.,* 2019; Rolland *et al.,* 2008).

Aging is accompanied by a reduction in voluntary physical activity, which contributes to significant decreases in maximal aerobic capacity and muscle function (e.g. muscular strength, power, and endurance), thereby resulting in physical disability (Walston *et al.*, 2006). Combined with physical inactivity are declines in skeletal muscle mass and muscle function, known as sarcopenia, which characterizes the most dramatic and significant of changes experienced during aging (Larsson *et al.,* 2019). Sarcopenia, derived from Greek terminology 'sarx' meaning flesh and 'penia' signifying loss, was originally proposed to describe the age-related loss of muscle mass (Rosenberg, 2011).

During aging, the loss of muscle mass occurs similarly to the loss of muscle function. However, these declines do not occur simultaneously, which has led to more contemporary sarcopenia definitions advocating the inclusion of muscle function, modifying the definition of sarcopenia to be the age-related loss of muscle mass and muscle function (Rolland *et al.*, 2008; Studenski *et al.*, 2014; Chen *et al.*, 2016; Landi *et al.*, 2017; Cruz-Jentoft *et al.*, 2019). Although a uniform definition and diagnostic criteria are still being debated, the dual nature of sarcopenia is generally accepted, which includes both quantitative and qualitative declines in skeletal muscle, characterized by reductions in muscle mass, muscular strength, muscular power, and muscular endurance (Trombetti *et al.*, 2016; Miller *et al.*, 2019).

Individuals with sarcopenia display a reduced ability to perform activities of daily living (Malmstrom *et al.*, 2016), a loss of independence (Akune *et al.*, 2014; dos Santos *et al.*, 2017; Steffl, Bohannon, *et al.*, 2017), have an increased risk for and experience more falls (Bischoff-Ferrari *et al.*, 2015; Schaap *et al.*, 2018) while also experiencing a higher prevalence of fractures (Hida *et al.*, 2014). Sarcopenia also contributes to the prevalence of cardiac, metabolic, and respiratory diseases (Srikanthan, Hevener and Karlamangla, 2010; Bahat and İlhan, 2016; Beaudart *et al.*, 2017). More recent studies have shown that sarcopenia accelerates the onset of cognitive impairment (Chang *et al.*, 2016) and mortality (De Buyser *et al.*, 2016). Sarcopenia also presents a growing economic burden contributing approximately $18.5 billion dollars to annual health care costs (Janssen *et al.*, 2004), which is even larger than the $16 billion annual cost of fractures due to osteoporosis (Ray *et al.*, 1997). Further, individuals with sarcopenia require greater hospital costs and an increase length of hospitalization compared to those

without sarcopenia (Antunes *et al.*, 2017; Cawthon *et al.*, 2017; Steffl, Sima, *et al.*, 2017). Increased hospital expenses and time of hospitalization are traditionally believed to be attributed to age alone, however, recent reports observed similar outcomes among individuals with sarcopenia below the age of 65 years, demonstrating the impact of sarcopenia on health regardless of age (Sousa *et al.*, 2016). Importantly, determining preventative approaches that combat the consequences of sarcopenia can reduce associated health care costs. In fact, previous estimations indicate that a 10% reduction in the prevalence of sarcopenia would decrease health care expenses by $1.1 billion dollars (Janssen *et al.*, 2004). Cumulatively, the impact of sarcopenia not only diminishes quality of life for individuals, but also strains the sustainability of our health care system (Cesari *et al.*, 2014). Therefore, identifying effective solutions capable of preventing the harmful consequences that sarcopenia exerts on our health care systems is a primary global objective (Rolland *et al.*, 2008; Studenski *et al.*, 2014; Cruz-Jentoft *et al.*, 2019).

The consequences of sarcopenia are worsened when coupled with negative changes in body composition (Prado *et al.*, 2012). Body composition comprises the amount of fat mass and muscle mass an individual possesses. With aging there are prominent shifts toward increased amounts of fat mass and decreased amounts of muscle mass. The importance of the shifts in fat and muscle mass, and which has a greater influence on physical function are inconclusive. For example, higher fat mass values are significantly related to a reduced ability to use the stairs (Zoico *et al.*, 2004), while lower body muscle mass has been reported to be the main predictor for physical disability in older individuals (Fantin *et al.*, 2007). More recently, studies have shown that it is the ability of a muscle to produce force relative to the amount of muscle mass, referred to as

muscle quality, rather than the amount of muscle or fat mass as the strongest predictor of physical function in older women (Straight, Brady and Evans, 2015a). Although these data present conflicting results suggesting which measure is most important regarding physical function, in either case women are more affected by decreases in muscle mass and increases in fat mass than men (Riebe *et al.*, 2009; Valentine *et al.*, 2009). Women possess lower levels of skeletal muscle mass and muscle function in addition to greater amounts of body fat mass. Each of these factors alone increases the risk of physical disability and sarcopenia. Additionally, these factors contribute to the increased prevalence of a new condition called sarcopenic obesity, which is characterized by low muscle mass, low muscle function, and obesity. Possessing the combined effects of each condition poses even greater risks to health than each alone (Barford *et al.*, 2006; Rolland *et al.*, 2008; Barazzoni *et al.*, 2018). Furthermore, the growing obesity and sarcopenia epidemics in the United States will combine to impose a significant health system challenge, which highlights the importance of determining when the significant changes in muscle mass, muscle function, and body composition occur across the lifespan (Sturm, Ringel and Andreyeva, 2004; Brownson, Boehmer and Luke, 2005).

Women display a greater likelihood of suffering from physical disability, and as age increases, the sex differences become more exaggerated with older women displaying twice the rate of physical disability (Newman & Brach, 2001). The National Center for Health Statistics reported that 85% of women 65 years and older depend on assistance for maintaining basic (i.e. using stairs, getting into and out of bed, etc.) and instrumental (i.e. brushing teeth, grooming, eating, etc.) activities of daily living (Schiller, Lucas and Peregoy, 2012). Challenging traditional beliefs that the incidence of physical disability

does not occur until older age, the National Health Survey reported that 1 out of 3 women between 40 and 60 years of age self-report physical limitations (Schiller, Lucas and Peregoy, 2012). Cumulatively, these findings indicate that women suffer from physical limitations more than men and that these physical limitations synergistically decrease independence and quality of life. Clearly, there is a need to examine the influence of age on skeletal muscle function for both the upper and lower body musculature to reduce the incidence of physical disability and improve quality of life for aging women.

Previous research suggests that muscle mass (Marjolein Visser *et al.*, 2002; Fragala *et al.*, 2014; Miller *et al.*, 2018) and muscle function, such as muscular strength, power, or endurance (Straight, Brady and Evans, 2015a; Correa-de-Araujo *et al.*, 2017; Frontera, 2017), significantly influence physical function (i.e. the ability to complete activities of daily living). Although it is widely accepted that muscle mass and muscle function decrease with age, there is no evidence outlining the onset or progression of decline in these parameters in women across the lifespan, highlighting an important gap in the literature. Since each measure has been shown to influence physical function, it is imperative to determine when each parameter begins to decline to effectively prescribe preventative measures to reduce the rate of physical disability. Furthermore, previous literature has generally examined the lower body given its inclusion in walking and additional activities of daily living, without assessing the upper body as well. However, upper body strength is required for activities of daily living such as eating, cooking, and grooming and can predict physical limitations, hospitalization, and mortality (Bohannon, 2008, 2015). One question that remains unanswered is when upper body muscle mass and function begins to decline in women and how this decline progresses with increased age.

What we know about aging in women comes from research conducted on men, yet the influence of age on muscle mass, muscle function (e.g. strength, power, endurance), body composition (e.g. fat and muscle mass), and physical disability rates are different for women (Jette and Branch, 1981; Schiller, Lucas and Peregoy, 2012; Deeg, 2016; Roberts *et al.*, 2018). Therefore, there is an urgent need to define the onset and progression of declining muscle mass, muscle function, and body composition to allow for more timely preventative interventions necessary for ensuring quality of life in women.

Purpose

The purpose of this investigation was to examine the influence of chronological age on muscular strength, power, endurance, and quality in recreationally active women.

Significance of Study

The aims of the present study were to 1) examine the influence of chronological age on quantitative and qualitative changes in skeletal muscle in recreationally active women; 2) determine the influence that age-related body composition changes have on skeletal muscle function; and 3) to provide a novel examination of biomarkers suggested to contribute to these changes with advanced age. The present aims remain unknown in the current literature, which limits the ability to develop effective preventative measures to ensure quality of life in aging women.

To our knowledge, the primary purpose of the present investigation, examining the influence of age on muscle mass and muscular strength, power, endurance, and quality in women, has yet to be explored by previous literature. Most importantly, women are

vastly underrepresented in both exercise science and biomedical research, including human, animal and basic cell studies (Beery and Zucker, 2012; Miller, 2014; Hunter, 2016). The present study offers a unique opportunity to specifically fill the void in the marginalized interests of women. Furthermore, census data indicates that women outnumber and outlive men (Howden and Meyer, 2011) and that women generate greater health care expenses than men (Alemayehu and Warner, 2004). Women also perform less physical activity (Sun, Norman and While, 2013), have more fat and less muscle mass, and display lower skeletal muscle function than men, each factor contributing to physical disability (Brady and Straight, 2014; Brady *et al.*, 2014; Charlier *et al.*, 2015; Da Boit *et al.*, 2016). Thus, women represent a group of the population that are particularly vulnerable to declines in physical function. Therefore, the ability to maintain physical function in women is paramount for reducing physical disability, hospitalization and mortality (Guralnik *et al.*, 1994). Consequently, distinguishing the interplay between aging, muscle mass, muscular strength, muscular power, muscular endurance, muscle quality, and body composition is a necessary first step toward decreasing the high rates of physical limitations in aging women.

This study includes practical and clinical measures of muscle function, as well as criterion standard measurements of skeletal muscle composition and total body composition. We chose to include multiple muscle function tests to ascertain dynamic muscular power, as well as assessing strength in terms of dynamic measures, isometric measures, and velocity related measures. Each assessment was strategically selected to provide unique and novel insight for evaluating the influence of chronological age on skeletal muscle and body composition in women. Incorporating multiple muscle groups

of the upper and lower body broadens the scope of observation to maximize our ability to find the key characteristics of skeletal muscle influenced by aging, with each muscle group differentiated by the daily amount of muscle use, muscle size, muscle fiber composition, and muscle location. Furthermore, we will examine muscular strength, power, endurance and quality (the ability to generate force relative to the amount of muscle mass present) for each muscle group, enabling the detection of the initial decline and progression of decline for each parameter across the lifespan of women.

Lastly, examining age-related changes in myostatin (a protein that inhibits muscular development) and interleukin-6 (an indication of stress and inflammation) in relation to muscle mass and muscle function changes is novel and may provide insight to further understanding of age-related changes in musculature. For example, previous literature has advocated the potential use of these biomarkers as an increase in these biomarkers may precede declining muscle function (Cesari *et al.*, 2012; Scharf and Heineke, 2012); however, the relationship between these biomarkers and muscle characteristics, and the age at which initial increases are evident remains unknown. Therefore, determining when these biomarkers initially increase may provide an early detection index of skeletal muscle declines and allow for early application of appropriate preventive interventions.

The recent establishment of an ICD-10-CM medical code for sarcopenia in 2016 is an important step toward increasing awareness of this debilitating condition, enabling sarcopenia to be recognized by the United States Food and Drug Administration and European Medicines Agency as a reportable condition (Vellas *et al.*, 2018). In October 2018, the European Working Group on Sarcopenia met and determined the primary

objectives for forthcoming sarcopenia research. The primary objective states "sarcopenia has long been associated with ageing and older people, but the development of sarcopenia is now recognized to begin earlier in life" (Cruz-Jentoft *et al.*, 2019). Therefore, the determination of the onset and progression of quantitative and qualitative changes in skeletal muscle across the lifespan demands further evaluation. The findings of this study will identify the onset and progression of significant alterations in skeletal muscle and body composition, permitting the proposal for critical age periods for deteriorating physical function in women. Ultimately, these data will provide the foundation for the development of preventative measures to reduce physical disability, ultimately improving independence and quality of life in a rapidly growing aging women population.

Research Question

1. Are there critical ages that can be identified in recreationally active women when significant decreases in muscular strength, muscular power, muscular endurance, and muscle quality occur?

Research Subquestions

1. Do age-related changes in muscle strength, power, endurance, and quality depend on muscle fiber type (type I versus type II), muscle location (upper versus lower body, proximal versus distal) or muscle size (large versus small)?
2. Are age-related changes in muscle mass and muscle function accompanied by changes in serum myostatin and interleukin 6?

Research Hypotheses

1. It was hypothesized that women between 25 to 29 years of age will display the greatest amount muscular strength for each muscle observed. Additionally, muscular strength will remain relatively stable among women within the 30-49 years of age intervals, with a more apparent decline beginning for women in the 50s, which has been suggested by previous literature (Kallman, Plato and Tobin, 1990; Lindle *et al.*, 1997). When transitioning into the sixth decade, muscle quality reductions will appear to become evident for women (Lynch *et al.*, 1999; Metter *et al.*, 1999). Further, it was hypothesized that women 25 to 29 years of age will display the greatest amount of muscular power with significant reductions occurring thereafter (>29 years) (Metter *et al.*, 1997; Dietzel *et al.*, 2013; Siglinsky *et al.*, 2015). In contrast to the hypothesized reductions in muscle strength, power, and quality, it was hypothesized that muscular endurance was maintained with age until the >80-year group, which may be due to the selective decrease in fast-twitch muscle fibers resulting in slow-twitch muscle fibers becoming the dominant fiber type.

Research Subquestion Hypotheses

1. It was hypothesized that muscles predominantly containing a type I fiber (soleus) composition was less affected with age when compared to a muscle predominantly composed of type II fibers (triceps brachii). This is supported by the selective alterations in fiber type accompanied with aging and that the number and requirement of powerful contractions are greatly reduced with age (Mitchell

et al., 2012; Tieland, Trouwborst and Clark, 2018). Additionally, it was hypothesized that the declines in the lower body muscle function was greater and occur sooner than the observed in the upper body, which has been reported previously (Frontera *et al.*, 1991, 2000; Hughes *et al.*, 2001). However, with age, the use of the upper extremities remains relatively unchanged given the habitual use during activities of daily living, which may lessen the age-related changes. Additionally, the lower body possesses greater muscle mass and greater force production capabilities; therefore, a greater reduction is possible. Further, it was hypothesized that muscle function in muscle groups located distally will undergo greater reductions with age when compared to those that are located proximally, given the previous observations of the preferential reduction in motor units (Campbell, McComas and Petito, 1973; Lexell *et al.*, 1983; Tieland, Trouwborst and Clark, 2018).

2. It was hypothesized that decreases in skeletal muscle mass was accompanied by increased myostatin and interleukin 6 levels, suggested by previous research (Schaap *et al.*, 2006; Ryall, Schertzer and Lynch, 2008; Beyer, Mets and Bautmans, 2012; White and Lebrasseur, 2014). The age of initial increase was hypothesized to be approximately 50 years where noticeable reductions in skeletal muscle mass have been reported (Fielding *et al.*, 2011; White and Lebrasseur, 2014).

Assumptions

1. Participants provided honest and accurate information while completing the included study documentation.
2. Participants were free of injury or disease.
3. Participants did not perform aerobic or resistance exercise 72 hours prior to the muscle function testing sessions.
4. Participants performed each of the included tests with their maximum effort.

Delimitations

1. The present observations only apply to healthy, recreationally active women above the age of 20.
2. Participants with a recent (<12 months) muscle or skeletal injury or a previous injury that may affect testing were excluded.
3. Participants with metal implants in the hip, knee, and spine were excluded.
4. The women were recruited from the surrounding areas of Norman and Oklahoma City, Oklahoma.

Limitations

1. The cross-sectional design limits the ability to infer a causal relationship.
2. Daily activities performed during participation were not measured or controlled.
3. Women that participated in the study were volunteers and may not provide an accurate representation of the entire population.
4. The study examined recreationally active women; therefore, the present data may not be representative of sedentary or highly active populations.

5. Participation was limited to those who fit within the dual-energy x-ray absorptiometry scanning area and within the peripheral quantitative tomography gantry.

Operational Definitions

Appendicular Skeletal Mass: The sum of bone-free lean body mass of the upper and lower extremities (Sergi *et al.*, 2015).

Bone-Free Lean Body Mass: The portion of body exclusive of stored fat and bone, including muscle, nervous tissue, connective tissue, organs and water (Duren *et al.*, 2008; Miller, Chambers and Burns, 2014).

Dual Energy X-Ray Absorptiometry: An enhanced form of low dose x-ray technology that is used to measure total and regional body composition and bone mineral content and bone mineral density by measurement of two x-ray beams, ~40kev and ~70kev, as they pass through the body (Duren *et al.*, 2008; Miller, Chambers and Burns, 2014).

Dynapenia: The age-related loss of muscle strength (Clark and Manini, 2008).

Fat Free Mass Index: The quantity of total body bone free lean body mass made relative the height squared (Cruz-Jentoft *et al.*, 2019).

Intramuscular Adipose Tissue: Deposition of adipose tissue located within the muscle (Kuk et al., 2009; Marcus, Addison, & Lastayo, 2013; Marcus et al., 2012; Scott et al., 2015).

Isokinetic Contraction: A muscular contraction in which the muscle contracts maximally through its full range of motion at a constant predetermined velocity (Haff and Triplett, 2015).

Isometric Contraction: A muscular contraction in which the muscle maintains the same length as tension in the muscle increases (Haff and Triplett, 2015).

Isotonic Contraction: A muscular contraction in which the external load is fixated, which must be overcome to perform a contraction (*System 3 Pro Application/Operation Manual*, 1988).

Lean Body Mass: The portion of body exclusive to stored fat, including muscle, bone, nervous tissue, connective tissue, organs and water (Shaw *et al.*, 2007; Visser and Harris, 2012).

Maximal Voluntary Isometric Contraction: The maximum amount of force that one can voluntarily exert by a muscle or group of muscles against an immovable object (Haff and Triplett, 2015).

Menopause: When there has been no menstrual period for 12 consecutive months and no other biological or physiological cause can be identified (Maltais, Desroches and Dionne, 2009).

Muscle Cross-Sectional Area: The area of muscle present on an image of a transverse slice of an appendicular lime measured using peripheral quantitative computed tomography (Engelke *et al.*, 2018).

Muscle Density: A function of protein, water, and lipid content within a muscle (Engelke *et al.*, 2018).

Muscular Endurance: The ability of the muscle to sustain repeated muscle contractions or resist fatigue during repeated contractions (Haff and Triplett, 2015).

Muscular Power: The product of force production and the velocity at which the force is produced (Haff and Triplett, 2015).

Muscle Quality: Muscular performance made relative to the quantity of muscle mass (Correa-de-Araujo *et al.*, 2017).

Peak Torque: The greatest rotational force produced during a maximal voluntary isokinetic contraction (*System 3 Pro Application/Operation Manual*, 1988).

Peripheral quantitative computed tomography: Peripheral quantitative computed tomography used the attenuation of x-rays through tissues to measure the composition of that tissue. This type of measurement is volumetric due to multiple slices being combined (mg/cm^3) and can provide a determination of cortical and trabecular bone in addition to muscle cross-sectional area. Specific sites for the current study included the 66% and 40% site of the tibia and femur, respectively (Duren *et al.*, 2008).

Sarcopenia: The age-related loss of skeletal muscle mass and function (Rolland *et al.*, 2008; Studenski *et al.*, 2014; Chen *et al.*, 2016; Cruz-Jentoft *et al.*, 2019).

Skeletal Muscle Mass Index: Appendicular bone free lean body mass made relative to height squared (Cruz-Jentoft *et al.*, 2019).

Specific Power: The amount of power a muscle group(s) can perform made relative to the quantity of muscle mass for a specific muscle group(s) (Correa-de-Araujo *et al.*, 2017; Alcazar *et al.*, 2020).

Time to Peak Power: The amount of time elapsed from the point of muscle force generation to the point where peak power is achieved (*System 3 Pro Application/Operation Manual*, 1988).

Time to Peak Torque: The amount of time elapsed from the point of muscle force generation to the point where peak torque is achieved (*System 3 Pro Application/Operation Manual*, 1988).

Time to Peak Velocity: The amount of time elapsed from the point of muscle force generation to the point where peak velocity is achieved (*System 3 Pro Application/Operation Manual*, 1988).

Work Fatigue: A ratio of the difference between the first 1/3 and the last 1/3 of work during isokinetic testing [WF = (work performed last 10 repetitions / work performed first ten repetitions) × 100] (*System 3 Pro Application/Operation Manual*, 1988).

List of Abbreviations

ASM- appendicular skeletal muscle mass

BFLBM- bone free lean body mass

DXA- dual energy x-ray absorptiometry

MQ- muscle quality

MVIC- Maximum voluntary isometric contraction

PP- peak power

pQCT- peripheral quantitative computed tomography

PT- peak torque

PV- peak velocity

RTD- rate of torque development

SP- specific power

TTPP- time to peak power

TTPT- time to peak torque

TTPV- time to peak velocity

UL- unloaded (1Nm) isotonic contraction

WF- work fatigue

Combined abbreviations examples:

PP_{20}- peak power at 20% MVIC

$TTPV_{20}$- time to peak velocity at 20% MVIC

$TTPP_{UL}$- time to peak power during unloaded (1Nm) condition

SP_{UL}- specific power during unloaded (1Nm) condition

Chapter II: Review of Literature

The purpose of this study was to examine the age-related changes of neuromuscular performance in recreationally active women above 20 years of age. The following literature review is divided into four major areas: 1) Muscle function with increased age; 2) Factors affecting muscle function with increased age; 3) Body composition changes with increased age; and 4) Characterizing muscle quantity and quality reductions.

Muscle Function with Increased Age

Muscle function can be characterized by several force production characteristics including muscular strength, power, endurance and quality. With increased age, muscular strength, power and quality decrease; however, muscular endurance appears to be relatively unaffected and perhaps increases depending on the task and nature of contraction (Mitchell *et al.*, 2012; Tieland, Trouwborst and Clark, 2018). Strength and power appear to reach maximum levels from the late teenage years into the fourth decade of life. When individuals extend later into the fourth decade, strength appears to decrease relatively slowly until the sixth decade of life where substantial decreases become evident. Muscular power tends to decrease at a greater rate than strength beginning for individuals in the fourth decade. Additionally, it appears that musculature of the lower body is affected to a greater degree than the upper body regarding muscle mass and strength losses. Although there is a tremendous amount of literature available regarding the age-related changes in muscle function, most of these studies only employ a young and old group, thus making the inference on where critical time points may occur difficult.

Furthermore, most of the investigations examine men, which makes any extrapolation to women difficult.

Isometric Strength

Isometric force production has been examined for a number of joints and muscle groups; however, when evaluating age-related changes, isometric grip strength can provide measures of functional strength and also an indication of and prediction of forthcoming morbidity and mortality (Bohannon, 2008). Kallman *et al.* examined the age-related decline in hand grip strength employing both a cross-sectional and longitudinal analysis observing a curvilinear decrease with maximal hand grip strength for individuals in their 30s, though not statistically different from the adjacent decades (i.e. 21 to 29 and 41 to 49 years) (Kallman, Plato and Tobin, 1990). Significant decreases were first observed for individuals in their 50s and continued to be observed with each subsequent age group until the oldest age group (80 to 89 years) displayed a 37% reduction in hand grip strength when compared to strongest group (30 to 39 years). Longitudinal analyses revealed an increased slope through the 30s, followed by a negative slope for the remaining age groups. Interestingly, the authors observed a trend with age suggesting that the older an individual is, the more likely they were to lose strength; however, 48%, 29% and 15% of the individuals less than 40, 40 to 59 and >60 years, respectively, did not experience strength loss during the longitudinal analysis. In contrast to these findings, Xue *et al.* reported marginal declines when longitudinally examining grip strength, knee extension, and hip flexion from women enrolled in the Women's Health and Aging Study II between the ages of 70 and 79 years (Xue *et al.*, 2010). Overall, there was a collective reduction in strength for each parameter over time with specific losses including a 1.10kg

per year loss of grip strength between 70 to 75 years and 0.5kg per year from 75 to 79 years. Knee extensor strength declined at a constant rate of 0.57kg per year, while hip strength declined an average of 1.31kg per year between 70 to 75 and 0.39kg per year between 75 to 79 years. Although these losses appear to be marginal, it should be mentioned that based off recently suggested criteria, following year 1.5 of the longitudinal analysis, the average grip strength would indicate that these women displayed clinical muscle weakness with a grip strength <22kg (Duchowny, Peterson and Clarke, 2017). Interestingly, these values do not meet the proposed values set forth from de Souza Vasconcelos et al. who used a grip strength value of <17.4kg or that proposed from Alley et al. suggesting <16kg to identify mobility limitations and clinically relevant weakness, respectively, in community dwelling individuals older than 65 years (Alley *et al.*, 2014; de Souza Vasconcelos *et al.*, 2016). The discordant proposals may be attributed to the different dynamometers used in the different studies since the Smedley and Jamar dynamometers were used, respectively. Lastly, Kallman *et al.* suggested that an individual with a greater amount of strength is more likely to lose strength and do so at a quicker rate than a weaker individual (Kallman, Plato and Tobin, 1990). In support of the observations from Kallman *et al.*, Aadahl *et al*. similarly reported maximum grip strength values in women were achieved between the ages of 30 to 39 years when examining women between the ages of 19 to 72 years (Aadahl *et al.*, 2011).

Rantanen *et al.* conducted a 27-year longitudinal analysis examining the influence of age on hand grip strength and reported an annual hand grip strength decline of 1% per year, while suggesting a 30% reduction between the youngest and oldest participants (Rantanen *et al.*, 1998). Additionally, the authors suggested that individuals greater than

50 years of age at the initial strength testing visit experienced a greater strength decline (1.5% per year). Dodds *et al.* evaluated 60,803 hand grip strength observations (26,687 women) and reported that peak hand grip strength is achieved around 30 years of age, followed by marginal reductions into the 50s with more substantial decrements beginning toward the end of the 50s and declining thereafter (Dodds *et al.*, 2014). Similar observations regarding maximal hand grip strength obtained in the 30s with marginal declines occurring until significant decreases observed in the 50s have been reported elsewhere (Metter *et al.*, 1997; Vianna, Oliveira and Araujo, 2007).

When looking at lower body isometric force, there appears to be a greater decline with increased age. Murray *et al.* sought to provide normative strength values for the knee flexor and extensor muscles in healthy women between the ages of 20 and 86 years (Murray *et al.*, 1985). The women were grouped into three age groups consisting of 20 to 35 years ($\bar{x}$ age 27), 42 to 61 years ($\bar{x}$ age 52), and 70 to 86 years ($\bar{x}$ age 75) and performed two knee extensor muscle contractions and then two knee flexor muscle contractions at 30, 45, and 60 degrees of knee flexion. For both muscle groups, across all joint positions, decreases in strength were found to parallel age, with the highest values in the youngest group and the lowest values in the oldest age group. Specifically, the middle-aged group displayed strength that was 77 to 95% of that of the youngest group, and the strength of the oldest group was 56 to 78% of that of the youngest and 69 to 88% of the middle-aged group. Similar to the findings of Murray *et al.*, Häkkinen & Häkkinen examined thirty women divided among three different age groups 30 years (range: 26 to 35 years) 50 years (range: 46 to 55 years) and 70 years (range: 66 to 75 years) (Häkkinen and Häkkinen, 1991). The participants completed testing to examine characteristics of muscle

cross-sectional area, maximal voluntary isometric force, isometric force-time and relaxation-time of their leg extensor muscles. There were no differences in cross sectional area between the 30 and 50-year-old groups, however the 70-year-old group displayed significantly smaller cross-sectional area when compared to the 20-year-old group ($p<0.01$). The 70-year-old group displayed significantly less strength compared to both groups (30: $p<0.01$; 50: $p<0.05$). Further, there were significant relationships between cross-sectional area and extensor strength across all age groups, and when isometric force was made relative to cross sectional area, there were no observed differences across groups. Additionally, the force-time curves revealed that the 30-year-old group could achieve the same absolute and relative force significantly quicker than the 70-year-old group ($p<0.05$), however relaxation times did not differ across groups. Also examining the knee extensors, Hunter *et al.* examined the rate of change with age of lower limb reaction time in women and sought to determine the relationship among reaction time, strength, and physical activity (Hunter, Thompson and Adams, 2001). Two-hundred seventeen women (20 to 89 years) performed reaction time testing and knee extensor maximum voluntary isometric strength testing. The authors observed a linear decrease with age regarding isometric knee extensor strength, however, there was no matching trend of reaction time. The regression analysis indicated that the baseline value for participants in this study was 224 Nm and for each year increase in age there was a decrease of 1.79 Nm. Of note, regardless of age and physical activity, the strongest women had the fastest reaction time.

Further supporting linear declines with age, Bohannon sought to determine how aging influences grip strength and knee extension strength in aging women (Bohannon,

2017). Eighty-five females between the ages of 20 and 79 years were separated into groups according to age (20 to 39 years, 40 to 59 years, and 60 to 79 years) and completed bilateral hand grip testing and isometric knee extension testing. The results showed that both grip strength and knee extension strength decreased significantly and in a linear manner with age ($p<0.001$). However, grip and knee extension strength normalized against the young group's strength did not differ significantly ($p=0.904$) for participants 40 to 59 years, but that did differ significantly ($p=0.012$) for the oldest group. One limitation regarding these observations would be the classification of age groups, by separating the participants into tertiles may mask or decrease the ability to detect specific age periods for the onset and progression of muscle function losses with age. In a similar study, Amaral *et al.* measured grip strength and knee extension strength in 63 women divided into three groups (young, $n=33$, 24.7±3.5 years; middle age, $n=15$, 58.6±4.2 years; and older adults, n=15, 72.0±4.2 years) (Amaral *et al.*, 2014). However, in contrast to Bohannon's observations, Amaral *et al.* noted no significant decreased for grip strength, whereas knee extensor strength was significantly decreased in all groups. The authors attributed these observations to the maintenance of habitual use for the upper extremities in activities of daily living, while there may be a significant reduction in the activity of the lower limbs with increasing age.

Christ *et al.* examined maximum voluntary isometric force production characteristics of the finger flexors, thumb extensors, forearm flexors, forearms extensors, dorsiflexors and plantar flexors in women between the ages of 25 to 74 years (Christ *et al.*, 1992). The authors reported an overall decrease in strength between 36.2% (forearm extensors) and 45.1% (plantar flexors). The age groups where significant

reductions were first observed was 45 to 49 years for the finger and forearm flexors, 55 to 59 years for the dorsiflexors, 60 to 64 years for the thumb extensors and plantar flexors, and 65 to 69 years for the forearm extensors. Interestingly, the individuals aged 65 to 69 years, not the oldest group, 70 to 74 years, showed the greatest reduction in maximal strength when compared to the 25 to 29-year-old group. Further, the authors indicated that the overall reduction in muscle mass could not account for the reductions in strength, thereby suggesting that the overall muscle quality may have been compromised. In contrast to these observations, and although not a primary aim of their study, Moraux *et al.* revealed that isometric plantar and dorsiflexion strength appears to decrease between the ages of 20 to 29 and 30 to 39 years, respectively, across individuals 5 to 80 years of age (Moraux *et al.*, 2013). The differing results may be due to methodological approach as the studies used different angles to assess muscle function.

Stoll *et al.* examined 51 functional muscle groups (FMG) in 543 men and women between the ages of 21 and 79 years (Stoll *et al.*, 2000). The FMGs included groups from the upper and lower body and the authors reported an average FMG strength reduction of 4% between years 25 and 55 with only the knee flexors decreasing significantly ($p<0.001$) in women. After 55 years of age, every FMG presented negative slopes; however, significant negative slopes were only observed for shoulder abduction, shoulder external rotation, elbow flexion, wrist pronation, supination and extension and hip internal rotation. When comparing upper and lower body FMGs, it was observed that between 21 to 55 years, the upper body isometric force production was preserved to a greater degree than that of the lower body and trunk. Marked decreases were observed for the upper and lower body as well as the trunk between 55 to 79 years; however, the

ability to suggest where critical time points occur is difficult given the dichotomy in age groupings.

Bohannon examined maximal isometric strength in women aged 20 to 79 years at the wrist extensors, hip flexors, knee extensors, elbow flexors and should abductors and reported no clear trend for strength reductions (Bohannon, 1996). For example, the elbow flexors and knee extensors demonstrated 83% and 45%, respectively, losses in muscle strength between the youngest (20 to 29 years) and oldest (70 to 79 years) groups. Additionally, the hip flexors and knee extensors demonstrated immediate reductions when comparing the 20 to 29 years of age and 30 to 39 years of age groups of 11%. The wrist extensors presented marginal decreases in strength between the youngest and the 60-69 years group, while no changes were revealed for shoulder abduction. Interestingly, using a similar dynamometer approach Akbari *et al.* examined women 21 to 80 years of age and observed significant differences ($p<0.001$) for the hip extensors and ankle dorsiflexors for women in their 40s while women in their 50s presented significant differences in hip abduction and knee extensors when compared to the youngest group (20s) (Akbari and Mousavikhatir, 2012). In contrast to these observations, Cheng *et al.* examined maximal isometric strength of the hip flexors, knee extensors, and ankle plantar flexors in men and women aged 40 to 89 years in relation to functional activities noting similar differences between sexes reporting significant differences between the youngest group (40 to 49 years) and the oldest group (>80 years) (Cheng *et al.*, 2014). Interestingly, there were no significant differences noted for either sex for plantar flexors, and the onset of significantly impaired performance in functional activities occurred prior to the significant strength decrease (70 versus 80 years, respectively) (Cheng *et al.*, 2014).

However, the divergent results may be attributed to the dynamometer used as Cheng et al. incorporated a handheld dynamometer for their testing.

Further, Young *et al.* measured the maximum voluntary isometric contraction strength of the quadriceps muscles of healthy women in their 70s ($\bar{x}$ age 74.4 years, n=25) and in their 20s ($\bar{x}$ age 24.2 years, n=25) and have compared it with the mid-thigh cross-sectional area of the same muscles (Young, Stokes and Crowe, 1984). Taking the best MVIC recorded for each subject, the older women were on average 35% weaker than the young women (p<0.001), which may have been attributed in part to the observed 33% less cross-sectional area (p<0.001). More recently, Francis *et al.* measured maximal isometric torque and isometric muscle quality of the knee extensors and flexors in healthy 50- to 70-year-old women providing several key findings for future research (Francis, Toomey, *et al.*, 2017). Interestingly, the authors noted: 1) a statistically significant learning effect (~5%) was present for assessing maximal strength across two testing days (7 days apart), 2) the combination of knee extensor and flexor peak strength muscle quality (KF + KE/ upper leg lean tissue mass) declined at twice the rate of upper leg lean tissue mass, and 3) differences in muscle strength of the legs is driven by knee extensor strength. Cumulatively, these findings indicate that participants must perform multiple familiarization trials in order to produce accurate strength values. Further, a 5% change in performance should be further investigated to determine whether this difference in performance translates into a "clinically significant" difference. Francis *et al.* also determined muscle quality by using the upper leg lean tissue mass as opposed to total leg lean tissue mass (Lynch *et al.*, 1999; Goodpaster *et al.*, 2006; Delmonico *et al.*, 2009), which more closely reflects the musculature involved in knee extension and flexion

testing. Further, the non-significant change in lean tissue mass may indicate that assessing lean tissue mass with dual-energy x-ray absorptiometry may mask age-related changes in muscle mass since this method cannot differentiate between skeletal muscle and non-skeletal muscle fat-free tissue (i.e. intermuscular fat, connective tissue, etc.).

Hughes *et al.* examined isometric shoulder strength in men and women aged 20 to 78 years and observed that strength peaked in the 30s although not statistically different from the 20s. Thereafter, a gradual decline to the 50s occurred where significant differences ($p<0.001$) were first observed (Hughes, Johnson, O'Driscoll, & An, 1999). Not all musculature appears to be impacted with age as findings from Salo *et al.* revealed no differences with increased age for the neck flexors, extensors or rotators (Salo *et al.*, 2006). However, Salo *et al.* only examined women aged 20 to 59 years which may explain the discrepant observations.

Dynamic Strength

The age-related reduction in dynamic muscle force appears to occur in similar fashion as isometric force production when slower movements are performed. However, when higher contraction velocities are employed there appears to be a widening in the force-velocity relationship between young and old individuals. These findings are likely attributed to changes in fiber type ratio (i.e. greater slow twitch to fast twitch fiber ratio), which has been supported from previous biopsy studies (Lexell, Henriksson-Larsen, Winblad, & Sjostrom, 1983; Sjöström, Lexell, & Downham, 1992). Furthermore, increased time to peak tension and relaxation time from previous twitch studies has revealed that both measures increase with age (Winegard, Hicks and Vandervoort, 1997). Differences may also be attributed to differences in physical activity, given that older

individuals may perform fewer fast and forceful contractions, thus the necessity to recruit fast twitch fibers is reduced possibly resulting in a decreased cross-sectional area and/or denervation from reduced use (Mitchell *et al.*, 2012; Tieland, Trouwborst and Clark, 2018).

Stanley and Taylor examined dynamic muscle characteristics of the knee flexors and extensors across four groups of women (20 to 25 years, n=15; 30 to 40 years, n=5) and older healthy women (50 to 59 years, n=9; 60 to 70 years, n=6) (Stanley and Taylor, 1993). The young participants completed testing at six angular velocities (60, 120, 180, 240, 300, and 400 degrees per second [deg/s]) while the older women completed testing at the five lowest velocities (60 to 300 deg/s). The results indicated that women between 20 to 40 years displayed greater flexor and extensor values for strength related measures (peak torque, angle of specific torque, work, and power) suggesting that changes in knee flexors and extensors may begin in the 4th decade. Additionally, Häkkinen *et al.* measured lower body dynamic force production capabilities in young and old men and women categorized into age groups consisting of a 40 or 70-year-old group (Häkkinen *et al.*, 1998). Dynamic explosive force was measured via vertical jump and standing long jump, while isometric force time curves, maximal isometric force, and maximal rate of isometric force development of the bilateral leg extensors were measured using an electromechanical dynamometer. Additionally, maximal dynamic strength (1RM) was assessed for the leg extensors, which quantified the explosive force characteristics using 50% of the participant's 1RM load. The results indicated that both groups of men, regardless of age, performed significantly greater (p<0.001) than either group of females. Presumably, the women in the 40-year-old group had significantly greater cross-sectional

area ($p<0.001$), bilateral 1RM ($p<0.01$), and jumping performance ($p<0.001$) than their older counterparts. Interestingly, no differences were present for isometric strength or rate of force development between the groups of women.

Jubrias *et al.* examined knee extensor isokinetic force in 57 individuals between the ages of 23 and 80 years and revealed that older individuals' knee extensor isokinetic force decreased significantly at all speeds tested (60, 120, 180, 240 deg/s, $p<0.001$) (Jubrias *et al.*, 1997). Interestingly, no changes were observed for the subjects divided into a young group (23 to 57 years); however, the individuals between 65 and 80 years revealed a drop of approximately 10 Newtons (N) per year, which indicated a 39% decline in isokinetic force between 65 to 80 years. Additionally, the reduction in cross-sectional area accounted for approximately half of the 39% force reduction, suggesting that quantitative changes alone do not explain the reduction in strength. Further, between the ages of 65 to 80 years, specific force dropped 1.5 N/cm^2 per year, indicating a 21% total reduction. The relationship between specific force, with regard to fiber type, revealed a greater percent of type I fibers (~44%) with an overall age-related decline in myosin heavy chain (MHC) type IIb fibers. However, the limited relationships between MHC composition and specific force at most velocities (r=0.01 to 0.11) limited the ability to suggest that the reduction in specific force was attributed to MHC composition (Jubrias *et al.*, 1997). Collectively, the authors suggested that the reduction in muscle force production appear to be credited to equal parts of muscle cross-sectional area and specific force and that the weak correlations between specific force and MHC composition indicate that the change in specific force with age is not attributed to changes in fiber type. Lastly, it is likely that the additional half of variance not accounted for was due to

muscle recruitment changes, contractile apparatus dysfunction, or excitation contraction coupling impairment (Jubrias *et al.*, 1997).

Akima *et al.* examined peak torque of the knee flexors and extensors in 164 individuals between the ages of 20 to 84 years of age and reported that at each angular velocity (0, 60, 180 and 300 deg/s), knee extension torque significantly decreased ($p<0.001$) with age (Akima *et al.*, 2001). Peak torque during knee extension and flexion was inversely related with age for men ($r=-0.79$ to -0.76, $p<0.001$) and women ($r=-0.64$ to -0.53, $p<0.001$), regardless of contraction speed. Further, women between the ages of 40 and 70 years displayed significantly lower peak torque than women in their 20s, and regression analyses indicated that the age-related decline in peak torque expressed as a percentage of the 20-year-old women was -0.5 to -0.7% with an 8% reduction per decade decline for knee flexors and extensors, respectively. Charlier *et al.* examined isokinetic knee extensor strength in 578 women in ten-year age groupings revealing no difference in torque at 60 and 240 deg/s in women aged 18 to 49 years; however significant differences were observed with each subsequent age group (18 to 49 years, >50 to 60 years, 60 to 70 years, and >70 years) (Charlier *et al.*, 2015).

Frontera *et al.* examined isokinetic force production of the knee and elbow flexors and extensors in men and women aged 45 to 78 years and reported that during the slow speed (60 deg/s) the oldest group (65 to 78 years) displayed significantly lower force production ($p<0.001$) for all muscle groups even after correcting for muscle mass (Frontera, Hughes, Lutz, & Evans, 1991). The difference in absolute strength ranged from 18.8 to 21.1% in the muscle groups, and when strength was expressed relative to muscle mass, the difference decreased to 3.6 to 10%. When evaluating the high-speed contraction

(240 deg/s) the oldest group produced significantly lower force production for all muscle groups ($p<0.001$); however, when the correction for muscle mass was made, the knee extensors did not present significant differences. Percent differences between the youngest and oldest groups were 18.7 to 23% and decreased to 3.8 to 14.2% when expressed relative to muscle mass. Furthermore, the data suggest that the proximal muscle of the legs decreased strength to a greater degree than that of the upper body. The authors suggested a preferential body composition alteration regarding intramuscular adipose tissue (IMAT), suggesting that IMAT may have increased in the legs but not in the arms. Additionally, the authors suggested that these differences could be attributed to changes in muscle morphology, decreased central nervous system activity, a loss in muscle mass or a combination of the factors. Similar observations of decreased peak torque in the knee extensors have been observed in men and women beginning in the 40s to 50s (Murray *et al.*, 1985; Lindle *et al.*, 1997).

Supporting the notion for a dynamic midlife period for changes in muscle function, Gajdosik *et al.* examined concentric isokinetic torque of the calf muscles in women between the aged of 20 and 84 years (Gajdosik, Vander Linden and Williams, 1999). Women were divided into three age groups consisting of 20 to 39 years (n=24), 40 to 59 years (n=24), and 60 to 84 years (n=33) and performed concentric contractions at 30, 60, 120 and 180 deg/s. The results indicated that advanced age results in decreases in peak and mean torques, with age displaying a significant negative correlation with peak and mean torques (r=-0.60 to -0.73), angular delay (defined as the angular displacement from the onset of movement to peak torque) at all velocities (r=-0.44 to -0.64), maximal passive DF angle (r=-0.73) and torque (r=-0.60), and with the peak torque velocity at 180

deg/s (r=-0.29). However, more apparent decreases were observed between the middle and older age groups. In an alternative task for quantifying ankle plantar flexion strength, Jan *et al.* measured 20 repetition one-leg heel-rise across three age groups of men and women (21 to 40 years, 41 to 60 years, and 61 to 80 years) observing significantly reduced performance for each adjacent age group as well as the youngest compared to the oldest group (p<0.017) (Jan *et al.*, 2005). Interestingly, there was a greater reduction in performance between the young and middle-aged group for men and a greater decrease between the middle-aged and older group for women, suggesting that advanced age may impact muscular performance to a greater degree in women.

Further, when comparing young and old men and women, Thelen *et al.* also noted significant differences in muscular performance noting that the older individuals require a substantially longer time reach various torque thresholds (5, 10, and 15 Nm) when compared to young adults (Thelen *et al.*, 1996). Of note, isometric rate of torque development was 25 to 36% lower in the older adults, while maximum isokinetic torques developed by the old were 20 to 40% lower than those of young adults. In agreement with additional research, these differences were widened with increasing velocity.

Similar findings were observed from Leyva *et al.* providing sex comparisons across the lifespan by decade in 195 women and 162 men, 18 to 80 years of age (Leyva, Balachandran and Signorile, 2016). Peak torque (PT) and average power (AP) during knee extension (KE), knee flexion (KF), ankle plantar flexion (PF), and dorsiflexion (DF) at 1.05, 3.14, and 5.24 rad/s were measured. A key observation from this study indicated that PT and AP declines are different between sexes and appear to occur at a younger age in women. For example, KEPT and KEAP values initially showed declines for men

beginning in the 50s, while similar decreases were observed in the 40s for women. Additionally, the authors noted that the losses observed at the KE muscles were velocity dependent, suggesting that strength can be maintained with advanced age at slower velocities. Losses of PF and DF PT and AP displayed curvilinear relationships for both sexes, again presenting an earlier onset of reduced muscle function with age in women. KEPT declined approximately 7.4% and 7.6% per decade in men and women, respectively. However, with advanced age the losses per decade for both sexes (40, 50, and 60 age groups) were increased to values of 16.9%, 18.9%, and 13.4% in women and 21.1%, 9.9%, and 17.5% in men. Collectively, these results suggest that muscle function maintenance strategies (i.e. exercise or physical activity interventions) should be introduced as early as the 30s and 40s, as the midlife can potentially present significant losses. Of note, the total sample (n=357) was divided into groups to test either the ankle or the knee, thus not all participants completed the testing. The suggestion of an earlier onset of muscle function loss conflicts those reported by Danneskiold-Samsøe *et al.* which reported a linear decrease with age in men but the onset of muscle function loss beginning at age 41 in women (Danneskiold-Samsøe *et al.*, 2009).

Most recently, Kemmler *et al.* proposed that aging related changes with muscle function do not uniformly present a linear or quadratic decline postulating that there may be a "changepoint" over the lifespan (Kemmler *et al.*, 2018). Specifically, the authors questioned whether there was a change in the rate of loss in muscle function with advanced age in non-athletic men aged 19 to 91 years. The study examined maximum isokinetic hip/leg extensor and flexor strength via isokinetic leg press testing, and it was hypothesized that at approximately 60 years of age, a "changepoint" would become

evident. Kemmler *et al.* incorporated a more rigorous statistical approach (i.e. segmental/spline model analyses), which is contrast to alternative approaches previously used (linear or quadratic regression). From the segmental analysis it was evident that there was a "changepoint" for maximum isokinetic extensor strength at 52 years of age to later age indicating a loss of 44 N per year, whereas up to 52 years of age there was a gradual loss of 5.2 N per year In contrast to maximal extensor strength, flexor strength did not display a significant "changepoint" until 59 years of age where the decline was 25 N per year while up to 59 years it was only 10 N per year. A conservative follow-up analyses (Davies, 2002) validated each change point presented from the preliminary analyses. Collectively, the takeaway from this novel analysis of age-related changes in muscle function illuminates that more rigorous statistical approaches need to be employed in order to quantify more precise changes across the lifespan. These observations further support previous suggestions that midlife may present the onset of muscle function decline, thereby warranting prophylactic approaches to be introduced prior to advanced age (Leyva, Balachandran and Signorile, 2016). Moreover, Samson *et al.* performed a similar analysis grip strength, knee extensor isometric strength, and knee extensor power, and suggested that the age of 55 years represented a critical period for age-related changes in muscle function (Samson *et al.*, 2000). Most recently, Alcazar employed a similar approach revealing that the 40s and potentially the 70s represent critical ages where changes in the rates of decline change for women (Alcazar *et al.*, 2020).

Muscular power, described as the rate at which work can be performed, typically measured through the vertical jump, also displays age-related declines. Metter *et al.* examined upper body muscular power production in 20 to 90-year-old individuals in ten

year intervals (Metter *et al.*, 1997). Power was measured through upper body cycling for 15 second work intervals with maximal power being observed for individuals in their 20s, followed by subsequent reductions within each decade. Sex differences were observed revealing that women showed a smaller reduction which may have been attributed to a lower baseline value. This could also indicate that even a marginal loss in muscular power could result in functional impairment. Using a similar cycling approach, however performed on the lower body and in men, Martin *et al.* revealed that maximal lower body muscular power was produced for men between the ages of 20 and 49 years (Martin *et al.*, 2000). Although the maximum values were displayed for men belonging to the 30 to 39-year-old group, they were not statistically significant from adjacent age groups. When examining the lower body, Aadahl *et al.* quantified lower limb knee extension power in women between the ages of 19 to 72 years revealing that maximal power was achieved between 19 to 39 years, declining thereafter (Aadahl *et al.*, 2011). The conflicting observations between when maximal upper and lower body muscular power is achieved could be attributed to testing modality or differences in muscle mass. Dietzel *et al.* examined jumping mechanography in men and women between the ages of 20 to 85 years and reported similar findings to that of the upper body from Metter et al. (Metter *et al.*, 1997; Dietzel *et al.*, 2013). Dietzel *et al.* reported that men and women were affected equally, with reductions of jump power varying between 40 to 50% between the 20 to 29 and >80-year groups.

Although there appears to be a substantial reduction in muscular power with advanced age, few studies have attempted to identify the primary determinant for this reduction. Recent work from Alcazar *et al.* revealed that there does not appear to be

uniform reductions in either the force or velocity component in older adults. Interestingly, the authors observed that bimodal deficits were associated with a lower physical function and reduced quality of life, higher frailty incidence, whereas the absence of force only was associated with a reduced cognitive function (Alcazar *et al.*, 2018). Kostka suggested that age-related decrease in maximum quadricep power reflects changes in muscle mass, thus force production capability, from young adulthood to middle-aged in addition to an insidious decline in velocity just prior to middle age (Kostka, 2005). Work from De Vito *et al.* aimed to illuminate whether force or velocity was the primary determinant of muscular power loss in women between the ages of 50 to 75 years (De Vito *et al.*, 1998). Muscle power was quantified using a counter movement jump and a squat jump technique. Absolute watts, peak watts, average watts, and vertical velocity each revealed significant age-related declines for both jumping conditions. However, vertical force displayed a paralleled reduction with increasing age but did not achieve statistical significance, except for during the counter movement jump. Therefore, the main finding indicates that vertical jump velocity is responsible for the significant reduction in power in the group of elderly women. Further supporting the main determinant responsible for power losses with age is velocity, Dionyssiotis *et al.* measured jumping mechanography quantifying jump force, velocity, and power in 179 women between the ages of 20 to 79 years categorized by decade (e.g. 20 to 29 years, 30 to 39 years, etc.) (Dionyssiotis, 2009). Jump velocity, power, and power/weight significantly decreased with advanced age ($p<0.001$), while the force produced during the jump did not decrease ($p=0.85$). Interestingly, the authors noted a 56% decrease from the 20 to 29 years decade versus the 70 to 79 years decade and the authors additionally noted an accelerated decrease

following the time of menopause. More recently, Edwén *et al.* examined the force and velocity changes with increasing age in men and women aged 18 to 81 years (Edwén *et al.*, 2014). Intuitively, men revealed significantly greater reductions for both parameters as a function of age when compared to women. However, the authors suggested that in men there was a greater reduction of force output while women displayed greater reductions in velocity. Several additional investigations are available regarding the influence of aging and power production assessing power by vertical jump or cycle ergometer testing reporting similar findings that power begins to decrease in the third decade (Runge *et al.*, 2004; Tsubaki *et al.*, 2009; Siglinsky *et al.*, 2015).

Rapid force characteristics, such as rate of force or rate of torque development (RFD or RTD) display greater reductions with advanced age than strength (39 to 65% and 29 to 46%, respectively) (Izquierdo, Aguado, Gonzalez, Lopez, & Hakkinen, 1999; Thompson et al., 2014). Paasuke *et al.* examined knee extensor RFD in women belonging to three age groups ($\bar{x}$ age of groups: 20 ± 0.2 years, 54.8 ± 0.9 years and 70.8 ± 0.8 years) observing that RFD was significantly greater ($p<0.001$) in the young women when compared to both the middle and older age groups, with no differences being observed between the middle and elderly aged groups (Paasuke, Ereline and Gapeyeva, 2003). More recently, Van Driessche *et al.* took a novel approach for determining the influence of aging on peak power, rate of power development, peak velocity, and rate of velocity development and how they correspond to functional parameters in young (22 ± 2 years) and old (68 ± 5 years) men and women (Van Driessche, Delecluse, Bautmans, Vanwanseele and Van Roie, 2018). Isometric knee extensor strength followed by isotonic knee extensor testing at 40%, 20%, and 60% maximum isometric strength was quantified

using a Biodex dynamometer. With the exception of peak velocity at 20%, the young adults performed significantly better for the additional strength-, velocity-, and power-related variables for both sexes ($p<0.05$). The key observation from this study was that both rate variables displayed greater differences between young and older individuals compared to peak values. Further, the differences were greater when examining the lower load (20%) compared to the higher load (60%). Interestingly, the authors speculate that the greater differences may be attributed to the inclusion of maximal strength and acceleration during the assessment of rate of power development. Nonetheless, the authors advocate the use of low loads to potentially detect age-related declines in muscle function. A number of alternative studies examining young and older individuals are available and indicate that rapid force characteristics are reduced with age; however, the ages at which these reductions occur remain unidentified due to methodology consisting of only a young (~20 to 30 years) and older (>60 years) groups (Izquierdo *et al.*, 1999; Korhonen *et al.*, 2006; Klass, Baudry and Duchateau, 2008; Power *et al.*, 2016).

Bemben *et al.* examined the influence of advanced age on force time characteristics in men aged 20 to 74 years analyzing the finger flexors, thumb abductors, forearm extensors, dorsiflexors and plantar flexors (Bemben *et al.*, 1991). Although no significant differences were observed for time to maximal force, significant differences between age groups were observed for maximal RFD for each muscle group. The forearm extensors, dorsiflexors and plantar flexors declined after 35 years of age while the finger flexors and thumb abductors did not reveal reductions until the late 50s. In a similar design, Runnels et al. examined age-related changes in force time characteristics for isometric and isokinetic contractions in men aged 20 to 83 years (Runnels *et al.*, 2005).

Time to maximal isometric force for the elbow extensors, knee flexors and knee extensors displayed a significant trend ($p<0.001$) increasing from the youngest to the oldest group. Maximal isometric RFD revealed significant differences between age groups for each muscle group (elbow extensors $p<0.05$; elbow flexors $p<0.005$; knee flexors $p<0.05$; and knee extensors $p<0.005$). The elbow flexors and extensors increased through the 30s and 40s, respectively, followed by sharp declines through the oldest group. The knee flexors displayed a linear decrease with age and the knee extensors remained relatively similar through the 50-59-year-old group followed by subsequent significant reductions ($p<0.05$) for the 60s and 70s group. In addition to the aforementioned observations, no distinct pattern was observed for time to isokinetic peak torque, with the exception that the slowest time was in the oldest age group. Congruent to similar findings, the authors reported an overall decline between 39 to 45% decline in maximal RFD (Izquierdo et al., 1999; Thompson et al., 2014).

Kostka examined quadriceps maximal power and shortening velocity in 335 individuals between the ages of 23 to 83 years noting initial decreases in the 30 to 39 and 40 to 49 year groups for optimal velocity and max power, relative power, power relative to the amount of quadricep mass, respectively (Kostka, 2005). Kostka noted an approximate 11% decrease in maximal power, which was greater than normal reports, but an overall linear decrease beginning in the 30s (Kostka, 2005). Interestingly, advanced age appeared to result in an increased rate of per annum decrease between the sixth and seventh decade (1.03%), seventh and eighth decade (1.42%), and the eighth to ninth decade (2.36%). Similar to the magnitude of loss, and more recently, Van Driessche *et al.* examined healthy adults between the ages of 20 and 70-years having participants

perform dynamic unilateral knee extension and multi-joint testing (Van Driessche, Van Roie, Vanwanseele, Van Leemputte, *et al.*, 2018). Variables of interest included peak power and rate of power development through the contraction. A significant interaction was observed suggesting that peak power declines greater in single- when compared to multi-joint contractions. Further, the authors noted that leg extension rate of power development declines to a greater degree (-1.42 to -1.92%) across the life span than peak power declines (-1.04 to -0.77%). Interestingly, the authors speculated that by only obtaining measures of multi-joint movements, there may be an underestimation of the actual age-related declines in maximal power production, advocating the inclusion of single joint measures.

Muscular Endurance

Several studies examining young and older cohorts provide a consensus that fatigue may be preserved or even increased in older individuals depending on the task (Avin and Law, 2011; Christie, Snook and Kent-Braun, 2011). Bilodeau *et al.* employed a fatiguing protocol which involved a sustained submaximal voluntary contraction at 35% maximum voluntary isometric contraction (MVIC) for the elbow flexors (Bilodeau *et al.*, 2001). Older individuals (70.8 ± 3.9 years) displayed significantly longer endurance time ($p<0.05$) than the younger group (26.3 ± 3.1 years), with no differences observed between genders within either age group. The authors suggested that these findings may be reflective of the increase in type I to type II fiber area observed with increased age. Hunter et al. examined time to task failure (TTF) of the elbow flexors in young (18 to 35 years) and older (65 to 80 years) adults and reported that TTF was significantly longer ($p<0.05$) for the older group (22.8 ± 9.1 min) when compared to the younger group (14.4 ± 7.6

min), and suggested the findings may have been due to an increased oxidative capacity and/or a greater proportion of type I fibers (Hunter, Critchlow, & Enoka, 2004). Similar observations have been reported when young and old participants were matched for strength or performed paced dynamic and isometric tasks (Callahan, Foulis, & Kent-Braun, 2009; Kent-Braun, Ng, Doyle, & Towse, 2002; Lanza, Towse, Caldwell, Wigmore, & Kent-Braun, 2003; Petrella, 2004; Yoon, Schlinder-delap, & Hunter, 2014).

Lindstrom *et al.* employed a fatiguing protocol consisting of 100 repeated knee extensions at a fixed rate of 90 deg/s and concluded that when fatigue was made relative to strength, fatigability was equal between young and old individuals (Lindstrom *et al.*, 1997). This observation was later supported from Baudry *et al.* examining dynamic contractions in the ankle dorsiflexors employing five sets of 30 contractions, observing no age differences (Baudry *et al.*, 2007). These observations suggest that speed of contraction may influence fatigability in older individuals. To examine this proposition, Callahan et al. examined the fatigability of the knee extensors in 11 young (23.5 ± 0.9 years) and 10 old (68.9 ± 4.3 years) women employing three protocols: 1) an isometric protocol (MVIC), 2) 120 dynamic contractions at 270 deg/s (MVC_{HI}), and 3) 120 dynamic contractions at a velocity corresponding to 75% of baseline maximum voluntary contraction (MVC_{INT}) (Callahan & Kent-braun, 2011). As expected, the older group exhibited greater fatigue resistance after the MVIC protocol (old: 71.1 ± 3.7% initial vs. young: 59.8 ± 2.5% initial; $p=0.02$) and experienced greater fatigue during the MVC_{HI} protocol (old: 28.0 ± 3.9%, young: 52.1 ± 6.9%, $p<0.01$). During MVC_{INT}, old and young subjects fatigued to a similar degree (old: 50.9 ± 6.0% and young: 53.5 ± 4.8%; $p=0.74$) confirming that differences were attributed to contraction velocity.

Regarding the lifespan, Bemben *et al.* examined isometric intermittent endurance of the finger flexors, thumb abductors, dorsiflexors, and plantar flexors characterized as peak force, impulse, percent total impulse (PTI), and percent force decrement (PFD) employing a protocol of 11 consecutive 2s maximal contractions followed by 3s rest for each muscle group (Bemben *et al.*, 1996). When expressed as PFD and PTI, no significant differences between age groups were observed; however, the ability to maintain muscular endurance between different muscle groups revealed significant differences. When averaged across age groups the PFD for each muscle group was as follows: finger flexors (18.6%), thumb abductors (14.1%) dorsiflexors (8.7%) and plantar flexors (2.5%), revealing that the strongest muscle group, the plantar flexors, showed a marginal decrement while the weakest muscle group, the thumb abductors, showed a more profound decrease. PTI ranged from 2% (plantar flexors) to 11% (finger flexors and thumb abductors) with the only significant difference being observed between the ages of 20 to 69 year and 70 to 74 years. These observations suggest that the ability to maintain muscular endurance may vary based on muscle location (i.e. upper versus lower extremity) or muscular strength (i.e. weaker versus stronger muscle groups).

Recently, Charlier *et al.* examined absolute and relative endurance in 1,397 adults (578 women) aged 18 to 78 years (Charlier *et al.*, 2015). The endurance test consisted of 25 knee extensions and flexions at a velocity of 180deg/s where total work (J) was recorded as a measure of resistance to fatigue for both muscle groups. The endurance task revealed a significant age x gender interaction ($p<0.01$) with an identical interaction observed for relative endurance. Men and women showed a 34.9% and 41.4% average drop by the age of 60-70 years with an average drop up to 54% and 58% for the oldest

age group (>70y). Significant reductions in endurance were first observed for women in their 40s and 50s when expressed as a relative or absolute measure, respectively.

Muscle Quality & Specific Power

While declines in muscle force have traditionally been attributed to an age-related decrease in muscle mass, recent evidence suggests that the quality of the muscle may have greater relevance than a measure of quantity. Coupled with aging is an increase in the deposition of intra- and intermuscular adipose tissue as well as non-contractile tissue (Haus *et al.*, 2007; Zamboni *et al.*, 2013). Therefore, with age, some individuals may not observe substantial differences in limb or muscle girth; however, the overall ability of a muscle may be reduced (Correa-de-Araujo *et al.*, 2017). Muscle quality has typically been measured in terms of muscle strength normalized to a quantity of muscle mass, often obtained through dual-energy x-ray absorptiometry, computed tomography, or ultrasound imaging. For example, Lynch *et al.* examined muscle quality of the dominant arm and leg in a group of 703 adults (339 women) aged 19 to 93 years (Lynch *et al.*, 1999). Appendicular skeletal mass was determined by dual-energy x-ray absorptiometry and the muscular function testing consisted of eccentric and concentric peak torque in the dominant elbow flexors and extensors at an angular velocity of 45 deg/s and in the dominant knee flexors and extensors at an angular velocity of 30 deg/s. Arm and leg muscle quality was calculated by dividing peak torque values for both parts of contraction by the amount of muscle mass for each extremity. The authors reported a linear decrease in arm muscle quality while the changes in muscle quality of the leg displayed a curvilinear relationship, with no or marginal decline through the 50s followed by accelerated reductions. Lastly, the authors observed that the muscle quality for the arm

was higher than that observed for the leg during both contractions, and leg muscle quality revealed a greater age-related decline than arm muscle quality, which would parallel the greater reduction in strength and muscle mass observed with age.

Lindle *et al.* examined muscle quality of the dominant leg knee extensors in 654 subjects (308 women) from the Baltimore Longitudinal Study of Aging using three contraction speeds (0, 30, and 180 deg/s) (Lindle *et al.*, 1997). The results presented significant age-related declines for each concentric contraction for each speed beginning at age 40 years. Metter *et al.* employed a cross-sectional and longitudinal analysis of muscle quality in 617 individuals (106 women, aged 17.6 to 84.4 years) (Metter *et al.*, 1999). The authors reported that when examining muscle quality, the quotient of muscle function and muscle CSA or muscle function and fat free mass, an age-related decline is observed. However, when using creatinine, a decline was not observed. The discrepancy in findings regarding creatinine was also demonstrated by Frontera *et al.*, which found marginal age-related changes in muscle quality when using creatinine and hydrostatic weighing (Frontera et al., 1991). Although many of the aforementioned studies suggest that muscle quality is reduced with age, it has been observed that young (32 ± 1 years) and older women (72 ± 1 years) may display similar muscle quality (Kent-Braun, Ng, Physiol, & Kjaer, 2008). Despite significant strength differences between age groups, no differences were observed in muscle quality. This observation is common when employing studies slower speed or isometric contractions; however, it appears that when greater speeds of contraction are employed, the reduction in muscle quality becomes much more evident (Frontera *et al.*, 1991; Overend *et al.*, 1992; Jubrias *et al.*, 1997).

An alternative reason for the conflicting observations regarding age-related changes in muscle quality could be attributed to the methodological techniques employed. For example, previous research has observed a two- to threefold increase in quadriceps non-contractile tissue content in elderly compared with younger individuals (Jubrias *et al.*, 1997; Kent-Braun, Ng and Young, 2000; Mitchell *et al.*, 2012). Therefore, the ability to differentiate between contractile and non-contractile elements of a muscle will impact the determination of muscle quality. Although magnetic resonance imaging and computed tomography techniques are not easily accessed, these methods possess the greatest validity regarding muscle measurements and reveal a reduced attenuation coefficient due to augmented noncontractile elements. Alternatively, dual energy x-ray absorptiometry can be used to determine muscle quality; however, this method does not possess the ability to differentiate between non-contractile and contractile elements. Recently, ultrasound imaging has been evaluated for the ability to separate non-contractile and contractile elements of a specific muscle and involve the gray-scaling of an image referred to as echo intensity. It has been demonstrated that older individuals present greater gray-scale values when compared to younger individuals, indicating a greater non-contractile volume, and that echo intensity is a valid and reliable measure possesses strong associations with muscle strength, power and cardiovascular performance in older individuals (Cadore *et al.*, 2012; Fukumoto *et al.*, 2012; Watanabe *et al.*, 2013; Osawa *et al.*, 2017), which may provide a more accessible muscle quality assessment tool. Collectively, it appears that the major discrepancy between previous studies measuring muscle quality can be attributed to two methodological aspects. First, researchers should attempt to indicate and assess the amount or region of lean tissue mass

that most closely reflects the target musculature assessed. For example, Francis *et al.* proposed that major differences in previous findings of lower-limb muscle quality may be attributed to the included segment of lean tissue mass (Francis, Toomey, *et al.*, 2017). The knee extensors and flexors are commonly studied; however, previous research has opted to include total leg lean tissue mass as opposed to upper-leg lean tissue mass (Lynch *et al.*, 1999; Goodpaster *et al.*, 2006; Delmonico *et al.*, 2009). Therefore, these findings warrant future research to provide a comparison of total leg and upper-leg lean tissue mass to identify potential discrepancies. Second, the protocol used for muscular performance should be consistent with alternative studies and should allow participants to become familiar with the testing. The former factor was difficult to perform since many approaches used to measure performance have been related to functional status (i.e. 60, 120, 180, 240 deg/s). However, the latter factor, familiarization should be much simpler to achieve since familiarization trials should be performed for performance testing. However, the balance between diminishing a learning effect and not allowing for acute adaptation warrants future research. However, previous research has reported and also not reported a significant learning effect between testing trials (Frontera *et al.*, 1991; Lindle *et al.*, 1997; Lanza *et al.*, 2003).

Factors Affecting Muscle Function with Increased Age

Neural Factors

Changes in the intrinsic force generating properties (i.e. neurological factors) appear to provide a greater contribution for the observed decrease in force production with advanced age (D'Antona, 2003; Taaffe, 2006; Narici and Maffulli, 2010; Mitchell

et al., 2012). Multiple changes occur in the nervous system that can alter force production such as a reduction in neuron body size (Haug and Eggers, 1991), cortical atrophy (Salat *et al.*, 2004), a reduction in the total length and conduction velocity of myelinated fibers (Stetson *et al.*, 1992; Kumar *et al.*, 2017) and changes in the brain white matter (Allman & Rice, 2001; Doherty, Vandervoort, & Brown, 1993; Madden et al., 2004). With increased age, some motor neurons will die, as previous research suggests a 25 to 50% reduction in the number of motor neurons in individuals aged 20 to 90 years (Tomlinson and Irving, 1977; Roos, Rice and Vandervoort, 1997; Aagaard *et al.*, 2010). There is evidence indicating a substantial loss of motor units after 60 years of age with more apparent decreases in distal as opposed to proximal muscles (Campbell, McComas and Petito, 1973; Lexell *et al.*, 1983, 1988). Additionally, in lifelong endurance trained individuals there appears to be a preferential reduction in the number of motor units in the elbow flexors as opposed to lower extremities when compared to younger individuals (Power *et al.*, 2012). The number of motor units recruited, the firing frequency and the variability of motor unit discharge have also been observed to change with age (Kamen *et al.*, 1995; Christou, 2011). Expanding upon the variability of force output, previous research has observed increased variability in older versus younger individuals, and these differences appear to be influenced by contraction type. As motor neurons are lost with, the remaining fibers are reinnervated by neighboring motor neurons through collateral axonal sprouting resulting in an increased size of motor units with age (Campbell, McComas and Petito, 1973; Tomlinson and Irving, 1977; Brown, Strong and Snow, 1988). Fiber type is partially dependent on innervation and the aforementioned denervation reinnervation process accounts for the changes observed in fiber type

differences with increased age (Welle, 2002; Hepple and Rice, 2016). The increase in motor unit size has been observed to display increased fatigability, which may contribute to the reduction in strength but maintained muscular endurance. Often, the faster motor neurons die resulting in the slower motor neurons reinnervating the orphaned muscle fibers, resulting in larger and slower motor units, consequently decreasing motor unit discharge rate (Kamen *et al.*, 1995; Connelly *et al.*, 1999; Patten, Kamen and Rowland, 2001; Rubinstein and Kamen, 2005). Kamen *et al.* observed that during maximal voluntary contractions, the first dorsal interosseous, had slower motor unit discharge rates in older individuals; however, at 50% maximum voluntary contraction, no differences were observed between young and old individuals (Kamen *et al.*, 1995). Further, across a range of intensities (maximal and submaximal), the tibialis anterior has demonstrated reduced discharge rates in older muscles, which has also been observed for additional muscle groups (Connelly *et al.*, 1999; Patten, Kamen and Rowland, 2001; Rubinstein and Kamen, 2005). In contrast to the aforementioned results, few investigations have noted no changes in discharge rates with advanced age. For example, Roos *et al.* observed no differences with age when examining the knee extensors and tibialis anterior (Roos, Rice, Connelly, & Vandervoort, 1999). However, the conflicting observations regarding age-related alterations in discharge frequencies have been suggested to be affected by physical activity and muscle specificity (Dalton *et al.*, 2009; Christie and Kamen, 2010). The force-frequency relationship has been demonstrated to shift in older individuals indicating that force plateaus at a lower activation (Allman, 2003; Narici, Bordini, & Cerretelli, 1991; Ng & Kent-Braun, 1999; Tevald, Foulis, Lanza, & Kent-braun, 2010).

Conduction velocity has been shown to decrease in peripheral nerves with age. For example, when examining the relationship between age and median nerve grip function, Metter *et al.* reported a slow linear decline in peripheral nerve conduction velocity beginning between 30 to 40 years of age (Metter *et al.*, 1998). This reduction contributed to a small but significant independent predictive role in the loss of strength with increased age. Additionally, Wagman and Lessee observed a 20m/sec difference in conduction velocity between young (20 years) and older individuals (67.5 years) (Wagman and Lesse, 1952). The reduction in conduction velocity is in part due to the drop out of large axonal fibers, reduced myelination, changes in the fiber membrane and is related to the reduction observed in muscle strength sand power (Kumar *et al.*, 2017).

Christie *et al.* observed a longer after-hyperpolarization of the motor neuron in older individuals (Christie and Kamen, 2010). With an increased hyperpolarization period, this reduces the rate at which the motor neuron can produce additional action potentials. Moreover, decreases in neuromuscular activation have been observed in those with mobility impairment, which could explain the reduction in power production (Manini & Clark, 2012). Reduced central activation in older adults has been reported; however, most literature suggests that these impairments can be mitigated following subject familiarization (Allman and Rice, 2001; Stackhouse *et al.*, 2001; Chung, Callahan and Kent-Braun, 2007; Callahan, Foulis and Kent-Braun, 2009). The excitability of the motor cortex may be reduced with advanced age (Oliviero *et al.*, 2006). Additionally, antagonist coactivation may be responsible for reduced force production; however, many factors contribute to these findings such as exercise, muscle and contraction type and no study has thoroughly examined this suggestion with increased age (Klein, Rice and

Marsh, 2001; Macaluso *et al.*, 2002). Some evidence suggests that older adults require a greater amount of effort to achieve similar levels of relative force during a muscle contraction. Ng and Kent-Braun observed that older individuals displayed a reduced ratio of voluntary force production obtained from surface EMG measures (Ng and Kent-Braun, 1999). However, alternative research has indicated that although older adults display greater variability in activation, there were no differences in mean voluntary activation (Rozand *et al.*, 2017). Nonetheless, it is plausible that a higher EMG in older individuals reflects a greater need for increased neuromuscular drive to achieve a given force output.

Degenerative changes of the neuromuscular junction may impact impulse transmission, which include increased fragmentation in the distribution of acetylcholine receptors and an increase in the incidence of branches or boutons that are spatially separated or only connected by fine nerve filaments, indicating fragmentation of the nerve terminal (Delbono, 2003; Luff, 1998; Manini, Hong, & Clark, 2013). Excitation contraction coupling (ECC) refers to the process of converting a neural signal for muscle activation into muscle force production. Aging has been shown to result in a decreased amount of dihydropyridine receptors (DHPR), ryanodine receptors (RyR), and display increased uncoupling between the DHPR and RyR resulting in a decreased calcium release in response to muscle excitation and a reduced calcium supply to contractile proteins, thereby reducing force production (Renganathan and Delbono, 1998; Wang, Messi and Delbono, 2000; Delbono, 2003; Moreno *et al.*, 2006). Alternative proteins involved in ECC alterations regarding muscle weakness and aging have been observed. For example, in aged animal models, there is a reduced expression of the sarcoplasmic

reticulum junctional face protein, which alters the expression of DHPR subunits and affects DHPR and RyR interactions (Zorzato *et al.*, 2000).

Muscle Factors

Studies have reported a substantial reduction in muscle fiber size in older individuals, which appear to be preferential, indicating a predominant decrease in size of type II fibers between 10 to 40% resulting in a larger proportion of type I fibers, when older individuals are compared to younger populations (Mitchell *et al.*, 2012; Tieland, Trouwborst and Clark, 2018). Conversely, type I fiber size appears to be relatively unchanged with advanced age (Larsson, Sjodin and Karlsson, 1978; Martel *et al.*, 2006; Verdijk *et al.*, 2006; Nilwik *et al.*, 2013). Previous studies have reported a decrease in total muscle fiber number with increased age (Lexell *et al.*, 1983, 1988). Lexell *et al.* observed an 18% smaller vastus lateralis muscle size in older individuals with an accompanied 25% reduction in fiber number, suggesting that atrophy could be attributed to the loss of muscle fibers (Lexell *et al.*, 1983, 1988). However, Nilwik *et al.* reported that vastus lateralis fiber number was not different between young and old individuals, but there was a preferential reduction in type II fiber size in the older individuals (Nilwik *et al.*, 2013).

The use of individual fibers allows for a better understanding of muscle behavior. It has been demonstrated that with aging, shortening velocity of type I and II fibers decreases by 10 to 30% and 20 to 50%, respectively (Höök, Sriramoju, & Larsson, 2001; Larsson, Li, & Frontera, 1997). Within the fibers, myosin concentration decreases with age, and within each fiber type, specific tension is determined by the myosin concentration indicating that the loss in specific tension is caused by a decrease myosin

concentration (D'Antona, 2003). Specific tension has been observed to decrease with age for men and women by approximately 16 to 33% for type I, 14 to 25% in type IIa, and close to 50% in type IIx fibers (Larsson, Li and Frontera, 1997; Höök, Sriramoju and Larsson, 2001; D'Antona, 2003). Previous studies have shown that the age-related decrease in specific tension (~16 to 50%) is associated with a decrease in the number of myosin heads in the strong binding, force generating state (Lowe, 2004; Lowe, Surek, Thomas, & Thompson, 2001; Thompson, Lowe, Ferrington, & Thomas, 2001). This age-related loss of myosin content relative to muscle fiber cross-sectional area, consequently, results in a decreased number of actomyosin interactions. Additionally, aging is associated with an accumulation of glycation end products which can alter the structure and function of myosin, leading to decreases in shortening velocity and specific tension while increasing collagen cross linking (Haus *et al.*, 2007; Narici and Maffulli, 2010). Collagenous cross linking is believed to increase muscle stiffness, thereby impairing muscle function (Haus *et al.*, 2007). Furthermore, the speed of actin sliding decreases with age resulting in a reduced maximal shortening velocity (Larsson, Li and Frontera, 1997; Höök, Sriramoju and Larsson, 2001). Shortening velocity is greatly influenced by myosin isoforms, in that type IIa have greater amounts of myosin ATPase and display three times faster velocity than MHC type I fibers (Trappe *et al.*, 2003). Therefore, any reduction or shift from fiber type II to I would result in a reduced contractile speed. The rate of muscle relaxation in whole muscle also declines with aging and has been associated with a lower proportion of type IIa fibers and lower sarcoplasmic reticulum maximal rate of calcium uptake and calcium ATPase activity (Hunter *et al.*, 1999; Callahan and Kent-braun, 2011). Interestingly, older women that perform resistance

training for 12 weeks have been shown to significantly increase sarcoplasmic reticulum calcium uptake and calcium ATPase activity; however, these improvements did not produce changes in speed of relaxation (Hunter *et al.*, 1999).

Lieber *et al.* suggested that the architecture of muscle is a major determinant of the force producing capability (Lieber & Friden, 2000). Changes in muscle architecture, such as fascicle length and pennation angle have been observed to decrease with age, which contribute to a reduction in cross-sectional area, thus a reduction in force generating capacity (Häkkinen and Häkkinen, 1991; Overend *et al.*, 1992; Kubo *et al.*, 2003; Narici and Maffulli, 2010). In the gastrocnemius, it has been observed that a decrease in muscle volume of 24 to 31% between young and older men was not attributed to only fewer fibers but also a decrease in fiber length (Narici, Maganaris, Reeves, & Capodaglio, 2007; Thom, Morse, Birch, & Narici, 2007). Conversely, Kubo *et al.* reported that pennation angle was decreased with age for the vastus lateralis ($p<0.001$) but not for the medial gastrocnemius or triceps brachii; additionally, increased age did not influence fascicle length (Kubo *et al.*, 2003). The mechanisms responsible for the alterations in muscle architecture is the atrophy of a specific muscle, therefore the muscle packing along the aponeuroses decreases (Narici & Maffulli, 2010). Decreased fascicle length represents a loss of sarcomeres in series and implicates a loss of shortening velocity, whereas a decrease in pennation angle reflects a loss of sarcomeres in parallel (i.e. cross-sectional area), thereby reducing force production potential. Given the product of force and velocity is power, changes in muscle architecture inevitably play a role in age-related loss of muscle power.

Considering the key roles of mitochondria for skeletal muscle function, namely fueling the metabolic demands with muscle fibers (i.e. contractile function, maintaining membrane potential, calcium handling, homeostasis, etc.), a shift in focus has turned to the mitochondria as a profound contributor to age-related changes in muscle mass and muscle function (Gonzalez-Freire, Adelnia, *et al.*, 2018; Coen *et al.*, 2019). Specifically, aging has been observed to result in skeletal muscle displaying a reduced activity of mitochondrial enzymes, mitochondrial volume and an increase in mitochondrial abnormalities (Conley, Jubrias and Esselman, 2000). It was first observed that two mitochondrial enzymes, citrate synthase and cytochrome c oxidase decrease with increasing age from skeletal muscle biopsies in both sexes (Rooyackers *et al.*, 1996). Further, Portions of diseased mitochondria, termed 'ragged red fibers' can accumulate in the sarcolemma region of the muscle fiber and may indicate an age-related decline in mitochondrial function (Rifai *et al.*, 1995). Although some have suggested that impaired mitochondrial function can lead to reduced muscle size and function, alternative literature has suggested that the impact of senescent mitochondria can be combatted through exercise, such that Dodds *et al.* demonstrated that physically active individuals >85 years (11 females and 8 males) retain mitochondrial respiratory chain function and content (Dodds *et al.*, 2018). Nonetheless, mitochondrial dysfunction results in an imbalance of reducing equivalents (i.e. NADH), thereby increasing reactive oxygen species in turn causing oxidation of cellular components (Coen *et al.*, 2019). Moreover, the reduced capacity of skeletal muscle mitochondria has been associated with reduced gait speed, fatigability, and sarcopenia, among other skeletal muscle characteristics and conditions (Santanasto *et al.*, 2015; Gonzalez-Freire, Scalzo, *et al.*, 2018). For example, Zane *et al.*

initially reported that mitochondrial function affects muscle strength and that a decreased capacity for muscle bioenergetics contributes to differences in walking performance in men enrolled in the Baltimore Longitudinal Study of Aging (Zane *et al.*, 2017).

Noting the ambiguity of the present literature regarding skeletal muscle oxidative capacity, Fitzgerald *et al.* composed a systematic review and meta-analysis to determine what the current evidence suggests (Fitzgerald, Christie and Kent, 2016). The authors noted that while the overall influence of age on skeletal muscle oxidative capacity is positive (i.e. greater oxidative capacity) in vivo, there was significant heterogeneity across the literature, of note, the findings are greatly affected by muscle group, physical activity, and sex. Of greatest importance, Fitzgerald *et al.* reported a clear discrepancy between muscle groups in the analysis nothing that oxidative capacity is lower in the knee extensors of older adults, similar across ages for the plantar flexors, and displays a greater capacity in the arms and dorsiflexors in older adults (Fitzgerald, Christie and Kent, 2016).

Most recently, Ahn *et al.* used mutated mice to examine the influence of elevated mitochondrial oxidative stress on muscle mass and contractile function observing quite paradoxical findings (Ahn *et al.*, 2019). Of note, the elevated reactive oxygen species lead to a reduction in neuromuscular junction morphology and function in additional to skeletal muscle contractile abnormalities. Interestingly, there was an increase (~10 to 15%) in muscle mass, suggesting that impaired mitochondrial function may induce fiber branching as a compensatory mechanism to maintain muscle mass (Ahn *et al.*, 2019). Collectively, it is important to remember that mitochondrial changes observed in muscle with aging are attributed to aging but are largely influenced by environmental and lifestyle factors (Aversa *et al.*, 2019).

Markers of oxidative stress increase with age. For example, lipofuscin which is the result of the polymerization of lipids and an antioxidant enzyme, glutathione, have been observed to decrease with age (Weindruch, 1995). Cellular metabolism generates free radical particles which include reactive oxygen particles, reactive nitrogen particles and reactive aldehydes which can cause damage to proteins, DNA and lipids. Rodent studies have provided evidence for mitochondrial dysfunction leading to dysfunction in the neuromuscular junction in mice that lacked superoxide dismutase (Jang *et al.*, 2010). Further, coupled with advanced age is a reduction in redox homeostasis, which leads to a progressive oxidation of contractile proteins resulting in skeletal muscle dysfunction (Lourenço dos Santos *et al.*, 2015).

Satellite cells are myogenic precursor cells, which are activated in response to muscle stress or injury, which then undergo proliferation and differentiate into myoblasts. Myoblasts fuse with additional myoblasts to form myotubes, which can then form a new muscle fiber or fuse with an existing fiber. These cells are the essential skeletal muscle stem cell and are essential for skeletal muscle regeneration following injury (Aversa *et al.*, 2019). It appears that the transmembrane receptor notch is responsible for the activation of satellite cells and the activity of the notch declines with age (Carlson *et al.*, 2009). Moreover, insulin like growth factor 1 (IGF-1) can trigger the activation of satellite cell division, however IGF-1 is decreased with advanced age (Perrini *et al.*, 2010), and the number of satellite cells per muscle fiber has been observed to decrease by 24% when comparing young and old women (Verdijk *et al.*, 2014). Further, elegant parabiosis experimental analysis, which combines two organisms resulting in a "sharing" of a common circulatory system has facilitated the dichotomization of progeronic and

antigeronic factors from an old and young circulatory system, respectively, and previous data indicates that progeronic factors hinder the health and function of cells in the younger circulation, while the antigeronic factors improve the health and function of cells in an older circulation (Conboy *et al.*, 2005; Carlson *et al.*, 2009).

Muscle protein metabolism has been suggested as a possible factor for a reduction in skeletal muscle mass. The net balance between synthesis and degradation is largely responsible for the maintenance of muscle mass (Fry and Rasmussen, 2011). Previous evidence indicates that fasting and basal metabolic protein synthesis rates are similar between young and old individuals (Cuthbertson *et al.*, 2004; Katsanos *et al.*, 2005). Therefore, an additional proposition was made suggesting that older individuals may display an 'anabolic resistance' associated with feeding and physical activity. For example, previous studies have observed that when older individuals ingest essential amino acids, there is a diminished accretion of muscle proteins (Katsanos *et al.*, 2005; Katsanos, 2006). Likewise, following an acute bout of resistance training, a blunted protein synthesis rate in older individuals has been observed (Sheffield-Moore *et al.*, 2004). In addition to a blunted post prandial and post-exercise response, some evidence indicates an increased protein breakdown with age. Vastus lateralis biopsies were obtained from old and young women and messenger mRNA expression of atrogin-1, a ubiquitin proteasome related gene, was upregulated by 2.5-fold following resistance exercise (Raue *et al.*, 2007).

Changes in Physical Activity

Physical inactivity can lead to a reduction in muscle mass and function any time throughout the life span (Paddon-Jones, 2006; English and Paddon-Jones, 2010).

Unfortunately, there is a substantial disagreement between what adult's self-report and what is actually performed regarding physical activity. For example, Tucker *et al.* suggested that 60% of adults (American and European) self-report that they meet physical activity guidelines, however, objectively measured physical activity indicates that less than 10% of adults in the United States meet these guidelines (Tucker, Welk and Beyler, 2011). Moreover, measuring accelerometry to quantify physical activity from the National Health and Nutrition Examination Survey displayed a 55% decreases in moderate to vigorous physical activity above the age of 39 years, in addition to a 75% decrease in the time spent performing such activities (Troiano *et al.*, 2008).

Nonetheless, aerobic exercise has been observed to stimulate protein synthesis, satellite cell activity and increase muscle mass (Coggan *et al.*, 1992; Sheffield-Moore *et al.*, 2004). Similarly, resistance training has also demonstrated the ability to increase protein synthesis, muscle mass and muscle strength (Yarasheski *et al.*, 1993, 1999; Welle, Thornton and Statt, 1995; Jozsi *et al.*, 1999; Ivey and Roth, 2000). Initial results regarding changes with lifelong physical activity are conflicting with observed decreases in muscle mass and function in masters athletes that have performed resistance training throughout their lifetime (Hameed, Harridge, & Goldspink, 2002; The & Ploutz-Snyder, 2003; Trappe, Lindquist, & Carrithers, 2001). In contrast, more contemporary evidence has shown that lifelong exercise may display a greater 'preservation capacity' with advanced age. Wroblewski *et al.* examined lifelong masters triathletes in their 40s, 50s, 60s, and >70 years and observed no significant differences in muscle mass with advanced age and only marginal differences for peak torque of the knee extensors between age groups (Wroblewski *et al.*, 2011). Aagaard *et al.* reported that lifelong strength and endurance

trained older individuals produced significantly greater knee extensor strength ($p<0.05$) than age matched lifelong sedentary controls (Aagaard *et al.*, 2007). RFD was significantly greater ($p<0.01$ – $p<0.05$) for strength trained men when compared to sedentary males; though not significantly greater than endurance trained men. Muscle fiber area was significant larger in the strength trained men ($p<0.05$) for fiber types I, IIa and IIx, with strength trained men having greater values than sedentary men for each fiber type but only type IIa and type IIx greater than endurance trained men. Similarly, Zampieri *et al.* showed that maximal isometric torque ($p<0.01$), 10-meter max gait distance ($p<0.05$), 5-repetition chair rise ($p<0.01$), and timed up and go test ($p<0.05$) were significantly better in individuals who were lifelong exercisers (Zampieri *et al.*, 2015). The authors reported several key findings, among those i) greater muscular force with lifelong exercise, ii) better preserved fiber morphology and calcium handling with lifelong exercise, iii) preserved muscle size from a more efficient reinnervation, and iv) genes related to autophagy and reactive oxygen species were much lower in lifelong exercises.

Hormonal Factors

Evidence suggests that the changes associated with menopause can impact skeletal muscle mass and function (Maltais, Desroches and Dionne, 2009; Carvalho *et al.*, 2018). Postmenopausal women lose approximately 0.6% of muscle mass per year and the non-contractile volume of a muscle is nearly double that of premenopausal women (Jubrias *et al.*, 1997; Rolland *et al.*, 2007). There is an increase in oxidative stress caused by an inadequate antioxidant system, which creates an increased production of reactive oxygen species from the mitochondria, which may lead to apoptosis (Signorelli *et al.*,

2006; Hiona and Leeuwenburgh, 2008; Pansini *et al.*, 2008). It has been suggested that the mitochondrial DNA is damaged via oxidative stress leading to a reduction in energy production from the electron transport chain, referred to as the vicious cycle theory (Bandy and Davison, 1990). The reduced capacity of the mitochondria to produce energy makes it susceptible to apoptosis, which may impact the muscle fiber. It was proposed and later confirmed that the increased total body and intramuscular adiposity the menopausal transition can be attributed to the increased oxidative stress (Wing, Matthews and Kuller, 1991; Mittal and Kant, 2009).

In older women, vitamin D deficiency has been associated with muscular atrophy and an increase in intramuscular adipose tissue (Visser, Deeg and Lips, 2003). A decrease in circulating dehydroepiandrosterone (DHEA) occurs during the menopausal transition and is associated with reduced muscle mass and function (Yen, Morales and Khorram, 1995; Labrie *et al.*, 2005). Circulating growth hormone levels decline with menopause and have been suggested to contribute to the loss in muscle and bone tissues during the menopausal transition (Van den berg *et al.*, 1996; Leung *et al.*, 2004). Insulin-like growth factor 1 (IGF-1) decreases with menopause and is believed to contribute to an increased amount of circulating inflammatory cytokines (IL-6 and TNFα), which are associated with muscle protein breakdown (Tsujinaka *et al.*, 1995; Pfeilschifter *et al.*, 1996). Insulin sensitivity is impaired with age and therefore protein synthesis is reduced while protein breakdown may be increased (Chevalier *et al.*, 2005). Most notably, the menopausal transition is associated with a reduction of estrogen and some believe that the simultaneous reductions in muscle function and estrogen are causal (Calmels *et al.*, 1995; Cooper *et al.*, 2007, 2011). It has been proposed that estrogen has an anabolic effect on

muscle through IGF-1 stimulation leading to an increased protein synthesis (Sitnick *et al.*, 2006; Velloso, 2008). Estrogen receptors have been observed in human muscles, (estrogen receptor α and estrogen receptor β) and are reduced in postmenopausal women when compared to young women and young and old men (Wiik *et al.*, 2009). In contrast, some evidence suggests that estrogen and muscle strength are not related. Humphries *et al.* observed women in age groups of 45 to 49, 50 to 54, 55 to 59 and 60 to 64 years and suggested that age, as opposed to estrogen, provided a larger contribution to decreased strength (Humphries *et al.*, 1999). Interestingly, whether age or menopause causes the decrease in muscle function, it should be noted that estrogen receptors are expressed in a greater amount in type II fibers, which undergo greater age-related changes (Brown, 2008). Lastly, it has been suggested that the loss of estrogen could impact the contractile properties of the muscle. Wohlers *et al.* examined ovariectomized mice and observed a reduced capacity to activate adenosine monophosphate kinase (AMPK) (Wohlers *et al.*, 2009). AMPK is necessary for glucose uptake and lipid oxidation with the muscle and could therefore explain part of the insulin insensitivity and adipose tissue infiltration observed during the menopausal transition (Ley, Lees and Stevenson, 1992; Osler and Zierath, 2008).

Myostatin and Interleukin-6

Myostatin

Myostatin, also referred to as growth differentiation factor 8 (GDF8), is a member of the transforming growth factor beta family and a negative regulator of muscle growth. Myostatin is expressed largely in skeletal muscle, but also can be observed in adipose and

cardiac tissues. Initial evidence of this relationship was first observed in rodent models, where the iconic “mighty-mouse” model was first described (McPherron, Lawler and Lee, 1997). Shortly after, the capacity for myostatin to regulate muscle growth, via null models or overexpression, was observed among additional species (e.g. Piedmontese and Blue Belgian cattle, hamsters, etc.). These animals display significant amounts of muscle mass, which is also shown, though not to the same degree in a set of racing dogs (whippets). Some believe it was the genetic mutation observed in whippets that lead investigation between myostatin, muscle mass, and muscle performance. Altogether, these observations have facilitated the ideology that inhibition or blocking of GDF8 may result in increased amounts of muscle mass and strength. For example, more than a dozen clinical trials are underway, some revealing promising, while others reveal detrimental outcomes (Lee and Jun, 2019).

Since McPherron’s foundational observations (McPherron, Lawler and Lee, 1997), relationships and mechanisms between myostatin and skeletal muscle have been under investigation. Myostatin effects both protein synthesis and satellite cell activity (Lee, 2004; Elkina *et al.*, 2011). Once bound to its activin type 2 B receptor (ACTR2B), the binding recruits then phosphorylates the activin receptor-like kinase (ALK) 4 or ALK5 units. Following this phosphorylation, mothers against decapentaplegic homolog (SMAD) 2 and SMAD3 are phosphorylated and then form a heterodimer with SMAD-4. The heterodimer then has the capacity to translocate to the nucleus and alter transcriptional events. The SMAD2/SMAD3 complex also has demonstrated the capacity to influence the downstream events of protein kinase b (Akt) signaling. Once SMAD2/SMAD3 exert the inhibitory effects of Akt, protein synthesis is decreased

(though influenced by multiple factors) in addition to the break that Akt exerts on the Forkhead box (FOXO) family regulation of atrogenes (e.g. atrogin-1 and muscle RING finger 1 (MuRF1) is now decreased which increased the signaling for the ubiquitin proteasome system, resulting in protein degradation. Moreover, myostatin also hinders the capacity for satellite cells to undergo the requisite stages for muscle recovery following damage (proliferation, differentiation, and fusion). In brief, the proliferation step is impacted through myostatin increasing levels of the p21 gene, in turn, inhibiting cyclin dependent kinase (CDK) 2 and 4 (Thomas *et al.*, 2000). The inhibitory effects of p21 on the CDK family result in hyperphosphorylation of retinoblastoma protein (rb), which is normally phosphorylated by stable levels of the CDK family. The importance of this hyperphosphorylation is that rb inhibits the mitotic cycle, specifically the transition between G1 and G2 phases, often referred to as “cycle arrest”. Myostatin has also been shown to inhibit differentiation and fusion of satellite cells. Regarding differentiation, decreased levels of myogenic regulatory factors (Myf5, MyoD, myogenin, and Pax7) have all been observed (Langley *et al.*, 2002; Joulia *et al.*, 2003).

In human models, the inverse relationship between myostatin and muscle mass was first reported in a study including both HIV patients and healthy individuals (Gonzalez-Cadavid *et al.*, 1998). Additional clinic conditions have been associated with elevated levels of myostatin (Wang, Maxwell and Yu, 2019). Given the associations between wasting conditions and myostatin, myostatin may represent a potential biomarker of aging and age-related dysfunction of skeletal muscle. Nonetheless, the influence of advanced age and the 1) levels and activity of myostatin and 2) the relationships between skeletal muscle characteristics (e.g. force production, physical

function, and muscle mass) remain unclear. The ambiguity in results is likely due to the difficulty in assessing myostatin levels or the procedure used to analyze myostatin levels (Seibert *et al.*, 2001; White and Lebrasseur, 2014; Walker *et al.*, 2016). For example, a big concern in the assessment of myostatin levels is its close homology to GDF11, where there is a difference of only 11 amino acid sequences, resulting in a 90% homology. Further, traditional ELISA techniques have resulted in a large range of observed values, thus hindering the capacity to suggest 'normal' values. With this in mind, it is no surprise that myostatin levels with increased age, whether assessed in young versus old, or across the lifespan have provided inconsistent results. For example, previous research has observed no change with increasing age (Sandri *et al.*, 2013; Schafer *et al.*, 2016; Semba *et al.*, 2019), decreases with increasing age (Olson *et al.*, 2015; Poggioli *et al.*, 2016), and increases with advanced age (Yarasheski *et al.*, 2002; Egerman *et al.*, 2015; Parker *et al.*, 2017; Shibaguchi *et al.*, 2018).

In regards to aging and skeletal muscle, initial reports from Yarasheski *et al.* revealed increases with age and relationships between myostatin and muscle mass (Yarasheski *et al.*, 2002). This study examined myostatin immunoreactive protein levels in three groups of men and women (19 to 35 years, 60 to 75 years, and 76 to 92-year-old frail women). Average serum myostatin immunoreactive protein concentrations increased with advancing age. Concentrations were greater in the 60 to 75-year-old men and women in comparison to the 19 to 35-year-old women ($p<0.05$). Further, concentrations were greatest in the 76 to 92-year-old frail women, whom even after correcting for a potential outlier remained significantly greater than the remaining groups of men and women ($p<0.05$). Moreover, the increased concentrations were inversely

correlated with both fat free mass relative to height (r=-0.48, p<0.001) and muscle mass relative to height (r=-0.96, p=0.017).

In contrast to those observations, Ratkevicius *et al.* compared members of the TGF beta family between young (22 ± 2 years) and older (69 ± 3 years men) (Ratkevicius *et al.*, 2011). Serum concentrations of myostatin did not differ between group, nor did myostatin correlate with knee extensor strength or quadriceps cross-sectional area. Of note, both knee extensor strength and cross-sectional area both decline with age and displayed additional differences between those with mild and severe sarcopenia. Moreover, in a similar comparison in women, supporting observations were reported by Hofmann *et al.* compared members of the TGF beta family between young (22 to 28 years) and older (65 to 92 years) women (Hofmann *et al.*, 2015). There were no differences between myostatin levels of the two age groups, even when classified based off different levels of dynapenia and sarcopenia.

More recent observations continue to provide to the uncertain influence of myostatin on skeletal muscle. For example, Bergen *et al.* developed a liquid chromatography with tandem mass spectrometry assay to assess members of the TGF beta family in two groups of men and women aged less and 40 years or greater than 65 years of age (Bergen *et al.*, 2015). Older women displayed 33% greater circulating myostatin concentrations than their younger counterparts (p<0.001). Expressed relative to bone free lean body mass, older women and sarcopenic women displayed 40 and 23% greater circulating myostatin concentrations than the younger women (both p<0.01). In contrast, younger men displayed significantly greater myostatin concentrations when compared to the older men with or without sarcopenia, with and without adjusting for

bone free lean body mass (p<0.01). Moderate relationships between myostatin and relative appendicular skeletal muscle mass were observed for both sexes (both r=0.24, p<0.01). Significant positive and trending relationships between myostatin and grip strength and knee extensor strength were observed in the men (r=0.20, p=0.026 and r=0.17, p=0.073, respectively), but not for women.

Fife *et al.* investigated the relationships between muscle function and TGF beta members in men and women over the age of 60 years (Fife *et al.*, 2018). Participants performed muscle strength and power assessments, in addition to having their body composition assessed via bioimpedance analysis. No significant relationships were observed between the markers and any measures in the older men, however, the old women displayed significant negative relationships between myostatin and grip strength (r=-0.296, p<0.05) and optimal velocity (r=-0.329, p<0.05), but not for any of the skeletal muscle mass parameters. Peng *et al.* investigated the associations between serum myostatin levels and skeletal muscle mass in older community dwelling adults as part of the I-Lan Longitudinal Aging Study (Peng *et al.*, 2018). Limited to only older adults, the sample included 463 adults, with approximately half men and women (49.5 and 50.5%, respectively) aged 53 to 92 years. When comparing the sample by age, there were not significant differences (p=0.085) for those aged 53 to 70 years compared to those above the age of 70 years. In contrast to previous observations, Peng *et al.* reported that lower relative appendicular skeletal muscle mass was associated with lower serum myostatin levels. Further, this relationship was evident for the men in the cohort not the women. Chew *et al.* investigated the potential for serum myostatin to serve as a biomarker of frailty and low relative appendicular skeletal muscle mass and further investigated the

influence of sex on this possibility (Chew *et al.*, 2019). Two-hundred participants above the age of 50 years were analyzed and categorized into one of four groups: 1) frail/prefail with low relative appendicular skeletal muscle mass; 2) frail/prefrail with normal relative appendicular skeletal muscle mass; 3) robust with low relative appendicular skeletal muscle mass; and 4) robust with normal appendicular skeletal muscle mass. Normalized myostatin levels (expressed relative to total lean body mass) were higher in the frail/low relative appendicular skeletal muscle mass compared to the frail/normal relative appendicular skeletal muscle mass groups. In contrast, there were no differences in myostatin for the groups belonging to the robust groups, regardless of the quantity of muscle mass. Further, myostatin was significantly associated (p=0.05) with frail/low relative appendicular skeletal muscle mass across the entire cohort. However, when the cohort was separated by sex, the relationship between myostatin and relative appendicular skeletal muscle mass was observed only in men. Moriwaki *et al.* examined myostatin levels in regard to age, sex, body composition, and physical function in community dwelling individuals above the age of 65 years (Moriwaki *et al.*, 2019). There were no differences between sexes for myostatin concentrations and it was not correlated with age for either sex. Further, myostatin did not correlate with height, weight, body mass index, skeletal muscle index, grip strength, or gait speed for the entire cohort, or each sex individually. Of note, the authors suggested the lack of findings may be attributed to the difficulty in distinguishing between the active and inactive forms of myostatin.

Few studies have sought to influence the relationships in regard to baseline and post-intervention between myostatin and skeletal muscle characteristics. Of note, Arrieta *et al.* determined the association of serum myostatin concentration with body

composition, physical fitness, physical activity level, and frailty in long term nursing care and see how these are influenced by exercise (Arrieta *et al.*, 2019). There were no differences between men and women for concentrations of myostatin. At baseline, myostatin was related to body fat percentage (r=-0.232, p<0.05) and lean mass (r=0.252, p<0.05) in women but not men. Further, most measures of physical fitness were significantly associated with myostatin in men but only timed up and go test was related to myostatin levels in women, while each measured used to quantify physical activity was positively associated with women (all p<0.005), but not men. Following the intervention, myostatin increased in the exercise group, while decreasing in the control group (p-0.028). Regarding frailty status, elevated levels were associated with frailty, but only reached significance in the male participants. Altogether, the authors revealed elevated myostatin concentrations in leaner, fitter, and more physically active long-term nursing care residents and suggested that elevated levels of myostatin are indicative of frailty status. Planella-Farrugia *et al.* conducted a prospective and controlled clinical trial in which participants were randomized into one of three groups: 1) control group; 2) low intensity resistance exercise group; or 3) low intensity resistance exercise and nutritional support, each for 16 weeks (Planella-Farrugia *et al.*, 2019). At baseline, myostatin was positively associated with body weight (r=0.316, p=0.039), muscle arm circumference (r=0.396, p=0.009), basal metabolism (r=0.365, p=0.016), fat free mass (r=0.358, p=0.018), total water in kg (r=0.364, p=0.017). The control group revealed a significant decrease in myostatin (p=0.003), whereas the two exercise groups did not (p>0.203) across the 16-week intervention. The change in myostatin in the control group paralleled a decrease in fat mass, whereas fat free mass increased in the exercise groups. Following

the intervention, there were significant differences between groups (p=0.048) with the control group being lower.

Moreover, there is evidence that obesity may negatively influence skeletal muscle through myostatin (White 2014). Although a relatively newer postulation, myostatin is believed to contribute to the onset of sarcopenic obesity primarily through 1) inhibiting skeletal muscle Akt phosphorylation, 2) inhibiting skeletal muscle AMPK and lipid oxidation; 3) inhibiting GLUT 4 expression; and 4) influencing adipose tissue composition (Argilés *et al.*, 2012; LeBrasseur, 2012; Consitt and CLARK, 2018). Regarding obesity status, Hittel *et al.* compared protein expression in cultured myotubes from extremely obese compared to healthy nonobese women (Hittel *et al.*, 2009). The authors reported a 2.9-fold increase in the secretion of myostatin from the extremely obese women, which was significantly related to insulin resistance (p<0.05). Of note, the regression analyses indicated an R-squared value of 0.737 (p<0.001) between myostatin levels and body mass index. Further, there were no differences between obese women and lean women in regard to myostatin protein, suggestive of a threshold needed to be achieved for the relationship to be present. Although these observations were based off body mass index and not fat mass per se, it has been documented that inhibiting myostatin is associated with reduced fat mass (Tang *et al.*, 2014). Moreover, in patients that have undergone biliopancreatic diversion resulting in substantial weight loss (~40%), of which most of the weight loss was attributed to fat mass loss, myostatin mRNA levels were significantly reduced (p<0.05) (Milan *et al.*, 2004).

Interleukin 6

Interleukin 6 (IL-6) is a cytokine with pleiotropic functions spanning a number of tissues and organs. In regard to skeletal muscle, IL-6 is associated with stimulation of hypertrophic adaptation by increasing the regenerative capacity of satellite cells, in addition to contributing to energy metabolism regulation of contracting skeletal muscle. On the other hand, elevated levels of IL-6 have been associated with deleterious effects of skeletal muscle, such as wasting and atrophy (Muñoz-Cánoves *et al.*, 2013). Interleukin-6 signaling is mediated by the transmembrane protein gp130. However, the precise mechanisms of signaling are complicated given the ability to signal via traditional and trans-signaling mechanisms. In the traditional signaling, IL-6 binds to the membrane bound IL-6 receptor, which is induced to form a homodimer of gp130, thereby transmitting intracellular signaling. Of note, the IL-6 receptor to specific cell types, therefore the range of these actions are suggested to be limited (Rose-John *et al.*, 2006). In contrast to this signaling, trans-signaling is made possible by alternative splicing and proteolytic events resulting in a soluble IL-6 receptor that is found systemically. Further, the IL-6 binding to the soluble receptor can bind, in turn activating, gp130 homodimers on cells that do not typically express the membrane bound IL-6 receptor, thereby increasing the potential effects of IL-6 (Rose-John *et al.*, 2006). Typically, signaling is mediated through the Janus kinase/signal transducer and activator of transcription (JAK/STAT) pathway, in which the IL-6 effects are exerted.

Increasing age is associated with a chronic low-grade inflammation revealing increased levels IL-6, tissue necrosis factor alpha (TNFα) and C-Reactive protein (CRP) (Bruunsgaard, Pedersen and Pedersen, 2001; Curtis *et al.*, 2016). Although the degree of

increase remains difficult to determine, many observations have reported increases regardless of being in the presence of lifelong exercise (Wei *et al.*, 1992; Ferrucci *et al.*, 2005; Mikkelsen *et al.*, 2013; Lavin *et al.*, 2020). Nonetheless, this culmination of low-grade inflammatory markers has been referred to as "inflammaging" and contributes to chronic diseases (i.e. cardiovascular disease, sarcopenia, frailty, among others) (Ferrucci and Fabbri, 2018). These cytokines play an important role of the normal proinflammatory response associated with injury or illness, thereby promoting tissue repair and regeneration by activation of the complement system and increased phagocytosis (Addison *et al.*, 2012). For example, when tissues are damaged or illness occurs, macrophages are secreted to assist in repair and regeneration. These macrophages secreted a number of cytokines (IL-6 and TNFα) that exert autocrine, paracrine, and endocrine effects. Interleukin 6 specifically has been classified as a pro- and anti-inflammatory cytokine (Muñoz-Cánoves *et al.*, 2013). In response to TNFα production, IL-6 induces T-cell differentiation and assists T-cells in resisting apoptosis, while also producing CRP by hepatocytes and activation of the complement system thereby increasing phagocytic activity. On the other hand, IL-6 results in the production of IL-10, TNF soluble receptor, and IL-1 receptor antagonist, which assist in decreasing the production of TNFα and IL-1, in turn, limiting the proinflammatory cascade of events (Addison *et al.*, 2012). What is concerning is that eventually the production results in a 'spillover' from the tissue of origin, resulting in the ability for these cytokines to act in an endocrine manner.

Consequently, chronic low-grade inflammation can lead to reduced muscle mass, quality and function (Marjolein Visser *et al.*, 2002; Beyer, Mets and Bautmans, 2012).

Inflammation can induce its adverse effects through a myriad of way. Cytokines have the ability to upregulate the proteolytic ubiquitin proteasome pathway, specifically FOXO family, Atrogin-1, and others, resulting in an increased protein degradation, which may contribute to the reductions in skeletal muscle mass with advanced age (Schaap *et al.*, 2006; Skipworth *et al.*, 2006). Rodent models have demonstrated the capacity to induce skeletal muscle apoptosis by DNA fragmentation (Skipworth *et al.*, 2006). However, often the levels of inflammation may be supraphysiological, thus may not represent the inflammaging process. Elevated levels of IL-6 have been observed to limit the capacity and efficiency of IGF-1 signaling, thereby diminishing the effects of a potent anabolic hormone (Al-Shanti and Stewart, 2012). Age-related changes in body composition, notably increased fat mass, can result in increased cytokine production (Maachi *et al.*, 2004), and as the body increases fat mass, the quantity of secreted IL-6 and/or TNFα parallels this increase (Skurk *et al.*, 2007). Accompanied with age-related muscle weakness, this change inevitably places older individuals at risk for developing sarcopenic obesity. More recently, there has been evidence that suggests that an accumulation of inflammatory factors could result in detrimental consequences to the mitochondria by affecting both the quantity and quality (Franceschi *et al.*, 2017; Giuliani *et al.*, 2017).

In regards to IL-6 changes with age, Wei *et al.* reported significant increases in IL-6 in men (p=0.02) but not for women with increasing age (p>0.10) (Wei *et al.*, 1992). Of note, this analysis was performed on a small sample and dichotomized age by 26 to 54 years and 55 to 75 years. Nonetheless, plasma IL-6 was significantly correlated with age (r=0.28, p<0.05). Ahluwalia *et al.* reported no changes in IL-6 between young and

old women when adequate health and nutrition are maintained (Ahluwalia *et al.*, 2001). Ferrucci *et al.* observed that in both men and women, aging was associated with higher levels of IL-6 while the sIL-6 receptor only increased in men (Ferrucci *et al.*, 2005). Blain *et al.* reported a trend (p=0.063) for increasing IL-6 levels in asymptomatic women aged 20 to 72 years (Blain *et al.*, 2012). Altogether, the current evidence suggests that there are gradual increases in IL-6 with age, but these increased are attenuated through a healthy lifestyle and exercise (Mikkelsen *et al.*, 2013; Lavin *et al.*, 2020).

Inflammation and the effects on skeletal muscle studies including individuals across the lifespan are scarce. In regard to a chronic inflammatory state (rheumatoid arthritis, RA), Beenakker *et al.* revealed a steeper decline in strength in those with RA compared to healthy age-matched controls, which was not associated with age (Beenakker *et al.*, 2010). Although the investigation noted the relationship between increasing age and decline grip strength, the inflammatory state was strongly associated with grip strength. Blain *et al.* measured serum IL-6 in 220 asymptomatic women between the ages of 20 and 72 years and reported that those in the group of the lowest IL-6 levels displayed the fastest six meter walking speed (>1.4 m/s) (Blain *et al.*, 2012). In contrast to this observation, there were no relationships between IL-6 levels and maximum grip strength, knee extension strength, or lean body mass.

Longitudinal observations of older individuals indicate that elevated levels of IL-6 may contribute to the worsening of skeletal muscle characteristics. Ferrucci *et al.* examined whether accelerated sarcopenia in older persons with elevated IL-6 levels contributes to the association between inflammation and disability (Ferrucci *et al.*, 2002). Six hundred women from the Women's Health and Aging Study completed functional

status, walking performance, and knee extension strength testing at baseline and over six semiannual follow-up visits. At baseline, those with higher IL-6 levels were more likely to be disabled and displayed lower walking speeds. Further, after adjusting for confounders, women in the highest IL-6 tertile (>3.10 pg/mL) were at greater risk for developing incident mobility (risk ratio: 1.50), having a reduced ability to perform activities of daily living (risk ratio: 1.41), displaying severe limitations in walking (risk ratio: 1.61), and displayed greater declines in walking speed (p<0.001) than women in the lowest tertile. Of note, differences were not observed for knee extensor strength, and when adjusting for the change in knee extensor strength overtime, the associations between IL-6 and physical limitations were no longer significant. Payette *et al.* assessed the prognostic role of IL-6 in predicting two-year changes in fat free mass while controlling for potential confounders of the Framingham Heart study in men and women aged 72 to 92 years (Payette *et al.*, 2003). Loses in fat free mass were significantly greater in the two highest quartiles of IL-6 in comparison to the lowest quartile (p<0.05). Aléman *et al.* investigated the influence of high levels of IL-6 and CRP on appendicular skeletal muscle mass in 115 community dwelling non-sarcopenic men and women between the ages of 60 and 84 years at baseline and five years later (Alemán *et al.*, 2011). Collectively, men and women demonstrated a 1.6 kg loss of appendicular skeletal muscle mass. Of note, the risk of loss was 1.29 times greater (p=0.03) per unit increase of IL-6 (pg/mL) and 1.28 times greater (p=0.01) per unit increase in CRP (mg/l). Further, the risk of loss was 4.85 time higher with participants with serum IL-6 levels greater than 2.71 pg/mL and 3.97 times higher with participants with serum CRP greater than 3.74 mg/l, and remained after adjusting for potential confounders (e.g. age, sex, and five year weight

change). Sanders *et al.* tracked changes in IL-6 in relation to functional measures over nine years in older adults (Sanders *et al.*, 2014). The authors observed that greater increases in IL-6 were consistently associated with worsening decline in function. For example, each standard deviation higher increase in IL-6 was associated with concurrent larger decline in grip strength (β=-0.463), gait speed (β=-0.018) and DSST score (β=-0.83). Newman *et al.* followed 5,888 participants from the Cardiovascular Health Study for ageing and longevity since 1989 to 1990, measuring IL-6 (and additional biomarkers), gait speed and grip strength, among additional non-physical function parameters, at baseline and at follow-up in 2005 to 2006 (Newman *et al.*, 2016). The trajectories of functional decline revealed strong age associated acceleration late in life for both sexes, with IL-6 paralleling those declines. In fact, IL-6 was independently associated with grip strength and gait speed for both sexes ($p<0.001$). In contrast to the previous observations, Westbury *et al.* as part of the Hertfordshire Cohort Study baseline grip strength and skeletal muscle measures were not associated with IL-6 but additional inflammatory factors (Westbury *et al.*, 2018). The non-significant relationships were also observed following the 10.8-year (10.2 to 11.6 year) follow-up time.

Collectively, these data advocate for the development of certain IL-6 thresholds that may represent declines in skeletal muscle. For example, Barbieri *et al.* suggested that IL-6 levels greater than 1.73 pg/mL should be considered a risk factor that reduces muscular performance, thereby resulting in disability (Barbieri *et al.*, 2003). Further, IL-6 levels of 2.5 pg/mL or greater resulted in successful prediction of functional disability in community dwelling elderly, in the absence previous function limitations (Ferrucci *et al.*, 1999). This value is similar to more recent suggestion of greater than 2.71 pg/mL for

losses in muscle mass (Alemán *et al.*, 2011). Ferrucci *et al*. suggested that a threshold value of 3.1 pg/mL or greater in community dwelling elderly for worsening function (Ferrucci *et al.*, 2002). Penninx *et al.* postulated that the cutoff of baseline IL-6 levels resulting to long-term damage in regard to functional performance was 2.18 pg/mL (Penninx *et al.*, 2004). More recently, Newman *et al.* suggested a critical value for declining physical function of 2.2 pg/mL for both men and women (Newman *et al.*, 2016). Of note, a recent systematic review and meta-analysis regarding IL-6 and grip strength in men and women suggested that sex specific cut offs be distinguished in future longitudinal work (Mikó *et al.*, 2018).

Regarding cross-sectional studies, the influence of IL-6 on skeletal muscle is controversial but appears to be an issue of concern. From baseline data of the Health ABC study, Visser *et al.* examined muscle cross-sectional area, appendicular skeletal muscle mass, knee extensor strength, grip strength, and plasma levels of IL-6 and TNFα in 3,075 men and women participants aged 70 to 79 years, revealing that elevated levels of cytokines were generally associated with reduced muscle mass and strength (M. Visser *et al.*, 2002). Of note, the most consistent association was between IL-6 and grip strength, which indicated that per standard deviation increase in IL-6, grip strength was 1.1 to 2.4 kg lower ($p<0.05$). Further, older individuals that displayed IL-6 and TNFα levels of greater than 1.80 pg/mL and 3.2 pg/mL, respectively, displayed smaller muscle cross-sectional area, lower appendicular skeletal muscle mass, and lower muscular strength compared to older individuals with cytokine levels lower than the above-mentioned values. Cesari *et al.* assessed physical performance and inflammatory factors as part of the InCHIANTI study in 1,020 participants above the age of 65 years (Cesari *et al.*, 2004).

Levels of IL-6 were significantly correlated with physical performance (r=-0.210, p<0.05) and grip strength (r=-0.089, p<0.05). The relationship between IL-6 and worse physical performance remained after adjusting for potential confounders (p<0.001). Based off quartiles scores, those with IL-6 levels between 1.46 and 2.28 pg/mL and those greater than 2.28 pg/mL displayed significantly lower physical performance scores than those less than 0.86 pg/mL (p<0.05 and p<0.001, respectively). Further, quartile analyses revealed that only those with IL-6 levels greater than 2.28 pg/mL displayed significantly lower grip strength compared to those with less than 0.86 pg/mL (p<0.01).

Oliveira *et al.* assessed 57 women aged 71 ± 7.38 years, observing a significant negative correlation between plasma IL-6 levels (1.95 ± 1.77 pg/mL) and muscle strength for knee flexion (r=-0.265; p=0.047) and extension (r=-0.315; p=0.017) (Oliveira *et al.*, 2008). No significant correlation was observed between IL-6 levels and the functional tests. Pereira *et al.* evaluated sixty three community dwelling elderly women between the ages of 60 to 88 years that completed grip strength testing and observed an inverse relationship between IL-6 plasma levels (2.56 ± 3.44 pg/mL) and grip strength (22.9 ± 4.62 kg) (r=-0.267, p=0.037) across the cohort (Pereira *et al.*, 2009).

Tiainen *et al.* measured physical performance in 197 women and 65 men aged 90 years and reported that elevated levels of CRP, IL-6, and IL-1 receptor were significantly associated with poor grip strength (p=0.041, p=0.023, and p<0.001, respectively) (Tiainen *et al.*, 2010). Further after adjusting for confounders, IL-6 and IL-1 receptor remained significantly associated with lower grip strength (p=0.048 and p=0.004, respectively). Felicio *et al.* examined the relationships between plasma levels of IL-6 and muscle performance of the knee extensors and flexors, grip strength, and 10 meter gait

speed (Felicio *et al.*, 2014). The sample consisted of a total of 221 women aged 71.1 ± 4.93 years whom were overweight (determined by body mass index) moderately active and presented a small number of comorbidities. Plasma levels of IL-6 were positively correlated with the variables mean power of knee extensors (r=0.14; p=0.03) and knee flexors (r=0.16; p=0.01), but none of the additional parameters displayed significant relationships. Further, Santos *et al.* assessed 80 older women (71.2 ± 5.3 years) and demonstrated a negative correlation of IL-6 (1.42 ± 1.15 pg/mL) with peak torque/body mass of knee flexors (r=-0.23; p=0.03) and agonist/antagonist ratio (r=-0.25; p=0.02) (Santos *et al.*, 2011). Bian *et al.* examined 441 participants over the age of 60 years (235 men, 206 women) that were divided into 'sarcopenia' and 'non-sarcopenia' groups (Bian *et al.*, 2017). In the sarcopenia group, both TNFα and IL-6 were significantly greater (p=0.01 and p=0.03, respectively) than the non-sarcopenia group. Further, significant correlations between IL-6 and skeletal muscle mass (r=-0.239, p=0.039), body mass index (r=0.373, p=0.004), visceral fat mass (r=0.464, p<0.001), were observed. Dutra *et al.* reported that IL-6 was positively associated with age (r=0.19, p<0.05) and age adjusted significant correlations were observed across entire cohort for body mass index (r=0.19, p<0.05) and fat mass (r=0.022, p<0.05) with IL-6, however in the sarcopenic obesity group, age adjusted correlations were observed for body mass index (r=0.44) waist circumference (r=0.38), fat mass (r=0.45), and percent body fat (r=0.47), all p<0.05 (Dutra *et al.*, 2017). Further, grip strength was reduced in the group that has higher IL-6 levels (p=0.02) when split by median value. Miko *et al.* performed a systematic review and meta-analysis on the sex comparison between grip strength and IL-6 (Mikó *et al.*, 2018). Altogether, the results showed a negative correlation between plasma IL-6 levels

and grip strength across both sexes and within both sexes independently and this was observed in the presence of low plasma IL-6 levels (2 to 2.5 pg/mL) in healthy individuals.

In contrast to these observations, Silva *et al.* did not observe a correlation between IL-6 (3.56 ± 6.96 pg/mL) and muscle fatigue index (r=-0.0001; p=0.99) across 135 community dwelling women aged 71.2 ± 4.7 years (Silva *et al.*, 2011). Pereira *et al.* reported similar findings between IL-6 (3.13 ± 4.4 pg/mL) and knee extensor strength (r=0.087; p=0.30) or knee flexor strength (r=-0.011; p=0.89) (Pereira *et al.*, 2011). Lustosa *et al.* compared sarcopenia status with levels of plasma IL-6, and although there were no differences in IL-6 levels between groups (p=0.39) there were differences observed during knee extensor performance at 180 deg/s (power: p=0.01; normalized work: p=0.01) but this was not observed during the 60 deg/s contraction (Lustosa *et al.*, 2017).

Body Composition Changes with Increased Age

Skeletal Muscle Mass

Several studies have attempted to quantify the onset and rate of age-related reductions in muscle mass as if it occurs in a linear manner. Previous literature suggests a uniform rate around 1 to 2% per year after the age of 50 (Rolland *et al.*, 2008; Mitchell *et al.*, 2012; Tieland, Trouwborst and Clark, 2018). However, the proposed reduction in muscle mass is not uniform between genders or for different areas of musculature within the body. Muscle mass muscle begins to decrease around 30 years of age with a suggested decline between 0.5 to 2% per year, 3.7% per decade, or approximately 20 to 30%

between the 30s and 80s for healthy, active individuals (Frontera *et al.*, 2000; Trappe, Lindquist and Carrithers, 2001; Goodpaster *et al.*, 2006; Narici and Maffulli, 2010; Mitchell *et al.*, 2012). The reductions do not appear to become identifiable until approximately 45 years of age and remain statistically insignificant until 50 years of age, when compared to a young adult (Janssen *et al.*, 2000; Kyle, Genton, *et al.*, 2001; Kyle, Genton, *et al.*, 2001; Hughes *et al.*, 2002). The loss in muscle mass appears to occur at a greater rate for individuals older than 70 years, with previous literature suggesting rates close to 10% per decade (Newman *et al.*, 2003; Goodpaster *et al.*, 2006; Delmonico *et al.*, 2009).

Different areas of musculature appear to be affected more than others, such that musculature of the lower body appears to decline at a greater rate than the upper body (Janssen *et al.*, 2000; Narici and Maffulli, 2010). This is of great importance when considering the lower body contains the muscle involved in locomotion and activities of daily living. Lynch *et al.* estimated appendicular skeletal mass by dual-energy x-ray absorptiometry in men and women between the ages of 19 to 93 years (n=703). Women displayed a greater rate of decline during midlife (30 to 60 years) for leg (5%) and arm (4%) muscle mass when compared to men (Lynch *et al.*, 1999). Janssen *et al.* replicated the findings observing a greater reduction in women during the midlife for the lower body (6% versus 4%) but similar values for the upper body (3.9% and 4.3%) (Janssen *et al.*, 2000). Additionally, lower body muscle losses may present a preferential reduction in the anterior compartment (5.7% total, 0.6% annual) when compared to the posterior (3.2% total, 0.35% annual) over a 10-year span (Frontera, Reid and Phillips, 2008). Ogawa *et al.* supports the preferential anterior muscle reduction reporting that age was inversely

related to ultrasound derived muscle thickness of the quadriceps (r=-.30, p=0.04) but not for the hamstring (r=.10, p=0.50) (Ogawa, Yasuda and Abe, 2012). Maden-Wilkinson *et al*. reported similar findings between young (22 years) and older (72 years) individuals observing a 30% and 18% smaller quadriceps and hamstring muscles, respectively (Maden-Wilkinson *et al.*, 2013).

Total Body Weight and Body Fat

Maximum body weight in women is achieved during the 60s and 70s, followed by a gradual decline (Chumlea *et al.*, 2002; Hughes *et al.*, 2002; Coin *et al.*, 2012). Total body fat or percent body fat, reveals a similar trend with age, increasing in women into the 70s, followed by marginal reductions for the remainder of life (Kuk *et al.*, 2009). Kyle *et al.* examined the body composition of 2,490 women between 15 to 98 years by bioelectrical impedance analysis and reported a 1.7% decade increase in percent body fat through women in their 70s with marginal declines thereafter(Kyle, Genton, *et al.*, 2001; Kyle, Genton, *et al.*, 2001). Chumlea *et al.* reported similar findings when analyzing the National Health and Nutrition Examination Survey data revealing a body fat increase between 11 to 13% in women between 13 and 55 years (Chumlea *et al.*, 2002). Paralleled with increased body fat is also a marked alteration in the distribution of body fat. A decrease in subcutaneous adipose tissue has been confirmed using computed tomography and magnetic resonance imaging techniques (Delmonico *et al.*, 2009). Since subcutaneous adipose tissue displays an impaired ability to act as a fat reservoir, there is a central redistribution of fat in tissues, which are not regularly responsible for excessive fat storage such as visceral organs, muscle, and the heart. Skeletal muscle has two lipid reservoirs: intermuscular and intramuscular fat. The diagnostic processes for obtaining

such measures are relatively new, and much of the available literature uses the terms interchangeably, predominantly referring to this adiposity as intramuscular adipose tissue (IMAT). However, intramuscular fat is the lipid located within the muscle cell while intermuscular fat is the more visible marbling of fat that lines between the muscle fibers, both of which are increased with aging, associated with decreased functional capacity and metabolic impairments (Kuk *et al.*, 2009; Marcus *et al.*, 2010, 2012; Buford *et al.*, 2012; Addison *et al.*, 2014). It has been suggested that IMAT increases at a rate of 6% per year for women with this increase being observed even during periods of weight loss (Delmonico *et al.*, 2009). Recent data has revealed that muscle attenuation, an estimation of IMAT, is equally and independently associated with peak torque and rate of torque development in older men and women (Frank-Wilson *et al.*, 2018), which may be attributed to altered muscle architecture or a proinflammatory state.

Whether the alterations in body composition are attributed to menopause is still debated. Weight gain is commonly reported during the menopausal transition and women tend to have a greater amount of subcutaneous adipose tissue before the FMP while after a greater amount of visceral fat has been observed, nearly doubling in amount (Palmer & Clegg, 2015). The influence of changes in sex hormones regarding body composition have been observed in both women undergoing surgical menopause and animal models such as oophorectomized rats. Rodent models typically display increased obesity, decreased lipolysis, and reduced energy expenditure (Darimont *et al.*, 1997; Heine *et al.*, 2000; D'Eon *et al.*, 2005; Babaei, Mehdizadeh and Ansar, 2010). In contrast, when estrogen is supplemented, it has been shown to attenuate weight gain and abdominal adiposity deposition (Rachon *et al.*, 2007). Within human models, the alterations in

estradiol (E2) and androgen production following surgical menopause may induce weight gain (Cooper *et al.,* 2007). The Study of Women's Health Across the Nation suggested that women who underwent surgical menopause had much higher odds (5x) of developing severe obesity and a more profound increase in BMI when compared to women experiencing natural menopause (Sutton-Tyrrell *et al.,* 2010; Gibson *et al.,* 2013). Opposing the suggestion that body composition changes are attributed to aging and not menopause per se, would be observations in women that have premature ovarian failure (POF), in which POF often tend to be leaner than age matched controls (Davis *et al.*, 2012). However, much of a case is failed to be made due to an insufficiency in the data regarding POF.

Traditionally, it has been thought that larger individuals tend to possess greater amounts of skeletal muscle mass, in turn demonstrating greater amounts of strength. Therefore, when comparing age-related changes in muscle function, skeletal muscle mass must be accounted for. When assessing skeletal muscle mass, dual energy x-ray absorptiometry (DXA) is commonly performed. The principle underlying DXA is the attenuation of x-rays with high- and low-photon energies is measurable and dependent on the thickness, density, and chemical composition of the underlying tissue (Duren *et al.*, 2008). Estimations of fat and lean tissue from DXA software is based on inherent assumptions regarding several factors, including hydration status, tissue density and manufacturer. Although not as common, computed tomography (CT) can determine musculoskeletal composition through differentiating body tissues based on signal attenuation. Unlike DXA, CT also provides the ability to delineate between contractile

and non-contractile elements of a muscle, which provides a substantial benefit when determining muscle quality (Duren *et al.*, 2008).

Characterizing Muscle Quality and Quantity Reductions

The age-related reduction of skeletal muscle mass coupled with reduced muscle function is referred to as sarcopenia (Rosenberg, 2011). Originally described as a loss of skeletal muscle mass, the disorder has since been denoted as the reduction in skeletal muscle mass with the accompanied reduction in skeletal muscle function. The initial criterion for sarcopenia was the quotient of appendicular lean mass (ALM, kg) relative to body height (kg/m^2) referred to as the skeletal muscle index (SMI) (Baumgartner *et al.*, 1998). The classification proposed for sarcopenia was a ratio of muscle mass to height 2 standard deviations below the mean found in healthy young individuals from the Rosetta Stone project. However, one of the main criticisms associated with this criterion is that reduced skeletal muscle mass is not always associated with adverse events or functional impairment. Therefore, several international groups have been formulated to further examine and progress toward determining more effective sarcopenia classification cut off points.

In 2010, the European Working Group on Sarcopenia in Older People (EWGSOP), defined sarcopenia as "a syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength with a risk of adverse outcomes such as physical disability, poor quality of life and death" (Cruz-Jentoft *et al.*, 2010). Therefore, classification of sarcopenia should represent a combination of reduced muscle mass and reduced muscle strength and/or function. The EWGSOP suggested that

sarcopenia is not strictly related to older individuals; therefore, the EWGSOP suggested two sarcopenia classifications; primary and secondary sarcopenia. An individual is classified as having primary sarcopenia when the reductions in skeletal muscle mass are attributed to increased age. Secondary sarcopenia is classified when some individual displays reduced muscle mass combined with reduced physical activity (i.e. activity related sarcopenia), when combined with alternative diseases or conditions (i.e. disease-related sarcopenia) or when combined with malnutrition (i.e. nutrition-related sarcopenia). In addition, the EWGSOP suggested that stages should also be implemented depending on the severity of reduction in skeletal muscle mass, strength and physical performance (i.e. pre-sarcopenia, sarcopenia, and severe sarcopenia). When screening and assessing sarcopenic status, the EWGSOP developed an algorithm based on gait speed over a 6m course. When an individual produces a pace less than 0.8 m/s the next step in screening, obtaining a skeletal muscle mass measure should be employed. However, if an individual produces a gait >0.8 m/s but reveals reduced grip strength performance (<30 or <20 kg, men and women, respectively), a skeletal muscle mass measurement should be obtained. Following the skeletal muscle mass measurement, the EWGSOP identified a SMI of <7.26 or <5.45 indicative of sarcopenia for men and women, respectively (Cruz-Jentoft *et al.*, 2010). More recently, the EWGSOP re-released new criteria and a screening process for sarcopenia. However, the values for screening do not deviate much from the original definitions, of note, further sarcopenia screening is warranted following the measurement of low muscle strength or function (grip strength or gait speed, respectively) (Cruz-Jentoft *et al.*, 2019).

In 2011, the International Working Group on Sarcopenia (IWGS) suggested that individuals who underperform during gait speed testing (<1.0 m/s) should be further screened for sarcopenia (Fielding *et al.,* 2011). For example, the IWGS suggests using values of ≤7.23 and ≤5.67 kg/m^2 for men and women, respectively. In contrast to the aforementioned groups, the Foundation for the National Institute of Health (FNIH) examined data from nine previous studies encompassing 26,625 participants (11,427 men and 15,198 women) (Studenski *et al.,* 2014). The FNIH provided several cut points for weakness and low lean mass in men and women. For example, two measures of weakness identified as max grip strength (<26 kg and <16 kg men and women, respectively), max grip strength adjusted for body mass index (BMI, <1.0 and <0.56 men and women, respectively) and two measures of low lean mass characterized as appendicular lean mass (ALM) adjusted for BMI (<0.789 and <0.512, men and women, respectively) and total ALM (<19.75 kg and <15.02 kg men and women, respectively) (Studenski *et al.,* 2014).

Congruent to the originally proposed SMI from Baumgartner, the Asian Working Group for Sarcopenia (AWGS) suggested classifying sarcopenia as a skeletal muscle mass below 2 standard deviation a young reference group or the lower quintile of the study population (Chen *et al.,* 2016). The AWGS also suggested a height adjusted (m^2) index reporting values of <7.0 and <5.4 kg/m^2 for men and women, respectively. Reduced grip strength values of <26.0 and <18.0 kg (men and women, respectively) and reduced physical performance measured from gait speed of <0.8 m/s are also indicative of sarcopenia. Although the AWGS proposed such criterion, the authors suggested that further work needs to be done since many of the included entities had difficulty defining and agreeing on criterion.

Summary

With the exception of muscular endurance, decreases in muscular strength, power and quality are widely supported in the literature. The decreases in strength, power, and quality do not appear to happen in concert and are impacted by muscle composition and location. The precise contribution for the mechanisms responsible for the changes in muscle function remains unsolved, but the progression appears to be multifactorial process including alterations at the central and peripheral level, with physical activity also contributing. Unfortunately, a relatively finite amount of literature is available examining the influence of aging on muscle function. Traditionally, the studies have examined a young and older cohort, and most have examined men, making the application for middle-aged individuals and women difficult. Since women possess lower levels of skeletal muscle mass, greater amounts of fat mass and live longer than men; women undoubtedly increase the chance of experiencing a reduced quality of life attributed to sarcopenia.

Chapter III: Methodology

The purpose of this investigation was to examine the influence of chronological age on muscular strength, power, endurance, and quality in recreationally active women between the ages of 20 and 89 years.

Experimental Design

The present study employed a cross-sectional design that examined recreationally active women divided into thirteen, five-year, age intervals according to chronological age that was determined at each participant's initial visit to the Neuromuscular Laboratory. In brief, the study consisted of four total visits to the Neuromuscular Laboratory, in addition to a fasted blood draw completed at the University of Oklahoma Goddard Health Center prior to the second visit. The visits occurred in the following order: Visit 1- consenting, questionnaires, testing familiarization; Visit 2- fasted blood draw, visit 3-body composition analyses, muscle function testing; Visit 4- repeated muscle function testing; and Visit 5- repeated muscle function testing. Visit 1 required approximately 1 hour, while Visits 3, 4, and 5, required approximately 90 to 120 minutes, whereas the blood draw required five to 10 minutes.

Participants

Recreationally active women at least 20 years of age were recruited by mass email, flyers, newspaper advertisements, and by word of mouth from the Norman, Oklahoma and the surrounding areas to participate in this investigation. The participants were divided into the following age group intervals: 20 to 24, 25 to 29, 30 to 34, 35 to 39, 40 to 44, 45 to 49, 50 to 54, 55 to 59, 60 to 64, 65 to 69, 70 to 74, 75 to 79, and 80 to 89

years. Prior to participating, each participant was required to review and sign a written informed consent document, and those who were over the age of 45 years were required to obtain physicians clearance prior to participating.

Inclusion Criteria

1. Women 20 years of age and older that were ambulatory and possess the ability to perform routine activities of daily living (i.e. stair navigation, running errands, etc.) without assistance.
2. Women that did not have known orthopedic disorders or previous disorders that would impact participation.
3. Women free from pulmonary, cardiovascular or metabolic diseases (asthma, diabetes, uncontrolled hypertension, or COPD).

Exclusion Criteria

1. Women younger than 20 or older than 100.
2. Women that were actively training for a competitive event (i.e. power lifting, body building, extended length races, etc.).
3. Women that were current smokers.
4. Women that had known pulmonary, cardiovascular or metabolic diseases (asthma, diabetes, uncontrolled hypertension, or COPD).
5. Women that had a body weight that exceeded 300 pounds and/or height of 75 inches and/or do not fit within the peripheral quantitative computed tomography gantry (mid-thigh circumference equal to or greater than 250mm).
6. Women that had recently experienced a musculoskeletal injury.

7. Women that currently have metal inserts or a joint replacement at the hip, knee, or spine.

Questionnaires and Documentation

Multiple questionnaires were completed to provide the most accurate representation regarding each participant's current and previous health status, current and previous menstrual history, and current and previous physical activity. The following documentation and questionnaires were required for all participants:

Written Informed Consent

All participants were required to provide written informed consent prior to participating this study. Participants were provided detailed information regarding the study and were informed of the potential risks and benefits involved. Additionally, all participants were encouraged to ask any questions during the consenting process. Lastly, at the day of providing written informed consent, participants were provided a copy of the form.

Health Insurance Portability and Accountability Act

This health insurance portability and accountability act (HIPAA) documentation informed the participants of the potential use of protected health information during this project.

Health Status Questionnaire

The health status questionnaire consisted of a series of health, wellness, and previous medical history questions that assisted in the determination of participant inclusion while providing pertinent information regarding health status. This document

collected information related to age, demographics, medical history, previous and current exercise habits, family medical history, and previous and current medications, and is a lab derived questionnaire.

Menstrual History Questionnaire

The menstrual history questionnaire included a series of questions related to the menstrual cycle. These questions were broken down into two sections: 1) Current Menstrual Status and 2) Previous Menstrual Status. Questions from the first section included those related to cycle regularity, current hormonal use, and menopausal status, among others. Section 2 included questions regarding age of menarche, potential cycle irregularities, and previous hormone use.

International Physical Activity Questionnaire

The international physical activity questionnaire (IPAQ) included five sections detailing participant physical activity from the previous seven days as part of the participant's routine daily living. The five sections examined within the IPAQ include: 1) job related physical activity, 2) transportation physical activity, 3) housework, house maintenance and caring for family, 4) recreation, sport, and leisure-time physical activity, and 5) time spent sitting. Based off the responses from each section, participants were stratified into low, moderate, or high physical activity levels.

Physical Activity Readiness Questionnaire

The physical activity readiness questionnaire (PAR-Q) is used as the initial screening tool before engaging in physical activity. The questionnaire provided a series of questions determining the participant's overall ability to participate. When a

participant responded with ‘yes’ to any of the questions, physician’s clearance was sought out prior to participation regardless of the participant’s age.

Body Weight and Height

Standing height and weight were measured upon arrival at Visit 3. A wall mounted stadiometer (Stadi-0-Meter®, Novel Products, Inc., Rockton, Illinois, USA) measured height to the nearest cm. Participants placed their feet together with heels, buttocks and upper back against the wall with back straight while being positioned in the middle of the stadiometer. Participants were instructed to look straight ahead, position their chin at a 90-degree angle, take a deep breath and fully exhale. Weight was determined using a digital scale recorded to the nearest 0.1 kg (TANITA Digital Scale, model BWB-800A, Japan). Participants removed their shoes, excess clothing (i.e. scarves, jacket, etc.) and emptied their pockets of any items. The digital scale was turned on, set to kg and participants stood on the scale with both feet.

Pregnancy and Hydration Testing

A urine sample was obtained prior to the body composition analyses performed in Visit 3. The sample was used to determine pregnancy and hydration status for each participant. Pregnancy tests were measured using a SAS pregnancy strip (SAS Scientific, Mega Cor, GmbH Europaplatz 88131 Lindau, Germany) and hydration status was assessed by a pen refractometer (Brix 0-32PCT .2 VEE GEE Scientific). Participant’s hydration statuses were all between the values of 1.004 to 1.031 urine specific gravity.

Dual-Energy X-ray Absorptiometry

Lunar Prodigy dual-energy x-ray absorptiometry (DXA, GE Medical Systems, Lunar Prodigy) was used to assess body composition requiring four scans the following scanning procedures: total body scan, AP lumbar spine (L1-L4) and dual proximal femur scan (femoral neck, trochanter, total hip). All scans were analyzed using the enCORE software, version 16 (GE Healthcare, Madison, WI) and by the same trained technician. At the beginning of each testing day, the DXA machine was calibrated per manufacturer guidelines and all scanning procedures were standardized for each participant. Participants were instructed to arrive dressed in light clothing with no attenuating materials (i.e., metal zippers, buttons, bra wires, etc.). Participants were asked to lie in a supine position on the table, with their head approximately 2 to 3 cm below the horizontal line located at the top of the table. The technician performing the scan positioned the participant's hips and shoulders evenly spaced in the middle of the table. The participant was instructed to position their arms close to the sides of their body. Lastly, the participant's knees and ankles were secured with one strap each to keep the legs straight and in place during the scan. Following the total body scan, a foam block was placed under the participant's legs resulting in a knee flexion between 45 to 60 degrees. The participant was instructed to locate their navel to adjust the scanning arm accordingly for the lumbar spine scan. Following the lumbar spine scan, the participants legs were secured to the manufacturer provided brace with moderate internal rotation. The hip scans started with the left leg and then an identical procedure was performed for the right leg. Each DXA scan consisted of two x-ray beam attenuation values of 40 and 70kV, which were attenuated based on the differences in densities, to assess bone mineral density, fat

mass, and bone free lean body mass. The radiation exposure from DXA ranges from 0.08 to 0.18 mrem which is similar to that of daily exposure to environmental radiation and less than the typical radiation exposure found in X-rays and CT scans (25 to 270 mrem). Precision values from the Bone Density Laboratory for total, regional, and appendicular bone free lean muscle mass are 1.21% to 3.97%, while bodyfat percent and mass values are 1.56% to 2.53% (Appendix G).

Peripheral Quantitative Computed Tomography

Peripheral quantitative computed tomography (pQCT, XCT 3000, version 6.00 Stratec Medizintechnik gmbH, Pforrzheim, Germany) was a supplement to the DXA procedures and provided detailed information soft tissue at the 40% femur and 66% tibia sites. Scans of the 4% and 38% tibia were also capture but were not included in the current analyses. Images of cross-sectional slices were acquired from the Stratec software and were analyzed used BoneJ (Doube *et al.*, 2010). Density distribution and soft tissue were analyzed to determine muscle density and muscle cross sectional area.

The pQCT was calibrated daily prior to use with the cone phantom to ensure reliability, while additional calibration procedures with the cortical phantom was performed every seven days per manufacturer guidelines. Lengths of the tibia and femur were recorded manually (mm) using a tape measure. Tibia length was measured as the distance from the inferior articular surface of the tibia to the medial tibial plateau of the medial condyle, while femur length was measured from the top of the greater trochanter to the end of the lateral condyle of the tibia. Before each scan, participant and scan (tibia first, followed by femur) information was entered into the computer and the participant's

right leg was adjusted according to scan. Participants were asked to sit comfortably in the pQCT chair with their right leg resting on manufacturer supports located beneath the knee and foot. Velcro straps were then wrapped securely around the foot and knee to minimize participant movement. Initially, a scout view was performed to identify the distal end of tibia where the reference line could be identified. Three separate scans were performed at the 4%, 38% and 66% site of the right tibia. Following the tibia scan, the participant was asked to stand up and sit adjacent to the pQCT while the pQCT attachments could be adjusted appropriately for the femur scan. During the femur scan, the participant's right leg was supported and was parallel with the floor. Once a parallel placement was determined, the participant's leg was secured with velcro straps to minimize movement. A scout view was then performed to determine the end of the femur, where the reference line was placed prior to performing the 40% scan. During both scans, the gantry moved to the respective sites in a distal to proximal manner and the participant's left leg was positioned adjacent to the gantry in a comfortable position. Across all scans, a scan speed of 20mm/sec with a voxel size of 0.4 mm and a slice thickness of 2.2 mm was employed. Muscle cross-sectional precision values for the midthigh and calf are 2.92% and 1.4% to 1.73%, respectively (Appendix G).

Performance Measure Familiarization

After meeting the eligibility criteria and completing the required documentation, each participant was familiarized on the correct techniques for each of the muscle function tests. Participants received verbal instruction, were provided physical demonstration, and were required to perform familiarization trials for each testing

procedure. During this time, proper orientation for the handgrip dynamometer and Biodex were recorded and prepared for subsequent visits.

Handgrip Test: Maximal Isometric Force Production

Grip strength was assessed for both hands through a Jamar handgrip dynamometer (Takei Scientific Instruments, Japan). Participants were seated in a chair with their back supported and feet placed flat on the ground. Participants had their elbow flexed at 90 degrees with the forearm in a neutral position, wrist dorsiflexed between zero and 30 degrees and zero to 15 degrees ulnar deviation in the dominant hand. The grip width of the dynamometer was adjusted to the participants comfort prior to measured testing. Once a comfortable grip width was determined in the right hand, the participant was verbally cued to squeeze as hard as possible or until the needle on the dynamometer fails to increase, each repetition lasting approximately 3 to 5 seconds. Following the contraction, the dynamometer was alternated to the left hand, and after 30 seconds of rest, an additional contraction was performed. This alternating right to left procedure was performed 3 times for a total of 6 repetitions. Each repetition was measured to the nearest 0.1kg, with average and max grip strength included in statistical analyses.

Lower Body Muscular Power Testing

Muscular power was assessed using the Tendo FiTRODYNE (Tendo unit, Tendo Sports Machines, Slovak Republic) and Just Jump mat (Just Jump, Probiotic, AL). Each participant performed three vertical jump repetitions while positioned on the jump mat with the Tendo unit safely secured to their waist. Participants were instructed to descend to a comfortable depth prior to jumping, incorporate an arm motion that is comfortable,

jump straight up, refrain from bending their legs in the air, and to land with both feet on the mat. Each repetition was separated by 1-minute of rest and spotters were positioned on both sides and behind the participant. Watts, velocity, time in air, and jump height were collected for each trial.

Biodex Muscular Strength and Endurance Testing

Muscular strength and endurance were assessed using the Biodex Systems 3 dynamometer system (Biodex Medical Systems, Shirley, New York). Following standardized calibration procedures, each participant started testing at the right elbow, followed by the right knee, and ending at the right ankle. Initially, each participant performed 6 maximum voluntary isometric contractions (MVICs), followed by 4 sets of isotonic contractions at loads corresponding to 1Nm, 20%, 40%, and 60% MVIC, then performed 30 isokinetic contractions at 240 deg/s and 60 deg/s. During all modes of contraction, the first contraction was always extension at the elbow and knee, and plantarflexion at the ankle. Each contraction mode was administered in the concentric-concentric mode to measure opposing musculature (e.g. biceps and triceps for elbow flexion and extension, respectively). Before each testing modality, the participant performed 3 to 5 submaximal trials of the designated test.

Variables of Interest

The variables to be collected and included in statistical analyses were the following. During the isometric contraction: maximal isometric force (Newton meters, Nm) and rate of torque development (Newton meters per second, Nm/s). Isotonic variables of interest included: peak velocity (degrees per second, deg/s), peak power

(Watts), time to peak velocity (seconds, s), and time to peak power (s). Isokinetic testing provided measures of muscular strength from peak contraction values and measures of muscular endurance across the 30-repetition test. The isokinetic strength testing variables included were: peak torque (newton meters, Nm) and time to peak torque (s), while across the 30 repetitions, muscular endurance was measured through the total work from the first and last ten repetitions (J) and calculated as work fatigue (%, work expressed as a ratio of first ten repetitions relative to last ten repetitions).

Participant Orientation

Testing started at the elbow; therefore, the chair was set to 90-degrees and the participant was positioned up-right in the seat with straps placed across their chest and fastened to the seat back. After securing the participant to the seat, the dynamometer was aligned with the participants elbow and then stabilized with a velcro strap to the appropriate dynamometer attachment. The attachment arm was then modified to allow the subject to easily grab the attachment handle, doing so in a comfortable manner. When performing the testing at the knee, participants remained seated at a 90-degree angle. The participant's anatomical axis of the right knee was aligned with the dynamometer and then stabilized with a velcro strap at the distal tibia. The attachment was adjusted to the participant's comfort, with the shin pad secured just proximal to the ankle. When performing the testing at the ankle, the seat was adjusted to a 70-degree tilt, the participant had a knee flexion angle of 90-degrees, an ankle flexion angle between 20 and 30-degrees, the axis of rotation was aligned with the talus and fibular malleolus. A limb support pad was positioned just beneath the distal femur and secured with a velcro strap.

Testing Procedures

Isometric Elbow Extension and Flexion

Testing started at the elbow with participants initially completing the MVIC protocol. The elbow joint was oriented to 90-degrees flexion, and the participant received a verbal cue of "3-2-1, go!" and were verbally encouraged to push as hard as they can for 3 seconds. Following this contraction, 60 seconds of rest was provided before starting the subsequent contraction. During the second contraction the participant received the same verbal cue but was instructed to pull as hard as they can for 3 seconds. This alternating, antagonistic musculature contraction pattern was employed 3 times for a total of 6 repetitions. Once all 6 repetitions were completed, the Biodex protocol was changed to the isotonic testing procedure. Between the final MVIC and initial isotonic testing bout, 3 minutes of rest was provided.

Isotonic Elbow Extension and Flexion

Isotonic testing consisted of 4 loads corresponding to 1Nm, 20%, 40%, and 60% MVIC with participants completing 3 repetitions for each load. The loads were determined from the previous MVIC values. Prior to testing, the elbow joint was fully flexed, and the participant received a verbal cue of "3-2-1, go!" and was instructed to push (triceps extension) as hard and as fast as they can when extending the elbow. Once the participant reached full extension, the participant rested for 30 seconds and following an additional "3-2-1, go!", pulled (biceps curl) as hard and as fast as they could when flexing the elbow. All participants completed the isotonic testing in the similar order (e.g. 1Nm, 20%, 40%, then 60%) and rested 60 seconds between loads. Once the last trial at 60% was complete, the participant moved onto isokinetic testing.

Isokinetic Elbow Extension and Flexion

Isokinetic testing consisted of 2 velocities, 240 deg/s and 60 deg/s, with each protocol consisting of 30 repetitions. Prior to testing, the elbow joint was fully flexed, and the participant received a verbal cue of "3-2-1, go!" and was instructed to push when extending the elbow and pull when flexing the elbow. The first speed was 240deg/s and once the initial 30 repetitions were completed, a 5-minute rest interval was provided then testing at 60deg/s was performed. Once the 30 contractions at 60deg/s were finished the participant was removed from the Biodex seat, was instructed to sit in a nearby chair, and the device was orientated for testing at the knee.

Isometric Knee Extension and Flexion

When measuring the knee extensors and flexors, the same protocol mentioned above was employed. The knee joint was oriented to 70-degrees flexion, and the participant received a verbal cue of "3-2-1, go!", and were verbally encouraged to kick as hard as they can for 3 seconds. Following the initial contraction, 30 seconds of rest was provided before starting the subsequent contraction. During the second contraction the participant received the same verbal cue and were instructed to pull as hard as they can for 3 seconds. This alternating, antagonistic musculature contraction pattern was employed 3 times for a total of 6 repetitions. Once all 6 repetitions were completed, the Biodex protocol was changed to the isokinetic testing procedure. Between the final MVIC and initial isokinetic testing bout, 3 minutes of rest was provided.

Isotonic Knee Extension and Flexion

Isotonic testing at the knee consisted of 4 loads corresponding to 1Nm, 20%, 40%, and 60% MVIC with participants completing 3 repetitions for each load. Prior to

testing, the elbow joint was fully flexed, and the participant received a verbal cue of "3-2-1, go!" and be instructed to kick (knee extension) when extending the knee. Once the participant reaches full extension, the participant rested for 30 seconds and following an additional "3-2-1, go!" cue, pulled (knee curl) when flexing the knee. All participants completed the isotonic testing in the same order (e.g. 1Nm, 20%, 40%, then 60%) and between loads will rest for 60 seconds. Once the last trial at 60% is complete, the participant moved onto isokinetic testing.

Isokinetic Knee Extension and Flexion

Isokinetic testing consisted of 2 velocities, 240 deg/s and 60 deg/s, with each protocol consisting of 30 repetitions. Prior to testing, the knee was fully flexed, and the participant will receive a verbal cue of "3-2-1, go" and be instructed to kick when extending the knee and pull when flexing the knee. The first speed was 240deg/s and once the initial 30 repetitions are completed, a 5-minute rest interval was provided then testing at 60deg/s was performed. Once the 30 contractions at 60deg/s are finished the participant was removed from the Biodex seat, be instructed to sit in nearby chair, and the device was orientated for testing at the ankle.

Isometric Ankle Plantar and Dorsiflexion

The ankle joint was oriented to 20-degrees plantar flexion, and the participant will receive a verbal cue of "3-2-1, go" and be verbally encouraged to push as hard as they can for 3 seconds. Following the initial contraction, 30 seconds of rest was provided before starting the subsequent contraction. During the second contraction the participant will receive the same verbal cue and be instructed to pull as hard as they can for 3 seconds. This alternative, antagonistic musculature pattern was employed 3 times for a total of 6

repetitions. Once all 6 repetitions have been completed, the Biodex protocol was changed to the isokinetic testing procedure. Between the final MVIC and initial isokinetic testing bout, 3 minutes of rest was provided.

Isokinetic Ankle Plantar and Dorsiflexion

Isokinetic testing consisted of 2 velocities, 240 deg/s and 60 deg/s, with each protocol consisting of 30 repetitions. Prior to testing, the ankle was fully dorsi flexed the participant will receive a verbal cue of "3-2-1, go" and be instructed to push when plantar flexing the ankle and pull when dorsi flexing the ankle. The first speed was 240deg/s and once the initial 30 repetitions are completed, a 5-minute rest interval was provided then testing at 60deg/s was performed. Once the 30 contractions at 60deg/s are finished the participant was removed from the Biodex seat and the testing was complete.

Muscle Quality & Specific Power

Muscle quality (MQ) and specific power (SP) were determined using variables collected from body composition analyses and muscle function testing. MQ of the upper and lower leg from the pQCT was calculated as the sum of peak torque (PT) for knee extension (KE) and flexion (KF) divided by the sum of muscle area. Upper arm MQ was calculated as the sum of peak torques (elbow extension + flexion [EE, EF, respectively] relative to the quantity of BFLBM obtained from DXA (Barbat-Artigas *et al.*, 2012; Correa-de-Araujo *et al.*, 2017).

$$MQ_{DXA} = (EE\ PT + EF\ PT) / (BFLBM)$$

$$MQ_{pQCT} = (KE\ PT + KF\ PT) / (mCSA)$$

$$SP_{UL} = (EE\ PP_{UL} + EF\ PP_{UL}) / (BFLBM)$$

Blood Sampling

A blood draw (7.5ml) was collected by a registered nurse or phlebotomist by venipuncture at the antecubital fossa. The blood draw was performed in the morning between 0800 and 1000 following an overnight fast, which were then allowed to clot, centrifuged, and then transferred into 8 micro-tubes. These micro-tubes were stored and frozen at -84 degrees Celsius in the Bone Density Laboratory until biomarker analyses were performed. Biochemical analyses of serum myostatin (MyBioSource, San Diego, CA) and interleukin 6 (R&D Systems, Minneapolis, MN) were performed following step by step instructions provided within each kit (see appendix C for respective procedures). Intra-assay CVs for myostatin and interleukin 6 were to 3.2% and 2.2%, respectively, while the inter-assay CVs were 9.6% and 11.0%, respectively. Intra-assay CVs were calculated as replicate samples placed as the first and last sample during each of the assays.

Statistical Analyses

All statistical procedures were performed using R Version 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria) (R Core Team, 2019). Descriptive characteristics for all variables among each age group were determined and are presented as mean ± SE unless otherwise reported. An a priori significance level was set at $p \leq 0.05$ for all analyses.

Participant Demographics

Categorical and interval data were compared across groups by the Kruskall-Wallis or Chi-square tests, respectively. One-way analysis of variance was used to compare the

age groups with the corresponding reference age interval (i.e. the group showing the greatest quantity of muscle mass) for each variable. The Sidak-Bonferroni post hoc correction was used to identify the source of significance. Participant characteristics representing muscle mass (e.g. total body bone free lean body mass, skeletal muscle index, etc.) underwent identical procedures as those described below in neuromuscular performance analyses, however, the alternative parameters did not (e.g. total body fat mass, body fat percentage, etc.)

Neuromuscular Performance Reliability

Relative reliability was quantified using the two-way mixed effects, absolute agreement intraclass correlation coefficient (ICC). Presently, there is no universally accepted criteria for ICC vales, thus the present analyses considered values of <0.5, 0.50-0.75, 0.76-0.90, and >0.9 corresponding to poor, moderate, good, and excellent reliability, respectively (Koo and Li, 2016). Absolute reliability for each outcome was determined as follows. The standard error of the measurement (SEM) was included to determine the extent to which a score varied across repeated measurements, calculated as the product of the SD and the square root of 1 – ICC. The SEM value was then used to calculate the minimal difference needed to be considered real (MDCR) for each test. The MDCR was calculated as 1.96 × SEM × square root of 2. Additionally, both the SEM and MDCR are expressed in the unit of measurement, thus were transformed into relative percentages of the mean for all observations (SEM% = (SEM/mean) × 100; MDCR% = (MD/mean) × 100. Ranges of relative and absolute reliability are presented in Appendix D.

Neuromuscular Performance Analyses

The primary aim of the present study was to illuminate potential critical age periods for adverse changes in quantitative and qualitative muscle performance characteristics in recreationally active women. Initially, one-way analyses of variance were used to compare the age groups with a corresponding reference age interval (i.e. the group showing the greatest muscle strength) for each variable. The Sidak-Bonferroni post hoc correction was used to identify the source of significance in comparison to each parameter's respective reference value. As expected, preliminary scatter plot inspection revealed that many variables deviated from a linear change with increasing age, therefore, in addition to a linear model, a quadratic and segmental model were also fit. The addition of a quadratic age term often results in a greater fit when compared to linear regression models but does not provide as transparent of a description regarding precise locations of critical changes (e.g. change in muscle performance or change in muscle performance loss). Segmental (also known as piecewise or stick-) models can provide estimates regarding where a change in slope (i.e. rate of change) occurs, and thus, can serve to identify critical age periods, as well as the rate of change associated with the proposed breakpoint. The critical age proposed by the segmental analysis was then assessed initially using the score-test and further verified using the Davies test for difference in slope (Davies, 2002; Muggeo, 2016). Segmental analyses were performed using an iterative approach, where each five-year increment of age (e.g. 25, 30, 35, etc.) in addition to different age intervals (e.g. 20 to 50, 25 to 50, 30 to 55, etc.) were evaluated. Each five-year interval was evaluated irrespective of the neuromuscular performance measures, whereas the age ranges that were evaluated were determined based off visual inspection

of the scatter plots. Then the final segmental model was constructed using the breakpoint or breakpoints where a statistically significant change in slope was observed. Last, the relationships between qualitative and quantitative characteristics of skeletal muscle, in addition to myostatin and interleukin 6 were assessed using Pearson's or Spearman's Rho correlations.

Sample Size Justification

Sample size was determined a priori after evaluating similar cross-sectional aging designs in both men and women. The current study included several variables representing muscle mass and function; thus, sample size determination was calculated considering multiple variables that have been previously examined in similar research. These variables included: jump power, knee extension peak velocity and power, grip strength, maximal isometric strength, maximal isokinetic strength, etc. Based off power calculations from 14 previously investigated muscle function parameters, the average required sample size needed to achieve a statistical power of 0.80 at an alpha level of 0.05, was a minimum of 131 participants. Therefore, a minimum of 11 participants were recruited, representing each five-year interval (13 total groups) over the age of 20 years. Given the possibility of participant attrition and previous analytical suggestions and guidelines, we sought to include at least 15 participants per five-year interval. The previous observations were included in the sample size determination (Lindle *et al.*, 1997; Lynch *et al.*, 1999; Harbo, Brincks and Andersen, 2012; Charlier *et al.*, 2015; Zhang and Yuan, 2018; Kemmler *et al.*, 2018; Van Driessche, Delecluse, *et al.*, 2018; Van Roie *et al.*, 2018; Wang *et al.*, 2018; Suetta *et al.*, 2019; Alcazar *et al.*, 2020).

Chapter IV: Results and Discussion

The primary purpose of this investigation was to identify critical age periods across the lifespan in recreationally active women where changes in quantitative and qualitative skeletal muscle parameters occur. Therefore, given the ability for segmental modelling techniques to provide estimates of critical ages and ranges of ages where these changes occur, in addition to having displayed superior R^2 and standard error of the estimate values when compare to the linear and quadratic models, only the segmental model estimates are described in the results, with the exception for a few parameters where linear changes were not different. Parameter estimates are displayed as mean value (95% confidence interval [CI]).

Following traditional participant demographics, the results section was divided into the following order: 1) functional measures (i.e. grip strength and vertical jump parameters); 2) maximum isometric strength; 3) maximum dynamic strength; 4) muscular power; 5) local muscular endurance, and 6) muscle quality and specific force. For each metric, the reference group with the 'best' value is underlined (e.g. highest grip strength, lowest body fat percent), while asterisks depict a significant difference from the corresponding reference group. Further, the age(s) that were deemed critical from the segmental analyses are referenced by superscript denoted in the respective tables "*Note"*. Last, the group effects from the ANOVA are not presented within the text and are displayed within each individual parameter's corresponding table.

Participants

Three-hundred forty-seven (*n*=347) females between the ages of 20 and 89 years were screened for study enrollment. From the initial 347 participants 168 did not meet

initial screening criteria, however, 179 met the criteria and completed Visit 1 providing written informed consent. Unfortunately, 27 participants dropped out of the study due to unrelated reasons (e.g. pregnancy, job relocation, etc.), which resulted in a total of 152 participants that completed all requirements of the study.

Anthropometrics and Lifestyle

Table 1 displays each five-year interval and the corresponding number of participants along with general anthropometric assessments. As anticipated, there was a significant effect of age (F=7.15, p<0.001), which revealed that each five-year interval was significantly different in age, apart from the two youngest groups (p=0.063). There were no differences observed for height (F=1.28, p=0.237), weight (F=1.37, p=0.186), or body mass index (F=0.714, p=0.736). Of the 152 participants, 75 women were premenopausal, 19 were perimenopausal, and 58 were classified as postmenopausal. Further, 52/75 of the premenopausal women were using a form of contraceptive (e.g. intrauterine device or combined oral contraceptive), whereas 6/19 perimenopausal and 12/58 postmenopausal women were using exogenous hormones. Among all age intervals, there were no differences observed for the number of medications currently being prescribed (F=0.78, p=0.66), as well as for the number of current medical diagnoses (F=1.43, p=0.16, Table 2). Additionally, there were no differences in the number of hours worked or volunteered among the different age intervals (x^2: 39.23, p=0.32).

Table 1. Participant Anthropometrics

Age Group	*n*	Age (years)	Height (cm)	Weight (kg)	BMI (kg/m^2)
20-24	15	22.7±1.31	164.4±1.99	65.0±2.88	24.1±1.08
25-29	13	25.8±0.27	166.3±2.19	67.2±3.24	24.2±1.03
30-34	11	31.7±0.42	164.3±2.14	71.7±3.51	26.7±1.53
35-39	13	36.4±0.34	165.3±1.77	67.5±3.45	24.7±1.21
40-44	13	42.8±0.47	167.4±2.38	72.3±1.87	26.1±0.84
45-49	12	46.4±0.29	164.2±2.11	67.9±4.37	25.1±1.43
50-54	13	52.2±0.33	164.8±1.86	63.2±2.80	23.3±1.16
55-59	14	57.1±0.37	165.7±1.82	68.3±2.41	25.1±1.29
60-64	11	61.9±0.43	162.1±2.32	60.5±3.18	23.3±1.15
65-69	11	67.4±0.92	167.1±1.30	70.2±2.29	25.1±0.75
70-74	10	71.6±0.60	162.0±1.89	64.3±2.23	24.6±0.95
75-79	8	75.9±0.54	162.0±2.85	66.6±6.86	25.3±2.23
80-89	8	85.3±1.16	155.7±3.97	61.4±3.39	25.3±0.96

Note: Values are presented as mean ± SE. *Abbreviations*: cm- centimeters, kg- kilograms, BMI- body mass index, kg/m^2- kilograms per meter squared.

Across all age intervals, no differences were observed for the number of medications currently being prescribed (F=0.78, p=0.66), as well as for the number of current medical diagnoses (F=1.43, p=0.16, Table 2). Additionally, there were no differences in the number of hours worked or volunteered among the different age intervals (x^2: 39.23, p=0.32). Physical activity characteristics are presented in Table 3. As expected, there were no differences among groups for met minutes per week (mm/w, F=0.49, p=0.98), and all participants were classified as moderately active (Hagströmer, Oja and Sjöström, 2008). There were no differences in the number of days exercised per week (x^2: 8.89, p=0.71) or the participant's perceived exertion when performing resistance exercise (x^2: 14.74, p=0.26) or aerobic exercise (x^2: 10.87, p=0.54).

Table 2. Participant Lifestyle Characteristics

Age	Medications	Diagnoses	Occupational and Volunteer Hours			
			0 hours	0 to 20 hours	20 to 40 hours	>40 hours
20-24	3.0 (0-6)	2.0 (0-4)	2	6	6	1
25-29	3.0 (0-5)	2.0 (0-3)	2	4	2	4
30-34	4.0 (0-5)	2.0 (1-3)	1	4	2	4
35-39	4.0 (1-7)	3.0 (0-5)	3	3	3	6
40-44	4.0 (0-7)	3.0 (1-4)	3	4	3	3
45-49	5.0 (0-8)	3.0 (0-4)	3	3	3	3
50-54	4.0 (0-7)	3.0 (1-5)	4	5	3	1
55-59	3.0 (0-8)	2.0 (0-5)	3	5	4	2
60-64	4.0 (0-7)	3.0 (1-5)	2	3	5	1
65-69	3.0 (0-6)	2.0 (0-4)	2	5	3	1
70-74	4.0 (1-10)	3.0 (0-4)	3	4	2	1
75-79	5.0 (2-7)	3.0 (1-4)	1	5	2	0
80-89	4.0 (2-9)	2.0 (0-3)	2	3	3	0

Note: Medications and diagnoses are presented as mean number currently taking (minimum to maximum) and are based off self-report and/or medical documentation. There were no differences in current number of medications or diagnoses.

Table 3. Physical Activity Characteristics

Age	Physical Activity (mm/w)	Days per week	Resistance Exercise (RPE)	Aerobic Exercise (RPE)
20-24	2453.9±203.7	6.0 (3 to 7)	7.0 (4 to 8)	5.0 (3 to 9)
25-29	2318.5±115.0	5.0 (3 to 7)	6.0 (4 to 8)	7.0 (3 to 9)
30-34	2311.4±117.8	5.0 (4 to 7)	6.0 (4 to 8)	7.0 (3 to 8)
35-39	2401.4±130.9	5.0 (3 to 7)	7.0 (4 to 8)	7.0 (3 to 9)
40-44	2247.8±212.9	5.0 (3 to 7)	6.0 (4 to 7)	6.0 (3 to 8)
45-49	2311.2±119.8	5.0 (3 to 7)	6.0 (4 to 7)	6.0 (3 to 8)
50-54	2407.8±112.5	5.0 (4 to 7)	6.0 (4 to 9)	6.0 (3 to 8)
55-59	2228.6±109.1	5.0 (4 to 7)	5.0 (4 to 8)	7.0 (4 to 9)
60-64	2310.1±116.8	5.0 (4 to 6)	6.0 (4 to 7)	7.0 (4 to 9)
65-69	2310.5±183.3	5.0 (4 to 7)	6.0 (4 to 8)	7.0 (3 to 9)
70-74	2340.5±113.3	5.0 (4 to 7)	6.0 (4 to 8)	7.0 (4 to 8)
75-79	2205.8±248.4	6.0 (5 to 7)	7.0 (4 to 8)	6.0 (4 to 8)
80-89	2413.0±106.7	6.0 (3 to 7)	5.0 (4 to 8)	7.0 (3 to 9)

Note: Physical activity is presented as mean ± SE and was derived from the International Physical Activity Questionnaire. Days per week and RPE values are presented as mean (minimum to maximum). *Abbreviations*: mm/w- met minutes per week, RPE- rating of perceived exertion.

Body Composition

Significant group effects were observed for total body bone free lean body mass (BFLBM) (F=2.36, p=0.009), leg BFLBM (F=2.33, p=0.010), arm BFLBM (F=2.62, p=0.004), and appendicular skeletal muscle mass (ASM, F=2.58, p=0.004). However,

post-hoc analyses did not confirm differences among groups. Values are presented in Table 4 and Figure 2, panels A-F.

Total BFLBM displayed a significant increase at a rate of 0.63 kg per year (95% CI: 0.07 to 1.22 kg per year; p=0.028) to the age of 29 ± 2.6 years (95% CI: 24.8 to 35.1 years), after which a rate of decline of 0.15 kg per year (95% CI: -0.21 to -0.10 kg per year; p=0.02) was observed. Leg BFLBM displayed a non-significant increase of 0.21 kg per year (95% CI: -0.03 to 0.44 kg per year; p=0.08) to the age of 29.9 ± 3.2 years (95% CI: 25.1 to 35.2 years), thereafter a rate of decline of 0.06 kg per year (95% CI: -0.08 to -0.03 kg per year; p=0.04) was observed. Arm BFLBM displayed a non-significant increase of 0.08 kg per year (95% CI: -0.003 to 0.164 kg per year; p=0.06) to the age of 30.9 ± 3.2 years (95% CI: 25.6 to 36.1 years), then a significant rate of decline of 0.02 kg per year (95% CI: -0.03 to -0.01 kg per year; p=0.043) was observed. Appendicular skeletal muscle mass displayed a significant increase of 0.29 kg per year (95% CI: 0.002 to 0.585 kg per year; p=0.04) to the age of 30 ± 2.8 years (95% CI: 27.5 to 33.1 years). Following this breakpoint, a significant rate of decline of 0.08 kg per year (95% CI: -0.11 to -0.05 kg per year; p=0.001) was observed. Fat free mass index displayed a non-significant increase of 0.14 kg/m^2 per year (95% CI: -0.02 to 0.31 kg/m^2 per year; p=0.08) to the age of 30.7 ± 3.5 years (95% CI: 23.9 to 37.6 years), after which a rate of decline of 0.04 kg/m^2 per year (95% CI: -0.05 to -0.02 kg/m^2 per year; p=0.023) was observed. Last, SMI displayed a non-significant increase of 0.07 kg/m^2 per year (95% CI: -0.02 to 0.17 kg/m^2 per year; p=0.13) to the age of 30.9 ± 3.9 years (95% CI: 23.2 to 38.7 years). Following this age, a rate of decline of 0.02 kg/m^2 per year (95% CI: -0.03 to -0.01 kg/m^2 per year; p=0.021) was observed.

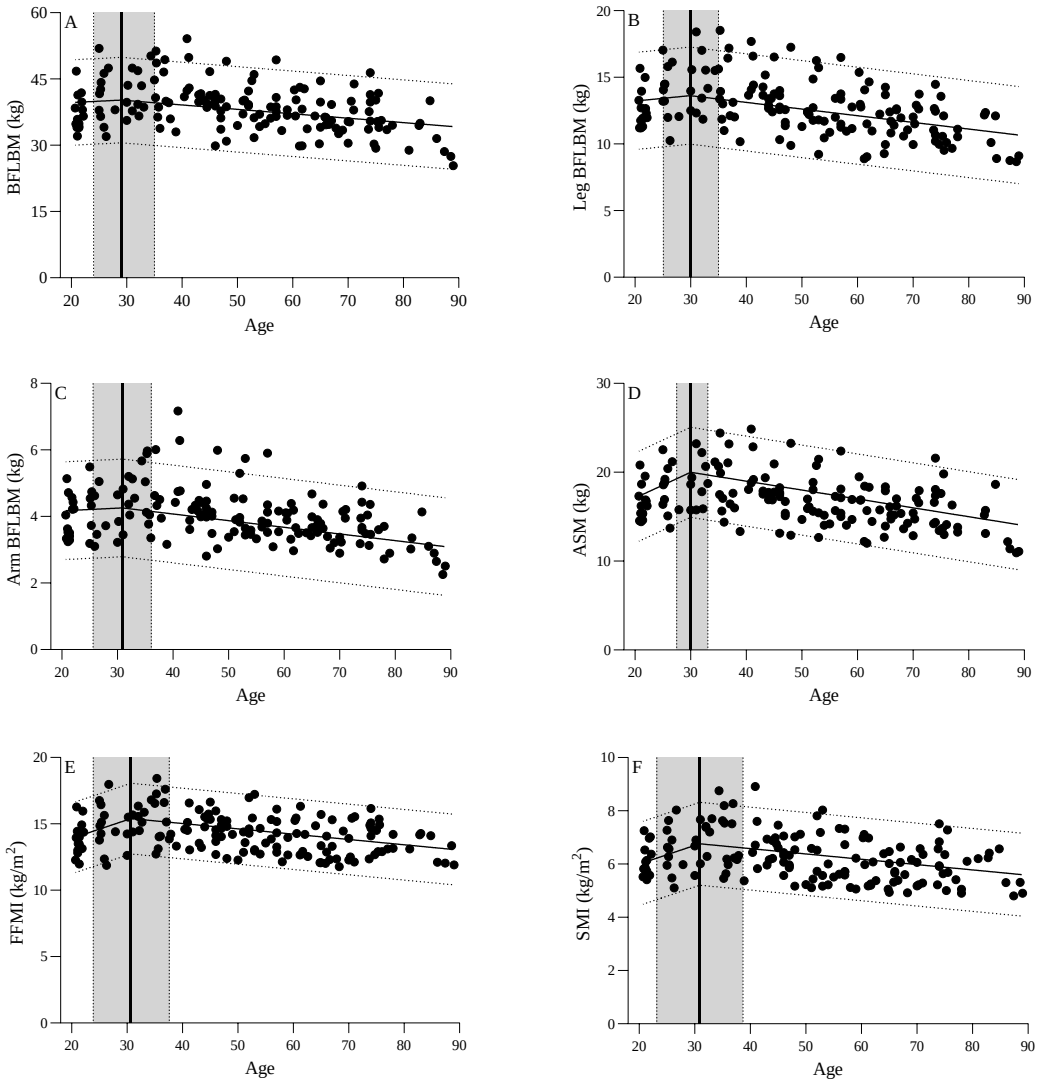

Figure 1. Bone Free Lean Body Mass Parameters

Figure Legend: *A- total body bone free lean body mass (BFLBM); B- legs BFLBM; C- arms BFLBM; D- appendicular skeletal muscle mass; E- fat free mass index; F- skeletal muscle index.*
Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval.
Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)

Table 4. DXA Bone Free Lean Body Mass Parameters

Age	Total (kg)	Legs (kg)	Arms (kg)	ASM (kg)	FFMI	SMI
20-24	38.5±1.49	12.96±0.48	4.16±0.26	17.13±0.73	14.23±0.49	6.33±0.24
25-29	41.2±1.82‡	13.81±0.61‡	4.18±0.24	18.06±0.83	14.85±0.55	6.53±0.27
30-34	41.7±1.47	14.57±0.62	4.45±0.23‡	19.02±0.79‡	15.51±0.61‡	7.11±0.27‡
35-39	41.5±1.69	13.72±0.69	4.52±0.27	18.24±0.93	15.15±1.90	6.65±0.29
40-44	41.6±0.92	13.97±0.35	4.47±0.21	18.44±0.51	14.87±0.35	6.59±0.16
45-49	39.3±1.57	13.03±0.64	4.14±0.24	17.16±0.85	14.52±0.36	6.32±0.19
50-54	38.6±1.14	12.52±0.56	4.07±0.21	16.59±0.71	14.24±0.44	6.12±0.28
55-59	38.3±1.26	12.50±0.51	3.94±0.23	16.44±0.72	13.93±0.39	5.99±0.24
60-64	36.7±1.57	11.98±0.68	3.73±0.13	15.71±0.78	13.93±0.43	5.96±0.24
65-69	38.1±1.22	12.58±0.53	4.00±0.14	16.58±0.59	13.63±0.42	5.93±0.19
70-74	35.8±1.09	11.79±0.39	3.53±0.12	15.32±0.49	13.66±0.39	5.84±0.18
75-79	37.2±1.59	11.93±1.11	3.54±0.29	15.47±1.37	14.17±0.48	5.88±0.43
80-89	33.1±2.30	11.29±1.13	3.08±0.32†	14.37±1.44	13.59±0.42	5.87±0.34

Note: Values are presented as mean ± SE with reference value underlined. ‡- denotes critical value from segmental analysis, †- denotes significant difference from reference group (underlined). *Abbreviations*: DXA- dual energy x-ray absorptiometry, kg- kilograms, ASM- appendicular skeletal muscle mass, FFMI- fat free mass index (FFM/ht^2), SMI- skeletal muscle index (ASM/ht^2).

Fat mass values obtained from the DXA are displayed in Table 5. Significant group effects for total percent fat (F=2.23, p=0.014), arm percent fat (F=2.45, p=0.007), and leg percent fat (F=2.54, p=0.005) were observed, however, post-hoc analyses did not confirm the differences.

Table 5. DXA Total Body and Regional Fat Mass Values

Age	Total		Arms		Legs	
	Total (kg)	Percent (%)	Total (kg)	Percent (%)	Total (kg)	Percent (%)
20-24	21.7±1.89	32.9±1.77	2.36±0.24	32.8±1.81	7.81±0.49	34.7±1.56
25-29	20.8±1.95	30.7±1.82	2.22±0.25	31.1±2.16	8.10±0.66	33.8±1.67
30-34	24.9±2.23	34.2±1.56	2.62±0.27	33.5±1.75	9.96±0.72	37.5±1.38
35-39	21.1±2.38	30.5±1.98	2.41±0.33	30.9±2.29	7.98±0.61	33.7±1.19
40-44	26.3±2.06	35.7±2.04	2.81±0.25	35.4±2.39	10.0±0.70	38.6±1.89
45-49	23.9±3.20	34.0±2.37	2.37±0.36	32.9±2.10	9.34±1.29	37.4±2.29
50-54	19.9±1.98	30.8±1.92	2.20±0.24	31.3±1.98	7.39±0.66	33.7±1.61
55-59	25.4±2.56	36.5±2.59	2.63±0.27	36.3±2.83	10.1±1.09	40.7±2.37
60-64	19.8±1.89	32.4±1.69	2.15±0.20	33.2±1.85	6.95±0.79	33.3±1.76
65-69	27.7±1.84	39.3±1.64	2.81±0.18	38.1±1.69	9.92±0.95	40.5±1.76
70-74	24.2±1.82	37.2±1.90	2.60±0.18	38.7±1.82	8.69±0.76	38.9±2.0
75-79	25.3±5.39	36.3±4.06	2.58±0.55	37.4±3.14	9.65±2.22	39.9±3.83
80-89	24.5±1.35	40.2±1.51	2.84±0.31	44.4±1.91	9.68±2.92	42.9±3.05

Note: Values are presented as mean ± SE. *Abbreviations*: kg- kilograms.

Table 6 displays upper and lower leg site specific muscle density and muscle area values. Muscle density (F=4.82, p<.0001) and muscle area (F=11.84, p<0.001) for the

upper leg revealed significant effects, while this was observed for muscle density (F=4.32, p<0.001) but not for muscle area (F=1.04, p=0.417). Post hoc analyses and visual representation are presented in Table 6 and Figure 2 (A-D), respectively.

For the upper leg, muscle density displayed a non-significant increase (p=0.73) of 0.02 mg/cm^3 per year (95% CI: -0.11 to 0.16 mg/cm^3 per year) to the age of 34.9 ± 1.3 years (95% CI: 32.7 to 37.1 years). After this age, a significant decrease (p<0.001) of 0.10 mg/cm^3 per year (95% CI: -0.11 to -0.05 mg/cm^3 per year) was observed. Muscle area displayed a non-significant increase of 10.21 cm^2 per year (95% CI: -1.96 to 22.4 cm^2 per year) to the age of 22 ± 0.8 years 95% CI: 20.4 to 23.5 years) which preceded a significant decline (p<0.001) of 0.75 cm^2 per year (95% CI: -0.88 to -0.62 cm^2 per year).

Table 6. Site Specific Muscle Density and Cross-Sectional Area

Age	Upper Leg		Lower Leg	
	Muscle density (mg/cm^3)	Muscle CSA (cm^2)	Muscle density (mg/cm^3)	Muscle CSA (cm^2)
20-24	81.33±0.31	100.78±3.48‡	80.07±0.31	64.95±2.62
25-29	81.74±0.42	<u>109.02±6.21</u>	78.83±0.39	64.61±2.73
30-34	81.68±0.39‡	106.52±4.34	79.51±0.49	66.47±3.65
35-39	<u>82.02±0.52</u>	106.45±4.82	<u>80.32±0.27</u>	<u>72.87±3.65</u>
40-44	81.55±0.37	100.32±4.72	79.60±0.44	62.80±2.55
45-49	80.83±0.26	91.96±3.16	78.78±0.32	66.39±2.68
50-54	80.40±0.26	92.45±4.47	79.12±0.22	68.76±3.37
55-59	79.53±0.52	82.06±3.01†	78.70±0.37	64.83±2.96
60-64	79.27±0.67	81.31±3.06†	78.25±0.80	65.42±3.62
65-69	78.80±0.51	80.56±3.16†	78.61±0.62‡	63.49±2.86
70-74	79.53±0.84	80.01±4.81†	77.91±0.37	64.72±2.21
75-79	79.48±1.91	67.44±3.93†	76.94±0.92†	59.09±2.65‡
80-89	77.11±0.74†	65.27±2.62†	76.51±0.99†	60.50±4.74

Note: Values are displayed as mean ± SE. Muscle density and CSA (cross-sectional area) values are excluding possible intramuscular adipose tissue. Upper leg: 40% femur length, lower leg: 66% tibia length. ‡- denotes critical value from segmental analysis, †- denotes significant difference from reference group (underlined). *Abbreviations*: mg/cm^3- milligrams per cubic centimeter, cm^2- centimeters squared.

Muscle density for the lower leg displayed a significant decline (p<0.001 of 0.03 mg/cm^3 per year (95% CI: -0.05 to -0.01) to the age of 69.8 ± 3.7 years (95% CI: 62.4 to 77.2 years) where an accelerated decline of 0.20 mg/cm^3 per year (95% CI: -0.34 to -0.08

mg/cm^3 per year) was observed. Muscle area displayed a non-significant (p=0.45) decline of 0.05 cm^2 per year (95% CI: -0.15 to 0.05 cm^2 per year) to the age of 79.0 ± 5.5 years (95% CI: 68.1 to 89.9 years) where an accelerated decline of 2.05 cm^2 per year (95% CI: -5.97 to -1.86 cm^2 per year) was observed.

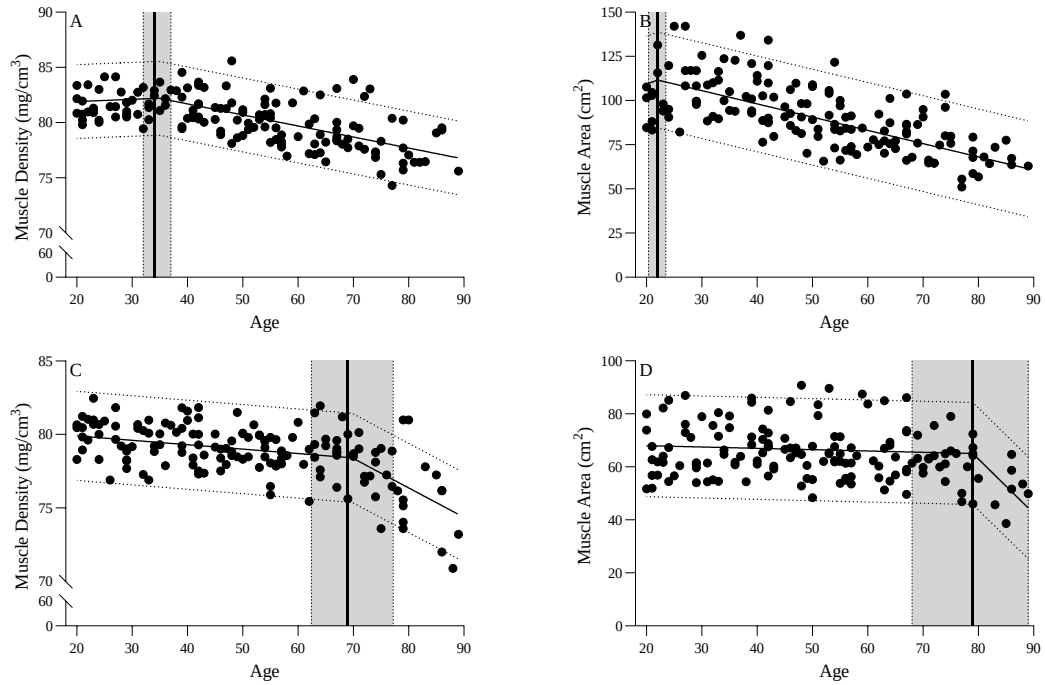

Figure 2. Site Specific Muscle Density and Cross-Sectional Area
Figure Legend: *A and B- upper leg; C and D- lower leg.*
Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval.
Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)

Reliability of Measures

The reader is directed to Appendix D for a comprehensive presentation of absolute and relative reliability for each muscle performance variable. In general, ICC values ranged from moderate to excellent across all performance measures (ICC: 0.61-0.98). The tables are displayed as a range, displaying the smallest and largest values across all age groups.

Functional Measures

Altogether, mean grip strength was maintained to the late 60s, whereas jump power and velocity both increased to 41 and 35 years of age, respectively, thereafter each decreased with increased age.

Dominant and non-dominant grip strength displayed significant group differences presented in Table 7 (right: F=11.37, p<0.001; left: F=17.70, p<0.001). For the dominant hand grip strength, there was a non-significant rate of decline of 0.036 kg per year (95% CI: -0.065 to 0.006 kg per year; p=0.17) until the age of 67 ± 2.2 years (95% CI: 62.6 to 71.3 years), after which a significantly accelerated rate of decline of 0.328 kg per year (95% CI: -0.478 to -0.251 kg per year; p<0.001) was observed. Non-dominant grip strength displayed a non-significant rate of decline of 0.077 kg per year (95% CI: -0.109 to -0.04 kg per year; p=0.54) to the age of 67.5 ± 3.14 years (95% CI: 61.3 to 73.7 years) where a significantly increased rate of decline of 0.312 kg per year was observed (95% CI: -0.552 to -0.228 kg per year; p<0.001).

Table 7. Functional Measures

Age	Grip Strength		Vertical Jump	
	Dominant hand* (kg)	Non-Dominant hand (kg)	Power (Watts)	Velocity (m/s)
20-24	32.8±1.5	35.2±1.3	1156.1±73.4	1.31±0.11
25-29	32.6±1.2	34.0±1.1	1186.7±67.8	1.41±0.09
30-34	33.1±1.9	36.6±1.5	1256.4±75.8	1.38±0.11
35-39	33.6±1.4	35.9±1.5	1209.5±82.7	1.43±0.09‡
40-44	32.4±1.7	33.4±1.6	1302.9±77.0‡	1.28±0.10
45-49	33.4±1.2	33.7±1.3	1098.8±93.2	1.23±0.11
50-54	31.3±1.6	32.3±1.4†	1089.9±101.3†	1.22±0.10
55-59	32.1±0.9	32.3±1.4†	955.5±73.9†	1.11±0.08†
60-64	31.5±1.7	32.2±1.8†	987.8±77.5†	1.09±0.10†
65-69	31.9±1.5‡	33.6±1.4‡	803.5±99.5†	1.01±0.10†
70-74	29.0±2.0†	29.6±1.9†	641.1±79.9†	0.99±0.10†
75-79	27.6±1.9†	27.6±1.5†	583.1±77.3†	0.95±0.11†
80-89	25.7±1.6†	25.6±1.9†	535.3±72.8†	0.72±0.13†

Note: Values presented as mean ± SE. *determined as hand used to complete activities of daily living, ‡- denotes critical age (breakpoint) from segmental analysis, †- significantly different from reference group (underline). *Abbreviations*: kg- kilograms, m/s- meters per second.

Vertical jump power and jump velocity data are presented in Table 7 and Figure 3, panels C and D. Both vertical jump metrics displayed significant group differences (jump power: F=72.4, p<0.001; jump velocity: F=66.91, p<0.001). Jump power displayed a significant rate of increase of 5.34 Watts per year (95% CI: 0.13 to 10.56 Watts per year; p=0.044) to the age of 41 ± 1.8 years (95% CI: 37.4 to 44.6 years). Thereafter, a significant decline of 15.03 Watts per year (95% CI: -19.84 to -10.55 Watts per year; p<0.001). Jump velocity displayed a non-significant rate of increase of 0.005 m/s per year (95% CI: -0.005 to 0.016m/s per year; p=0.328) to the age of 35 ± 3.7 years (95% CI: 28.3 to 41.6 years), after which a significant rate of decline of 0.017 m/s per year (95% CI: -0.014 to -0.010m/s per year; p<0.001) was observed.

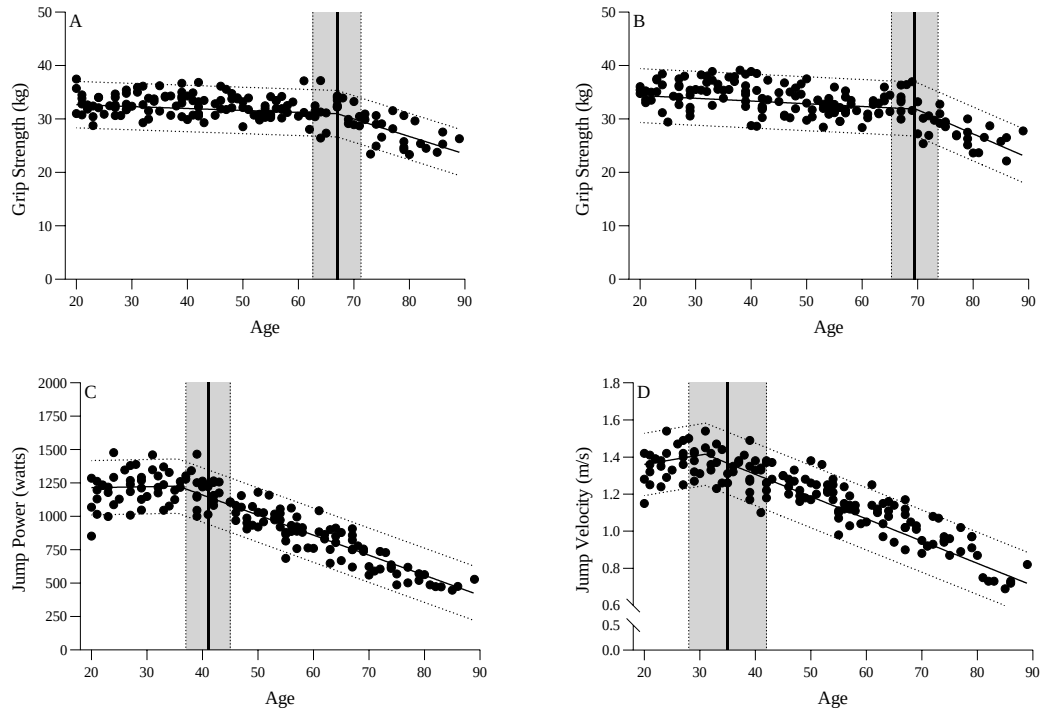

Figure 3. Functional Measures

Figure Legend: *A- dominant hand; B- non-dominant hand; C- vertical jump power; D- vertical jump velocity Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval. Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)*

Isometric Strength

Collectively, maximal isometric strength values revealed critical age periods during the mid-40s for the knee extensors and flexors (43 and 45.7 years, respectively), whereas the early to mid-60s represented critical age periods the alternative muscle groups investigated (elbow extensors: 61.3 years, elbow flexors: 61.2 years, plantar flexors 66.2 years, and dorsiflexors 63 years).

Elbow Extension

Maximal voluntary isometric strength and rate of torque development for the elbow extensors and flexors are displayed in Table 8 and Figure 4. As expected, there were significant age effects for both maximal isometric strength (F=21.37, p<0.001) and rate of torque development (F=48.60, p<0.001; Table 8). Maximal isometric strength for the elbow extensors displayed a non-significant rate of decline of 0.08 Nm per year (95% CI: -0.16 to 0.001 Nm per year; p=0.43) to the age of 61.3 ± 2.2 years (95% CI: 56.9 to 65.7 years), after which a significantly accelerated rate of decline of 0.85 Nm per year (95% CI: -1.06 to -0.64 Nm per year; p=0.02) was observed. Rate of torque development displayed a significant rate of decline of 0.36 Nm/s per year (95% CI: -0.49 to -0.03; p=0.021) to the age of 63.2 ± 1.23 years (95% CI: 61.3 to 66.3 years) which then displayed a significantly accelerated rate of decline of 4.58 Nm/s per year (95% CI: -5.18 to -3.77 Nm/s per year; p=0.009).

Table 8. Isometric Elbow Flexion and Extension Parameters

Age	Elbow Extensors		Elbow Flexors	
	MVIC (Nm)	RTD (Nm/s)	MVIC (Nm)	RTD (Nm/s)
20-24	94.3±3.1	253.3±7.8	74.2±3.0	216.2±5.5
25-29	95.3±4.4	244.3±10.1	77.9±4.3	206.5±4.4
30-34	94.9±3.8	244.7±7.5	72.1±3.8	208.6±8.1
35-39	92.3±3.8	246.0±6.6	78.4±4.1	209.6±4.4
40-44	97.2±3.4	252.7±10.7	76.1±3.0	202.9±7.8
45-49	94.7±3.4	242.7±9.9	73.5±3.2	206.4±7.2‡
50-54	91.3±3.5	236.4±10.2	73.1±3.9	205.9±4.9
55-59	90.5±3.5	236.5±9.4	71.4±3.4	179.6±4.8†
60-64	93.9±3.5‡	248.5±11.7‡	72.7±3.4‡	169.3±7.2†
65-69	87.4±2.8†	231.0±8.7	68.5±2.9†	149.1±7.9†
70-74	80.1±4.4†	196.1±11.4†	61.9±3.9†	150.3±5.6†
75-79	79.8±4.8†	164.3±10.4†	55.3±5.0†	128.2±6.3†
80-89	72.8±3. 5†	156.4±9.9†	56.4±3.4†	118.1±4.3†

Note: Values presented as mean ± SE. ‡- denotes critical age (breakpoint) from segmental analysis, †- denotes significant difference from reference group (underline). *Abbreviations*: MVIC- maximum voluntary isometric contraction, RTD- rate of torque development, Nm- Newton meters, Nm/s- Newton meters per second.

Elbow Flexion

Group effects indicated differences among age groups for elbow flexor maximal isometric strength (F=21.96, p<0.001) and rate of torque development (F=150.66, p<0.001, Table 8). Maximal isometric elbow flexion strength displayed a slow but significant rate of decline of 0.09 Nm per year (95% CI: -0.18 to 0.01 Nm per year; p=0.02) to age 61.2 ± 2.4 years (95% CI: 56.5 to 66.0 years). After this point, the rate of decline significantly increased to 0.82 Nm per year (95% CI: -1.04 to -0.62 Nm per year; p=0.035). Rate of torque development displayed a significant rate of decline of 0.36 Nm/s per year (95% CI: -0.63 to -0.10 Nm/s per year; p=0.04) to age 49.6 ± 1.47 years (95% CI: 46.7 to 52.5 years). Following this age, the rate of decline was significantly increased to 2.56 Nm/s per year (95% CI: -2.79 to -2.34 Nm/s per year; p=0.050).

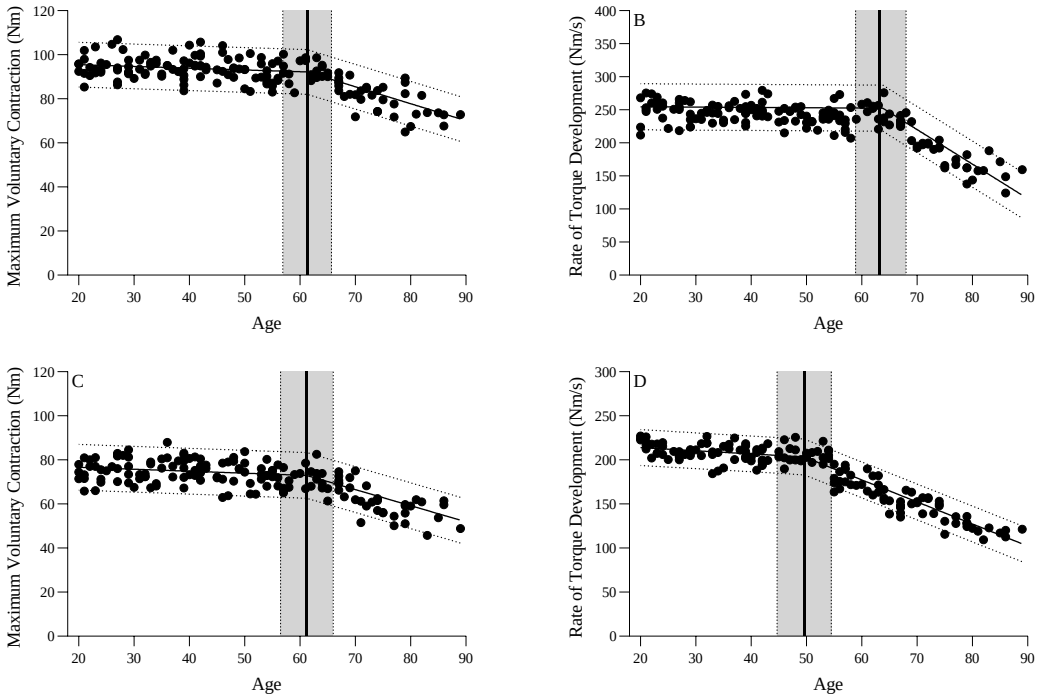

Figure 4. Elbow Extension and Flexion Isometric Parameters
Figure legend: *A and B- elbow extensors; C and D- elbow flexors*
Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval.
Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)

Knee Extension

Table 9 and Figure 5 present the maximal isometric performance parameters for the knee extensors and flexors. As expected, significant differences were observed for both maximal isometric strength (F=106.28, p<0.001) and rate of torque development (F=48.11, p<0.001; Table 9). Knee extensor maximal isometric strength demonstrated a marginal increase of 0.14 Nm per year (95% CI: -0.32 to 0.61 Nm per year; p=0.31) up to the age of 43 ± 1.4 years (95% CI: 40.1 to 45.9 years), after which displaying a significant rate of decline of 3.07 Nm per year (95% CI: -3.50 to -2.53 Nm per year; p=0.006). Knee extensor rate of torque development displayed a non-significant rate of decline of 9.44 Nm/s per year (95% CI: -8.51 to 6.58 Nm/s per year; p=0.83) to 36.1 ±

3.23 years (95% CI: 29.6 to 42.4 years), thereafter a significantly accelerated rate of decline of 13.47 Nm/s per year (95% CI: -16.1 to -12.7 Nm/s per year; p=0.04) was observed.

Table 9. Isometric Knee Extension and Flexion Parameters

Age	Knee Extensors		Knee Flexors	
	MVIC (Nm)	RTD (Nm/s)	MVIC (Nm/s)	RTD (Nm/s)
20-24	240.7±2.91	1179.5±30.83	133.6±1.83	455.2±21.57
25-29	237.9±2.20	1168.7±22.94	131.6±3.46	438.2±23.58
30-34	235.1±4.54	1133.9±43.84	142.4±3.34	397.9±19.79
35-39	242.3±2.92	1205.8±35.32‡	130.1±2.10	443.7±32.45
40-44	244.3±5.11‡	1038.6±42.50	133.3±2.29	465.4±23.40
45-49	231.6±3.62	1042.6±30.39	132.7±1.75‡	491.7±21.53‡
50-54	226.7±4.40	909.2±31.08†	126.9±2.24†	422.9±19.71
55-59	199.6±2.94†	865.8±34.97†	122.2±1.75†	412.5±21.58
60-64	179.9±4.15†	787.2±36.37†	106.1±2.24†	432.8±20.35
65-69	169.6±3.03†	696.4±27.41†	98.5±1.52†	397.2±25.70
70-74	151.6±3.47†	568.3±36.37†	93.9±2.01†	382.7±36.83
75-79	148.5±4.31†	574.4±27.33†	99.2±1.97†	374.2±27.35
80-89	136.7±5.05†	530.8±30.54†	88.6±2.09†	320.4±25.17†

Note: Values presented as mean ± SE. ‡- denotes critical age (breakpoint) from segmental analysis, †- denotes significant difference from reference group (underline). *Abbreviations*: MVIC- maximum voluntary isometric contraction, RTD- rate of torque development, Nm- Newton meters, Nm/s- Newton meters per second.

Knee Flexion

Both isometric parameters displayed significant age effects (both p<0.001, Table 9). Knee flexor isometric strength displayed a significant rate of decline of 0.05 Nm per year (95% CI: -0.10 to -0.01 Nm per year; p=0.043) to the age of 45.7 ± 2.3 years (95% CI: 41.2 to 50.2 years), where the rate of decline increased significantly to 1.28 Nm per year (95% CI: -1.44 to -1.11 Nm per year; p=0.005). Knee flexor rate of torque development revealed a small decline of 1.09 Nm/s per year (95% CI: -1.22 to 3.40 Nm/s per year; p=0.327) to the age 45.9 ± 5.5 years (95% CI: 34.2 to 58.2 years), thereafter a significantly accelerated rate of decline of 4.23 Nm/s per year (95% CI: -4.5 to -7.77 Nm/s per year; p=0.002) was observed.

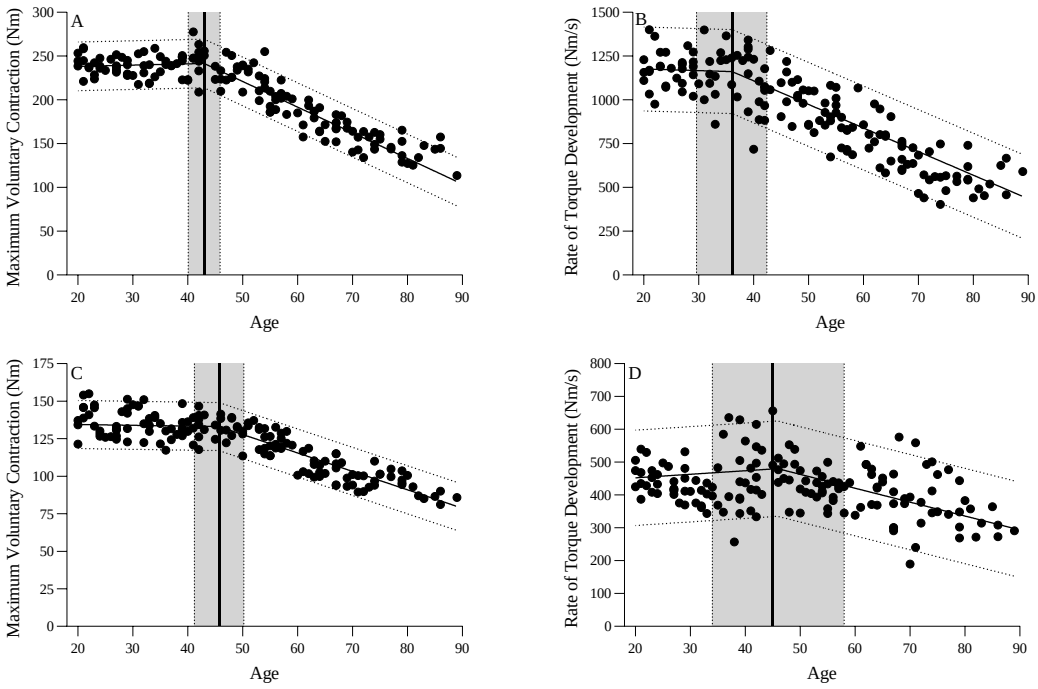

Figure 5. Knee Extension and Flexion Isometric Parameters
Figure Legend: *A and B- knee extension; C and D- knee flexion*
Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval.
Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)

Plantarflexion

Plantar and dorsiflexion isometric strength parameters are displayed in Table 10 and Figures 6. Significant age effects were observed for plantarflexion maximal isometric strength (F=16.52, p<0.001) and rate of torque development (F=33.71, p<0.001; Table 10). Plantarflexion maximal isometric strength displayed a significant rate of decline in strength of 0.05 Nm per year (95% CI: -0.10 to -0.01 Nm per year; p=0.02) to the age of 66.2 ± 2.1 years (95% CI: 62.3 to 70.1 years), where the rate of decline was significantly accelerated to 0.64 Nm per year (95% CI: -0.83 to -0.46 Nm per year; p=0.01). Rate of torque development revealed a significant rate of decline of 1.73 Nm/s per year (95% CI: -2.14 to -1.31 Nm/s per year; p=0.001) to the age of 51 ± 4.72 years (95% CI: 43.7 to

58.2 years) where the rate of decline was significantly reduced to 0.70 Nm/s per year (-1.51 to -0.67 Nm/s per year; p=0.006).

Table 10. Plantar- and Dorsiflexion Isometric Parameters

Age	Plantarflexion		Dorsiflexion	
	MVIC (Nm)	RTD (Nm/s)	MVIC (Nm)	RTD (Nm/s)
20-24	38.5±1.30	200.2±13.7	30.6±1.10	113.5±12.3
25-29	39.7±0.98	202.1±17.7	30.0±0.91	118.6±17.4
30-34	38.2±2.41	200.1±14.9	29.6±1.88	111.2±14.1
35-39	40.9±2.23	199.2±14.0†	29.1±1.65	107.9±11.8
40-44	38.2±1.09	168.5±14.5†	27.6±1.51	107.7±13.8
45-49	39.9±1.85	161.1±12.5†	29.1±1.75	98.7±12.7†
50-54	38.0±2.12	154.1±16.7†‡	25.5±2.41	107.4±11.8
55-59	36.3±3.15	149.8±13.9†	27.7±1.94	101.9±11.9†
60-64	37.7±2.98	146.6±14.2†	30.0±1.65‡	97.4±12.1†‡
65-69	36.6±3.21‡	144.7±14.6†	23.0±2.38†	96.2±11.9†
70-74	33.3±2.45†	140.1±14.1†	24.2±2.12†	85.5±12.0†
75-79	29.8±3.1†	132.7±15.6†	17.8±1.73†	78.4±10.2†
80-89	25.3±1.87†	116.7±16.5†	15.3±1.10†	74.4±8.9†

Note: Values presented as mean ± SE. ‡- denotes critical age (breakpoint) from segmental analysis. †- denotes significant difference from reference group (underline). *Abbreviations*: MVIC- maximum voluntary isometric contraction, RTD- rate of torque development, Nm- Newton meters, Nm/s- Newton meters per second.

Dorsiflexion

Dorsiflexion maximal isometric strength (F=19.24, p<0.001) and rate of torque development (F=25.53, p<0.001) displayed significant group differences (Table 10). Maximal dorsiflexion isometric strength displayed a significant rate of decline of 0.07 Nm per year (95% CI: -0.12 to -0.01 Nm per year; p=0.007) to the age of 63 ± 2.58 years (95% CI: 56.5 to 69.3 years) where a significantly accelerated rate of decline of 0.55 Nm per year (-0.72 to -0.39 Nm per year; p=0.03) was observed. Rate of torque development for the dorsiflexors displayed a significant rate of decline of 0.44 Nm/s per year (95% CI: -0.57 to -0.30 Nm/s per year; p<0.001) to the age of 64 ± 3.87 (95% CI: 56.3 to 71.6 years) where the rate of decline significantly increased to 1.21 Nm/s per year (95% CI: -1.60 to -0.80 Nm/s per year; p=0.01).

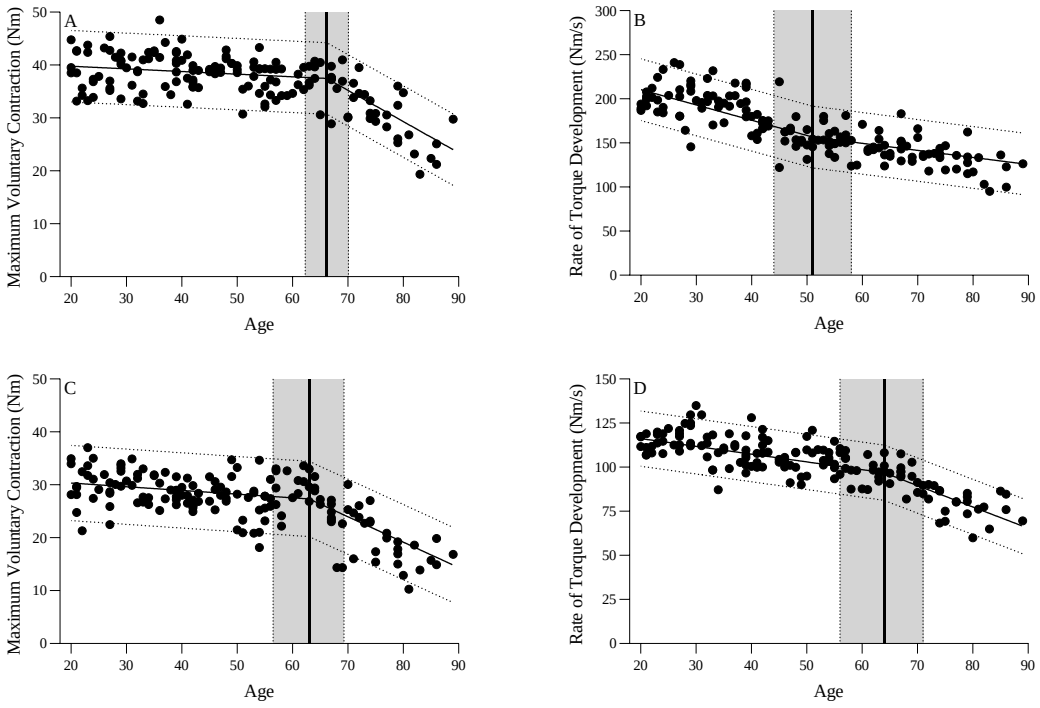

Figure 6. Plantar- and Dorsiflexion Isometric Parameters
Figure Legend: *A and B- plantar flexion; C and D- dorsiflexion*
Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval.
Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)

Dynamic Strength

Overall, dynamic strength (isokinetic contractions) displayed critical age periods well before those observed from the isometric strength contractions. For the slow contraction velocity (60 deg/s) the late 30s to 40s represented critical ages for the elbow extensors (48.5 years), knee extensors (39 years), knee flexors (44 years), and the dorsiflexors (45 yeas), whereas the late 50s early 60s represented critical aged for the elbow flexors (57 years) and plantar flexors (63.2 years). With the exception of the dorsiflexors (64 years), each of the muscle groups again displayed earlier critical ages for the higher contraction velocity (240 deg/s). Apart from the dorsiflexors (64 years) the

plantar flexors displayed critical changes during the early 50s (51 years), whereas the remaining muscle groups displayed critical ages between the late 20s to 30s (elbow extensors and flexors: 39 years and knee extensors and flexors: 29 years).

Elbow Extension

Values are displayed in Table 11 and Figure 7. Significant differences were observed across groups for elbow extensor peak torque (PT, F=32.44, p<0.001) and time to peak torque (TTPT, 41.56, p<0.001; Table 11). PT_{60} values displayed a marginal rate of decline of 0.12 Nm per year (95% CI: -0.28 to 0.05 Nm per year; p=0.158) until age 48.5 ± 3.1 years (95% CI: 42.4 to 54.5 years), where a significantly accelerated rate of decline of 0.75 Nm per year (95% CI: -0.88 to -0.62 Nm per year; p=0.003) was observed. $TTPT_{60}$ displayed a significant increase (i.e. took longer to achieve) of 0.005 seconds per year (95% CI: 0.004 to 0.006 seconds per year; p<0.001) to the age of 75 ± 1.8 years (95% CI: 71.4 to 78.6 years) where an accelerated rate of increase of 0.029 seconds per year (95% CI: 0.017 to 0.040 seconds per year; p=0.004) was observed.

Table 11. Elbow Extension Dynamic Strength Parameters

Age	60 degrees per second		240 degrees per second	
	PT (Nm)	TTPT (s)	PT (Nm)	TTPT (s)
20-24	82.3±3.7	0.617±0.05	58.6±3.1	0.400±0.07
25-29	80.3±3.1	0.663±0.06	56.8±4.0	0.471±0.09
30-34	79.3±4.2	0.753±0.05†	57.9±3.6	0.381±0.08
35-39	78.9±4.0	0.696±0.05	58.3±3.9‡	0.471±0.08
40-44	79.1±3.9	0.702±0.05	56.4±3.7	0.415±0.10
45-49	79.5±3.5‡	0.750±0.04†	50.3±3.5	0.411±0.09‡
50-54	74.1±3.4	0.888±0.05†	50.4±3.8	0.482±0.07
55-59	75.9±4.5	0.901±0.05†	46.7±4.1†	0.548±0.07
60-64	67.5±3.5†	0.863±0.06†	42.6±3.8†	0.551±0.10
65-69	63.1±3.9†	0.841±0.05†	38.5±3.3†	0.696±0.09†
70-74	56.5±4.3†	0.858±0.06†	41.9±4.8†	0.841±0.09†
75-79	53.9±4.5†	0.952±0.07†‡	37.1±3.3†	0.869±0.11†
80-89	55.7±5.2†	1.23±0.08†	34.1±5.2†	0.867±0.10†

Note: Values are presented as mean ± SE. ‡- denotes critical age (breakpoint) from segmental analysis, †- denotes significant difference from reference group (underline). *Abbreviations*: PT- peak torque, Nm- Newton meters, TTPT- time to peak torque, s- seconds.

During the 240 deg/s contractions, PT and TTPT both displayed significant group differences (both $p<0.001$, Table 11). Elbow extensor PT_{240} revealed a non-significant rate of decline of 0.117 Nm per year (95% CI: -0.39 to 0.15 Nm per year; $p=0.405$) until age 38.9 ± 4.9 years (95% CI: 29.2 to 48.8 years), where a significantly accelerated rate of decline of 0.507 Nm per year (95% CI: -0.61 to -0.42 Nm per year; $p=0.047$) was observed. Elbow extensor $TTPT_{240}$ displayed a negligible increase in $TTPT_{240}$ of 0.0006 seconds per year (95% CI: -0.004 to 0.003 seconds per year; $p=0.71$) to the age of 48 ± 2.7 years (95% CI: 42.5 to 53.4 years) where the rate of increase for $TTPT_{240}$ significantly increased to 0.0156 seconds per year (95% CI: 0.011 to 0.017 seconds per year; $p=0.03$).

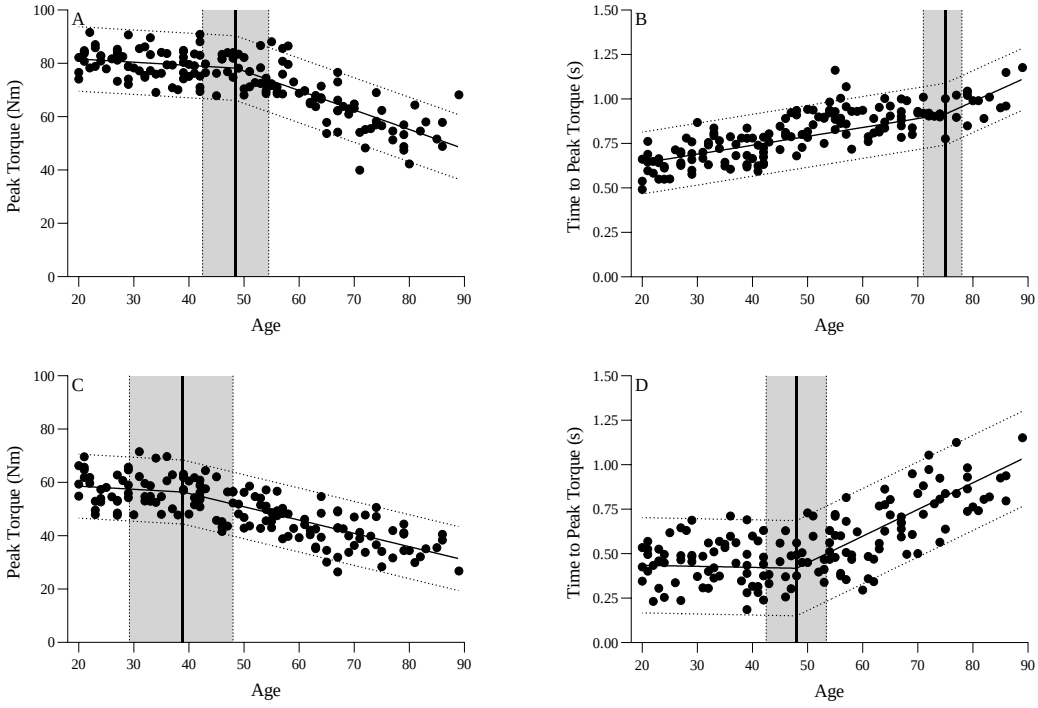

Figure 7. Elbow Extension Dynamic Strength Parameters
Figure Legend: *A and B contractions at 60 deg/s; C and D- contractions at 240 deg/s*
Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval.
Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)

Elbow Flexion

As expected, there were significant group differences for both peak torque and time to peak torque (PT and TTPT, both $p<0.001$, Table 12, Figure 8). Elbow flexor PT_{60} displayed a non-significant rate of decline of 0.02 Nm per year (95% CI: -0.09 to 0.06 Nm; $p=0.69$) to the age of 57 ± 3.5 years (95% CI: 50.1 to 63.8 years) where a significantly accelerated rate of decline of 0.468 Nm per year (95% CI: -0.62 to -0.31 Nm per year; $p<0.001$) was observed. Elbow flexor $TTPT_{60}$ displayed a significant rate of decline (i.e. improved) of 0.002 seconds per year (95% CI: -0.005 to -0.001 seconds per year; $p<0.001$) to the age of 65.1 ± 2.4 years (95% CI: 60.2 to 69.9 years) where the slope reversed and displayed a significant increase in rate corresponding to 0.023 seconds per year (95% CI: 0.011 to 0.026 seconds per year; $p=0.012$).

Table 12. Elbow Flexion Dynamic Strength Parameters

Age	60 degrees per second		240 degrees per second	
	PT (Nm)	TTPT (s)	PT (Nm)	TTPT (s)
20-24	61.6±2.9	0.907±0.08	41.8±2.5	0.489±0.08
25-29	57.1±3.5	0.900±0.08	45.5±2.0	0.469±0.08
30-34	59.4±3.7	0.980±0.10	46.0±2.6	0.421±0.09
35-39	62.3±4.7	0.942±0.06	45.0±2.1‡	0.509±0.07‡
40-44	57.5±4.3	0.955±0.10	44.0±2.7	0.502±0.10
45-49	57.8±2.8	0.905±0.08	41.9±2.2	0.444±0.08
50-54	59.6±4.3	0.942±0.08	43.2±2.2	0.512±0.05
55-59	55.3±3.7‡	0.813±0.05	40.2±1.8	0.526±0.05
60-64	54.1±3.6†	0.792±0.09	39.0±2.7	0.715±0.08†
65-69	45.1±4.1†	0.913±0.09‡	37.8±1.5†	0.733±0.09†
70-74	46.8±4.9†	0.856±0.08	31.7±2.9†	0.660±0.10†
75-79	42.9±4.8†	1.09±0.11	26.1±2.0†	0.698±0.11†
80-89	39.1±4.9†	1.19±0.10†	22.3±2.1†	0.671±0.09†

Note: Values are presented as mean ± SE. ‡- denotes critical age (breakpoint) from segmental analysis, †- denotes significant difference from reference group (underline). *Abbreviations*: PT- peak torque, Nm- Newton meters, TTPT- time to peak torque, s- seconds.

During the 240 deg/s contractions significant group differences were observed for PT and TTPT (both $p<0.001$, Table 12, Figure 8). With age, there was a non-significant increase in elbow flexion PT_{240} of 0.05 Nm per year (95% CI: -0.12 to 0.22 Nm per year;

p=0.41) to the age of 39 ± 3.7 years (95% CI: 31.1 to 46.9 years), thereafter a significant rate of decline of 0.265 Nm per year (95% CI: -0.32 to -0.20 Nm per year; p=0.004) was observed. Elbow flexion $TTPT_{240}$ displayed a marginal decrease in $TTPT_{240}$ of 0.004 seconds per year (95% CI: -0.014 to 0.006 seconds per year; p=0.21) to the age of 35 ± 2.1 years (95% CI: 23.8 to 44.1 years), where a significantly larger rate of increase of 0.014 seconds per year (95% CI: 0.004 to 0.017 seconds per year; p<0.001) was observed.

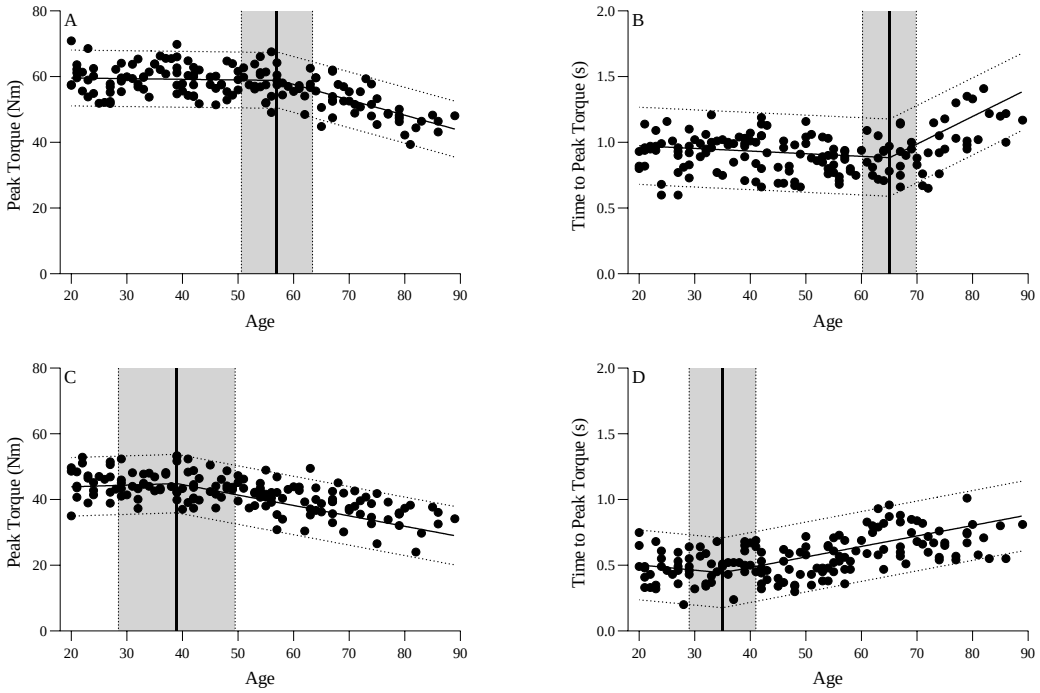

Figure 8. Elbow Flexion Dynamic Strength Parameters
Figure Legend: *A and B- contractions at 60 deg/s; C and D contractions at 240 deg/s*
Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval.
Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)

Knee Extension

Significant age effects for knee extension PT and TTPT at both contraction velocities (all p<0.001) were observed and are displayed in Table 13, Figure 9. PT_{60} displayed a non-significant decline of 0.240 Nm per year (95% CI: -0.99 to 0.51Nm per

year; p=0.15) to the age of 39 ± 4.27 years (95% CI: 30.5 to 47.4 years), where the rate of decline was significantly accelerated to 1.45 Nm per year (95% CI: -1.64 to -1.25 Nm per year; p=0.01). $TTPT_{60}$ displayed a non-significant increase of 0.001 seconds per year (95% CI: -0.004 to 0.007 seconds per year; p=0.21) until the age of 31 ± 4.49 years (95% CI: 22.1 to 39.8 years), thereafter a significantly greater rate of increase of 0.006 seconds per year (95% CI: 0.006 to 0.007 seconds per year; p=0.007) was observed.

Knee extensor PT_{240} displayed a marginal increase of 0.70 Nm per year (95% CI: -0.99 to 2.40 Nm per year; p=0.31) to the age of 29 ± 3.07 years (95% CI: 22.9 to 35.1 years) where a significant rate of decline of 1.04 Nm per year (95% CI: -1.19 to -0.85 Nm per year; p=0.03) was observed. Knee extensor $TTPT_{240}$ displayed a non-significant improvement (decreased time) of 0.0006 seconds per year (95% CI: -0.005 to 0.004 seconds per year; p=0.54) to the age of 34 ± 1.91 years (95% CI: 30.2 to 37.8 years) where a significant rate of increase of 0.0139 seconds per year (95% CI: 0.011 to 0.015 seconds per year; p=0.02) was observed.

Table 13. Knee Extension Dynamic Strength Parameters

Age	60 degrees per second		240 degrees per second	
	PT (Nm)	TTPT (s)	PT (Nm)	TTPT (s)
20-24	151.8±10.1	0.532±0.09	117.6±21.7	0.217±0.04
25-29	150.4±12.7	0.543±0.08	115.9±36.2‡	0.211±0.03
30-34	146.5±9.9	0.565±0.08‡	111.2±36.4	0.215±0.03‡
35-39	150.9±10.7‡	0.586±0.15	116.2±20.1	0.276±0.03
40-44	140.3±13.7	0.636±0.11	108.7±44.9	0.302±0.04
45-49	135.9±9.9	0.645±0.12	112.9±10.5	0.316±0.04
50-54	128.9±6.2†	0.661±0.08†	86.2±17.9†	0.485±0.04†
55-59	117.8±9.9†	0.741±0.12†	79.7±14.3†	0.484±0.04†
60-64	118.9±8.9†	0.766±0.10†	88.1±11.4†	0.528±0.06†
65-69	112.7±5.9†	0.852±0.11†	85.8±23.1†	0.659±0.05†
70-74	98.6±5.2†	0.863±0.15†	80.3±14.7†	0.722±0.06†
75-79	87.5±7.5†	0.850±0.15†	69.9±16.4†	0.734±0.06†
80-89	79.7±8.8†	0.869±0.10†	59.6±12.3†	0.844±0.09†

Note: Values are presented as mean ± SE. ‡- denotes critical age (breakpoint) from segmental analysis, †- denotes significant difference from reference group (underline). *Abbreviations*: PT- peak torque, Nm- Newton meters, TTPT- time to peak torque, s- seconds.

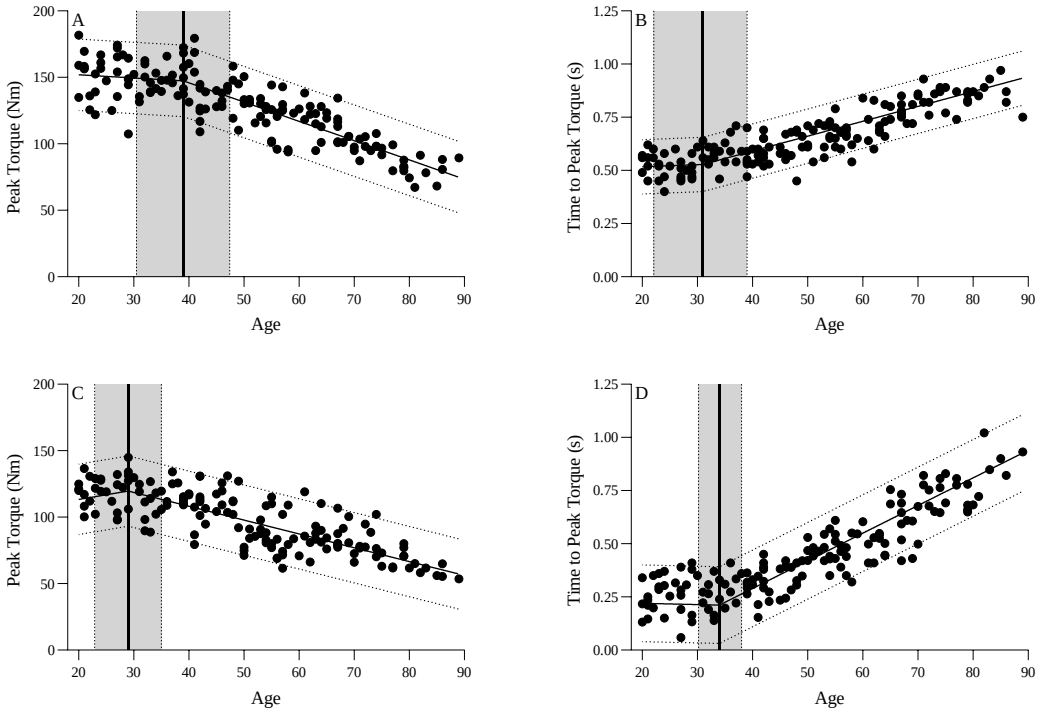

Figure 9. Knee Extension Dynamic Strength Parameters
Figure Legend: *A and B- contractions at 60 deg/s; C and D contractions at 240 deg/s*
Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval.
Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)

Knee Flexion

Age effects were observed for both dynamic strength parameters across both speeds and are displayed in Table 14, Figure 10 (all $p<0.001$). PT_{60} displayed a significant decrease of 0.236 Nm per year (95% CI: -0.45 to -0.02 Nm per year; $p=0.03$) to the age of 44.3 ± 2.7 years (95% CI: 39.0 to 49.7 years) where a significantly accelerated rate of decline of 0.98 Nm per year (95% CI: -1.11 to -0.87 Nm per year; $p=0.007$) was observed. $TTPT_{60}$ displayed a marginal increase in $TTPT_{60}$ of 0.001 seconds per year (95% CI: -0.001 to 0.004 seconds per year; $p=0.18$) to the age of 46 ± 2.8 years (95% CI: 40.4 to 51.6 years) where a significantly accelerated rate of increase of 0.008 seconds per year (95% CI:0.008 to 0.010 seconds per year; $p<0.001$) was observed. PT_{240} displayed a non-

significant rate of decline of 0.192 Nm per year (95% CI: -1.32 to 0.94 Nm per year; p=0.738) to the age of 29 ± 2.9 years (95% CI: 23.4 to 35.6 years) where a significantly accelerated rate of decline of 0.813 Nm per year (95% CI: -0.89 to -0.73 Nm per year; p=0.04) was observed. $TTPT_{240}$ displayed a linear decline with age, suggestive of a loss of 0.006 seconds per year (95% CI: 0.005 to 0.007 seconds).

Table 14. Knee Flexion Dynamic Strength Parameters

Age	60 degrees per second		240 degrees per second	
	PT (Nm)	TTPT (s)	PT (Nm)	TTPT (s)
20-24	114.5±3.2	0.283±0.03	91.1±3.6	0.135±0.02
25-29	113.7±3.9	0.307±0.03	90.9±3.3‡	0.152±0.03
30-34	112.1±3.7	0.301±0.03	90.8±5.2	0.153±0.04
35-39	112.1±2.9	0.322±0.02	87.5±3.3	0.136±0.03
40-44	108.1±3.7‡	0.311±0.03	73.8±3.5†	0.245±0.03†
45-49	109.5±4.1	0.292±0.04‡	66.9±4.2†	0.276±0.04†
50-54	95.2±4.8†	0.355±0.05	70.4±5.1†	0.266±0.04†
55-59	96.5±4.5†	0.446±0.04†	70.3±5.1†	0.284±0.03†
60-64	94.8±4.9†	0.512±0.05†	64.2±4.4†	0.351±0.06†
65-69	91.1±3.4†	0.536±0.05†	58.2±3.3†	0.376±0.05†
70-74	83.8±5.4†	0.608±0.06†	57.2±4.9†	0.445±0.06†
75-79	74.6±5.2†	0.616±0.06†	49.0±3.8†	0.477±0.05†
80-89	65.1±3.9†	0.612±0.09†	45.8±3.4†	0.493±0.07†

Note: Values are presented as mean ± SE. ‡- denotes critical age (breakpoint) from segmental analysis, †- denotes significant difference from reference group (underline). *Abbreviations*: PT- peak torque, Nm- Newton meters, TTPT- time to peak torque, s- seconds.

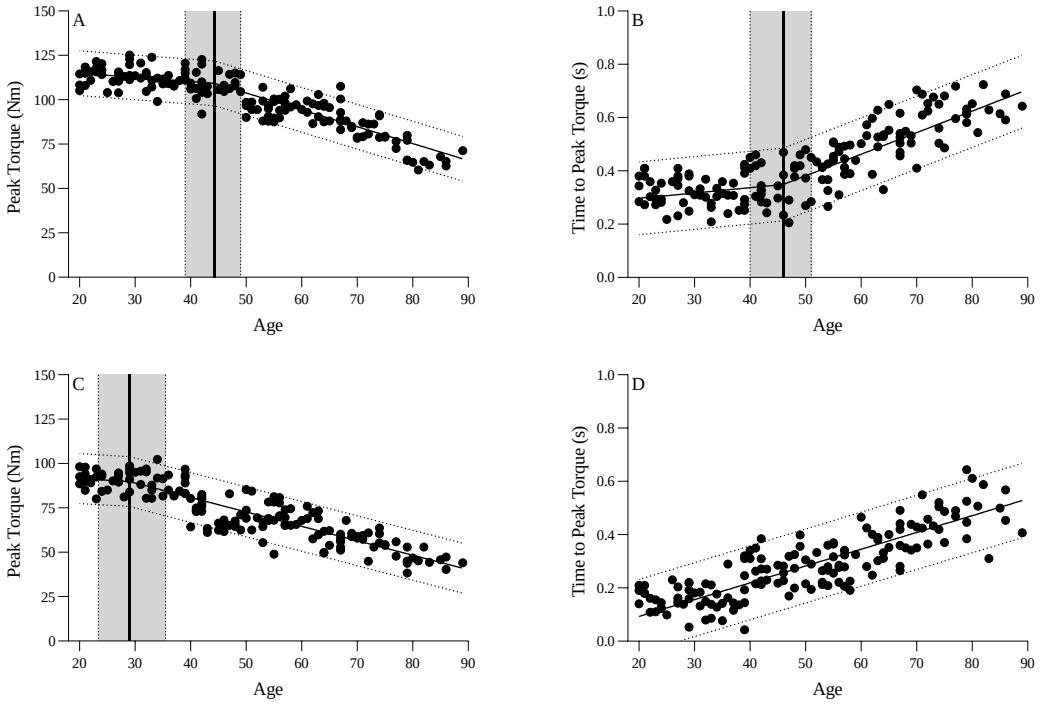

Figure 10. Knee Flexion Dynamic Strength Parameters
Figure Legend: *A and B- contractions at 60 deg/s; C and D- contractions as 240 deg/s*
Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval.
Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)

Plantarflexion

Group effects were observed and are displayed in Table 15, while Figure 11 displays the trends across the lifespan. With age, plantarflexion PT_{60} displayed a non-significant rate of decline of 0.05 Nm per year (95% CI: -0.09 to 0.003 Nm per year; p=0.06) to the age of 63.2 ± 2.1 years (95% CI: 59.1 to 67.4 years) where a significantly accelerated rate of decline of 0.61 Nm per year (95% CI: -0.77 to -0.45 Nm per year; p=0.031) was observed. Plantar flexor $TTPT_{60}$ displayed a significant rate of increase of 0.002 seconds per year (95% CI: 0.001 to 0.003 seconds per year; p<0.001) to the age of 60.1 ± 1.8 years (95% CI: 56.6 to 63.8 years), where a significantly larger rate of increase of 0.013 seconds per year (95% CI: 0.011 to 0.016 seconds per year; p<0.001) was

observed. For PT_{240}, a significant rate of decline of 0.09 Nm per year (95% CI: -0.17 to -0.014 Nm per year; p=0.019) was observed until the age of 51 ± 4.5 years (95% CI: 42.1 to 59.8 years), where a significantly greater rate of decline of 0.31 Nm per year (95% CI: -0.38 to -0.23 Nm per year; p=0.048) was revealed. Plantar flexor $TTPT_{240}$ displayed a borderline significant increase of 0.001 seconds per year (95% CI: -0.00004 to 0.003 seconds per year; p=0.056) until the age of 52.9 ± 4.2 years (95% CI: 44.6 to 61.4 years). Following this age, a significantly greater increase of 0.005 seconds per year (95% CI: 0.004 to 0.007 seconds per year; p=0.002) was observed.

Table 15. Plantarflexion Dynamic Strength Parameters

Age	60 degrees per second		240 degrees per second	
	PT (Nm)	TTPT (s)	PT (Nm)	TTPT (s)
20-24	33.9±1.5	0.256±0.03	24.3±1.6	0.192±0.03
25-29	33.5±2.1	0.259±0.03	23.2±2.2	0.196±0.04
30-34	35.5±2.6	0.257±0.04	22.2±2.0	0.222±0.03
35-39	36.6±2.5	0.314±0.04	21.9±2.4	0.214±0.03
40-44	33.5±2.2	0.279±0.03	21.5±2.0	0.236±0.04
45-49	33.9±1.6	0.273±0.04	22.2±1.7	0.223±0.03
50-54	31.3±2.3	0.296±0.04	22.3±2.2‡	0.208±0.04‡
55-59	31.9±1.9	0.338±0.04	17.9±2.1†	0.289±0.06†
60-64	35.1±2.8‡	0.307±0.04‡	16.5±2.9†	0.305±0.06†
65-69	30.2±2.2†	0.438±0.04†	16.1±2.6†	0.275±0.05
70-74	26.0±2.2†	0.491±0.05†	15.1±1.4†	0.363±0.06†
75-79	24.8±3.0†	0.528±0.04†	14.5±1.8†	0.357±0.06†
80-89	19.6±2.4†	0.634±0.05†	9.5±1.1†	0.427±0.07†

Note: Values are presented as mean ± SE. ‡- denotes critical age (breakpoint) from segmental analysis, †- denotes significant difference from reference group (underline). *Abbreviations*: PT- peak torque, Nm- Newton meters, TTPT- time to peak torque, s- seconds.

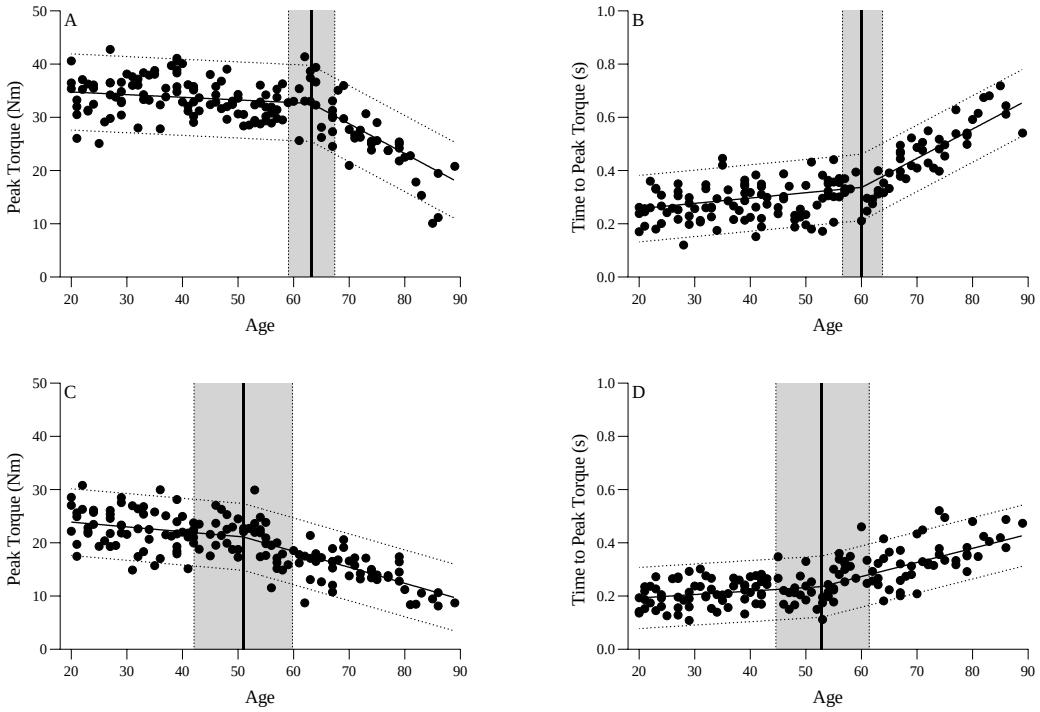

Figure 11. Plantarflexion Dynamic Strength Parameters
Figure Legend: *A and B- contractions at 60 deg/s; C and D- contractions at 240 deg/s*
Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval.
Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)

Dorsiflexion

Age effects in comparison to the reference group are displayed in Table16, Figure 12 (all $p<0.001$). Dorsiflexion PT_{60} displayed a significant rate of decline of 0.11 Nm per year (95% CI: -0.21 to -0.002 Nm per year; $p=0.044$) to the age of 45.2 ± 4.1 years (95% CI: 39.1 to 51.3 years), where a significantly larger rate of decline of 0.23 Nm per year (95% CI: -0.30 to -0.18 Nm per year; $p=0.04$) was observed. With age, dorsiflexion $TTPT_{60}$ significantly increased by 0.001 seconds per year (95% CI: 0.0002 to 0.002 seconds per year; $p<0.001$) to the age of 59 ± 1.3 years (56.3 to 61.7 years) where a significantly larger increase of 0.014 seconds per year (95% CI: 0.012 to 0.017 seconds per year; $p=0.03$) was observed. Dorsiflexion PT_{240} displayed a non-significant rate of

decline of 0.024 Nm per year (95% CI: -0.06 to 0.02 Nm per year; p=0.225) to the age of 64 ± 3.14 years (95% CI: 57.7 to 70.2 years), where a significantly larger rate of decline of 0.332 Nm per year (95% CI: -0.48 to -0.20Nm per year; p=0.009) was observed. A non-significant increase in $TTPT_{240}$ of 0.004 seconds per year (95% CI: -0.002 to 0.003s per year; p=0.39) was observed until the age of 39 ± 2.9 years (95% CI: 33.2 to 44.8 years), thereafter a significantly greater rate of increase of 0.006 seconds per year (95% CI: 0.006 to 0.007 seconds per year; p=0.023) was observed.

Table 16. Dorsiflexion Dynamic Strength Parameters

Age	60 degrees per second		240 degrees per second	
	PT (Nm)	TTPT (s)	PT (Nm)	TTPT (s)
20-24	24.3±1.9	0.355±0.03	21.0±2.3	0.321±0.03
25-29	22.6±2.4	0.361±0.02	22.2±1.8	0.302±0.04
30-34	21.6±1.8	0.371±0.03	23.5±1.7	0.315±0.02
35-39	22.2±2.7	0.391±0.03	21.4±1.4	0.316±0.02‡
40-44	21.4±2.0	0.401±0.03	19.2±2.0	0.338±0.03
45-49	21.1±1.9‡	0.347±0.04	19.5±1.7	0.364±0.03
50-54	21.3±2.4	0.401±0.03	20.7±1.8	0.430±0.05†
55-59	17.4±1.9†	0.401±0.03‡	20.6±2.0	0.438±0.04†
60-64	15.9±2.7†	0.423±0.05	19.7±1.8‡	0.469±0.05†
65-69	13.9±2.1†	0.544±0.05†	18.9±1.7	0.504±0.05†
70-74	13.7±1.5†	0.611±0.05†	16.9±1.9†	0.476±0.05†
75-79	13.8±1.9†	0.656±0.06†	15.2±1.6†	0.606±0.05†
80-89	13.6±1.1†	0.776±0.07†	13.0±1.6†	0.640±0.06†

Note: Values are presented as mean ± SE. ‡- denotes critical age (breakpoint) from segmental analysis, †- denotes significant difference from reference group (underline). *Abbreviations*: PT- peak torque, Nm- newton meters, TTPT- time to peak torque, s- seconds.

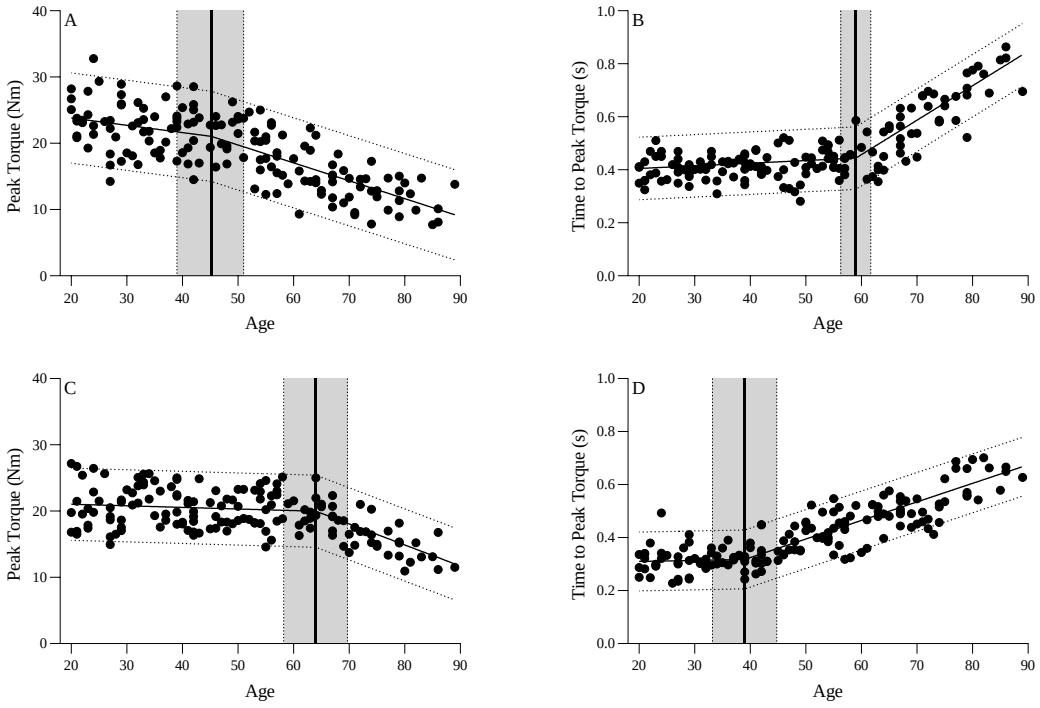

Figure 12. Dorsiflexion Dynamic Strength Parameters
Figure Legend: *A and B- contractions at 60 deg/s; C and D- contractions at 240 deg/s*
Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval.
Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)

Muscular Power

Muscular power was measured using isotonic testing of ballistic contractions tested at an absolute index of 1Nm followed by relative loads corresponding to 20, 40, and 60% of the participants' maximal isometric strength for each muscle group. The following results are separated by joint (elbow then knee) and then by intensity (1Nm to 60%). The four conditions will be referred to as the variable followed by the external load in subscript (e.g. peak power at 20% maximal isometric strength, PP_{20}). Altogether, muscular power revealed the earliest decline during the unloaded condition (absolute power), which was observed earliest in the knee extensors (35 years) followed by the

knee flexors (37 years), elbow extensors (42 years) and elbow flexors (56.4 years). When transitioning into the relative muscular power loads (20, 40 and 60% maximal isometric strength) muscular power was maintained longer during the lifespan, with the 60% condition resulting in critical ages at during the early 50s to 60s across all four muscle groups (elbow extensors: 62 years, elbow flexors: 61 years, knee extensors: 53 years, knee flexors: 60.3 years).

Elbow Extension

Tables 17 to 20 and Figures 13 to 16 display the mean values for each power parameter across each loading condition for the elbow extensors. Also presented in Tables 17 to 20 are the effects of age in comparison to the reference value (all $p<0.001$). PP_{UL} displayed a non-significant increase of 0.003 Watts per year (95% CI: -0.286 to 0.294 Watts per year; $p=0.979$) to the age of 41.9 ± 4.4 years (95% CI: 33.2 to 50.8 years) where a significant rate of decline of 0.581 Watts per year (95% CI: -0.723 to -0.427 Watts per year; $p=0.025$) was observed. PV_{UL} displayed a significant rate of decline of 1.18 deg/s per year (95% CI: -1.81 to -0.53 deg/s per year; $p<0.001$) to the age of 41.9 ± 1.7 years (95% CI: 33.2 to 50.8 years), where a significantly accelerated rate decline of 2.21 deg/s per year (95% CI: -2.72 to -1.71 deg/s per year; $p=0.012$) was observed. $TTPP_{UL}$ displayed a non-significant increase of 0.001 seconds per year (95% CI: -0.001 to 0.002 seconds per year; $p=0.70$) to the age of 38 ± 5.9 years (95% CI: 31.3 to 44.7 years), where a significantly accelerated rate of increase of 0.004 seconds per year (95% CI: 0.002 to 0.005 seconds per year; $p=0.004$) was observed thereafter. $TTPV_{UL}$ displayed a non-significant rate of increase of 0.001 seconds per year (95% CI: -0.0001 to 0.002 seconds per year; $p=0.07$) to the age of 41.4 ± 2.9 years (95% CI: 35.6 to 47.2

years), where a significantly larger rate of increase of 0.0047 seconds per year (95% CI: -0.000 to 0.002 seconds per year; $p<0.001$) was observed.

Table 17. Elbow Extension Unloaded (1 Nm) Power Parameters

Age	Peak Power (Watts)	Peak Velocity (deg/s)	Time to Peak Power (s)	Time to Peak Velocity (s)
20-24	60.1±5.2	271.5±15.9	0.272±0.02	0.293±0.02
25-29	61.2±5.5	263.4±14.9	0.296±0.02	0.327±0.02
30-34	58.2±5.6	253.1±15.5	0.292±0.03	0.306±0.03
35-39	60.4±5.4	241.1±19.2	0.282±0.02‡	0.315±0.02
40-44	62.4±3.8‡	247.3±15.3‡	0.283±0.02	0.314±0.02‡
45-49	59.5±3.9	245.2±15.3	0.319±0.02	0.334±0.03
50-54	62.5±4.8	238.8±11.9	0.325±0.03	0.375±0.02†
55-59	40.8±5.1†	209.5±15.6†	0.342±0.02†	0.408±0.02†
60-64	45.5±4.6†	204.6±14.9†	0.369±0.02†	0.449±0.03†
65-69	43.7±5.9†	184.4±17.2†	0.348±0.02†	0.457±0.02†
70-74	43.0±3.9†	182.7±16.7†	0.367±0.03†	0.475±0.03†
75-79	41.5±5.7†	169.8±18.2†	0.383±0.02†	0.491±0.03†
80-89	41.1±4.5†	167.4±14.8†	0.426±0.04†	0.497±0.03†

Note. Values are presented as mean ± SE. ‡- denotes critical age (breakpoint) from segmental analysis, †- denotes significant difference from reference group (underline). *Abbreviations*: deg/s degrees per second, s- seconds.

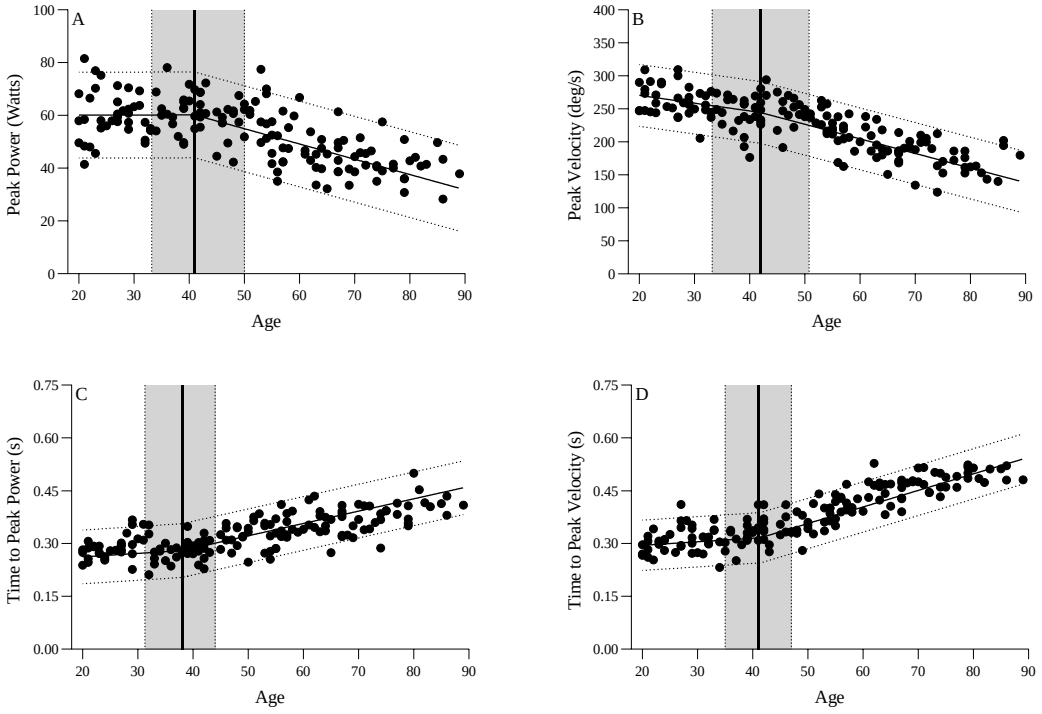

Figure 13. Elbow Extension Unloaded (1 Nm) Power Parameters
Figure Legend: *A- peak power; B- peak velocity; C- time to peak power; D- time to peak velocity Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval. Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)*

Age effects compared to the reference interval are displayed in Table 18. PP_{20} displayed a non-significant increase of 0.113 Watts per year (95% CI: -0.07 to 0.297 Watts per year; p=0.22) to the age of 43.8 ± 1.9 years (95% CI: 39.9 to 47.7 years) where a significant rate of decline of 0.77 Watts per year (95% CI: -0.86 to -0.66 Watts per year; p=0.02) was observed thereafter. PV_{20} displayed a non-significant decline of 0.618 deg/s per year (95% CI: -1.61 to 0.374 deg/s per year; p=0.221) to the age of 47 ± 6.2 years (95% CI: 34.7 to 59.2 years), where a significantly larger rate of decline of 2.32 deg/s per year (95% CI: -2.97 to -1.67 deg/s per year; p=0.001) was observed. $TTPP_{20}$ displayed a non-significant increase of 0.001 seconds per year (95% CI: -0.001 to 0.003 seconds per year; p=0.323) to the age of 39 ± 5.3 years (95% CI: 28.6 to 49.3 years), where a significantly accelerated rate of increase decline of 0.003 seconds per year (95% CI: 0.002 to 0.004 seconds per year; p=0.043) was observed. $TTPV_{20}$ displayed a non-significant increase of 0.001 seconds per year (95% CI: -0.0004 to 0.002 seconds per year; p=0.20) to the age of 43.3 ± 3 years (95% CI: 37.4 to 49.2 years), where then a significantly greater rate of increase of 0.005 seconds per year (95% CI: 0.003 to 0.007 seconds per year; p<0.001) was observed.

Table 18. Elbow Extension Power Parameters at 20% Maximum Strength

Age	Peak Power (Watts)	Peak Velocity (deg/s)	Time to Peak Power (s)	Time to Peak Velocity (s)
20-24	69.9±2.9	244.9±6.50	0.256±0.02	0.318±0.02
25-29	66.9±2.9	249.0±12.8	0.281±0.02	0.315±0.02
30-34	71.4±3.4	242.5±8.02	0.268±0.02	0.316±0.03
35-39	69.2±3.6	246.5±9.31	0.270±0.03‡	0.323±0.03
40-44	72.2±3.0‡	220.7±6.54	0.282±0.01	0.332±0.02‡
45-49	70.8±3.1	233.3±10.4‡	0.301±0.02	0.348±0.03
50-54	65.2±3.2	211.9±9.19	0.325±0.02†	0.381±0.03†
55-59	62.8±3.5†	228.4±12.4	0.329±0.02†	0.373±0.03
60-64	52.9±3.7†	192.0±8.18†	0.337±0.02†	0.429±0.03†
65-69	52.9±3.8†	174.6±8.60†	0.344±0.03†	0.468±0.02†
70-74	47.8±3.7†	172.3±10.4†	0.354±0.02†	0.485±0.04†
75-79	42.6±5.1†	141.4±12.3†	0.363±0.03†	0.527±0.04†
80-89	46.2±6.1†	165.4±5.59†	0.411±0.02†	0.503±0.04†

Note. Values are presented as mean ± SE. ‡- denotes critical age (breakpoint) from segmental analysis, †- denotes significant difference from reference group (underline). *Abbreviations*: deg/s degrees per second, s- seconds.

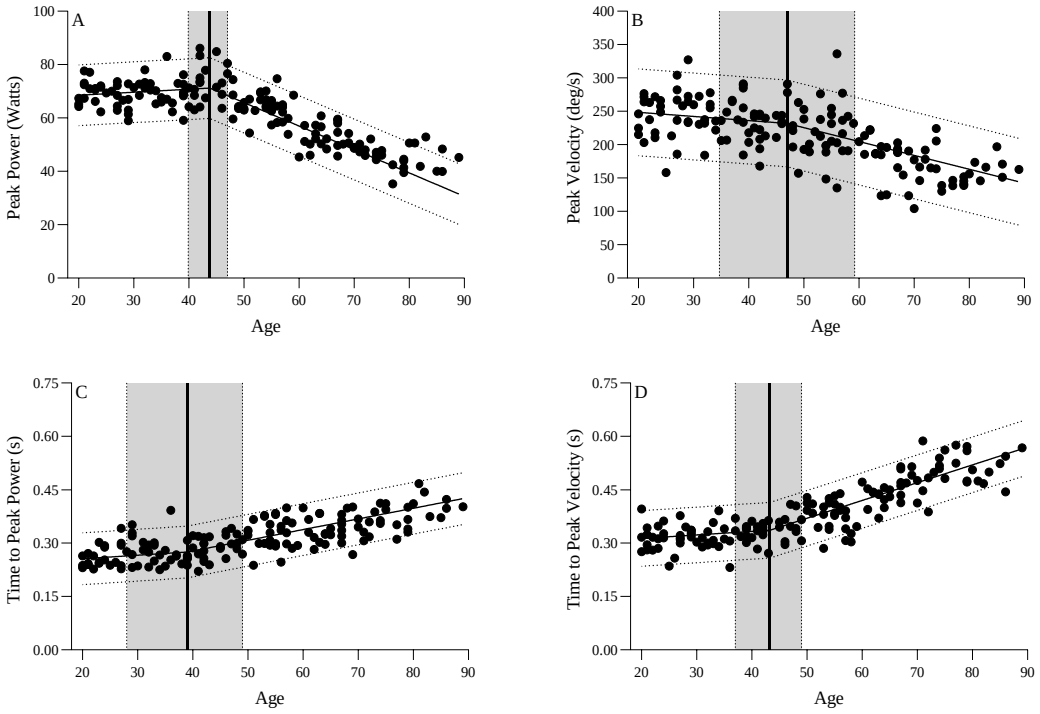

Figure 14. Elbow Extension Power Parameters at 20% Maximum Strength
Figure Legend: *A- peak power; B- peak velocity; C- time to peak power; D- time to peak velocity*
Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval.
Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)

Table 19 displays the mean values for the power parameters at 40% maximum strength. Significant effects for age were observed across all parameters (Table 19, all

$p<0.001$). PP_{40} displayed a non-significant increase of 0.017 Watts per year (95% CI: -0.10 to 0.13 Watts per year; $p=0.77$) to the age of 55.7 ± 2.6 years (95% CI: 50.6 to 60.7 years), where a significantly accelerated decline of 0.755 Watts per year (95% CI: -0.91 to -0.56 Watts per year; $p=0.04$) was observed. PV_{40} presented a significant rate of decline of 0.65 deg/s per year (95% CI: -1.04 to -0.25 deg/s per year; $p<0.001$) to the age of 53 ± 3.2 years (46.5 to 59.4), where a significantly accelerated rate of decline of 2.15 deg/s per year (95% CI: -2.89 to -1.68 deg/s per year; $p=0.018$) was observed. $TTPP_{40}$ displayed a non-significant increase of 0.0004 seconds per year (95% CI: -0.0004 to 0.001 seconds per year; $p=0.35$) to the age of 48.4 ± 4.3 years (95% CI: 39.8 to 56.9 years), where then a significantly accelerated rate of increase of 0.002 seconds per year (95% CI: 0.001 to 0.004 seconds per year; $p=0.006$) was observed. $TTPV_{40}$ displayed a non-significant increase of 0.0003 seconds per year (95% CI: -0.0006 to 0.001 seconds per year; $p=0.43$) to the age of 48.7 ± 2.2 years (95% CI: 44.4 to 53.2 years), where a significantly larger rate of increase of 0.006 seconds per year (95% CI: 0.004 to 0.008 seconds per year; $p=0.043$) was observed.

Table 19. Elbow Extension Power Parameters at 40% Maximum Strength

Age	Peak Power (Watts)	Peak Velocity (deg/s)	Time to Peak Power (s)	Time to Peak Velocity (s)
20-24	56.4±3.4	234.3±13.8	0.294±0.02	0.338±0.05
25-29	57.1±4.9	226.9±9.4	0.289±0.02	0.346±0.04
30-34	59.5±4.9	222.7±9.9	0.305±0.02	0.326±0.03
35-39	58.5±3.0	221.7±12.6	0.317±0.02	0.348±0.05
40-44	57.1±3.7	213.5±10.6	0.311±0.02	0.350±0.04
45-49	56.2±4.9	218.5±11.9	0.293±0.02‡	0.344±0.02‡
50-54	57.2±3.2	211.6±7.9‡	0.313±0.02	0.375±0.03
55-59	59.4±3.2‡	211.9±8.9	0.323±0.02	0.391±0.04†
60-64	51.2±4.0	188.2±12.5†	0.363±0.03†	0.410±0.03†
65-69	53.3±3.1	172.9±11.6†	0.376±0.03†	0.442±0.03†
70-74	37.8±4.2†	155.7±10.5†	0.382±0.03†	0.483±0.03†
75-79	42.8±4.3†	156.5±14.3†	0.391±0.04†	0.505±0.03†
80-89	39.5±4.0†	148.3±15.0†	0.394±0.04†	0.542±0.04†

Note. Values are presented as mean ± SE. ‡- denotes critical age (breakpoint) from segmental analysis, †- denotes significant difference from reference group (underline). *Abbreviations*: deg/s degrees per second, s- seconds.

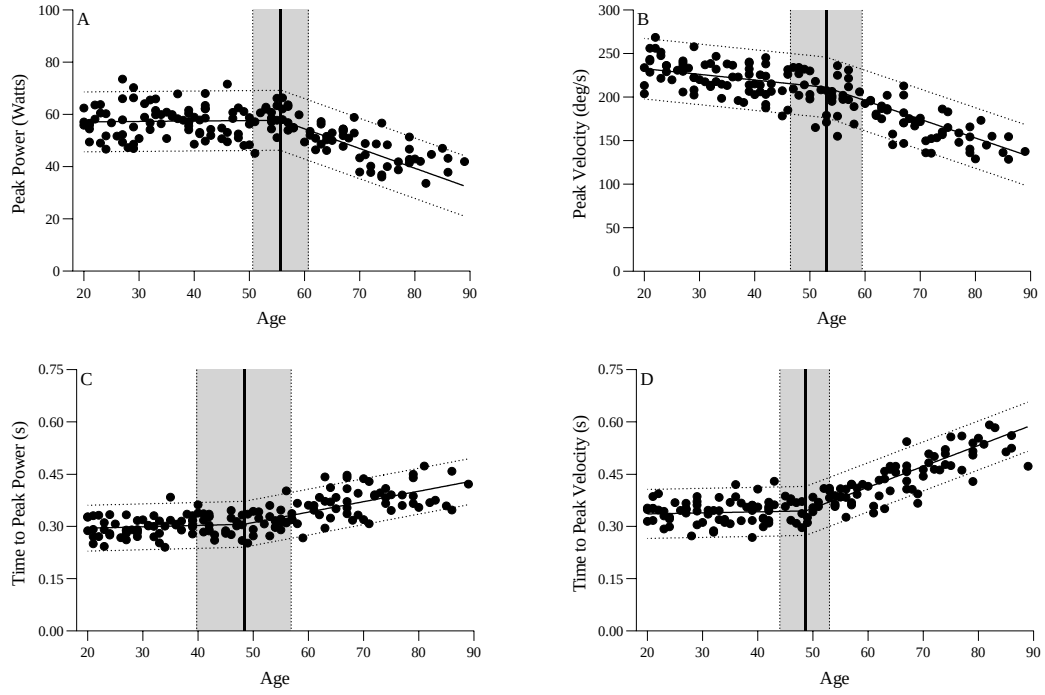

Figure 15. Elbow Extension Power Parameters at 40% Maximum Strength
Figure Legend: *A- peak power; B- peak velocity; C- time to peak power; D- time to peak velocity*
Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval.
Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)

Table 20 displays the mean elbow extensor parameters and effects of age (all $p<0.001$) in comparison to the reference group for each parameter for the 60% condition. PP_{60} displayed a significant rate of decline of 0.069 Watts per year (95% CI: -0.12 to -0.02 Watts per year; $p=0.012$) to the age of 62 ± 1.9 years (95% CI: 58.2 to 65.8 years), where a significantly accelerated rate of decline of 0.614 Watts per year (95% CI: -0.83 to -0.53 Watts per year; $p<0.001$) was observed. PV_{60} displayed a non-significant rate of decline of 0.168 deg/s per year (95% CI: -0.49 to 0.16 deg/s per year; $p=0.321$) to the age of 55.7 ± 2.9 years (95% CI: 49.9 to 61.7 years). Following this breakpoint, a significantly greater rate of decline of 1.98 deg/s per year (95% CI: -2.49 to -1.47 deg/s per year; $p=0.008$) was observed. $TTPP_{60}$ displayed a significant rate of increase of 0.001 seconds

per year (95% CI: 0.0001 to 0.001 seconds per year; p=0.027) to the age 63.4 ± 1.4 years (95% CI: 60.6 to 66.2 years), thereafter a significantly accelerated rate of increase of 0.009 seconds per year (95% CI: 0.007 to 0.010 seconds; p=0.01) was observed. $TTPV_{60}$ displayed a significant rate of increase of 0.0006 seconds per year (95% CI: 0.000014 to 0.0012 seconds per year; p=0.045) to the age of 64 ± 1.7 years (95% CI: 60.5 to 67.4 years), where a significantly larger rate of increase of 0.008 seconds per year (95% CI: 0.006 to 0.010 seconds per year; p=0.04) was observed.

Table 20. Elbow Extension Power Parameters at 60% Maximum Strength

Age	Peak Power (Watts)	Peak Velocity (deg/s)	Time to Peak Power (s)	Time to Peak Velocity (s)
20-24	34.7±1.7	138.5±12.8	0.306±0.01	0.349±0.01
25-29	37.2±2.4	140.2±12.3	0.320±0.02	0.340±0.02
30-34	34.9±1.7	133.9±10.9	0.310±0.02	0.339±0.02
35-39	33.7±2.2	141.1±12.8	0.320±0.02	0.339±0.02
40-44	34.1±1.9	135.8±10.3	0.305±0.01	0.350±0.01
45-49	33.2±1.9	135.6±11.2	0.337±0.02	0.343±0.02
50-54	34.8±1.7	129.5±10.7	0.329±0.02	0.365±0.02
55-59	31.9±2.2	134.3±10.5‡	0.329±0.02	0.373±0.02
60-64	34.8±3.0‡	123.9±14.3	0.319±0.02‡	0.351±0.02‡
65-69	28.5±2.4†	112.1±11.9	0.365±0.04†	0.377±0.02
70-74	25.5±2.9†	99.9±10.9†	0.408±0.05†	0.436±0.03†
75-79	20.7±2.3†	88.1±14.4†	0.470±0.04†	0.520±0.03†
80-89	18.7±3.6†	77.3±13.4†	0.499±0.04†	0.518±0.02†

Note. Values are presented as mean ± SE. ‡- denotes critical age (breakpoint) from segmental analysis, †- denotes significant difference from reference group (underline). *Abbreviations*: deg/s degrees per second, s- seconds.

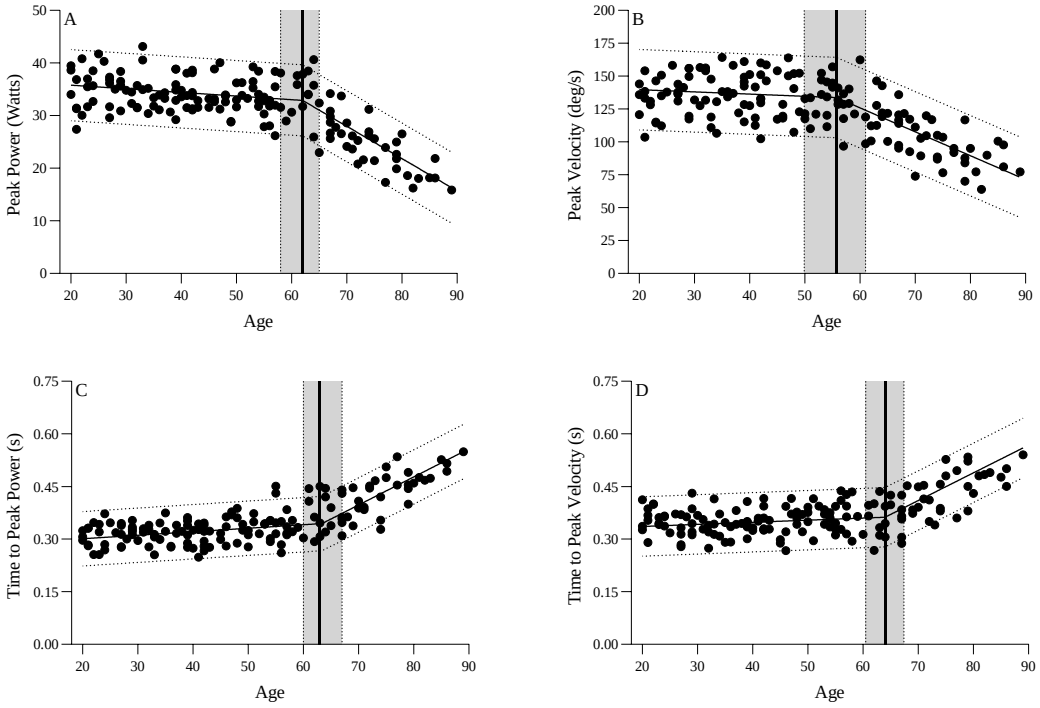

Figure 16. Elbow Extension Power Parameters at 60% Maximum Strength
Figure Legend: *A- peak power; B- peak velocity; C- time to peak power; D- time to peak velocity Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval. Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)*

Elbow Flexion

Elbow flexion power parameters are displayed in tables 21 to 24 and Figures 17 to 20. As expected, across all loading conditions, there were significant group effects (all $p<0.001$). Group differences when compared to the reference value (underlined in table) are displayed those tables (Tables 21 to 24, respectively). PP_{UL} displayed a non-significant increase of 0.020 Watts per year (95% CI: -0.07 to 0.11 Watts per year; $p=0.65$) to the age of 56.4 ± 2.5 years (95% CI: 51.5 to 61.4 years), where then a significant rate of decline of 0.645 Watts per year (95% CI: -0.78 to -0.46 Watts per year; $p=0.003$) was observed. PV_{UL} displayed a non-significant rate of decline of 0.304 deg/s per year (95% CI: -0.698 to 0.090 deg/s per year; $p=0.13$) to the age of 58.3 ± 3.4 years

(95% CI: 51.6 to 64.9 years), where then a significantly larger rate of decline of 2.35 deg/s per year (95% CI: -3.51 to -1.81deg/s per year; p=0.037) was observed. $TTPP_{UL}$ displayed a non-significant rate of increase of 0.001 seconds per year (95% CI: -0.0005 to 0.0008 seconds per year; p=0.74) to the age of 53.5 ± 1.9 years (95% CI: 49.7 to 57.2 years), where then a significantly larger rate of increase of 0.0051 seconds per year (95% CI: 0.0045 to 0.0061 seconds per year; p=0.004) was observed. $TTPV_{UL}$ displayed a non-significant increase of 0.0008 seconds per year (95% CI: -0.0007 to 0.0017 seconds per year; p=0.07) to the age of 53.8 ± 1.5 years (95% CI: 50.7 to 56.9 years). Following this age, a significantly larger rate of increase of 0.009 seconds per year (95% CI: 0.008 to 0.010 seconds per year; p=0.011) was observed.

Table 21. Elbow Flexion Unloaded (1 Nm) Power Parameters

Age	Peak Power (Watts)	Peak Velocity (deg/s)	Time to Peak Power (s)	Time to Peak Velocity (s)
20-24	33.2±2.6	221.9±12.8	0.318±0.01	0.351±0.02
25-29	36.9±2.9	226.5±13.5	0.324±0.02	0.361±0.02
30-34	35.9±3.3	213.4±15.7	0.313±0.02	0.392±0.02
35-39	32.7±3.5	228.6±12.3	0.286±0.02	0.367±0.02
40-44	35.6±2.8	228.3±11.8	0.322±0.01	0.381±0.01
45-49	35.1±3.1	204.8±12.9	0.329±0.02	0.369±0.02
50-54	34.7±2.7	208.9±16.5	0.318±0.02‡	0.390±0.02‡
55-59	36.5±3.7‡	223.8±11.9‡	0.331±0.02	0.396±0.02
60-64	36.3±3.3	209.6±13.5	0.379±0.02†	0.465±0.02†
65-69	23.4±3.8†	183.1±13.5†	0.369±0.02†	0.504±0.03†
70-74	22.2±2.4†	168.9±11.6†	0.422±0.02†	0.581±0.02†
75-79	22.4±3.8†	161.6±10.3†	0.448±0.02†	0.624±0.03†
80-89	21.4±2.9†	152.3±10.9†	0.485±0.03†	0.647±0.03†

Note. Values are presented as mean ± SE. ‡- denotes critical age (breakpoint) from segmental analysis, †- denotes significant difference from reference group (underline). *Abbreviations*: deg/s degrees per second, s- seconds.

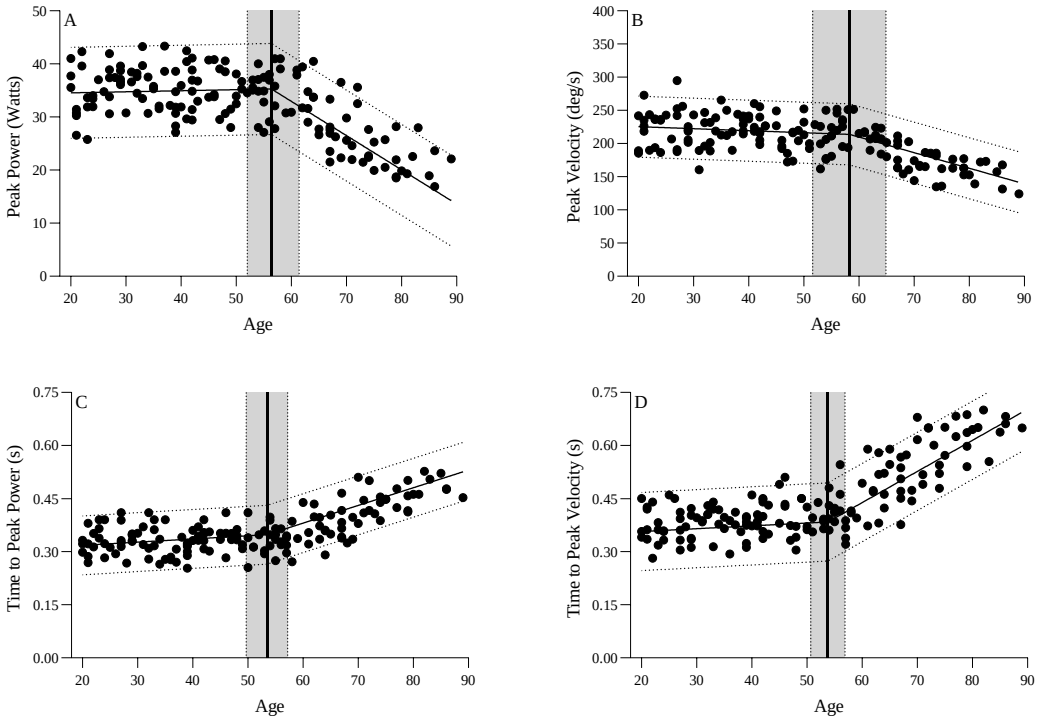

Figure 17. Elbow Flexion Unloaded (1 Nm) Power Parameters
Figure Legend: *A- peak power; B- peak velocity; C- time to peak power; D- time to peak velocity*
Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval.
Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)

PP_{20} (Table 22) displayed a non-significant rate of decline of 0.027 Watts per year (95% CI: -0.12 to 0.07 Watts per year; p=0.59) to the age of 54.8 ± 2.8 years (95% CI: 48.3 to 59.6 years), where then a significantly accelerated rate of decline of 0.497 Watts per year (95% CI: -0.641 to -0.372 Watts per year; p=0.042) was observed. PV_{20} displayed a significant rate of decline of 0.379 deg/s per year (95% CI: -0.62 to -0.14 deg/s per year; p=0.002) to the age of 62.8 ± 2.3 years (95% CI: 58.3 to 67.3 years), which was followed by a significantly greater rate of decline of 2.23 deg/s per year (95% CI: -3.26 to -1.96 deg/s per year; p=0.012). $TTPP_{20}$ displayed a significant increase of 0.0009 seconds per year (95% CI: 0.00035 to 0.0015 seconds per year; p<0.001) to the age of 60.4 ± 2.1 years (95% CI: 56.2 to 64.6 years). Following this breakpoint, a

significantly accelerated rate of increase of 0.008 seconds per year (95% CI: 0.0050 to 0.008 seconds per year; p=0.007) was observed. $TTPV_{20}$ displayed a non-significant rate of increase of 0.0008 seconds per year (95% CI: -0.0006 to 0.0007 seconds per year; p=0.82) to the age of 55 ± 3.8 years (95% CI: 47.4 to 62.5 years). Following this age, a significantly larger rate of increase of 0.004 seconds per year (95% CI: 0.008 to 0.010 seconds per year; p=0.007) was observed.

Table 22. Elbow Flexion Power Parameters at 20% Maximum Strength

Age	Peak Power (Watts)	Peak Velocity (deg/s)	Time to Peak Power (s)	Time to Peak Velocity (s)
20-24	43.2±2.6	183.7±10.1	0.338±0.03	0.371±0.01
25-29	44.8±2.7	184.1±11.3	0.332±0.01	0.379±0.02
30-34	44.9±3.3	180.7±11.5	0.349±0.02	0.372±0.02
35-39	43.5±3.2	179.1±10.1	0.359±0.03	0.396±0.02
40-44	42.4±2.8	177.8±11.0	0.349±0.02	0.366±0.02
45-49	44.7±2.6	170.7±10.7	0.376±0.02	0.383±0.02
50-54	43.1±2.6‡	182.1±10.0	0.377±0.02	0.375±0.02
55-59	41.5±3.3	168.6±10.4	0.350±0.02	0.385±0.02‡
60-64	39.4±3.0	172.1±12.0‡	0.392±0.02†‡	0.390±0.02
65-69	35.4±3.7†	151.7±13.4†	0.424±0.03†	0.400±0.02
70-74	33.1±2.4†	144.6±10.1†	0.432±0.02†	0.453±0.02†
75-79	31.5±3.4†	131.8±12.1†	0.496±0.03†	0.453±0.03†
80-89	27.2±3.2†	114.5±13.1†	0.534±0.03†	0.464±0.03†

Note. Values are presented as mean ± SE. ‡- denotes critical age (breakpoint) from segmental analysis, †- denotes significant difference from reference group (underline). *Abbreviations*: deg/s degrees per second, s- seconds.

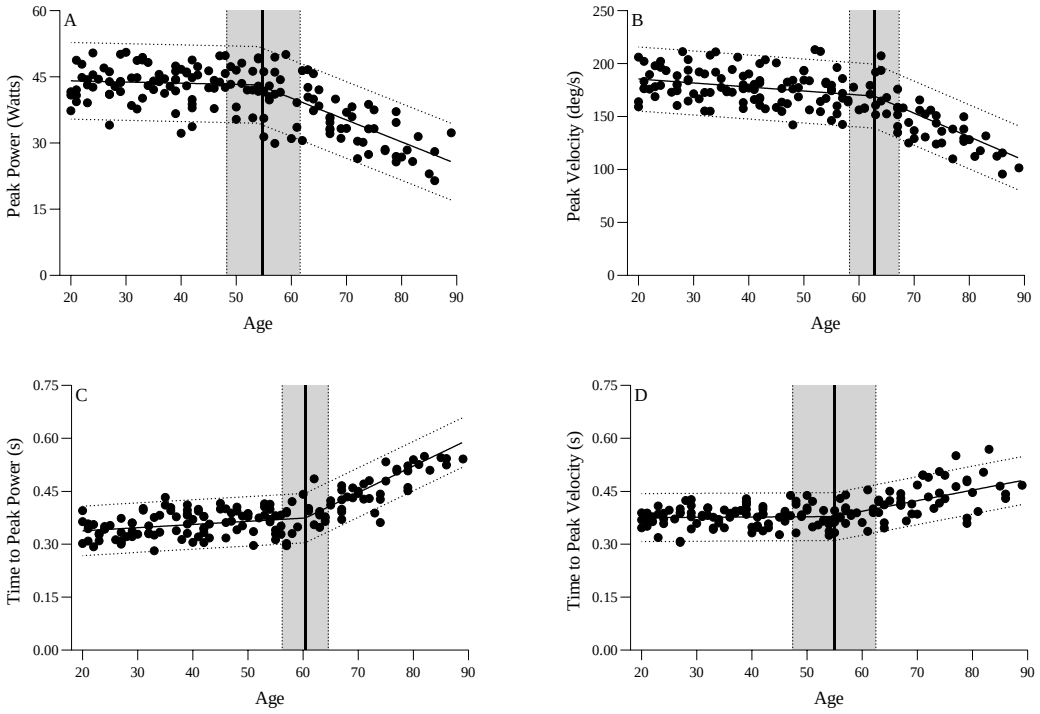

Figure 18. Elbow Flexion Power Parameters at 20% Maximum Strength
Figure Legend: *A- peak power; B- peak velocity; C- time to peak power; D- time to peak velocity*
Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval.
Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)

PP_{40} (Table 23) displayed a non-significant decline of 0.023 Watts per year (95% CI: -0.04 to 0.05 Watts per year; p=0.51) to the age of 61.1 ± 2.5 years (95% CI: 55.9 to 66.1 years), where then a significantly greater rate of decline of 0.540 Watts per year (95% CI: -0.59 to -0.32 Watts per year; p=0.021) was observed. PV_{40} displayed a non-significant decline of 0.18 deg/s per year (95% CI: -0.47 to 0.10 deg/s per year; p=0.21) to the age of 58.0 ± 2.6 years (95% CI: 52.8 to 63.2 years). Thereafter, a significantly larger rate of decline of 2.36 deg/s per year (95% CI: -2.98 to -1.75 deg/s per year; p=0.032) was observed. $TTPP_{40}$ displayed a significant rate of increase of 0.0005 seconds per year (95% CI: 0.0009 to 0.0015 seconds per year; p=0.04) to the age of 57.2 ± 2.7 years (95% CI: 51.8 to 62.5 years). Thereafter, a significantly larger rate of increase of

0.004 seconds per year (95% CI: 0.003 to 0.005 seconds per year; p=0.008) was observed. $TTPV_{40}$ displayed a non-significant rate of increase of 0.0004 seconds per year (95% CI: -0.0005 to 0.0008 seconds per year; p=0.08) to the age of 67 ± 4.6 years (95% CI: 57.9 to 76.1 years). Following this breakpoint, a significantly larger rate of increase of 0.0033 seconds per year (95% CI: 0.001 to 0.005 seconds per year; p=0.039) was observed.

Table 23. Elbow Flexion Power Parameters at 40% Maximum Strength

Age	Peak Power (Watts)	Peak Velocity (deg/s)	Time to Peak Power (s)	Time to Peak Velocity (s)
20-24	25.7±1.6	159.3±9.5	0.349±0.01	0.382±0.01
25-29	24.8±2.4	171.9±10.1	0.361±0.02	0.402±0.02
30-34	26.1±1.7	160.3±12.6	0.356±0.02	0.401±0.02
35-39	24.4±2.0	157.4±10.3	0.360±0.02	0.396±0.01
40-44	24.5±2.1	168.6±10.9	0.367±0.01	0.398±0.01
45-49	26.5±1.9	148.7±11.0	0.376±0.01	0.375±0.01
50-54	25.4±2.1	158.1±11.1	0.358±0.02	0.408±0.02
55-59	23.8±1.8	157.6±10.7‡	0.377±0.03‡	0.410±0.02
60-64	24.6±2.1‡	159.2±13.3	0.386±0.02	0.398±0.02
65-69	22.2±1.8	134.0±10.5†	0.432±0.03†	0.398±0.03‡
70-74	19.3±2.4†	112.2±10.1†	0.422±0.02†	0.438±0.01†
75-79	15.1±2.7†	108.3±11.2†	0.468±0.02†	0.433±0.04
80-89	15.1±2.0†	101.0±14.1†	0.497±0.03†	0.469±0.02†

Note. Values are presented as mean ± SE. ‡- denotes critical age (breakpoint) from segmental analysis, †- denotes significant difference from reference group (underline). *Abbreviations*: deg/s degrees per second, s- seconds.

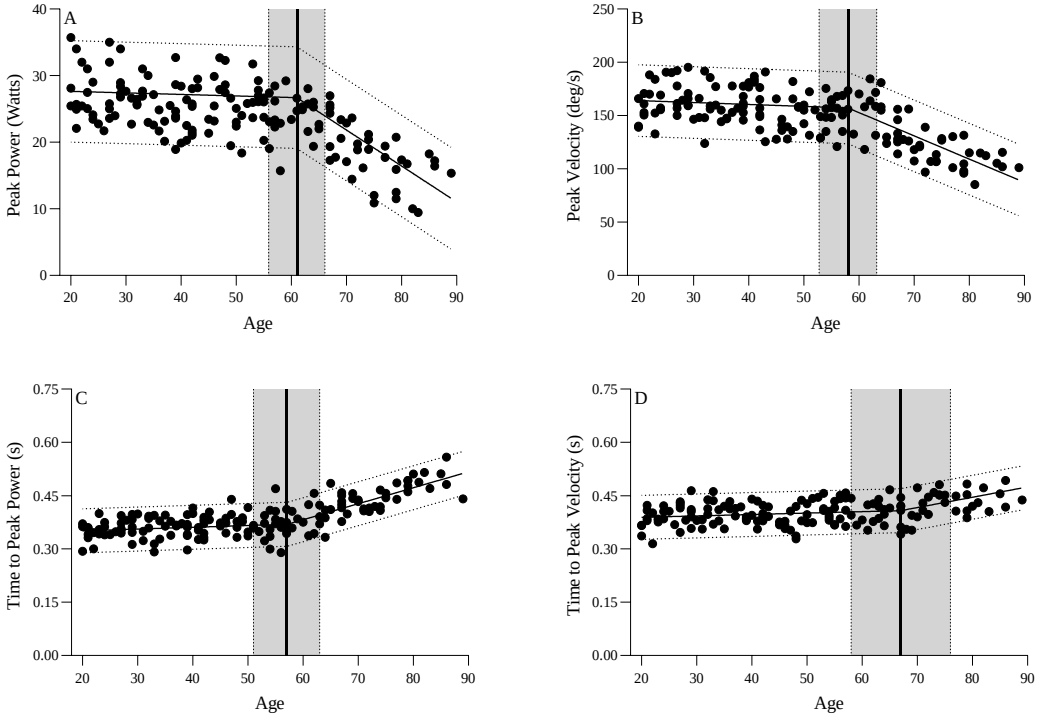

Figure 19. Elbow Flexion Power Parameters at 40% Maximum Strength
Figure Legend: *A- peak power; B- peak velocity; C- time to peak power; D- time to peak velocity*
Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval.
Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)

PP_{60} (Table 24) displayed a non-significant increase of 0.003 Watts per year (95% CI: -0.04 to 0.05 Watts per year; p=0.88) to the age of 61.1 ± 1.7 years (95% CI: 57.9 to 64.4 years) where then, a significantly larger rate of decline of 0.548 Watts per year (95% CI: -0.65 to -0.43 Watts per year; p<0.001) was observed. PV_{60} displayed a significant rate of decline of 0.336 deg/s per year (95% CI: -0.53 to 0.15 deg/s per year; p<0.001) to the age of 63.2 ± 2.8 years (95% CI: 57.7 to 68.8 years). Following this breakpoint, a significantly greater rate of decline of 1.575 deg/s per year (95% CI: -2.50 to -1.32 deg/s per year; p=0.034) was observed. $TTPP_{60}$ displayed a non-significant rate of decline of 0.0001 seconds per year (95% CI: -0.001 to 0.001 seconds per year; p=0.718) to the age of 60.2 ± 2.4 years (95% CI: 55.4 to 64.9 years). Thereafter, a significant rate of increase

of 0.005 seconds per year (95% CI: 0.003 to 0.007 seconds per year; $p<0.001$) was observed. $TTPV_{60}$ displayed a non-significant rate of increase of 0.0004 seconds per year (95% CI: -0.00001 to 0.001 seconds per year; $p=0.06$) to the age of 64.9 ± 2.9 years (95% CI: 59.2 to 70.7 years). Following this age, a significantly accelerated rate of increase of 0.0041 seconds per year (95% CI: 0.0028 to 0.0062 seconds per year; $p=0.007$) was observed.

Table 24. Elbow Flexion Power Parameters at 60% Maximum Strength

Age	Peak Power (Watts)	Peak Velocity (deg/s)	Time to Peak Power (s)	Time to Peak Velocity (s)
20-24	23.4±1.9	126.9±12.3	0.357±0.01	0.409±0.01
25-29	23.1±1.9	126.7±10.3	0.374±0.02	0.421±0.02
30-34	21.2±1.7	129.2±13.1	0.386±0.02	0.423±0.02
35-39	21.4±2.1	131.2±11.9	0.368±0.02	0.418±0.02
40-44	22.8±2.2	128.7±10.1	0.369±0.01	0.424±0.01
45-49	23.2±2.5	119.1±12.4	0.358±0.02	0.419±0.01
50-54	23.8±1.9	112.4±10.2	0.365±0.02	0.431±0.02
55-59	22.5±1.7	122.1±11.1	0.366±0.03	0.432±0.02
60-64	21.2±2.2‡	119.5±10.7‡	0.375±0.02‡	0.434±0.02‡
65-69	20.7±1.8	103.3±6.9†	0.385±0.04	0.443±0.03
70-74	16.1±1.7†	102.3±9.3†	0.450±0.04†	0.468±0.02
75-79	14.1±2.4†	84.52±10.5†	0.443±0.04†	0.487±0.03†
80-89	9.90±2.0†	78.31±9.0†	0.486±0.05†	0.522±0.02†

Note. Values are presented as mean ± SE. ‡- denotes critical age (breakpoint) from segmental analysis, †- denotes significant difference from reference group (underline). *Abbreviations*: deg/s degrees per second, s- seconds.

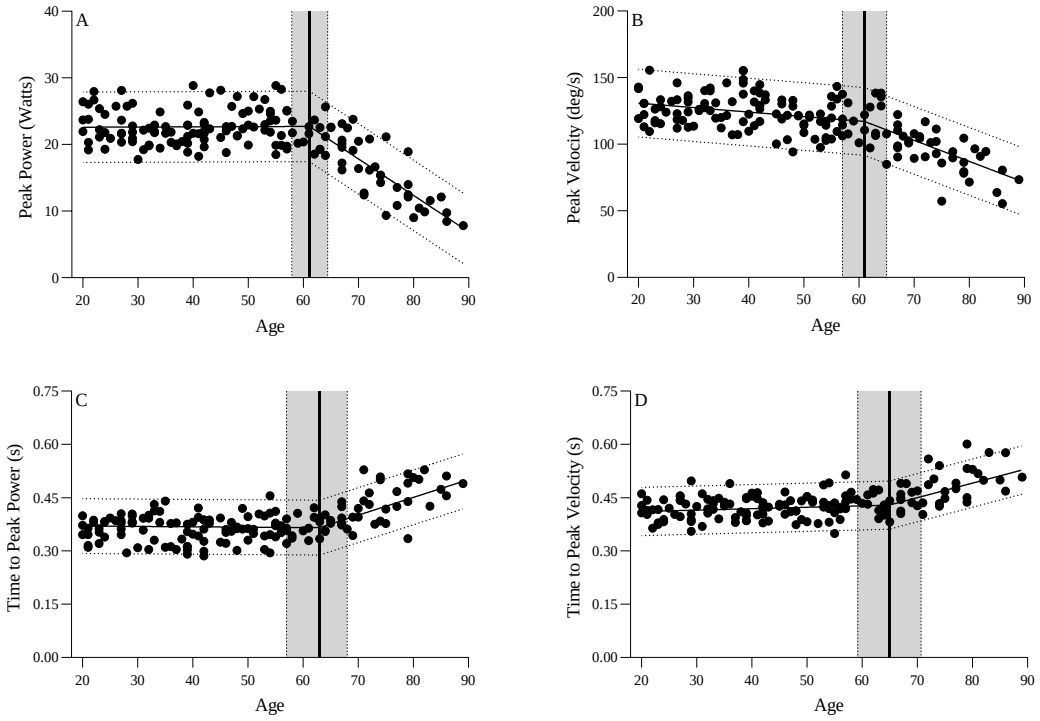

Figure 20. Elbow Flexion Power Parameters at 60% Maximal Strength
Figure Legend: *A- peak power; B- peak velocity; C- time to peak power; D- time to peak velocity*
Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval.
Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)

Knee Extension

Knee extension power parameters are presented in tables 25 to 28 and Figures 21 to 24. As expected, there were significant group effects across all loading conditions (all $p<0.001$). Group differences when compared to the reference value (underlined in table) are displayed accordingly (Tables 25 to 28, respectively). PP_{UL} displayed a non-significant rate of increase of 1.637 Watts per year (95% CI: -0.98 to 4.26 Watts per year; $p=0.22$) to the age of 35 ± 2.9 years (95% CI: 29.3 to 40.6 years), where then a significant rate of decline of 3.750 Watts per year (95% CI: -4.71 to -2.77 Watts per year; $p=0.003$) was observed. PV_{UL} displayed a non-significant rate of increase of 1.34 deg/s per year (95% CI: -2.91 to 5.59 deg/s per year; $p=0.54$) to the age of 37.3 ± 3.2 years (95% CI:

31.1 to 43.5 years). After this breakpoint, a significant rate of decline of 8.20 deg/s per year (95% CI: -9.13 to -7.04 deg/s per year; p=0.03) was observed. $TTPP_{UL}$ displayed a non-significant rate of decline of 0.0003 seconds per year (95% CI: -0.001 to 0.006 seconds per year; p=0.52) to the age of 37 ± 3.4 years (95% CI: 30.2 to 43.8 years). After this age, a significantly larger rate of increase of 0.002 seconds per year (95% CI: 0.001 to 0.002 seconds per year; p=0.047) was observed. $TTPV_{UL}$ displayed a non-significant rate of increase of 0.0003 seconds per year (95% CI: -0.0005 to 0.001 seconds per year; p=0.41) to the age of 40 ± 4.8 years (95% CI: 30.6 to 49.4 years). Thereafter, a significantly accelerated increase of 0.002 seconds per year (95% CI: 0.001 to 0.002 seconds per year; p=0.004) was observed.

Table 25. Knee Extension Unloaded (1 Nm) Power Parameters

Age	Peak Power (Watts)	Peak Velocity (deg/s)	Time to Peak Power (s)	Time to Peak Velocity (s)
20-24	309.7±70.5	524.5±105.8	0.179±0.01	0.230±0.01
25-29	330.8±65.4	538.3±64.5	0.170±0.02	0.236±0.02
30-34	318.5±57.1	541.3±100.9	0.177±0.01	0.237±0.01
35-39	326.7±66.0‡	540.7±120.8‡	0.173±0.02‡	0.238±0.02
40-44	325.8±58.7	492.8±116.9	0.177±0.02	0.230±0.02‡
45-49	284.3±63.5	479.5±116.9	0.174±0.02	0.247±0.02
50-54	269.5±78.4†	468.9±77.9	0.198±0.02	0.271±0.02†
55-59	250.5±73.2†	414.1±82.3†	0.208±0.02†	0.267±0.03†
60-64	247.2±75.8†	402.6±48.8†	0.205±0.05	0.266±0.05†
65-69	247.8±54.1†	315.3±79.6†	0.228±0.01†	0.294±0.01†
70-74	235.5±62.9†	269.5±92.3†	0.218±0.02†	0.300±0.02†
75-79	220.3±73.5†	251.4±46.3†	0.229±0.02†	0.299±0.02†
80-89	128.9±39.8†	227.1±53.6†	0.235±0.02†	0.299±0.02†

Note. Values are presented as mean ± SE. ‡- denotes critical age (breakpoint) from segmental analysis, †- denotes significant difference from reference group (underline). *Abbreviations*: deg/s degrees per second, s- seconds.

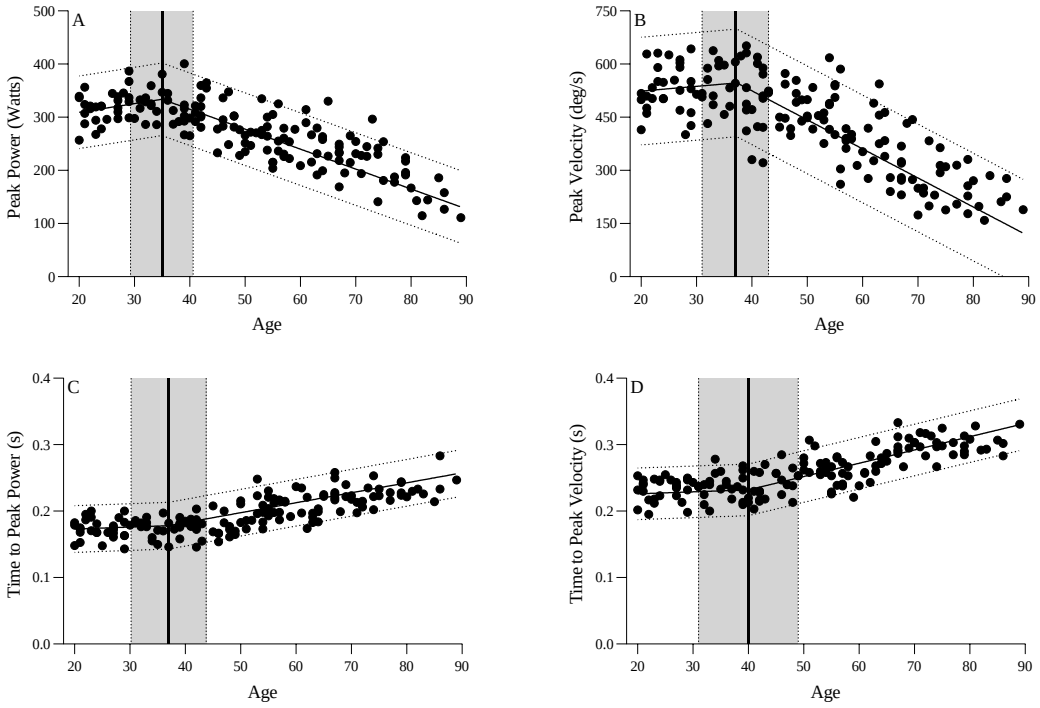

Figure 21. Knee Extension Unloaded (1 Nm) Power Parameters
Figure Legend: *A- peak power; B- peak velocity; C- time to peak power; D- time to peak velocity*
Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval.
Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)

PP_{20} displayed a non-significant rate of decline of 0.12 Watts per year (95% CI: -1.33 to 1.08 Watts per year; p=0.84) to the age of 43 ± 2.2 years (95% CI: 38.5 to 47.5 years) where then, a significantly accelerated rate of decline of 4.97 Watts per year (95% CI: -5.76 to -4.43 Watts per year; p<0.001) was observed. PV_{20} displayed a significant rate of decline of 1.66 deg/s per year (95% CI: -2.98 to -0.32 deg/s per year; p=0.014) to the age of 46 ± 3.7 years (95% CI: 38.6 to 53.3 years), which was followed by a significantly greater rate of decline of 3.31 deg/s per year (95% CI: -5.24 to -1.49 deg/s per year; p=0.07). $TTPP_{20}$ displayed a non-significant rate of increase of 0.0004 seconds per year (95% CI: -0.0001 to 0.001 seconds per year; p=0.14) to the age of 46 ± 2.8 years (95% CI: 40.1 to 52.5 years). Following this breakpoint, a significantly greater increase

of 0.0015 seconds per year (95% CI: -0.001 to 0.004 seconds per year; p=0.039) was observed. $TTPV_{20}$ displayed a linear increase of 0.0001 seconds per year (95% CI: -0.0001 to 0.0009 seconds per year; p<0.001).

Table 26. Knee Extension Power Parameters at 20% Maximum Strength

Age	Peak Power (Watts)	Peak Velocity (deg/s)	Time to Peak Power (s)	Time to Peak Velocity (s)
20-24	360.8±18.1	410.4±17.7	0.175±0.02	0.197±0.02
25-29	366.9±21.0	408.4±21.5	0.169±0.02	0.210±0.02
30-34	360.0±25.1	398.1±22.7	0.179±0.01	0.199±0.01
35-39	362.9±25.8	406.4±23.3	0.179±0.02	0.209±0.01
40-44	364.5±16.2‡	406.8±20.0	0.184±0.02	0.209±0.01
45-49	356.3±23.8	387.7±23.3‡	0.176±0.02‡	0.209±0.01
50-54	308.7±26.3†	394.4±27.2	0.186±0.02	0.215±0.02
55-59	284.4±23.8†	369.9±26.8	0.207±0.03	0.243±0.03†
60-64	263.9±21.0†	358.7±24.7	0.208±0.05	0.235±0.04†
65-69	224.1±23.6†	324.1±25.9†	0.227±0.01†	0.241±0.01†
70-74	194.9±21.7†	295.0±25.9†	0.220±0.02†	0.253±0.02†
75-79	195.1±24.5†	250.5±19.1†	0.228±0.02†	0.249±0.02†
80-89	168.3±21.7†	226.2±21.2†	0.241±0.02†	0.271±0.02†

Note: Values are presented as mean ± SE. ‡- denotes critical age (breakpoint) from segmental analysis, †- denotes significant difference from reference group (underline). *Abbreviations*: deg/s degrees per second, s- seconds.

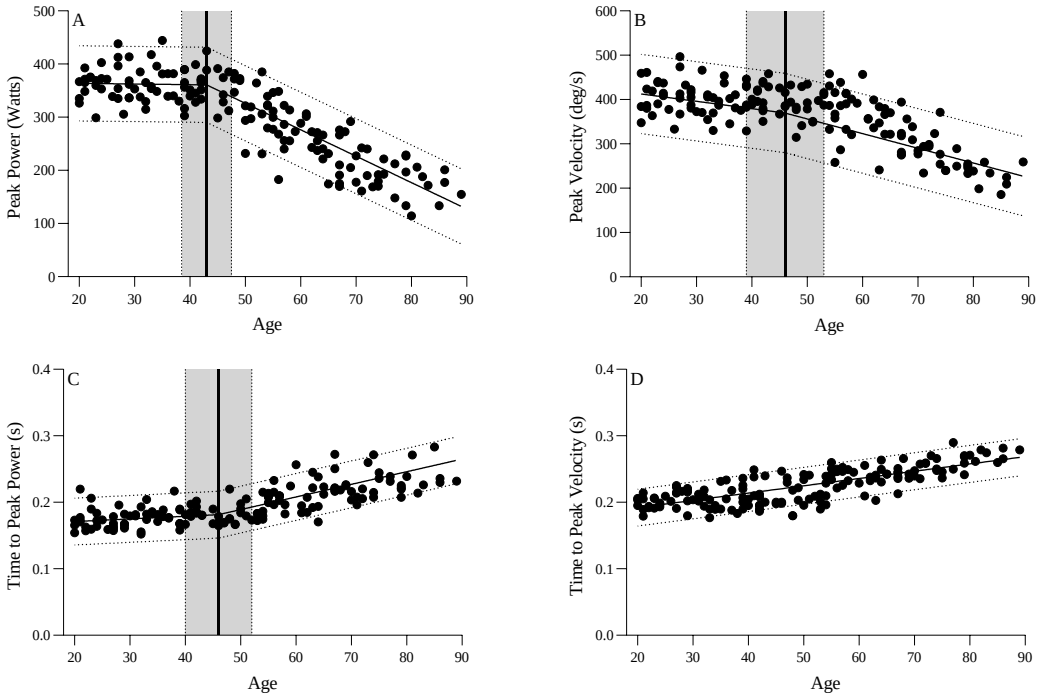

Figure 22. Knee Extension Power Parameters at 20% Maximum Strength
Figure Legend: *A- peak power; B- peak velocity; C- time to peak power; D- time to peak velocity Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval. Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)*

PP_{40} displayed a significant increase of 1.47 Watts per year (95% CI: 0.25 to 2.69 Watts per year; p=0.02) to the age of 43 ± 1.9 years (95% CI: 39.1 to 46.8 years). Following this breakpoint, a significant rate of decline of 4.27 Watts per year (95% CI: -4.82 to -3.58 Watts per year; p<0.001) was observed. PV_{40} displayed a non-significant rate of increase of 0.65 deg/s per year (95% CI: -1.02 to 2.34 deg/s per year; p=0.44) to the age of 41.8 ± 2.6 years (95% CI: 36.5 to 47.2 years). Thereafter, a significant rate of decline of 4.19 deg/s per year (95% CI: -5.18 to -3.79 deg/s per year; p=0.013) was observed. $TTPP_{40}$ displayed a non-significant increase of 0.001 seconds per year (95% CI: -0.0004 to 0.002 seconds per year; p=0.181) to the age of 41 ± 2.6 years (95% CI: 34.9 to 47.0 years). Thereafter, a significantly greater rate of increase of 0.002s per year

(95% CI: 0.002 to 0.003 seconds per year; p=0.041) was observed. $TTPV_{40}$ displayed a non-significant increase of 0.0006 seconds per year (95% CI: -0.0002 to 0.0014 seconds per year; p=0.146) to the age of 46 ± 5.5 years (95% CI: 35.0 to 56.9 years). Following this breakpoint, a significantly accelerated rate of increase of 0.0025 seconds per year (95% CI: 0.0016 to 0.0027 seconds per year; p=0.039) was observed.

Table 27. Knee Extension Power Parameters at 40% Maximum Strength

Age	Peak Power (Watts)	Peak Velocity (deg/s)	Time to Peak Power (s)	Time to Peak Velocity (s)
20-24	306.4±19.2	329.2±18.6	0.197±0.02	0.227±0.02
25-29	303.4±24.8	334.1±25.6	0.197±0.02	0.217±0.02
30-34	328.3±23.4	295.4±27.6	0.201±0.02	0.240±0.01
35-39	321.3±25.9	283.4±21.7	0.215±0.02	0.238±0.02
40-44	334.9±18.9‡	293.5±24.2‡	0.211±0.01‡	0.252±0.01
45-49	318.1±22.1	273.8±20.2†	0.226±0.02	0.236±0.02‡
50-54	288.8±22.9	287.8±19.5	0.220±0.02	0.277±0.02
55-59	275.5±28.9†	288.0±28.4	0.249±0.02†	0.255±0.02
60-64	265.0±22.8†	248.1±25.1†	0.287±0.02†	0.263±0.02†
65-69	224.4±22.5†	243.7±25.9†	0.271±0.02†	0.278±0.03†
70-74	213.9±23.2†	193.1±26.5†	0.292±0.02†	0.286±0.02†
75-79	203.6±22.7†	165.9±26.2†	0.273±0.03†	0.292±0.02†
80-89	147.8±25.8†	163.5±21.6†	0.309±0.03†	0.290±0.02†

Note: Values are presented as mean ± SE. ‡- denotes critical age (breakpoint) from segmental analysis, †- denotes significant difference from reference group (underline). *Abbreviations*: deg/s degrees per second, s- seconds.

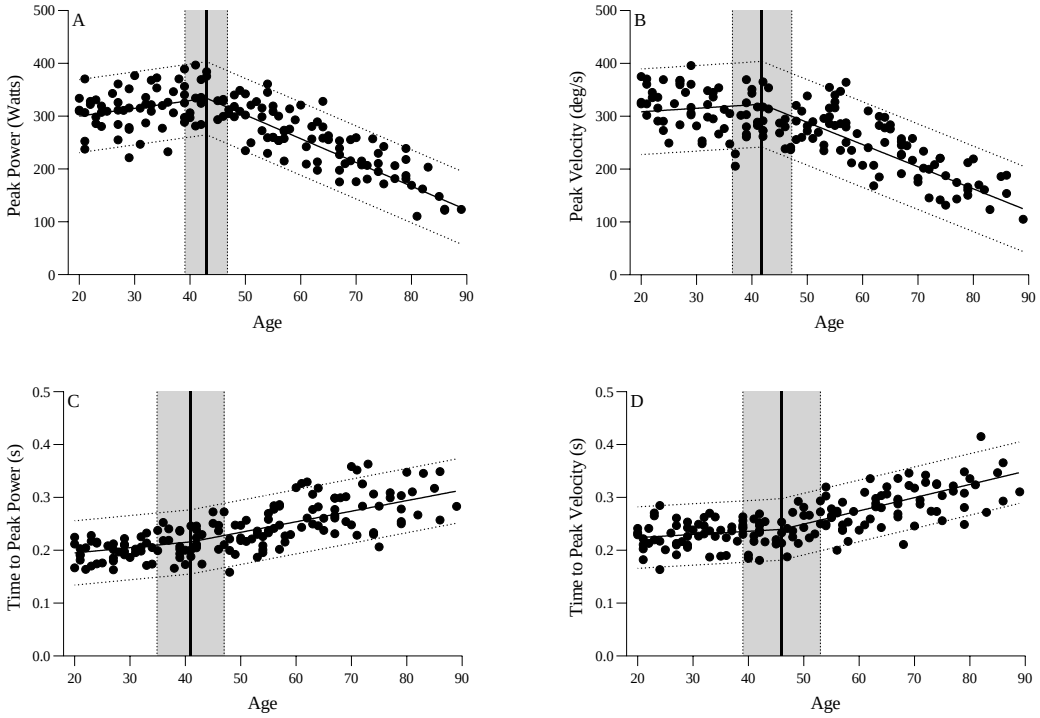

Figure 23. Knee Extension Power Parameters at 40% Maximum Strength
Figure Legend: *A- peak power; B- peak velocity; C- time to peak power; D- time to peak velocity*
Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval.
Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)

PP_{60} displayed a significant rate of decline of 0.628 Watts per year (95% CI: -1.06 to -0.19 Watts per year; p=0.005) to the age of 53 ± 2.5 years (95% CI: 48.0 to 57.9 years), where then a significantly accelerated rate of decline of 3.01 Watts per year (95% CI: -3.59 to -2.57 Watts per year; p=0.021) was observed. PV_{60} displayed a non-significant decline of 0.277 deg/s per year (95% CI: -0.88 to 0.32deg/s per year p=0.36) to the age of 45 ± 2.3 years (95% CI: 40.4 to 49.6 years). Following this breakpoint, a significantly accelerated rate of decline (p=0.045) of 2.73 deg/s per year (95% CI: -3.16 to -2.45 deg/s per year) was observed. $TTPP_{60}$ displayed a non-significant increase of 0.0002 seconds per year (95% CI: -0.0004 to 0.001 seconds per year; p=0.42) to the age of 50 ± 2.8 years (95% CI: 44.5 to 55.5 years). Following this breakpoint, a significantly

larger rate of increase of 0.0035 seconds per year (95% CI: 0.003 to 0.004 seconds per year; p=0.047) was observed. $TTPV_{60}$ displayed a non-significant increase of 0.0002 seconds per year (95% CI: -0.0005 to 0.001 seconds per year; p=0.54) to the age of 47.7 ± 2.1 years (95% CI: 40.6 to 54.7 years). Following this age, a significantly accelerated rate of increase of 0.002 seconds per year (95% CI: 0.001 to 0.003 seconds per year; p=0.05) was observed.

Table 28. Knee Extension Power Parameters at 60% Maximum Strength

Age	Peak Power (Watts)	Peak Velocity (deg/s)	Time to Peak Power (s)	Time to Peak Velocity (s)
20-24	284.6±13.7	229.4±11.8	0.207±0.02	0.226±0.04
25-29	281.4±11.9	220.1±10.0	0.213±0.02	0.231±0.03
30-34	270.3±15.9	224.4±12.1	0.199±0.02	0.230±0.02
35-39	270.0±14.2	217.4±10.7	0.204±0.02	0.239±0.03
40-44	267.2±12.9	219.6±11.3	0.212±0.01	0.234±0.03
45-49	264.0±14.2	213.1±11.4‡	0.222±0.02	0.225±0.04‡
50-54	278.7±12.5‡	198.8±13.3†	0.209±0.02‡	0.248±0.02
55-59	246.4±15.0†	184.8±11.7†	0.249±0.02†	0.252±0.04
60-64	229.4±15.6†	178.9±14.9†	0.243±0.03	0.270±0.02
65-69	214.3±19.0†	157.7±9.70†	0.285±0.03†	0.269±0.04
70-74	198.6±16.9†	136.6±12.3†	0.298±0.02†	0.273±0.04
75-79	203.8±16.6†	134.2±12.2†	0.325±0.03†	0.287±0.03†
80-89	161.5±15.4†	100.2±14.6†	0.323±0.03†	0.320±0.04†

Note: Values are presented as mean ± SE. ‡- denotes critical age (breakpoint) from segmental analysis, †- denotes significant difference from reference group (underline). *Abbreviations*: deg/s degrees per second, s- seconds.

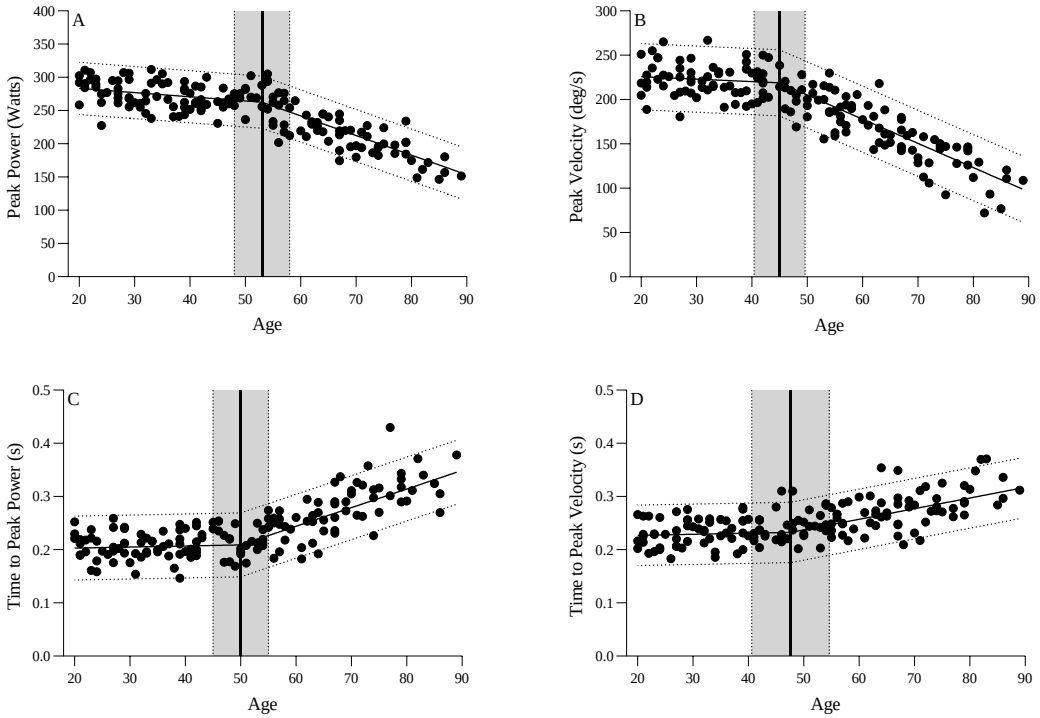

Figure 24. Knee Extension Power Parameters at 60% Maximum Strength
Figure Legend: *A- peak power; B- peak velocity; C- time to peak power; D- time to peak velocity*
Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval.
Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)

Knee Flexion

Values are displayed in Tables 29 to 32 and Figures 25 to 28. PP_{UL} displayed a non-significant increase of 0.207 Watts per year (95% CI: -0.965 to 1.38 Watts per year; p=0.73) to the age of 37 ± 3.1 years (95% CI: 30.8 to 43.2 years). Following this breakpoint, a significantly greater rate of decline of 2.08 Watts per year (95% CI: -2.35 to -1.82 Watts per year; p<0.001) was observed. PV_{UL} displayed a non-significant decline of 0.231 deg/s per year (95% CI: -3.14 to 2.68 deg/s per year; p=0.87) to the age of 36.5 ± 3.5 years (95% CI: 29.5 to 43.5 years). After this breakpoint, a significantly accelerated decline of 4.88 deg/s per year (95% CI: -5.37 to -4.46 deg/s per year; p<0.001) was observed. $TTPP_{UL}$ displayed a non-significant decrease of 0.0001 seconds per year (95%

CI: -0.001 to 0.001 seconds per year; p=0.81) to the age of 42.4 ± 3.3 years (95% CI: 35.9 to 48.9 years). After this breakpoint, a significant rate of increase of 0.003 seconds per year (95% CI: 0.002 to 0.004 seconds per year; p=0.021) was observed. $TTPV_{UL}$ displayed a non-significant increase of 0.001 seconds per year (95% CI: -0.0005 to 0.0014 seconds per year; p=0.36) to the age of 42.4 ± 4.8 years (95% CI: 33.7 to 52.9 years). Thereafter, the rate of increase was significantly accelerated to 0.003 seconds per year (95% CI: 0.0017 to 0.0048 seconds per year; p=0.041).

Table 29. Knee Flexion Unloaded (1 Nm) Power Parameters

Age	Peak Power (Watts)	Peak Velocity (deg/s)	Time to Peak Power (s)	Time to Peak Velocity (s)
20-24	224.5±12.6	438.5±28.9	0.217±0.02	0.240±0.01
25-29	221.9±14.7	459.2±30.5	0.210±0.03	0.229±0.02
30-34	220.2±15.0	427.6±42.6	0.216±0.02	0.240±0.02
35-39	221.2±13.9‡	433.5±34.2‡	0.224±0.03	0.247±0.02
40-44	224.7±15.1	430.0±38.8	0.210±0.02‡	0.245±0.01‡
45-49	199.7±11.8	384.1±27.9	0.221±0.02	0.260±0.02
50-54	191.1±14.0	346.5±29.2	0.242±0.03	0.262±0.02
55-59	181.8±12.1†	334.0±27.6†	0.245±0.02	0.265±0.02
60-64	174.2±15.4†	314.6±25.3†	0.265±0.03†	0.289±0.02†
65-69	163.2±12.9†	274.3±25.5†	0.282±0.02†	0.321±0.03†
70-74	158.6±14.1†	242.1±32.8†	0.298±0.03†	0.302±0.02†
75-79	146.3±15.1†	248.1±24.0†	0.314±0.03†	0.325±0.02†
80-89	116.5±15.2†	206.8±24.1†	0.307±0.04†	0.333±0.03†

Note: Values are presented as mean ± SE. ‡- denotes critical age (breakpoint) from segmental analysis, †- denotes significant difference from reference group (underline). *Abbreviations*: deg/s degrees per second, s- seconds.

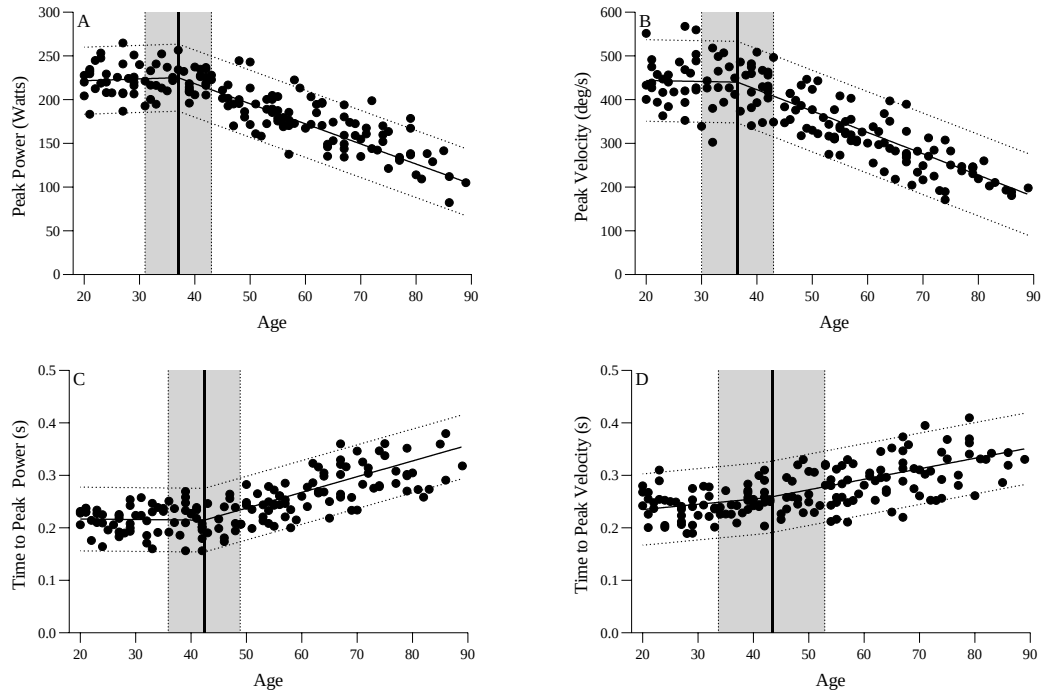

Figure 25. Knee Flexion Unloaded (1 Nm) Power Parameters
Figure Legend: *A- peak power; B- peak velocity; C- time to peak power; D- time to peak velocity*
Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval.
Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)

PP_{20} displayed a non-significant rate of decline of 0.33 Watts per year (95% CI: -0.89 to 0.22 Watts per year; p=0.24) to the age of 50 ± 2.7 years (95% CI: 44.6 to 55.4 years), where then a significantly larger rate of decline of 2.69 Watts per year (95% CI: -3.30 to -2.35 Watts per year; p=0.031) was observed. PV_{20} displayed a significant rate of decline of 1.66 deg/s per year (95% CI: -2.98 to -0.32 deg/s per year; p=0.015) to the age of 46 ± 3.7 years (95% CI: 38.6 to 53.3 years), which was followed by a significantly greater rate of decline of 5.36 deg/s per year (95% CI: -6.24 to -4.49 deg/s per year; p=0.027). $TTPP_{20}$ displayed a significant increase of 0.001 seconds per year (95% CI: 0.0001 to 0.002 seconds per year; p=0.02) to the age of 52.4 ± 3.8 years (95% CI: 45.1 to 60.0 years). Following this breakpoint, a significantly larger rate of increase of 0.003

seconds per year (95% CI: 0.002 to 0.004 seconds per year; p=0.002) was observed. $TTPV_{20}$ displayed a significant rate of increase of 0.001 seconds per year (95% CI: 0.0001 to 0.002 seconds per year; p=0.025) to the age of 50.5 ± 2.9 years (95% CI: 44.0 to 57.3 years). Thereafter, a significantly greater rate of increase of 0.0025 seconds per year (95% CI: 0.002 to 0.004 seconds per year; p=0.042) was observed.

Table 30. Knee Flexion Power Parameters at 20% Maximum Strength

Age	Peak Power (Watts)	Peak Velocity (deg/s)	Time to Peak Power (s)	Time to Peak Velocity (s)
20-24	250.3±12.8	415.6±23.2	0.215±0.02	0.238±0.02
25-29	234.6±15.3	376.1±31.8	0.220±0.03	0.229±0.02
30-34	232.7±14.9	399.7±24.9	0.212±0.03	0.245±0.02
35-39	244.9±15.0	371.3±31.4	0.229±0.03	0.247±0.02
40-44	240.4±13.5	380.2±26.5	0.223±0.02	0.253±0.01
45-49	231.7±13.8	381.7±28.2‡	0.242±0.03	0.254±0.02
50-54	235.5±12.4‡	339.0±30.4†	0.238±0.03‡	0.254±0.02‡
55-59	214.9±11.8†	297.2±28.2†	0.255±0.03	0.271±0.02
60-64	198.4±16.1†	254.7±30.4†	0.277±0.03†	0.285±0.03†
65-69	184.6±14.5†	249.2±19.8†	0.282±0.03†	0.312±0.03†
70-74	174.3±15.3†	210.1±18.8†	0.283±0.02†	0.312±0.23†
75-79	152.5±13.6†	209.9±17.2†	0.318±0.02†	0.308±0.03†
80-89	141.2±13.3†	178.4±24.1†	0.361±0.04†	0.334±0.03†

Note: Values are presented as mean ± SE. ‡- denotes critical age (breakpoint) from segmental analysis, †- denotes significant difference from reference group (underline). *Abbreviations*: deg/s degrees per second, s- seconds.

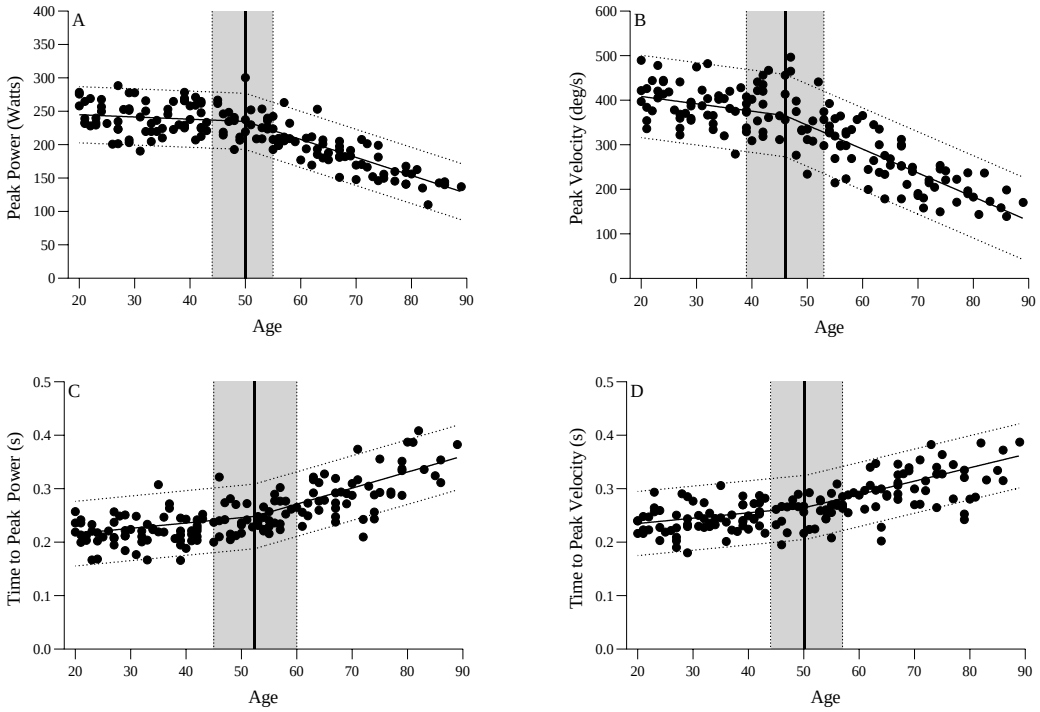

Figure 26. Knee Flexion Power Parameters at 20% Maximum Strength
Figure Legend: *A- peak power; B- peak velocity; C- time to peak power; D- time to peak velocity*
Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval.
Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)

PP_{40} displayed a non-significant rate of increase of 0.137 Watts per year (95% CI: -0.52 to 0.81 Watts per year; p=0.68) to the age of 47.3 ± 2.2 years (95% CI: 42.7 to 51.8 years). Following this breakpoint, a significant rate of decline of 2.25 Watts per year (95% CI: -3.53 to -1.59 Watts per year; p=0.002) was observed. PV_{40} displayed a significant rate of decline of 1.34 deg/s per year (95% CI: -2.01 to 0.06 deg/s per year; p<0.001) to the age of 56.4 ± 3.7 years (95% CI: 49.0 to 63.7 years). Thereafter, a significantly accelerated rate of decline of 4.50 deg/s per year (95% CI: -5.67 to -3.35 deg/s per year; p=0.011) was observed. $TTPP_{40}$ displayed a non-significant rate of increase of 0.0005 seconds per year (95% CI: -0.0004 to 0.0009 seconds per year; p=0.27) to the age of 47 ± 3.8 years (95% CI: 24.9 to 55.0 years). Thereafter, a significantly greater rate of increase

of 0.002 seconds per year (95% CI: 0.002 to 0.003 seconds per year; p=0.017) was observed. $TTPV_{40}$ displayed a linear increase of 0.001 seconds per year (95% CI: 0.001 to 0.003 seconds per year; p<0.001) with increasing age groups.

Table 31. Knee Flexion Power Parameters at 40% Maximum Strength

Age	Peak Power (Watts)	Peak Velocity (deg/s)	Time to Peak Power (s)	Time to Peak Velocity (s)
20-24	175.9±11.6	312.0±30.5	0.241±0.02	0.254±0.01
25-29	195.3±17.8	307.9±32.1	0.241±0.02	0.252±0.02
30-34	174.8±16.9	326.1±33.9	0.251±0.01	0.241±0.02
35-39	166.6±15.9	309.7±29.7	0.253±0.02	0.278±0.02
40-44	183.5±15.6	326.8±28.8	0.263±0.02	0.285±0.02
45-49	155.3±10.9‡	329.6±27.6	0.234±0.01‡	0.269±0.02
50-54	165.9±13.5	274.9±33.8	0.256±0.02	0.291±0.03
55-59	140.6±13.7	247.7±31.1†‡	0.304±0.02†	0.260±0.02
60-64	132.4±15.4†	219.2±27.6†	0.315±0.03†	0.276±0.02
65-69	126.5±11.5†	178.9±19.3†	0.320±0.03†	0.328±0.03†
70-74	124.0±12.4†	179.4±19.9†	0.329±0.02†	0.320±0.02†
75-79	114.2±14.2†	176.1±21.1†	0.340±0.02†	0.318±0.03†
80-89	116.2±14.7†	163.7±20.7†	0.362±0.03†	0.346±0.02†

Note: Values are presented as mean ± SE. ‡- denotes critical age (breakpoint) from segmental analysis, †- denotes significant difference from reference group (underline). *Abbreviations*: deg/s degrees per second, s- seconds.

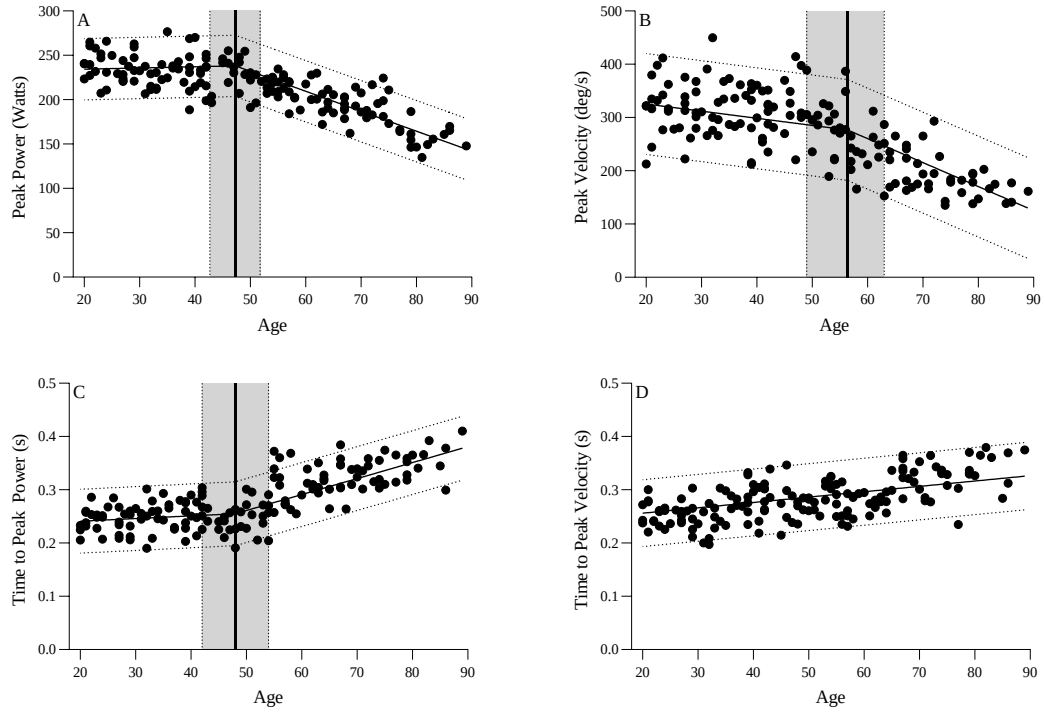

Figure 27. Knee Flexion Power Parameters at 40% Maximum Strength
Figure Legend: *A- peak power; B- peak velocity; C- time to peak power; D- time to peak velocity*
Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval.
Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)

PP_{60} displayed a significant rate of decline of 0.187 Watts per year (95% CI: -0.50 to 0.12 Watts per year $p=0.24$) to the age of 60.3 ± 1.8 years (95% CI: 56.8 to 63.9 years). After the breakpoint, a significantly greater rate of decline of 3.75 Watts per year (95% CI: -4.49 to -3.02 Watts per year; $p<0.001$) was observed. PV_{60} displayed a significant rate of decline of 0.655 deg/s per year (95% CI: -0.89 to -0.41 deg/s per year; $p<0.001$) to the age of 65 ± 1.6 years (95% CI: 62.0 to 68.5 years). Following this breakpoint, a significantly greater rate of decline of 3.78 deg/s per year (95% CI: -5.34 to -3.53deg/s per year; $p=0.039$) was observed. $TTPP_{60}$ displayed a non-significant increase of 0.0001 seconds per year (95% CI: -0.001 to 0.001 seconds per year; $p=0.74$) to the age of 62.3 ± 2.3 years (95% CI: 57.9 to 66.8 years). Following this age, a significantly greater rate

of increase of 0.006 seconds per year (95% CI: 0.004 to 0.01 seconds per year; p=0.014) was observed. $TTPV_{60}$ displayed a non-significant increase of 0.0004 seconds per year (95% CI: -0.00008 to 0.001 seconds per year; p=0.09) to the age of 60.1 ± 3.2 years (95% CI: 53.9 to 66.4 years). Following the breakpoint, a significantly accelerated rate of increase of 0.0035 seconds per year (95% CI: 0.002 to 0.005 seconds per year; p=0.038) was observed.

Table 32. Knee Flexion Power Parameters at 60% Maximum Strength

Age	Peak Power (Watts)	Peak Velocity (deg/s)	Time to Peak Power (s)	Time to Peak Velocity (s)
20-24	226.9±16.4	206.5±12.5	0.281±0.02	0.247±0.03
25-29	220.3±15.0	217.3±10.2	0.278±0.03	0.267±0.04
30-34	219.4±14.2	203.1±13.2	0.272±0.02	0.269±0.03
35-39	222.2±13.6	201.8±10.4	0.295±0.02	0.264±0.02
40-44	211.9±15.6	197.2±11.2	0.292±0.03	0.290±0.04
45-49	221.1±15.2	195.3±12.4	0.296±0.02	0.257±0.03
50-54	220.2±13.6	200.5±11.6	0.302±0.03	0.270±0.03
55-59	217.5±11.8	188.4±10.5†	0.274±0.02	0.270±0.04
60-64	209.5±17.8‡	178.6±11.9†	0.276±0.02‡	0.282±0.02‡
65-69	185.8±13.9†	177.8±10.7†‡	0.318±0.03	0.305±0.02†
70-74	177.6±14.6†	156.1±11.3†	0.352±0.03†	0.308±0.04†
75-79	152.0±12.5†	120.6±10.3†	0.409±0.03†	0.363±0.02†
80-89	124.5±11.3†	102.5±10.1†	0.399±0.03†	0.368±0.04†

Note: Values are presented as mean ± SE. ‡- denotes critical age (breakpoint) from segmental analysis, †- denotes significant difference from reference group (underline). *Abbreviations*: deg/s degrees per second, s- seconds.

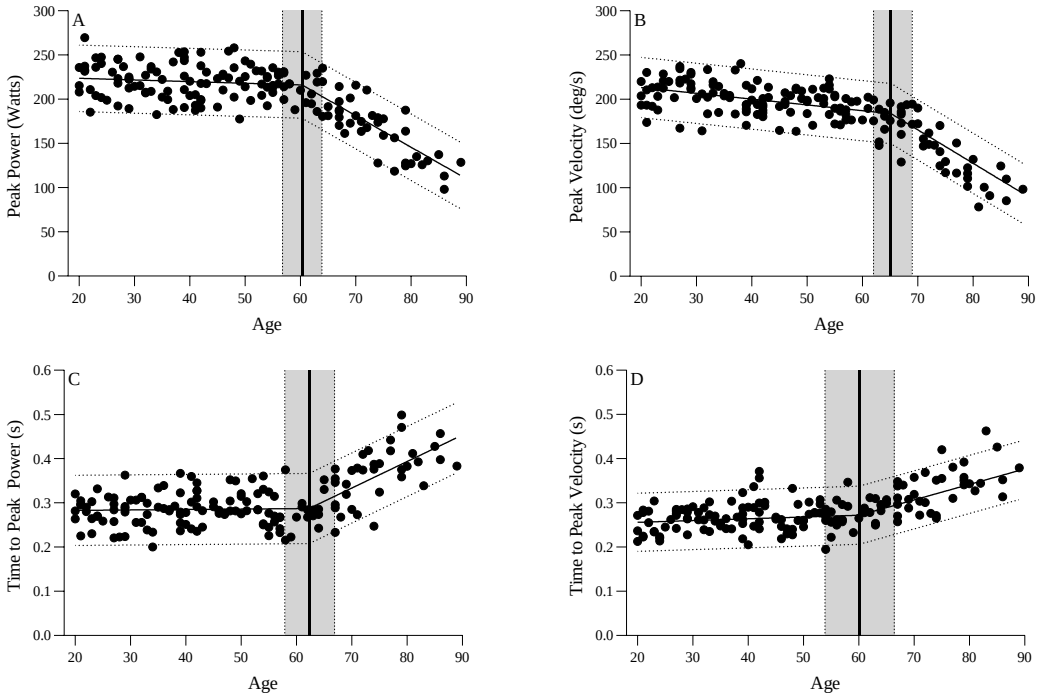

Figure 28. Knee Flexion Power Parameters at 60% Maximum Strength
Figure Legend: *A- peak power; B- peak velocity; C- time to peak power; D- time to peak velocity Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval. Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)*

Muscular Endurance

Local muscular endurance was assessed using a 30-repetition test where work fatigue (WF) was calculated by determining the percent change of the total amount of work that was performed during the first and last ten repetitions of each test. For clarity when reading the results, if the rate of change is increasing, this is representing of being more fatigable, conversely, if the rate of change is decline, this is representative of being less fatigable. For example, the faster contraction velocity (240 deg/s) resulted in greater fatigability, whereas the slower contraction velocity (60 deg/s) often displayed less fatigue to the critical age period.

The slower contraction velocity (60 deg/s) revealed a greater capacity to maintain endurance performance with increased age prior to meeting the critical age. During the 60 deg/s contraction, critical ages were no sooner than the early 60s to 70s. The critical ages during the slow contraction velocity were elbow extensors (67 years), elbow flexors (62.7 years), knee extensors (71 years), knee flexors (71 years), plantar flexors (73 years), and the dorsiflexors (67 years). The faster contraction velocity resulted in sooner critical age periods, each approximately 20 years prior to the 60 deg/s conditions. Those periods are as follows: elbow extensors (46 years), elbow flexors (47 years), knee extensors (36 years), knee flexors (52.9 years), plantar flexors (53 years), and the dorsiflexors (54 years). Across all muscle groups, both contraction velocities displayed significant group effects (all $p<0.001$). The reference interval and the corresponding comparisons are displayed in the following tables.

Elbow Extension

Mean values are displayed in Table 33 and Figure 29. WF_{60} displayed a non-significant rate of decline of 0.04% per year (95% CI: -0.079 to 0.001% per year; $p=0.054$) to the age of 67 ± 5.0 years (95% CI: 39.9 to 52.1 years). Thereafter, a significant rate of increase of 0.253% per year (95% CI: 0.010 to 0.417% per year; $p=0.012$) was observed. WF_{240} displayed a non-significant increase of 0.06% per year (95% CI: -0.045 to 0.157% per year; $p=0.281$) to the age of 46 ± 3.1 years (95% CI: 39.9 to 52.1 years). After this breakpoint, a significantly accelerated increase of 0.43% per year (95% CI: 0.336 to 0.469% per year; $p<0.001$) was observed.

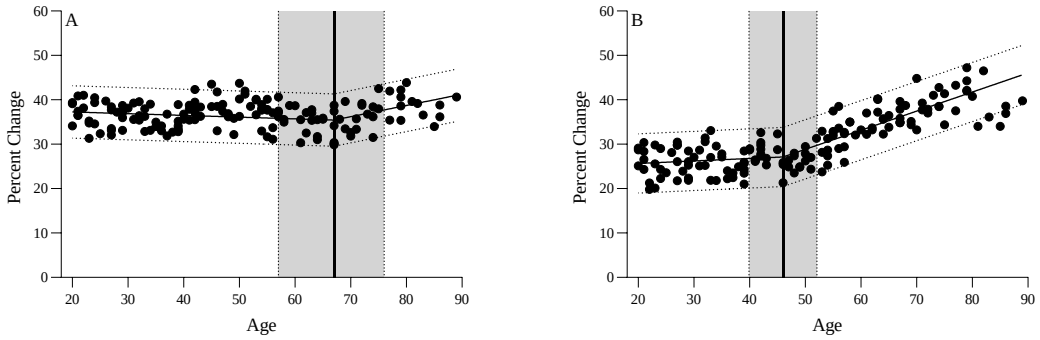

Figure 29. Elbow Extension Work Fatigue
Figure Legend: *A- contractions at 60 deg/s; B- contractions at 240 deg/s*
Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval.
Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)

Elbow Flexion

With age (Table 33, Figure 30), WF_{60} displayed a non-significant rate of decline of 0.04% per year (95% CI: 0.089 to 0.208s per year; p=0.282) to the age of 65.0 ± 4.1 years (95% CI: 60.7 to 70.8 years). After this age, a significant rate of increase of 0.50% per year (95% CI: 0.18 to 0.832% per year; p=0.029) was observed. WF_{240} displayed a non-significant rate of increase of 0.05% per year (95% CI: -0.044 to 0.152% per year; p=0.283) to the age of 46.9 ± 2.3 years (95% CI: 42.7 to 50.8 years). Thereafter, a significantly greater rate of increase of 0.27% per year (95% CI: 0.18 to 0.32% per year; p<0.001) was observed.

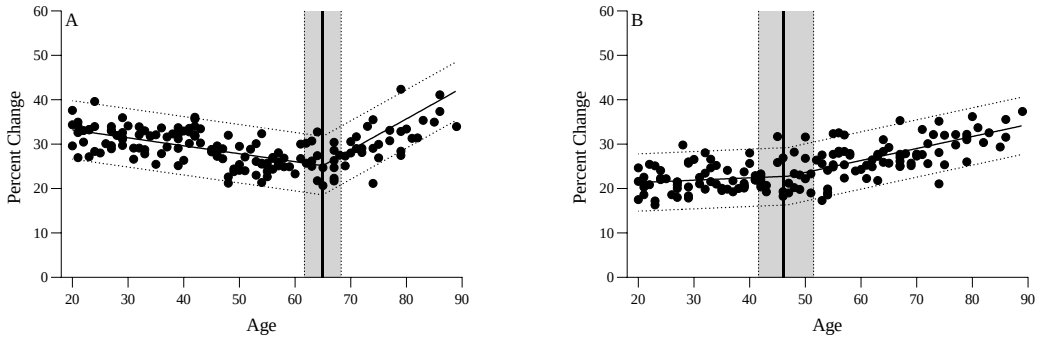

Figure 30. Elbow Flexion Work Fatigue
Figure Legend: *A- contractions at 60 deg/s; B- contractions at 240 deg/s*
Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval.
Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)

Table 33. Elbow Extension and Flexion Work Fatigue

Age	60 degrees per second		240 degrees per second	
	Extensors	Flexors	Extensors	Flexors
20-24	37.9±2.2	32.6±2.3†	25.6±2.2	21.3±2.2
25-29	35.9±1.6	31.5±1.7†	25.9±1.7	21.6±1.5
30-34	36.7±2.4	30.7±1.9	27.4±2.0	23.7±2.3
35-39	34.2±1.5	30.5±1.3	24.7±1.4	20.9±1.4
40-44	37.6±1.7	32.4±1.4	28.1±1.5	22.4±1.7
45-49	36.1±2.6	26.7±2.4	26.1±2.3‡	23.1±2.3‡
50-54	38.9±2.5†	26.4±2.2	27.9±2.1	23.2±2.0†
55-59	36.4±1.8	25.5±1.9	32.7±1.7†	27.6±1.7
60-64	34.8±1.9	27.3±1.5	35.5±1.9†	25.9±1.9†
65-69	33.9±1.8‡	25.4±2.2‡	36.1±1.9†	27.3±2.0†
70-74	35.4±2.1	29.6±3.1	39.1±2.6†	28.8±2.8†
75-79	39.4±2.8	31.5±3.6†	41.5±3.7†	30.0±3.9†
80-89	38.6±2.9	34.9±4.3†	38.3±3.5†	33.4±3.2†

Note: Vales are presented as mean ± SE. ‡- denotes critical age (breakpoint) from segmental analysis. †- denotes significant difference from reference group (underline).

Knee Extension

Mean values are displayed in Table 34 and Figure 31. WF_{60} displayed a significant rate of decline of 0.19% per year (95% CI: -0.23 to -0.14% per year; $p<0.001$) to the age of 71 ± 2.8 years (95% CI: 66.3 to 77.6 years). Thereafter, a significant increase of 0.62% per year (95% CI: -0.41 to 0.83% per year; $p=0.02$) was observed. WF_{240} displayed a non-significant increase of 0.07% per year (95% CI: -0.30 to 0.15% per year; $p=0.81$) to

the age of 36 ± 2.5 years (95% CI: 30.9 to 41.0 years). Thereafter, a significant rate of increase of 0.43% per year (95% CI: 0.38 to 0.48% per year; $p<0.001$) was observed.

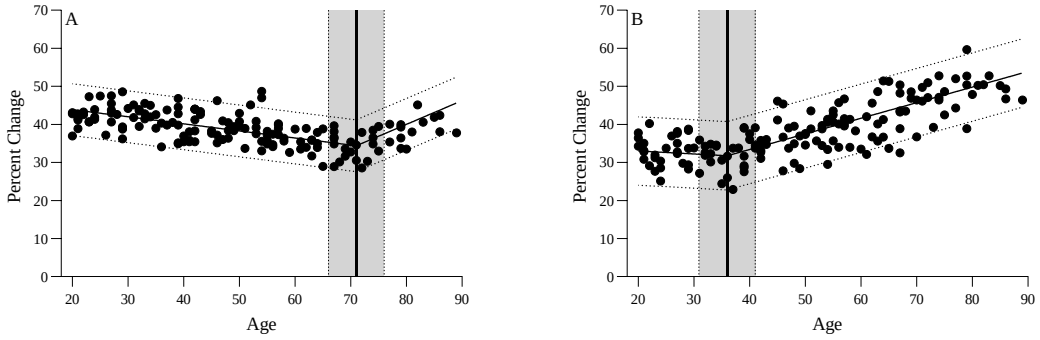

Figure 31. Knee Extension Work Fatigue
Figure Legend: *A- contractions at 60 deg/s; B- contractions at 240 deg/s*
Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval.
Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)

Knee Flexion

With age (Table 34 and Figure 32), WF_{60} displayed a significant rate of decline of 0.11% per year (95% CI: -0.244 to 0.351% per year; $p<0.001$) to the age of 71 ± 3.7 years (95% CI: 63.7 to 78.3 years). After this age, a non-significant increase of 0.37% per year (95% CI: -0.01 to -0.54% per year; $p=0.10$) was observed. WF_{240} displayed a non-significant rate of increase of 0.08% per year (95% CI: -0.01 to 0.15% per year; $p=0.058$) to the age of 52.9 ± 2.64 years (95% CI: 46.7 to 57.2 years). Thereafter, a significantly accelerated rate of increase of 0.42% per year (95% CI: 0.38 to 0.55% per year; $p<0.001$) was observed.

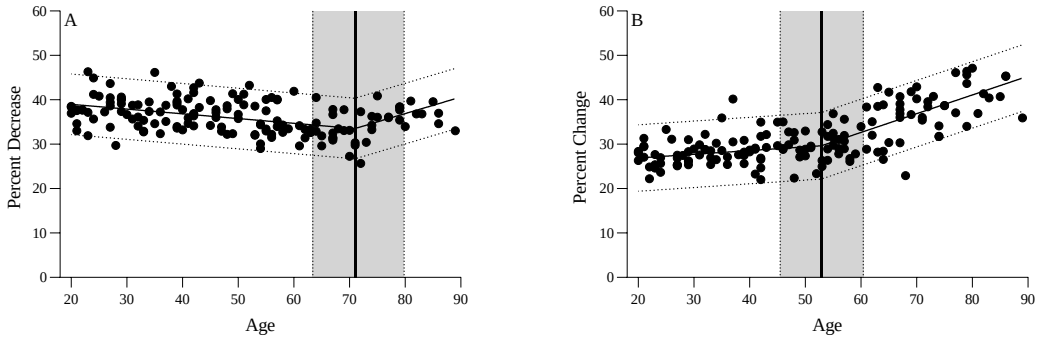

Figure 32. Knee Flexion Work Fatigue
Figure Legend: *A- contractions at 60 deg/s; B- contractions at 240 deg/s*
Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval.
Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)

Table 34. Knee Extension and Flexion Work Fatigue

Age	60 degrees per second		240 degrees per second	
	Extensors	Flexors	Extensors	Flexors
20-24	42.5±2.1†	37.9±1.8†	31.6±1.7	26.7±1.8
25-29	42.3±2.8†	38.6±2.3†	34.2±2.2	26.7±2.0
30-34	43.2±1.9†	36.2±1.6	32.8±1.7	28.5±1.9
35-39	40.3±1.8†	38.0±1.6†	30.6±2.9‡	29.5±2.7
40-44	39.6±2.3	37.9±2.5†	34.9±2.1	28.2±2.2
45-49	38.7±1.8	36.2±1.7	37.5±2.7†	30.2±3.1
50-54	40.2±2.4†	35.9±2.1	38.9±2.8†	28.9±2.5‡
55-59	36.6±2.3	35.6±2.1	39.4±2.5†	30.4±2.2
60-64	35.5±1.9	34.3±1.8	40.9±2.4†	33.8±2.3†
65-69	34.3±2.9	33.3±2.1	46.1±2.8†	35.8±2.8†
70-74	33.9±2.8‡	31.8±2.0‡	49.7±3.0†	37.1±3.0†
75-79	37.2±2.4	37.4±1.7	53.2±3.8†	41.3±3.5†
80-89	39.7±3.3	36.4±2.2	50.1±3.7†	41.7±3.3†

Note: Vales are presented as mean ± SE. ‡- denotes critical age (breakpoint) from segmental analysis. †- denotes significant difference from reference group (underline).

Plantarflexion

Mean values are displayed in Table 35 and Figure 33. WF_{60} displayed a non-significant rate of decline of 0.006% per year (95% CI: 0.001 to 0.101% per year; $p<0.001$) to the age of 72.9 ± 3.0 years (95% CI: 66.9 to 78.9 years). Thereafter, a significant increase of 0.627% per year (95% CI: 0.218 to 0.900% per year; $p=0.03$) was observed. WF_{240} displayed a linear increase of 0.08% per year (95% CI: 0.079 to 0.099% per year; $p<0.001$) with increasing age.

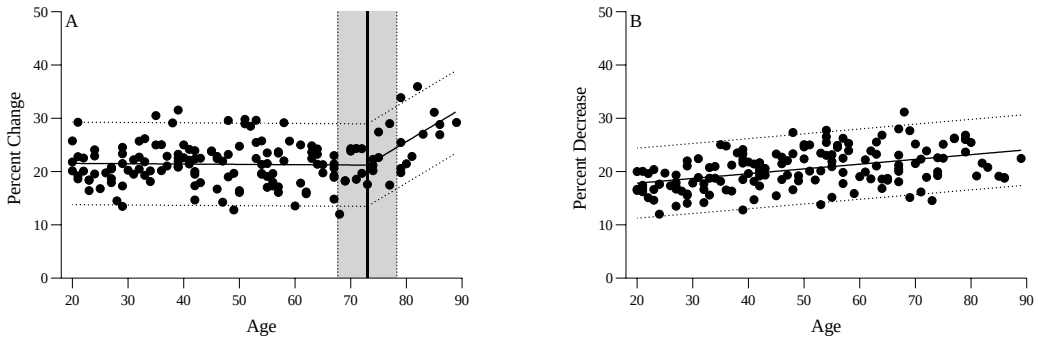

Figure 33. Plantarflexion Work Fatigue
Figure Legend: *A- contractions at 60 deg/s; B- contractions at 240 deg/s*
Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval.
Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)

Dorsiflexion

Mean values are displayed in Table 35 and Figure 34. With age, WF_{60} displayed a non-significant rate of increase of 0.02% per year (95% CI: -0.05 to 0.06% per year; p=0.06) to the age of 67 ± 2.1 years (95% CI: 63.2 to 45.4 years). After this breakpoint, a significantly accelerated rate of increase of 0.39% per year (95% CI: -0.185 to -0.064% per year; p=0.001) was observed. WF_{240} displayed a significant rate of increase of 0.151% per year (95% CI: 0.047 to 0.255% per year; p=0.004) to the age of 54 ± 2.06 years (95% CI: 49.9 to 58.1 years). Thereafter, a significantly accelerated rate of increase () of 0.25% per year (95% CI: 0.180 to 0.357%; per year p=0.048) was observed.

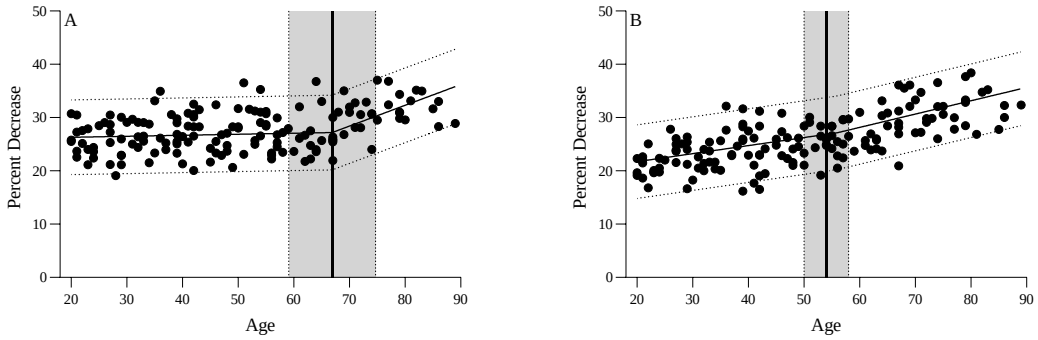

Figure 34. Dorsiflexion Work Fatigue
Figure Legend: *A- contractions at 60 deg/s; B- contractions at 240 deg/s*
Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval.
Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)

Table 35. Plantar- and Dorsiflexion Work Fatigue

Age	60 degrees per second		240 degrees per second	
	Plantarflexion	Dorsiflexion	Plantarflexion	Dorsiflexion
20-24	21.3±1.6	25.5±1.8	17.2±1.7	20.6±1.6
25-29	19.2±2.1	25.6±2.4	17.4±2.1	23.1±2.1
30-34	21.5±1.8	26.9±1.6	18.4±1.9	21.8±1.6
35-39	24.2±3.1	28.3±3.0	20.7±2.8	25.1±3.0
40-44	21.1±1.9	27.7±2.1	19.7±1.7	23.0±2.1
45-49	20.9±2.5	25.1±2.6	20.6±3.2	24.3±3.0
50-54	23.7±2.6	29.5±2.0	21.2±2.5	27.6±2.8‡
55-59	20.9±2.4	26.6±2.3	21.9±2.2	24.8±2.1†
60-64	20.8±2.9	25.6±3.1	21.5±2.5	26.9±2.7†
65-69	18.9±2.4	25.4±2.4‡	22.0±2.5	30.7±2.8†
70-74	21.6±2.9‡	30.0±2.9	20.5±2.9	29.9±2.4†
75-79	24.5±2.9	32.7±3.1†	25.4±3.4†	29.6±2.9†
80-89	27.9±3.9†	31.8±3.5†	20.8±3.5	31.3±3.6†

Note: Vales are presented as mean ± SE. ‡- denotes critical age (breakpoint) from segmental analysis. †- denotes significant difference from reference group (underline).

Muscle Quality & Specific Power

Muscle quality was defined as the quantity of muscular performance from the isometric, isokinetic, and isotonic contractions relative to the quantity of muscle mass. Therefore, the following section will be divided into 1) muscle quality determined from isometric and isokinetic strength, followed by 2) specific power determined from the power values collected during the isotonic testing (elbow and knee only). Further, muscle quality of the knee and ankle were quantified using the neuromuscular performance tasks

relative to the muscle area (pQCT) of the upper and lower leg. For the upper arm, muscle quality was determined by making neuromuscular performance relative to the region of interest of the arm from the DXA scan.

In general, there were few differences for the upper body muscle quality or specific power across each contraction conditions. Modest decreases were observed but the identification of a critical age period was not possible based off the collective rate of change with increasing age. For the lower body, more apparent declines were observed, such that the isometric and 60 deg/s for the upper thigh did not reveal critical age periods, whereas the 240deg/s and each of the four isotonic conditions did reveal critical age periods. Those are as follows: 240 deg/s (35.2 years), unloaded condition (1 Nm, 33 years), 20% condition (54 years), 40% condition (60 years), and the 60% condition (71 years). Further, the lower leg displayed critical age periods corresponding to isometric (63.6 years), 60 deg/s (54 years), and 240 deg/s (49 years).

Upper Arm Muscle Quality

Across all muscle quality parameters (isometric, both isokinetic contraction velocities, and all four isotonic external loads [specific power]), no age effects were observed ($p>0.05$). Of note, upper arm muscle quality determined from power output during the 20 and 60% isotonic conditions approached significance ($F=1.67$, $p=0.080$ and $F=1.61$, $p=0.095$, respectively). Mean values are displayed in Tables 36 and 37 and Figures 35 and 36.

During the isometric contraction, upper arm muscle quality displayed a linear rate of increase of 0.016 Nm/kg per year (95% CI: -0.027 to 0.061 Nm/kg per year; $p=0.45$). However, during the 60 and 240 deg/s contractions, upper arm MQ displayed linear rates

of decline of 0.124 Nm/kg per year (95% CI: -0.152 to -0.095 Nm/kg per year; $p<0.001$) and 0.131 Nm/kg per year (95% CI: -0.17 to -0.091 Nm/kg per year; $p<0.001$), respectively.

Table 36. Upper Arm Muscle Quality Parameters

Age	Isometric	60 deg/s	240 deg/s
20-24	86.8±3.78	53.5±2.71	51.4±2.82
25-29	86.2±4.92	50.9±3.21	50.5±3.50
30-34	76.5±4.03	49.2±2.96	47.4±2.95
35-39	77.8±4.18	47.4±3.21	48.2±2.73
40-44	79.8±3.34	47.8±1.94	47.0±1.64
45-49	85.5±5.91	51.5±3.10	48.5±3.41
50-54	84.1±3.91	50.4±2.67	47.7±2.15
55-59	84.8±4.35	50.9±2.25	47.2±2.41
60-64	85.4±2.61	49.7±2.08	47.2±1.70
65-69	84.4±3.18	43.6±1.71	45.4±2.16
70-74	84.5±3.89	45.2±2.16	43.9±1.39
75-79	81.6±5.79	41.6±5.12	42.3±3.05
80-89	85.1±4.92	48.7±5.49	43.2±1.94

Note: Values are presented as mean ± SE, No differences from reference group (underline). Muscle quality values were derived from right arm bone free lean body mass. *Abbreviations*: deg/s degrees per second

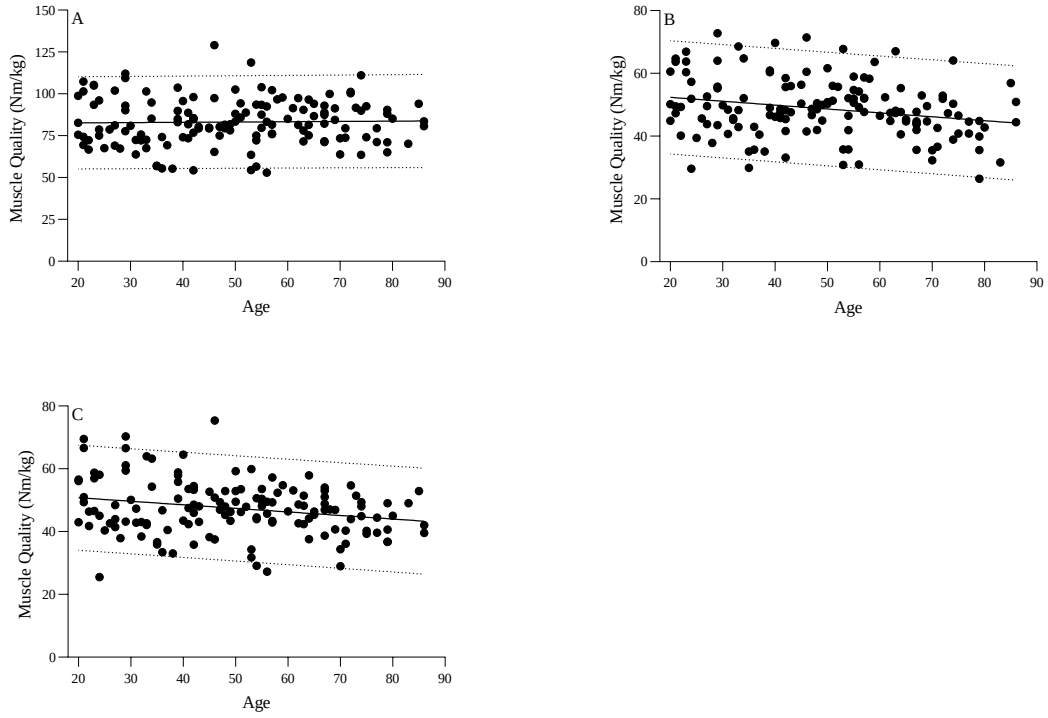

Figure 35. Upper Arm Muscle Quality Parameters

Figure Legend: *A- isometric contraction; B- contractions at 60 deg/s; C- contractions at 240 deg/s Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)*

Upper Arm Specific Power

Upper arm specific power during the unloaded condition displayed a linear rate of decline of 0.13 Watts/kg per year (95% CI: -0.15 to -0.10 Watts/kg per year; $p<0.001$). Specific power during the 20% MVIC condition displayed a linear rate of decline of 0.136 Watts/kg per year (95% CI: -0.16 to -0.11 Watts/kg per year; $p<0.001$). Specific power during the 40% condition displayed a linear decline of 0.04 Watts/kg per year (95% CI: -0.06 to -0.02 Watts/kg per year). Specific power during the 60% condition displayed a non-significant increase of 0.016 Watts/kg per year (95% CI: -0.04 to 0.08 Watts/kg per year; $p=0.41$) to the age of 67.9 ± 4.1 years (95% CI: 58.0 to 76.1 years), where a significant rate of decline of 0.47 Watts/kg per year (95% CI: -0.82 to -0.09 Watts/kg per year; $p<0.001$) was observed.

Table 37. Upper Arm Specific Power Parameters

Age	Unloaded	20% MVIC	40% MVIC	60% MVIC
20-24	51.4±1.86	56.6±2.67	41.5±2.50	28.9±1.30
25-29	48.8±3.15	54.7±2.78	43.1±2.65	29.7±1.67
30-34	46.7±1.70	53.9±3.41	38.5±1.86	26.0±1.47
35-39	46.3±2.45	51.4±2.72	38.3±2.03	25.7±1.40
40-44	45.1±2.10	52.2±1.95	37.2±1.54	25.8±1.44
45-49	46.4±2.42	55.6±2.96	41.6±2.28	28.4±1.78
50-54	48.9±2.37	52.7±1.79	41.1±1.85	29.3±1.38
55-59	47.3±2.38	55.5±2.71	40.7±1.90	28.7±1.62
60-64	44.1±1.96	53.1±2.39	42.9±1.41	28.2±0.88
65-69	42.4±1.48	46.9±1.50	39.4±1.59	28.2±1.22‡
70-74	43.2±2.36	47.9±2.26	37.8±2.56	25.4±1.39
75-79	43.4±2.82	48.2±1.87	39.4±2.16	23.1±0.87
80-89	43.9±5.13	47.2±1.91	39.4±5.18	23.7±2.94

Note: Values are presented as mean ± SE. Muscle quality values were derived from right arm bone free lean body mass. ‡- denotes critical age (breakpoint) from segmental analysis, No differences from reference group (underline). A*bbreviations*: MVIC- maximal voluntary isometric contraction.

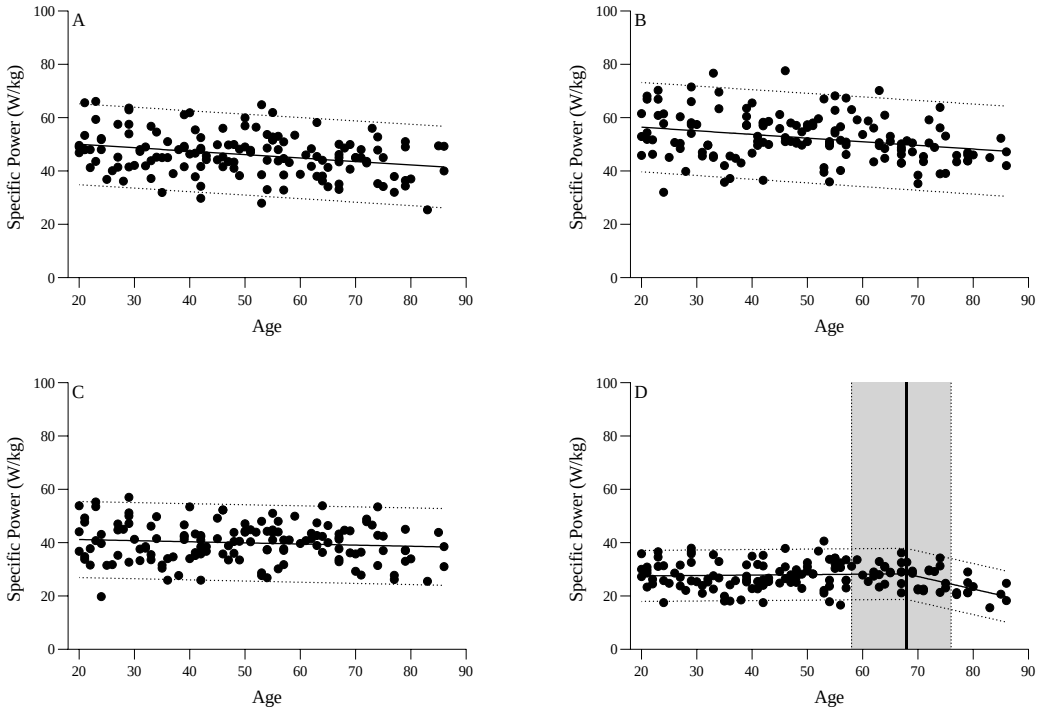

Figure 36. Upper Arm Specific Power

Figure Legend: *A- contractions at 1 Nm; B- contractions at 20% maximal isometric strength; C- contractions at 40% maximal isometric strength; D- contractions at 60% maximal isometric strength*
Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval.
Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)

Upper Leg Muscle Quality

There were no group differences observed for muscle quality of the upper leg during the isometric and 60 deg/s contractions. However, muscle quality during the 240 deg/s contraction and each of the four loaded isotonic conditions displayed significant groups differences (all $p \leq 0.007$); Tables 38 and 39 and Figures 37 and 38. Upper leg isometric muscle quality displayed a linear rate of decline of -0.001 Nm/cm^2 per year (95% CI: -0.007 to 0.003 Nm/cm^2 per year; p=0.44). Similar results were observed during the 60 deg/s contraction condition, which displayed a linear rate of decline of -0.002 Nm/cm^2 per year (95% CI: -0.005 to 0.002 Nm/cm^2 per year; p=0.55). Regarding the

240deg/s contractions, there was a non-significant increase of 0.0002 Nm/cm^2 per year (95% CI: -0.013 to 0.013 Nm/cm^2 per year, p=0.96) to the age of 35.2 ± 5.3 years (95% CI: 24.7 to 45.8 years), where a significant rate of decline of -0.014 Nm/cm^2 per year (95% CI: -0.016 to -0.011 Nm/cm^2 per year; p=0.021) was observed.

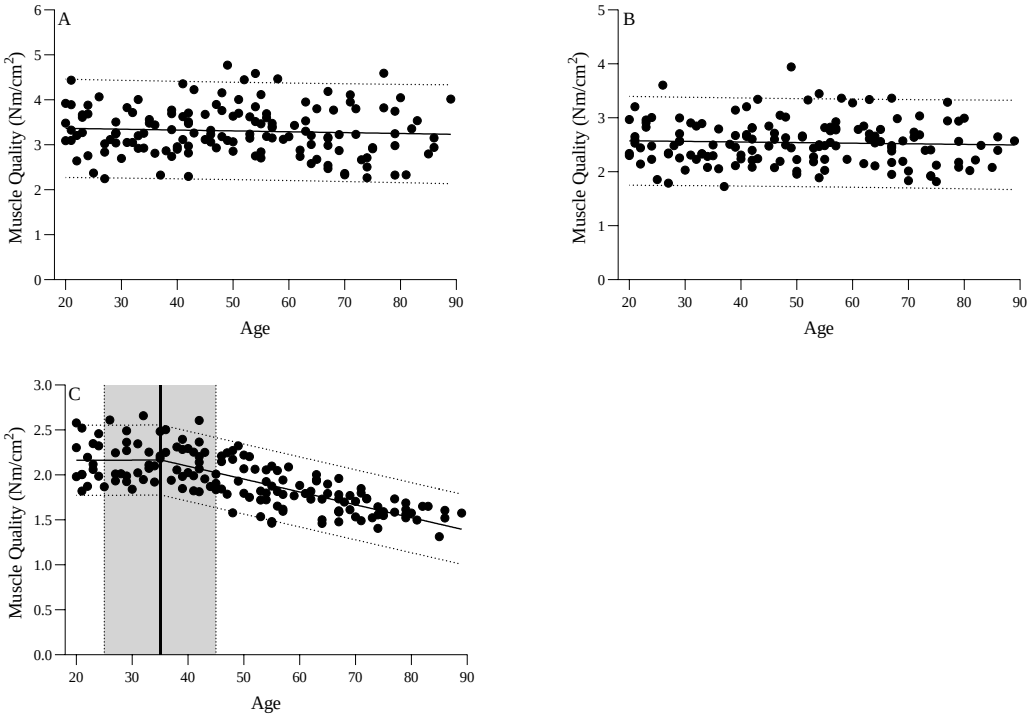

Figure 37. Upper Leg Muscle Quality Parameters

Figure Legend: *A- isometric contraction; B- contractions at 60 deg/s; C- contractions at 240 deg/s Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval. Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)*

Table 38. Upper Leg Muscle Quality Parameters

Age	Isometric	60 deg/s	240 deg/s
20-24	3.45±0.12	2.61±0.09	2.17±0.06
25-29	3.19±0.18	2.63±0.18	2.24±0.09
30-34	3.08±0.14	2.32±0.10	2.08±0.08
35-39	3.29±0.19	2.46±0.14	2.16±0.07‡
40-44	3.19±0.14	2.48±0.10	2.21±0.06
45-49	3.58±0.17	2.76±0.15	2.07±0.05
50-54	3.52±0.14	2.46±0.12	1.87±0.06
55-59	3.44±0.13	2.57±0.10	1.79±0.06
60-64	3.33±0.17	2.78±0.14	1.78±0.06†
65-69	3.26±0.13	2.67±0.10	1.75±0.04†
70-74	2.82±0.19	2.32±0.13	1.64±0.04†
75-79	3.52±0.25	2.55±0.16	1.66±0.05†
80-89	3.06±0.22	2.35±0.16	1.53±0.04†

Note: Values are presented as mean ± SE. Muscle quality values were derived from upper leg muscle cross-sectional area (pQCT). ‡- denotes critical age (breakpoint) from segmental analysis, †- denotes significant difference from reference group (underline). *Abbreviations*: deg/s degrees per second.

Upper Leg Specific Power

Specific power values of the upper leg derived from isotonic contractions are displayed in Table 39 and Figure 38. Upper leg specific power during the unloaded condition displayed a non-significant rate of increase of 0.024 Watts/cm^2 per year (95% CI: -0.023 to 0.073 Watts/cm^2 per year; p=0.31) to the age of 33.0 ± 3.5 years (95% CI: 26.1 to 39.8 years) where a significant rate of decline of 0.041 Watts/cm^2 per year (95% CI: -0.048 to -0.032 Watts/cm^2 per year; p=0.012) was observed. A similar non-significant rate of increase of 0.003 Watts/cm^2 per year (95% CI: -0.015 to 0.021 Watts/cm^2 per year; p=0.73) was observed during the 20% condition. After the age of 54 ± 5.2 years (95% CI: 43.7 to 64.2 years), a decline of 0.054 Watts/cm^2 per year (95% CI: -0.075 to -0.026 Watts/cm^2 per year) was observed. The 40% condition revealed a non-significant rate of increase of 0.002 Watts/cm^2 per year (95% CI: -0.01 to 0.016 Watts/cm^2 per year; p=0.72) to the age of 60 ± 4.5 years (95% CI: 51.2 to 68.9 years), where then a significant rate of decline of 0.062 Watts/cm^2 per year (95% CI: -0.092 to -

0.028 Watts/cm^2 per year; p=0.031) was observed. The 60% condition also revealed a non-significant rate of increase of 0.0001 Watts/cm^2 per year (95% CI: -0.006 to 0.007 Watts/cm^2 per year; p=0.84) to the age of 71.0 ± 2.6 years (95% CI: 66.9 to 75.1 years). Following this breakpoint, a significant rate of decline of 0.056 Watts/cm^2 per year (95% CI: -0.11 to -0.004 Watts/cm^2 per year; p=0.012) was observed.

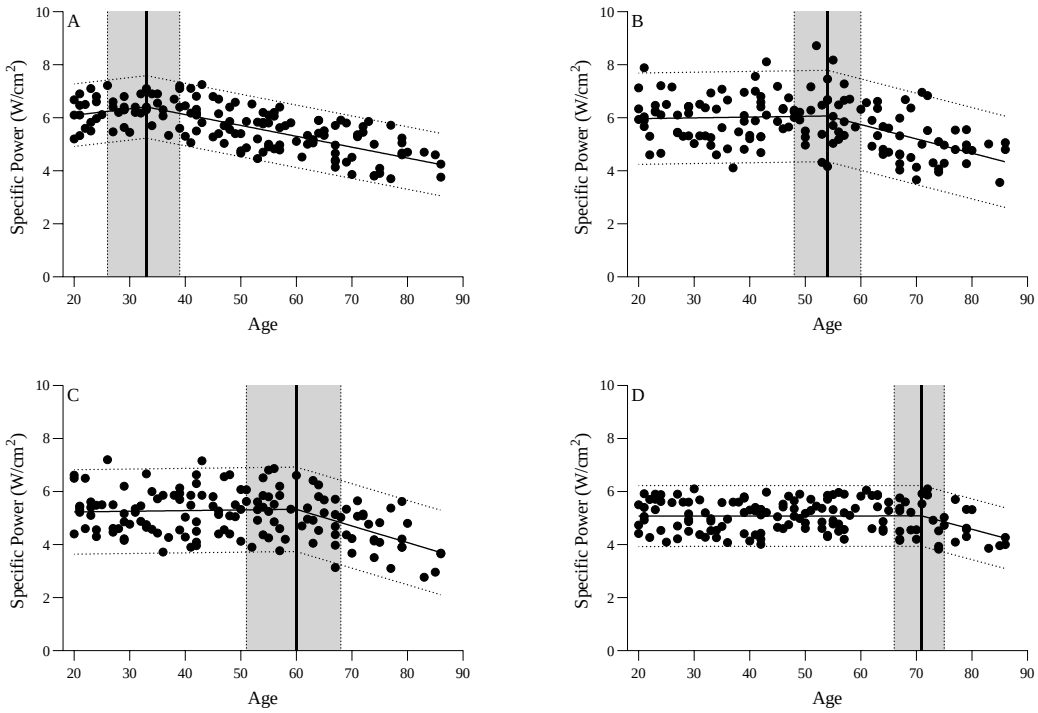

Figure 38. Upper Leg Specific Power Parameters
Figure Legend: *A- contractions at 1 Nm; B- contractions at 20% maximal isometric strength; C- contractions at 40% maximal isometric strength; D- contractions at 60% maximal isometric strength*
Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval.
Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)

Table 39. Upper Leg Specific Power Parameters

Age	Unloaded	20% MVIC	40% MVIC	60% MVIC
20-24	6.22±0.15	6.07±0.22	5.29±0.19	5.28±0.14
25-29	6.27±0.19	6.18±0.21	5.28±0.35	5.16±0.17
30-34	6.28±0.14‡	5.63±0.23	5.06±0.28	4.78±0.22
35-39	6.43±0.21	5.80±0.22	5.39±0.15	5.29±0.17
40-44	6.17±0.18	5.83±0.22	4.96±0.27	4.69±0.15
45-49	6.11±0.19	6.39±0.22	5.64±0.25	5.34±0.13
50-54	5.48±0.16	6.03±0.30‡	5.30±0.19	5.06±0.15
55-59	5.46±0.19	6.21±0.31	5.25±0.27	5.20±0.14
60-64	5.47±0.15	5.76±0.29	5.48±0.30‡	5.02±0.18
65-69	5.03±0.19†	5.51±0.29	4.99±0.16	5.39±0.17
70-74	4.88±0.24†	4.74±0.32†	4.40±0.21	4.79±0.24‡
75-79	4.76±0.29†	5.26±0.28	4.58±0.34	4.89±0.27
80-89	4.42±0.12†	4.48±0.19†	3.81±0.26†	4.51±0.21

Note: Values are presented as mean ± SE. Muscle quality values were derived from upper leg muscle cross-sectional area (pQCT). ‡- denotes critical age (breakpoint) from segmental analysis, †- denotes significant difference from reference group (underline). *Abbreviations*: MVIC- maximum voluntary contraction.

Lower Leg Muscle Quality

All three contractions revealed a significant group effect (all $p<0.001$) and the differences and corresponding reference values are displayed in Table 40 and Figure 39. Lower leg isometric muscle quality displayed a non-significant rate of decline of 0.002 Nm/cm^2 per year (95% CI: -0.005 to 0.006 Nm/cm^2 per year; $p=0.131$) to the age of 63 ± 6.6 years (95% CI: 49.8 to 76.1 years), where a significantly accelerated rate of decline of 0.011 Nm/cm^2 per year (95% CI: -0.19 to -0.003 Nm/cm^2 per year; $p=0.017$) was observed. During the 60 deg/s contractions, a linear rate of decline of -0.004 Nm/cm^2 per year (95% CI: -0.005 to -0.004 Nm/cm^2 per year; $p<0.001$) was observed. For the 240 deg/s contractions, there was a non-significant decline of 0.001 Nm/cm^2 per year (95% CI: -0.004 to 0.001Nm/cm^2 per year; $p=0.51$) until the age of 49 ± 3.9 years (95% CI: 41.3 to 56.7 years). Thereafter, a significantly accelerated rate of decline of 0.010 Nm/cm^2 per year (95% CI: -0.012 to -0.007 Nm/cm^2 per year; $p=0.04$) was observed.

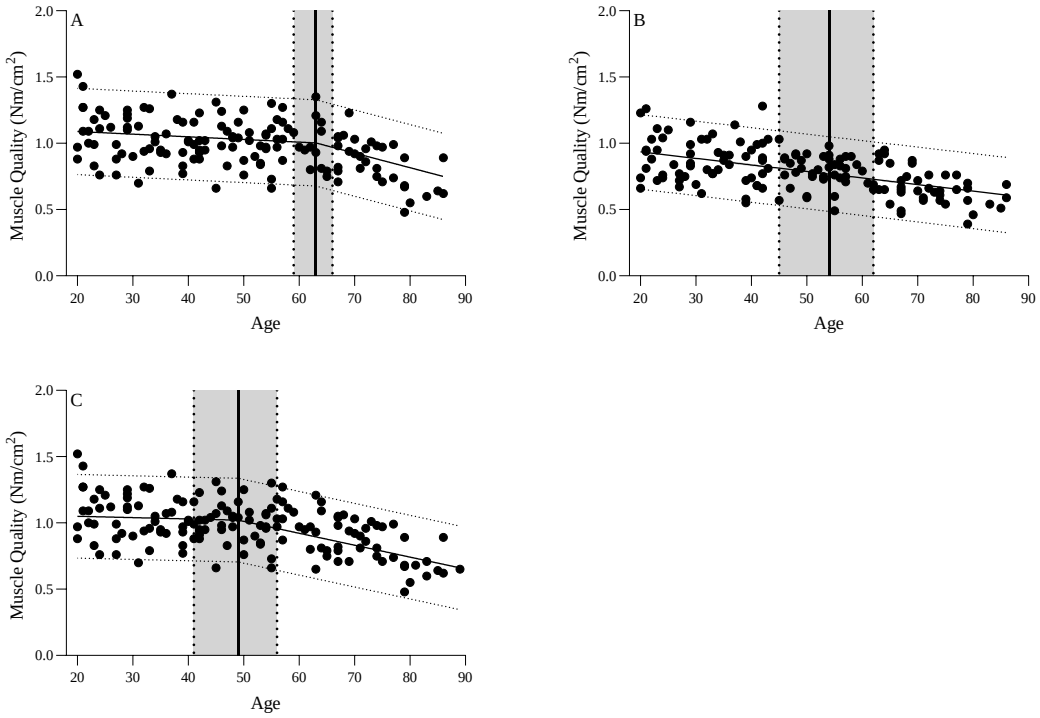

Figure 39. Lower Leg Muscle Quality Parameters

Figure Legend: *A- isometric contractions; B- contractions at 60 deg/s; C- contractions at 240 deg/s Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval. Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)*

Table 40. Lower Leg Muscle Quality Parameters

Age	Isometric	60 deg/s	240 deg/s
20-24	1.12±0.05	0.93±0.05	0.70±0.03
25-29	1.08±0.05	0.85±0.05	0.65±0.04
30-34	1.05±0.05	0.89±0.05	0.69±0.05
35-39	0.98±0.07	0.83±0.06	0.62±0.04
40-44	1.00±0.03	0.84±0.04	0.63±0.03
45-49	1.11±0.07	0.88±0.05	0.68±0.04‡
50-54	0.96±0.04	0.79±0.04‡	0.63±0.03
55-59	1.00±0.05	0.76±0.03	0.58±0.02
60-64	1.03±0.05‡	0.79±0.04	0.52±0.03
65-69	1.01±0.05	0.75±0.03	0.46±0.02†
70-74	0.89±0.03	0.61±0.03†	0.41±0.03†
75-79	0.85±0.04	0.65±0.03†	0.38±0.02†
80-89	0.65±0.04†	0.55±0.04†	0.26±0.02†

Note: Values are presented as mean ± SE. Muscle quality values were derived from lower leg muscle cross-sectional area (pQCT). ‡- denotes critical age (breakpoint) from segmental analysis, †- denotes significant difference from reference group (underline). *Abbreviations*: deg/s degrees per second.

Serum Biomarkers

The participants fell within the expected ranges for both myostatin and interleukin 6 (IL-6). Serum myostatin displayed significant group effects ($p<0.001$) while IL-6 did not ($p=0.206$; Table 41 and Figure 40). Both markers displayed significant positive relationships with age; myostatin: $r=0.420$, $p<0.001$ and IL-6: $r=0.249$, $p=0.003$, and both markers tended to display significant inverse relationships with the muscle function parameters. For example, IL-6 and knee extensor maximal isometric strength $r=-0.260$, $p=0.002$ and myostatin and elbow extensor maximal isometric strength $r=-0.257$, $p=0.001$. Altogether, myostatin displayed significant relationships with 109/126 muscle-related variables, while IL-6 displayed significant relationships with 81/126 variables. However, when controlling for age, the number of relationships dropped to 10/126 and 14/126 for myostatin and IL-6, respectively. There was also a significant positive relationship between both biomarkers ($r=0.187$, $p=0.026$).

Of all parameters, myostatin was the only to reveal two critical age periods. Initially, myostatin displayed a non-significant rate of increase of 0.002 ng/mL per year (95% CI: 0.001 to 0.003 ng/mL per year; $p=0.43$) to the age of 48.5 ± 2.2 years (95% CI: 43.2 to 53.1 years). Following this age, a significantly accelerated rate of increase of 0.018 ng/mL per year (95% CI: 0.009 to 0.027 ng/mL per year; $p=0.031$) to the age of 69.4 ± 2.1 years (95% CI: 64.1 to 75.5 years) was observed. Thereafter, an additional significant rate of increase of 0.034 ng/mL per year (95% CI: 0.025 to 0.043 ng/mL per year; $p=0.043$) was observed. Regarding IL-6, after removing outliers (values >3.77 pg/mL) a critical age period of 65.2 ±2.1 years (95% CI: 58.5 to 72.4 years) where prior to this age a non-significant rate of increase of 0.011 pg/mL per year (95% CI: 0.008 to

0.014 pg/mL per year; p=0.10) was observed. Thereafter a significant increase of 0.032 pg/mL per year (95% CI: 0.007 to 0.058 pg/mL per year; p=0.043) was observed.

Though not a focus of the current study, there did not appear to be any relationships between the circulating biomarkers and total fat mass or percent body fat. Of note, when expressed relative to muscle mass, the correlation between relative myostatin trended toward significance with total body fat mass (r=0.147, p=0.081).

Table 41. Serum Myostatin and Interleukin 6 Levels

Age	Myostatin (ng/mL)	Interleukin 6 (pg/mL)
20-24	0.865±0.10	1.569±0.21
25-29	0.753±0.06	1.017±0.19
30-34	0.724±0.05	1.095±0.15
35-39	0.732±0.06	1.127±0.16
40-44	0.958±0.06	1.030±0.21
45-49	0.825±0.05‡	1.342±0.18
50-54	0.940±0.10	1.329±0.31
55-59	0.899±0.10	1.483±0.18
60-64	1.110±0.11	1.557±0.31
65-69	1.058±0.08‡	1.781±0.27‡
70-74	1.120±0.11	1.487±0.16
75-79	1.670±0.21†	2.071±0.58
80-89	1.621±0.11†	2.150±0.52

Note: Values are presented as mean ± SE. ‡- denotes critical age period from segmental analysis, †- denotes significant difference from reference group (underline). *Abbreviations:* ng/mL- nanograms per milliliter; pg/mL- picograms per milliliter.

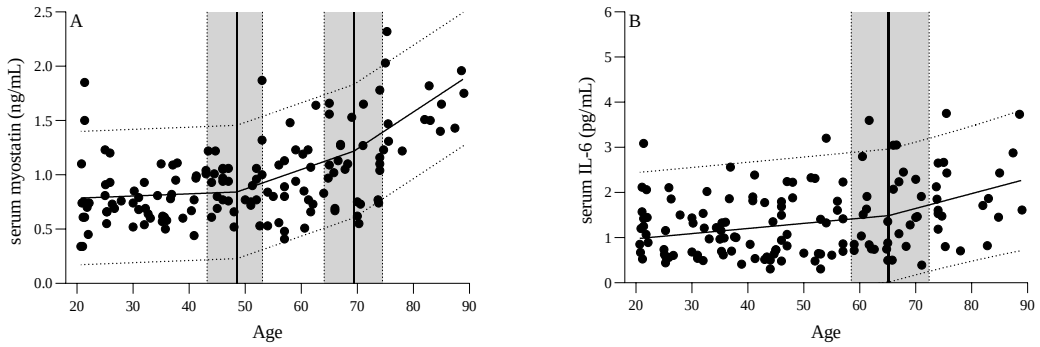

Figure 40. Serum Myostatin and Interleukin 6 Levels
Figure Legend: *A- myostatin; B- interleukin 6*
Vertical lines represent critical age (bold), dashed lines (gray fill) represent 95% confidence interval. Horizontal lines represent regression lines (bold), 95% confidence interval (dashed)

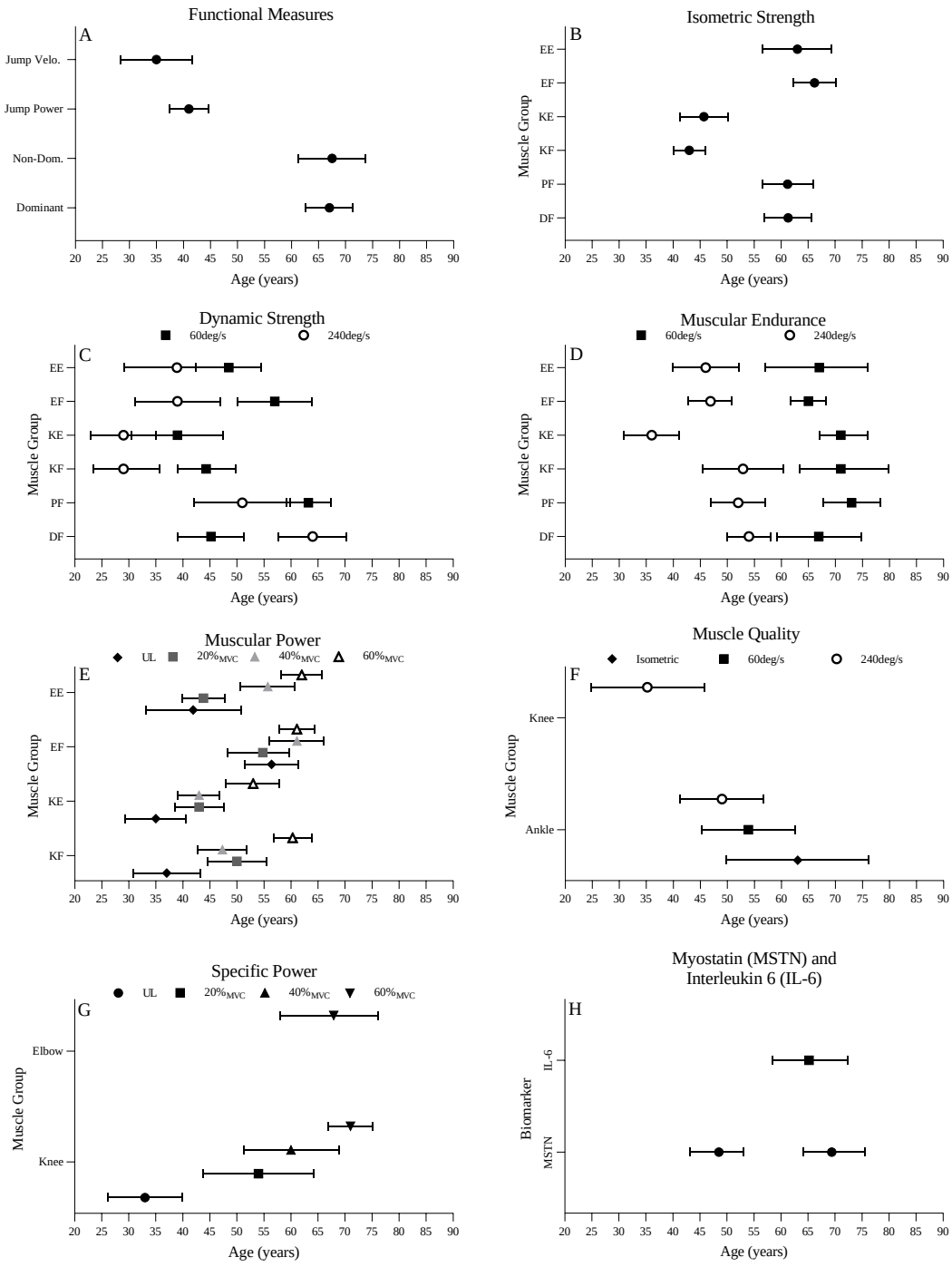

Figure 41. Critical Age Interval Summary

Figure legend: *A- functional measures, B- isometric strength, C- dynamic strength, D- muscular endurance, E- muscular power, F- muscle quality, G- specific power, H- serum biomarkers*

Figures present critical age period and corresponding 95% confidence interval

Discussion

The primary purpose of this investigation was to determine critical age periods in quantitative and qualitative skeletal muscle parameters in recreationally active women. The primary observations of the present study indicate that 1) skeletal muscle mass and function changes rarely occurred at similar age intervals; 2) the losses in skeletal muscle function (i.e. strength, power, and endurance) are greater than muscle mass, 3) muscle function specific parameters (i.e. isometric strength, dynamic strength, power, etc.) display declines at different ages and are further influenced by the muscle group and contraction being tested; 4) when assessing age-related changes in muscle function while accounting for muscle mass (i.e. muscle quality/specific power) declines across the lifespan were reduced but again are influenced by the muscle group and type of contraction; and 5) serum myostatin and interleukin 6 displayed significant positive and negative relationships with age and muscle parameters.

Participants

In the context of aging research, researchers often employ dichotomized design performing comparisons between a young and an older group inevitably observing differences between the two. In the current study, we sought to perform similar comparisons but allow for the identification of when skeletal muscle mass and skeletal muscle function changes, as well as the rate at which these parameters change. In order to isolate the effects of aging on these characteristics, rather than additional age-related factors per se, it was vital to have a strict recruiting and screening process (Harridge and Lazarus, 2017; Lazarus, Lord and Harridge, 2019). As displayed in Table 1, the only difference amongst physical stature parameters in the grouping of participants was the

mean age intervals, except for the two youngest groups. Therefore, the influence of factors that have been proposed to influence skeletal muscle parameters (e.g. height, weight, BMI) was trivial. Furthermore, each group of participants was currently prescribed and taking a similar number of medications and had a similar number of diagnoses, which were derived from our health status questionnaires. Despite the anticipated increase in hours during the mid-life period, the number of occupational work hours, which included those currently employed and those committed to volunteering in their community, were also similar amongst all groups (Table 2). The effects of physical activity on skeletal muscle cannot be refuted (Gries *et al.*, 2018; Lavin *et al.*, 2019), and given the context of the current study, it was important to identify the amount and type of physical activity that the participants were performing. Three approaches were used to quantify the total amount and level of perceived exertion of physical activity that each participant was currently performing. Table 3 reveals no differences across groups for total met minutes per week, with each participant being classified as 'moderately active'. In the case of the IPAQ questionnaire, a moderately active classification would include 1) three of more days of vigorous intensity activity and/or walking of at least 30 minutes per day, 2) five or more days of moderate intensity activity and/or walking of at least 30 minutes per day, 3) five or more days of any combination of walking, moderate intensity or vigorous intensity activities achieving a minimum total physical activity of at least 600 MET minutes a week (Hagströmer, Oja and Sjöström, 2008). Many of the participants fell into the categories 2 or 3, while a smaller portion met criteria 1. The participants completed a similar number of days (5 to 6) of physical activity and was being performed at similar levels of perceived exertion within each session for both resistance and aerobic

exercise (Table 4). For comparison, all participants met the recommended physical activity levels proposed from the American College of Sports Medicine, however, it must be mentioned that we did not quantify the extent to which stretching, or flexibility exercises were being performed. Further, although there is room for debate regarding whether individuals globally are currently meeting physical activity guidelines (Tucker, Welk and Beyler, 2011), the range of met minutes per week observed in the current study (1722.8 to 2984.9; $\bar{x} \pm SD$): 2331.16 ± 376.96) are just below the range where substantial gains in health outcomes are typically observed (3000 to 4000 met minutes per week) (Kyu *et al.*, 2016). Therefore, the results of the current study cannot be based off differences in physical activity levels with advanced age and may not be useful for generalization to inactive or sedentary populations.

It must be mentioned that we did not attempt to control for a specific menstrual cycle phase, contraceptive use, nor did we control for hormone replacement therapy use. Regarding the eumenorrheic women, there does not appear to be a consensus on whether changes in hormones across the menstrual cycle influence neuromuscular performance as both sides provide strong evidence (Janse De Jonge, 2003; Constantini, Dubnov and Lebrun, 2005; Tenan, Hackney and Griffin, 2016; Bondarev *et al.*, 2018; Ansdell *et al.*, 2019; Romero-Moraleda *et al.*, 2019; Weidauer *et al.*, 2020). Nevertheless, of the premenopausal women, 52/75 were using contraceptives, of which 58% (n=30) were using an intrauterine device and the remaining 42% (n=22) participants were using combined oral contraceptives. When performing comparisons among the three groups, no differences were observed for anthropometric measures, physical characteristics, or serum biomarkers (all p>0.05). Each of the 17 participants not using a form of

contraceptive reported having a normal menstrual cycle. To establish whether different phases of the menstrual cycle influence neuromuscular performance, the countback method was used to determine different phases corresponding to days 0 to 4 for follicular, days 11 to 15 for ovulatory, and days 21 to 25 for late luteal phase. Of the 17 participants, 13 of which were able to complete testing during each phase of the cycle, and no differences among any of the neuromuscular performance variables were observed. Further, differences between trials were also less than the typical errors associated with testing. Though the countback method is convenient, we are aware of the limitations, and suggest that future research regarding the menstrual cycle refer to and abide by the meticulous methodological considerations recently outlined (Sims and Heather, 2018; Janse De Jonge, Thompson and Han, 2019).

The menopausal transition has also revealed mixed results regarding decreases or no changes in muscular performance (Calmels *et al.*, 1995; Bassey, Mockett and Fentem, 1996; Kurina *et al.*, 2004; Cooper *et al.*, 2011; Cipriani *et al.*, 2012; Tseng *et al.*, 2012). What appears to be more clear is the full transition to the menopausal state where the absence of estrogens limits the function of myosin, thereby decreasing force production but exerting greater effects during moderate to high-velocity based contractions (Lowe, Baltgalvis and Greising, 2010; Sipilä *et al.*, 2013; Vitale, Cesari and Mari, 2016; Collins, Laakkonen and Lowe, 2019). The current data align with these suggestions since the collective critical age periods for the dynamic contractions and for peak power during the isotonic contractions decline around the menopausal transition (48 years). Additionally, with the exception of the knee extensors, each additional muscle group displayed critical changes during the menopausal transition for the high velocity muscular endurance tasks.

In this regard, it must also be mentioned that when reviewing the force time (i.e. RTD, TPT, TTPP, and TTPV) and velocity characteristics during the isotonic contractions, that the age intervals corresponding to the menopausal transition or the onset of typical menopause paralleled those in which critical changes were observed. These observations highlight the influence of female reproductive hormones on muscle performance with increasing age, particularly during contractions where velocity is an integral component.

Body composition parameters, specifically, fat mass and percent (total and regional), BFLBM (total and regional), SMI, FFMI, in addition to the site specific parameters derived from the pQCT were not different among groups representing the midlife period (45 to 49 years to 55 to 59 years, all $p>0.05$). These observations conflict with previous cross-sectional and longitudinal studies suggestion increases in fat mass and decreases in muscle mass, which are likely attributed to our smaller sample size and/or the cross-sectional design (Sowers *et al.*, 2007; Lee *et al.*, 2009; Jaff *et al.*, 2015; Karvonen-Gutierrez and Kim, 2016; Greendale *et al.*, 2019). An intriguing observation, is that given 1) the lack of changes of muscle and fat mass during this time; 2) the collective changes in velocity sensitive neuromuscular indices; and 3) a critical rate of increase for myostatin (to be discussed below), is that myostatin may induce its effects on performance, specifically velocity dependent parameters, which supports recent observations in older women but not men (Fife *et al.*, 2018).

Of the postmenopausal women, 21% ($n=12$) were supplementing with hormone replacement therapy. Conflicting data has also been reported on skeletal muscle and hormone replacement therapy (Bemben and Langdon, 2002; Greising *et al.*, 2009; Javed *et al.*, 2019), however, the most compelling evidence is from the Finnish Cohort study of

monozygotic twins discordant for exogenous hormone use, suggesting beneficial effects (Ronkainen *et al.*, 2009, 2010; Finni *et al.*, 2011; Qaisar *et al.*, 2013; Laakkonen *et al.*, 2017). Given the large number of postmenopausal women in the current sample, in addition to the low hormone replacement therapy users, we were able to perform age and size-matched comparisons discordant for hormone use. Although the comparison was not adequately powered, we did not observe any differences between groups. Further, the relatively wide age range of use may have impacted the differences, given the large decreases in performance observed across these age groups (~55 to 75 years).

Body Composition

Though not a focus of the current study, there were significant group effects for total and regional sites for percent body fat. However, when performing following up analyses, no differences were identified. The present values are similar to those reported elsewhere (Coin *et al.*, 2012; Jaff *et al.*, 2015; He *et al.*, 2018). Significant positive correlations between age and total percent body fat (r=0.284, p=0.001), arm percent body fat (r=0.331, p<0.001), and leg percent body fat (r=0.255, p=0.002) were observed. The trend for gradual increases in body fat with age was expected and supports previous observations of increase (Kyle, Genton, Hans, *et al.*, 2001; Sowers *et al.*, 2007; Coin *et al.*, 2012; Gába and Přidalová, 2014; He *et al.*, 2018; Westerterp, 2018). Of note, across most of the neuromuscular performance variables, significant negative relationships existed between total and regional percent body fat. For example, percent fat of the arms displayed significant negative relationships with elbow extensor (r=-0.304, p<0.001) and elbow flexor maximal isometric strength (r=-0.267, p=0.001), whereas percent fat of the legs displayed significant positive relationships with time to peak torque for both 60 deg/s

(r=0.271, p<0.001) and 240 deg/s (r=0.273, p<0.001). These relationships have been reported before (Lebrun *et al.*, 2006; Bouchard, Héroux and Janssen, 2011; Schaap, Koster and Visser, 2013); however, when controlling for the effects of age, most of the relationships were non-significant or completely disappear.

As expected, each muscle mass parameter declined with increasing age. The muscle mass parameters initially displayed concerted increases reaching the greatest values in the 30s, except for muscle area for the upper leg, which peaked at 25 to 29 years (Table 4, Figures 1 and 2) The ages at which the maximal values were displayed and the percent change from that maximal value to the oldest age group are displayed below (Table 42) Although particularly young breakpoints were identified and confirmed, it should be mentioned that no differences were observed between groups when performing post-hoc procedures on the DXA and three of the four pQCT (upper leg muscle area) muscle mass parameters. Nonetheless, the observed values for site specific, regional, and total body muscle mass values, in addition to the overall percent change, are congruent with what has been reported from previous literature (Gallagher *et al.*, 1997; Tankó *et al.*, 2002; Silva *et al.*, 2010).

Changes in muscle mass with increasing age is influenced by several factors (e.g. diet, exercise, occupation, among others), but it is promising that the present observations parallel previous research using larger scale data. To our knowledge, there is only one previous study that has employed a "breakpoint" analysis for assessing age-related changes in body composition (Silva *et al.*, 2010). The previous work consisted of 1280 female participants over the age of 18 years and observed a breakpoint at the age of 27 years, for which skeletal muscle begins to display a negative association with age (Silva

et al., 2010). The current observations support the previous observations indicating that the late 20s is likely a critical age period for changes in muscle mass.

Previous longitudinal observations reported a BFLBM decrease of 0.11kg per year, which is nearly identical to the 0.15kg per year observed in the current study (Guo *et al.*, 1999). Further, these observations support previous cross-sectional research that has observed increases from the youngest group included (typically 20 to 29 years) to the fourth decade (30 to 39 years), which is then followed by declines with increasing age (Chumlea *et al.*, 2002; Coin *et al.*, 2012; Gába and Přidalová, 2014). Alternative findings have been reported, which indicate that peak muscle mass is achieved between 40 to 60 years (Kyle, Genton, Hans, *et al.*, 2001; Borrud *et al.*, 2010; He *et al.*, 2018). Several reasons could explain the differences between studies; however, the most substantial differences would be the measurement device used in the current versus contrasting observations (DXA versus BIA) and the participant ethnicity/race. Previous observations from our lab, in addition to other work, has demonstrated the influence that race/ethnicity has on both fat and fat free mass (Silva *et al.*, 2010; Kaur *et al.*, 2019). Furthermore, we have also demonstrated that although there are strong relationships ($p<0.001$) between fat free mass measures of BIA and DXA, the values were significantly different, with BIA measures often displaying higher BFLBM values (Miller, Chambers and Burns, 2014). Thus, although large scale studies measuring the age-related changes in muscle mass using BIA provide information regarding when changes occur, the overall fat free mass values must be considered.

Overall, lower body skeletal muscle mass parameters displayed larger percent differences and slope coefficients between the reference and oldest age interval when

compared to the upper body, which supports previous observations in both men and women (Janssen *et al.*, 2000; Coin *et al.*, 2012) Additionally, it is important to note that the muscle area (derived from pQCT) revealed considerable declines across the lifespan (>26.9%), however the overall muscle density, a proxy for the quantification of intramuscular adipose tissue, displayed marginal changes (<6%) for both the upper and lower leg. Together, these findings support previous observations suggesting that the presence of physical activity may attenuate the anticipated infiltration of adipose tissue into the muscle with increased age, thereby maintaining muscle quality with advanced age, to be discussed later (Goodpaster *et al.*, 2008; Leskinen *et al.*, 2009; Santanasto, Newman, *et al.*, 2015).

Functional Measures

The current study included grip strength and vertical jump to determine the influence of aging on functional measures. The ability for grip strength measures to provide pertinent health information for aging populations cannot be argued (Bohannon, 2019), and the inclusion of the vertical jump has been used for years to predict and/or quantify an individual's physical function. Regarding grip strength, both hands displayed marginal declines to the late 60s, which preceded significant declines of approximately 0.04 and 0.08kg per year. The greatest grip strength values were displayed in the 30s, which supports previous observations of when maximal grip strength is achieved (Kallman, Plato and Tobin, 1990; Rantanen *et al.*, 1998; Vianna, Oliveira and Araujo, 2007; Dodds *et al.*, 2014; Amaral *et al.*, 2019). Interesting to note, most of the participants (n=142, 93%) were right-handed, yet the right hand did not display as great of grip strength values when compared to the left. Given that the dominant hand, in this case the

right hand, is often used to perform tasks that involve greater dexterity, such as unlocking or opening doors, picking things up off the floor, etc., it is not surprising that the left grip strength was higher, which is where any type of external load (e.g. a bag of groceries) would be placed to complete the aforementioned tasks. The observed strength values were similar to or marginally greater than those previously reported (Kallman, Plato and Tobin, 1990; Vianna, Oliveira and Araujo, 2007; Dodds *et al.*, 2014), with the exception of a recent epidemiological study from Brazil (Amaral *et al.*, 2019) for which the present values were substantially higher. Nonetheless, the epidemiological study did not specify the precise participant screening strategy, while the current study sought to include women that were recreationally active in order to delineate the effects of aging on skeletal muscle rather than additional age-related conditions. Further, to highlight the capacity of the current participants, none of the participants in the present study displayed a grip strength value that would have been beneath previously defined physical dysfunction thresholds (Duchowny, Peterson and Clarke, 2017; Duchowny, Clarke and Peterson, 2018).

Jump power increased to the age of 41 years and then displayed a precipitous decline, whereas jump velocity was relatively unchanged to the age of 35 years, which was then followed by a sharp decline. Although a multitude of devices have been used to measure vertical jump performance in the literature, the current declines of 59.9 and 49.7%, respectively, between the reference value and the oldest age group, in addition to maximal values being displayed in the late 30s and early 40s are consistent with previous literature (Runge *et al.*, 2004; Dionyssiotis, 2009; Siglinsky *et al.*, 2015). Further, given that the 13 age groups displayed no differences in body weight, the declines in jump

power are suggestive of substantial declines in jump velocity with increasing age. The decreased velocity would indicate that although the loads (body weight) were similar among groups, the load was becoming closer to maximal values for the older participants. Nonetheless, the vertical jump test provides a significant advantage in comparison to more laboratory-based tests in that it is an ecologically sound measure of neuromuscular performance and has been shown to have excellent reliability in a variety of populations (Heishman *et al.*, 2020; Miller *et al.*, 2020). For example, each of the desired vertical jump metrics depend on a value that is individualized to the subject being tested, which is also the same intrinsic resistance that individual encounters in everyday activities, which is certainly a potential advantage with respect to other methods such as dynamometry assessments.

Altogether, it appears that within the current cohort that decreases in jump power are largely explained by decreased in jump velocity, since body weight remained relatively similar among all age groups. Further, although we did not observe differences in body fat mass, increased fat mass has also been suggested to play a role with decrements in jump performance (Runge *et al.*, 2004). In this perspective, maximal force production of the legs (isometric contractions) did not display critical changes until after the observed changes for the vertical jump parameters. However, critical ages for changes in muscle cross-sectional area and muscle density paralleled those observed for both jump metrics, thereby suggesting a potential contribution to the observed changes. The decrease in cross-sectional area indicates a reduction in sarcomeres in parallel, thus a reduction in force generating capacity, which is a primary component of muscular power. Decreases in muscle density would suggest an increase in intramuscular adipose tissue,

which has also been shown to hinder muscular performance (Addison *et al.*, 2014). Altogether, these factors combined could influence muscle architecture, thereby potentially causing a reduction in maximum contraction speed.

Isometric Strength

As hypothesized, there were decreases in maximal isometric strength across all muscle groups. The losses appeared to be dependent upon muscle location in that the lower body displayed greater declines (nearly twice) in comparison to the upper body, which supports previous observations (Bemben *et al.*, 1991; Frontera *et al.*, 2000; Hunter *et al.*, 2000; Runnels *et al.*, 2005). Of note, the muscle groups of the elbow and ankle each appeared to be relatively unchanged to the early 60s, which proceeded significant declines, whereas the muscle groups of the knee displayed significant decreases during the mid-40s. This is important for two reasons. First, it is promising to note that the muscle group that has received the greatest amount of attention regarding its relationship with physical function, the knee extensors, displayed a significant increase prior to the decline. However, the significant rate of decline as in age group representing the 40s contains clinical implications. Given that muscular power is the product of force and velocity and is a strong predictor of physical function, if force is beginning to decline prior to the midlife, where consistent observations for decreases in contractile velocity have been observed, this sets up a problematic scenario for physical function following the menopausal transition.

Interestingly, the dorsiflexors (tibialis anterior), displayed the greatest percent difference from the reference value to the oldest group. This observation was interesting on two fronts. First, this opposes our hypotheses and was not expected since the

dorsiflexors were the weakest muscle group examined, thus suggestion a much lower amount that could theoretically be lost. Second, the dorsiflexors represent a muscle that tends to not be targeted during resistance training. However, the evaluation of this muscle group was important given the role in locomotion, but likely highlight the specificity concept. For example, during locomotion the toe rise is void of external resistance and usually happens at a rapid pace, which would be the opposite of the isometric testing procedure. In fact, the rate of torque development, a more muscle group specific measure, displayed a critical age period after the isometric contraction. Nonetheless, the present results are similar or slightly above those from previous research, which is to be expected given the recruitment criteria the current study employed.

To date, few studies have sought to identify critical age periods for changes in isometric strength and some bear major consideration. One of these performed a similar analytical technique and reported that the age of 55 years represented a period where changes in grip strength and knee extensor isometric strength occur (Samson *et al.*, 2000). Although the aforementioned observations regarding grip strength were supported later (Vianna, Oliveira and Araujo, 2007) with a much larger sample size, the initial observations had a total of 74 women spanning the age range of 20 to 90 years and no details regarding physical activity, with the exception of unassisted walking. Those observations conflict with the current observations, whereby the breakpoint in the current participants for knee extensor isometric strength was 43.0 years and was ~67 years for grip strength. Although the comparison between studies is difficult given the bleak methods, a few key differences between the two would be the use mean values in the present while the alternative used maximal values as well as the differences in sample

sizes. The use of mean values was selected based on providing a more appropriate representation of the participant's strength. Further, alternative observations have suggested that peak values are displayed between the 20s and 40s across muscle groups belonging to the upper and lower body (Danneskiold-Samsøe *et al.*, 2009). Again, a consistently observed difference between those observations and the current were differences in the health status of the participants. Although the physical activity levels are different between studies, this difference suggests that maintaining or completing recommended amounts of physical activity can delay the effects of aging on maximal isometric strength. In contrast, when recreationally active participants are included within the sample, the current observations support additional observations. For example, previous research has suggested that the muscle groups of the hand, ankle, and elbow display critical changes in the late 50s and early 60s (Christ *et al.*, 1992; Metter *et al.*, 1999). Interesting to note, when combining each of the isometric age groups in which critical changes were observed (50s), the current observations support those of Stoll *et al.* who measured 51 different muscle groups of the upper and lower body, combining each of the measures to form a surrogate muscle strength index revealing a critical age for women at 51 years (Stoll *et al.*, 2000).

The age-related changes observed regarding maximal isometric force production could be related to the declines in muscle area observed for the upper and lower leg, which would support previous suggestions of the close relationship between muscle area and force output (Jubrias et al., 1997; Larsson et al., 2019; Narici & Maffulli, 2010; Young et al., 1984), whereas much of the influence of neural deficits have been dismissed when appropriate methodological familiarization and orientation are performed (Klass,

2005; Klass, Baudry and Duchateau, 2007). Moreover, the decreased muscle area of the upper and lower leg, may have been a result of changes in muscle architecture, (e.g. fascicle length and pennation angle) in turn inducing a reduction in force generating capacity of the respective groups (Hakkinen & Hakkinen, 1991; Kubo *et al.*, 2003; Narici & Maffulli, 2010; Overend *et al.*, 1992). However, we did not perform pQCT scans of the upper arm or forearm, thus cannot confirm this change for each included muscle group. Nonetheless, it is interesting to note that arm BFLBM also displayed a critical age period for the onset of decline around 30 years of age, which corresponding to nearly half the age of the participants in the age group demonstrating a critical change for isometric force production for the elbow extensors and flexors. It should be mentioned that between the youngest age group (20 to 24 years) and those representing the critical age group for isometric force production, both upper arm muscle groups declined, but not at a significant rate.

Dynamic Strength

Dynamic strength parameters displayed greater percent declines between the reference value and the oldest group when compared to the maximal isometric contractions. Further, across all muscle groups, the faster contraction velocity as displayed greater percent declines and was also influenced by muscle group, supporting previous suggestions (Mitchell *et al.*, 2012; Hunter, Pereira and Keenan, 2016; Tieland, Trouwborst and Clark, 2018). With the exception of plantarflexion at 60 deg/s and dorsiflexion at 240 deg/s, each of the breakpoints for changes in slope occurred sooner than the isometric contractions. These observations were surprising but are likely contributed to their influence in normal ambulation, such as planting and pushing off the

toe slowly (plantarflexion) and rapidly raising the toe (dorsiflexion). Further, since many of the participants included walking and/or running as part of their physical activity, it is plausible that the exercise that the included participants were performing or had been performing may have been adequate to maintain dynamic force production for those muscle groups, but were not inducing a large enough stimulus to maintain dynamic force production for the knee extensors and flexors. Similar to the isometric changes, the lower revealed greater percent decreases across age. This is likely due to the fact that the upper body musculature is included more frequently in activities of daily living, which may culminate in a greater overall stimulus, in turn permitting the maintenance of muscular strength with increasing age. Further, it should be mentioned that many of the middle-aged and older participants included gardening as their physical activity, often spending times in a prone position while moving, carrying, or holding objects with upper body.

Altogether, it appears that dynamic strength begins to decline during the middle-age (29 to 64 years), and likely depends on the muscle and contraction velocity (Akima *et al.*, 2001; Frontera *et al.*, 1991; Hulens *et al.*, 2002; Jubrias *et al.*, 1997; Lindle *et al.*, 1997). Regarding peak torque values for each body part, the current observations are similar to those previously reported or marginally higher, again likely attributed to participant inclusion criteria (Harbo, Brincks and Andersen, 2012; Pereira *et al.*, 2019). Congruent to the current observations, Charlier *et al.* reported that women knee extensor peak torque values at 60 and 240deg/s were highest in those aged 18 to 30 and declined linearly with age (Charlier *et al.*, 2015). Further, in a more comprehensive study, Danneskiold-Samsøe *et al.* reported that the elbow extensors and both ankle muscle groups were relatively maintained until 50 to 59 years, then precipitously declined, while

the elbow flexors and both knee muscle groups displayed declines as early as 30 years of age (Danneskiold-Samsøe *et al.*, 2009). The current observations also support those of previous suggesting marginal changes of the ankle muscle groups through the middle-age, then observing greater declines after 60 years of age (Gajdosik, Vander Linden and Williams, 1999; Jan *et al.*, 2005). Recently, Leyva *et al.* measured dynamic strength of the knee extensors and flexors, in addition to the plantar- and dorsiflexors of men and women aged 19 to 80 years (Leyva, Balachandran and Signorile, 2016). The primary observation of this study indicates that age-related changes in peak torque were muscle group and contraction dependent. For example, when increasing contraction velocity within the knee extensors, there were differences between the 20 and 30-year-old group. However, for the knee flexors and the plantar flexors, significant differences were observed across all contraction velocities between the 20 and 30-year-old groups, while no dorsiflexion peak torque appeared to be similar among all age groups across all contraction velocities. Of note, only one study, to our knowledge, has employed a similar analytical technique for maximal dynamic strength across the lifespan, but was performed in men (Kemmler *et al.*, 2018). Nonetheless, critical age periods of 52 and 59 were identified for the knee extensors and knee flexors, respectively, which is later in the lifespan than the current observations in women, which would be suggestive of a sexual dimorphism with increased age. For example, in a similar study Runnels *et al.* examined isometric, isotonic, and isokinetic strength in recreationally active men reporting that across all contraction types that 60s represented a period for critical changes in muscle performance (Runnels *et al.*, 2005). In contrast to those observations, only two muscle

groups presented critical changes in the 60 to 64-year age group (plantar and dorsiflexors).

Muscular Power

Aside from the lower body power declines discussed from the vertical jump testing, the current study is the first to compare upper and lower body contractions across four different intensities to identify the influence of aging on muscular power output. Together, there was a trend for a longer maintenance of muscular power with increasing age as the external load increased. For example, the unloaded condition (1Nm) displayed the earliest breakpoint in slope across all four muscle groups, whereas the 60% maximal load displayed breakpoints five to 15 years later. Further, across all conditions, the observed breakpoint appeared to be fairly similar for all four power parameters examined (peak power, peak velocity, time to peak power, and time to peak velocity). It is interesting to note that there appears to be an inverse relationship between percent difference for the upper and lower body as the intensity increases.

The percent declines appeared to be similar to that during the dynamic contractions or slightly higher and were much greater than those displayed for isometric contractions. Previous research often delegates isotonic contractions as performing machine or free weight resistance exercises, thus limiting the ability to draw comparisons with the present observations. In the few studies that have included isotonic contractions using a dynamometer, the current values are similar to those across all age ranges (Van Roie *et al.*, 2011; Charlier *et al.*, 2015; Van Roie *et al.*, 2018; Van Driessche, Delecluse, *et al.*, 2018).

Similar to the dynamic contractions, changes in maximal power output appear to begin during the mid-life period, with the earliest onset occurring at ~35 years of age for the knee extensors, followed by the knee flexors and elbow extensors at ~40 years of age and last the elbow flexors at ~55 years. These observations support previous observations suggesting that the mid-life period results in significant decreases in knee extensor muscular power in women (Samson *et al.*, 2000; Aadahl *et al.*, 2011; Charlier *et al.*, 2015; Van Roie *et al.*, 2018; Suetta *et al.*, 2019; Alcazar *et al.*, 2020). To our knowledge, no previous research has examined knee flexion power, and it has recently been suggested that age-related increases in the hamstrings to quadriceps ratio with advanced age may negatively impact functional performance (Palmer *et al.*, 2017). Given the relationship between muscular power and fall risk, it is plausible that rapid force characteristics (i.e. peak torque or peak power) of the knee flexors contribute to an individual's fall risk. For example, the ability to recover from a balance perturbation requires the ability to quickly recover one's balance, but if the knee flexors do not possess an adequate amount of strength, they may not be able to withstand the individual's body mass, ultimately resulting in a fall. Nonetheless, since isotonic contractions across a wide range of external loading intensities, including the current observations, have been shown to be reliable, further research is needed to ascertain the relationship between knee flexor isotonic performance and physical function, as well as the influence of age-related changes in the hamstring to quadriceps ratio with advanced age. The current observations support previous findings (Van Driessche, Van Roie, Vanwanseele and Delecluse, 2018), that suggest using certain isotonic loads (e.g. >60% maximal strength) there may be a slight decrease in reliability and perhaps the inability to perform the contraction. For example,

the 60% contraction in the current study was anecdotally much more difficult to complete and resulted in lower reliability values than lower intensities.

To date there is a dearth of literature exploring age-related changes in upper body power. One study that included women revealed that maximal power was displayed in the 20s, which is neither refuted nor supported by the current observations since the elbow flexors and extensors each displayed some parameters that were highest in the 20s (Metter *et al.*, 1997). However, the methods for assessing muscular power were different, such that the current used isotonic dynamometry, whereas as the aforementioned study used upper body cycle ergometry.

Declines in dynamic strength and muscular power could be attributed to similar reasons addressed during the isometric strength deficits. In addition to the preferential loss of type II fibers with advanced age, there is a compensatory increased proportion of type I fibers resulting in slower contractile characteristics (Lexell *et al.*, 1983; Larsson, Li and Frontera, 1997; Larsson *et al.*, 2001; Nilwik *et al.*, 2013; Roberts *et al.*, 2018). Of note, recently Roberts *et al.* suggested that based of the severe type II atrophy with age, increased size variability, and type I myofiber grouping, that females may display a better capacity to retain myofiber quantity, but are unable to retain type II myofiber size, thereby resulting in substantial losses in force production and force-velocity characteristics (i.e. contractile speed). Given the differences between fiber types (Trappe *et al.*, 2003), this would be clinically and functionally relevant resulting in decreases in dynamic strength and muscular power. Moreover, changes in shortening velocity (Larsson, Li and Frontera, 1997; Krivickas *et al.*, 2001), architectural factors (Kubo *et al.*, 2003; Reid and Fielding, 2012), and potentially age-related changes in central activation (Klass, Baudry and

Duchateau, 2008). Further, type I grouping is believed to be a compensatory mechanism following denervation (Lexell and Downham, 1991), whereby the integrity of the neuromuscular junction may ultimately moderate the denervation reinnervation process (Kelly, Hammond, Bickel, *et al.*, 2018). Of note, Kelly *et al.* also identified that the greater myofiber grouping was associated with a reduced motor unit activation efficiency (e.g. great activation needed to complete same task) during a functional task, thus the reinnervation process may be protective against fiber less, it appears to present a significant functional disadvantage (Kelly, Hammond, Bickel, *et al.*, 2018). Changes proximal to the muscle may have also contributed to the decreases in dynamic strength and muscular power (D'Antona, 2003; Narici and Maffulli, 2010; Mitchell *et al.*, 2012). These changes may have included the motor neuron (e.g. decreased number, reduced voluntary activation, conduction velocity, recruitment strategies, etc.) and/or the neuromuscular junction (e.g. changes in transmitter release, changes in structural integrity, stability, etc.) (Hepple and Rice, 2016; Tieland, Trouwborst and Clark, 2018; Larsson *et al.*, 2019).

Muscular Endurance

Recent systematic reviews and meta-analyses have demonstrated that increasing age may provide an advantage for sustaining muscular endurance (Avin and Law, 2011; Kruger *et al.*, 2018). Specifically, older appear to be less fatigable with isometric or low intensity fatiguing tasks when compared to younger individuals. What is less clear is how increasing age influence muscular endurance during dynamic contractions. Determining whether age provides an advantage for muscular endurance is essential for creating effective lifestyle interventions since activities of daily living depend on not only the

ability to exert force but the ability to sustain force, which is often dependent on contractile velocity.

The current observations suggest that increasing age may provide an inherent advantage during slow contraction velocities (i.e. 60 deg/s) but may result in a disadvantage during high velocity contractions (i.e. 240 deg/s). Considering the changes in skeletal muscle, these changes were expected as the aging "slower" muscle would provide an advantage during slower or isometric contractions. Conversely, the slowing of the muscle would provide a significant disadvantage during faster contractions, resulting in an accumulation of metabolite, resulting in an impaired muscle contraction. The elbow extensors and flexors, knee extensors and flexors, and the plantar flexors each displayed modest improvements in work fatigue to the late 60s or early 70s, which was then followed by a significant decrease in work fatigue thereafter, which supports previous observations regarding a time where age may no longer provide an advantage for endurance or fatiguing tasks (Justice *et al.*, 2014). In contrast, during the high velocity contractions, each muscle group showed significant decreases in work fatigue during at a younger age.

Given the importance of dynamic force production for completing activities of daily living, recent efforts have been made to understand age-related changes in dynamic contractions via isokinetic or isotonic dynamometry. The current observations support previous research suggesting that slow contraction velocities display minimal differences across the lifespan (Callahan *et al.*, 2009; Lindstrom *et al.*, 1997; Senefeld *et al.*, 2017) and are also in agreement with those revealing that fast contraction velocities induce

greater fatigue in older adults (Callahan & Kent-braun, 2011; McNeil & Rice, 2007; Petrella, 2004).

Of note, most of the endurance or fatigue data compares pre to post muscular contractions (e.g. MVIC or power), whereas we compared the amount of work completed between the first 10 repetitions and the last 10 repetitions, thus posing a key different between observations. Recently, Senefeld *et al.* compared the elbow flexor and knee extensors muscle revealing greater differences in the lower body, whereas we saw similar differences across both contraction velocities (Senefeld, Yoon and Hunter, 2017). Nonetheless, differences in participants (men versus women) and the testing protocols could partly explain differences in observations. Further, most of the literature has focused on the knee flexors or plantar flexors, and we expand upon those observation by observing congruent findings for the elbow extensors, knee flexors, and dorsiflexors.

There are a number of mechanisms that contribute to age-related changes in muscular endurance/fatigue and these factors are further impacted by the type of contraction being performed and the muscle group in which the contraction is being performed (Hunter, Critchlow and Enoka, 2004; Kent-Braun, 2009; Avin and Law, 2011; Taylor *et al.*, 2016; Kruger *et al.*, 2018). Though a complete determination understanding the impact advanced age has on muscular endurance/fatigue is not available; recent evidence is compiling suggesting that the age-related fatigability during high velocity contractions is due to metabolite accumulation, in turn impacting the contractile apparatus within the muscle (Sundberg *et al.*, 2018; Sundberg *et al.*, 2019; Sundberg and Fitts, 2019). Specifically, the accumulation of the H^+ and Pi increase proportionally with exercise intensity as it exceeds the basal level of oxidative phosphorylation (Jones *et al.*,

2008; Vanhatalo *et al.*, 2010). During the slower contraction velocity, these byproducts ca be adequately removed by a "slower" aging muscle, thus resulting in a collective critical age period during the late 60s and early 70s. However, during the fast contraction velocity, the ability to remove these byproducts is limited given the increased energetic demand, thereby resulting in an increased reliance on anaerobic metabolism. The effects of these metabolites and their distinct roles in the facilitation of fatigue have been outline previously (Allen, Lamb and Westerblad, 2008; Hunter, Pereira and Keenan, 2016; Sundberg and Fitts, 2019). In short, the accumulation of metabolites reduces contractile function by inhibiting cross bridge cycle, reducing the force per bound cross bridge, reduced calcium affinity to its target binding sites, and alters the mechanics of cross bridge cycling (e.g. early myosin dissociation) (Allen, Lamb and Westerblad, 2008; Longyear *et al.*, 2014; Debold *et al.*, 2016; Sundberg *et al.*, 2018).

Interestingly, critical ages for the upper and lower body appeared to be relatively similar across both contraction velocities, with the exception of the knee extensors, which demonstrated a critical change in the 35 to 39-year group. Considering that muscle mass and maximal strength influence fatigability, this is not surprising. It was surprising to note that the older age groups were less fatigable than the young age groups for the knee extensors across the entire cohort, where the influence of muscle mass and strength, play the reciprocal role as mentioned above. Collectively, these observations suggest that with advanced age, contractile velocity plays a pertinent role in the fatigability of muscle groups, however the slower contraction velocity (60 deg/s) resulted in less fatigue than the higher contraction velocity (240 deg/s), which agree with recent suggestions (Senefeld, Yoon and Hunter, 2017).

Muscle Quality

Recently muscle quality, or the capacity of a muscle to exert force relative to the quantity of muscle, has been suggested to be a vital attribute regarding physical function (Straight, Brady and Evans, 2015b). To date, conflicting results have been reported regarding age-related changes in muscle quality, which consistently differ based on the type of contraction being performed (e.g. isometric, isotonic, or isokinetic) in addition to the imaging technique used to measure muscle (e.g. ultrasound, DXA, CT, MRI, etc.), or the quantity of muscle mass included in the measure (Francis, Lyons, *et al.*, 2017). For example, in the current study muscle quality was derived from isometric, isokinetic, and isotonic parameters and was made relative to muscle mass values measured via pQCT (upper and lower leg) or DXA (arm). Further, we included both antagonistic muscle groups, and these factors, among others, make comparisons among studies difficult.

Muscle quality of the upper arm increased with age, whereas subtle declines were observed during the 60 and 240 deg/s contractions. The increased muscle quality with age has been observed before (Chambers *et al.*, 2020) and demonstrates the capacity for aged muscle to produce adequate relative amounts of strength when given time to develop tension. The decreases during dynamic contractions were expected and the rate of decline increased slightly with increasing speed, which supports previous observations in men and women (Lynch *et al.*, 1999). During the specific power tests for the upper arm, expected declines were observed during the UL, 20% and 40% MVIC conditions, whereas the 60% MVIC was maintained until the 65 to 69-year group, and then declined significantly through the older groups. We are not aware of previous research that has performed specific power estimates for the upper arm, but the marginal changes were

expected given the physical activity level of the current cohort and the greater inclusion of the upper body with activities of daily living.

Marginal declines were observed during isometric and 60 deg/s conditions for the upper leg, which supports previous observations across young, middle-age, and older women during isometric contractions (Häkkinen and Häkkinen, 1991). Our results differ from those of Lynch *et al.* during slow contraction velocities, which may be due to the differences in participants, or since they only included the knee extensors, and different body composition devices were used to quantify muscle mass (Lynch *et al.*, 1999). However, our results generally support those of Moore *et al.* observing subtle linear decline for upper leg muscle quality with increasing age during a slow contraction velocity (30 deg/s) (Moore *et al.*, 2014). Interestingly, during the 240 deg/s contraction, upper leg muscle quality revealed a critical age period in the mid-30s, which was followed by significant rate of decline with increasing age. In contrast to the isometric or slow contraction, these observations suggest that women in their 30s do not possess the ability to effectively produce force relative to their muscle mass during high velocity contractions. Of note, this age was nearly identical to that observed for decreases in muscle density which would suggest that infiltration of intramuscular adipose tissue may be a profound candidate for these declines and occurred in an older age group than when the critical age was observed for cross-sectional area. Additional explanations have been discussed above under dynamic strength and power but are likely a combination central and peripheral factors. Specific power for the upper leg revealed a gradual increase for the critical age period as the intensity of contraction increased (i.e. from UL to 60% MVIC). Considering the isotonic function of the Biodex, each external resistance must

be overcome prior to the attachment moving and assessing power. Further, TTPP was increased with increasing intensity, thus the increased time taken to achieve the external load, likely shifted the critical age to older age groups. The current observations differ slightly from those of Alcazar *et al.* suggesting that the 45 years was a critical age period for specific power in women across the lifespan (Alcazar *et al.*, 2020). Few methodological differences exist between studies, such as different devices for both lower body power assessments and imaging devices for muscle mass, which may explain some of the differences. Further, the authors noted an additional critical age period in the 70s for the women, whereas we did not. However, it should be mentioned that their sample size was much larger, which would have increased the likelihood of observing that change.

With the exception of a few parameters, most of the observed critical age periods occurred during the midlife period, which agrees with previous research suggesting the onset of critical changes in muscle quality or specific power across the lifespan. (Lindle *et al.*, 1997; Lynch *et al.*, 1999; Metter *et al.*, 1999; Alcazar *et al.*, 2020). Collectively, these observations suggest that the midlife period is critical for age-related changes in muscle characteristics. Given that the midlife period, and many of the current critical age periods occurred during the menopausal transition, it is possible that the changes in female sex hormones are driving these changes in muscle quality. The presence of estrogen has been implicated in the ability to augment strength and thus may provide a larger effect during velocity dependent contractions (e.g. power) given the direct influence on the actomyosin complex (Lowe, Baltgalvis and Greising, 2010; Sipilä *et al.*, 2013; Tiidus, Lowe and Brown, 2013; Collins, Laakkonen and Lowe, 2019).

Force Time Characteristics

Most previous cross-sectional research has focused on maximal strength by means of identifying the influence of age on muscle function. Though important, it is suggested to take approximately 500ms, or longer (Häkkinen and Häkkinen, 1991), to display such performance. In the context of aging, this length of time may be functionally irrelevant as recovering from a fall or balance perturbation requires significantly less time (Bean *et al.*, 2013; Ward *et al.*, 2019). Arguably the greatest effect increased age had on the included parameters were the force time characteristics. In most cases, the oldest group took approximately twice the amount of time to display peak power and peak velocity, as well as reach peak torque values. Further, the average decline for rate of torque development across muscle groups was 42.1% supporting previous observations of 36 to 56% (Ditroilo *et al.*, 2010; Thompson *et al.*, 2013, 2014; Morcelli *et al.*, 2016). Recently, Thompson and others evaluated the influence of age-specific knee extensor muscle function in a cohort of 136 men divided into groups with mean ages of 21.9 years, 49.8 years, 58.9 years, and 71.3 years (Thompson, Sobolewski and Ryan, 2020). Supporting and expanding upon those observations, the mid-life period in the current women cohort appears to be a crucial time for force time characteristics, which is likely attributed to the changes in sex hormones and the resultant effects on contractile function (Lowe, Baltgalvis and Greising, 2010; Collins, Laakkonen and Lowe, 2019). Aside from the hormonal changes, these deficits are likely to be induced by early contractile neuromuscular characteristics, such as motor neuron recruitment speed, motor unit discharge, as well as structural changes and reduced efficiency of the actomyosin complex (De Ruiter *et al.*, 2004; Thompson, 2011; Del Vecchio *et al.*, 2019). In contrast

to Thompson *et al.*, we did not observe a potential improvement for force time characteristics during the mid-life (Thompson, Sobolewski and Ryan, 2020). The largest differences between studies were the differences in how the age groups were determined and the men versus women. Thompson *et al.* included four groups, while the current study had 13, in attempt to provide a more thorough representation of the lifespan, and the sex of the participants, where they investigated males and we included females. Further, we included multiple muscle groups, whereas they only evaluated the knee extensors. Few studies have sought to determine the influence of age on force time characteristics including participants across the entire lifespan. Bemben *et al.* examined men aged 20 to 74 years and noted significant differences across groups for maximal rate of force production and depended on the muscle group (Bemben *et al.*, 1991). The current results partially support those of Bemben *et al.* in that each of the muscle groups displayed different critical ages, with the lower body revealing changes in younger groups when compared to the upper body. In contrast to the current observations and those from Bemben *et al.*, Runnels *et al.* did not reveal differences across muscle groups for isokinetic TTPT parameters across the muscle groups of the elbow and knee but suggested that the age groups above 60 to 69 years may represent a critical group (Runnels *et al.*, 2005). The current observations support the observations from Van Roie *et al.* who measured rate of power development across the lifespan in 1,387 Flemish adults suggesting that to 40s represents a critical age period for both sexes (Van Roie *et al.*, 2018). Further, the authors speculated that the muscle-tendon unit may influence rate of power development more so than muscular power by relying on effective force transmission (Van Roie *et al.*, 2018). Additionally, it is interesting to note that as intensity

increased, force time characteristics were maintained to the older age groups. These observations may be explained by the findings of Earp *et al.* suggesting that at greater external loads, tendon strain decreases thereby resulting in the tendon acting to increase power (Earp *et al.*, 2014) Maffiuletti *et al.* suggested that the main factor for rate of force development is the ability to effectively display maximal levels of voluntary activation within the first 75ms, which is likely attributed to an increased motor unit firing rate (Maffiuletti *et al.*, 2016).

Muscle Characteristics

By including multiple muscle groups, we were able to identify whether the changes were uniform across the body. Traditionally, it has been suggested that peak muscle strength is displayed in the 30s maintained to the middle to late-50s and rapidly declines following thereafter (Francis, Lyons, *et al.*, 2017). Here we show this belief is not acceptable as the changes depend on several factors. For isometric strength, the lower body (knee extensors and flexors) showed greater muscle performance declines and critical age periods in younger age groups (40s versus 60s) when compared to the elbow extensors and flexors. However, the plantar and dorsiflexors displayed similar decrements for isometric force as the elbow flexors and extensors with advanced age. This may be attributed to the high inclusion in activities of daily living in which the actions including those muscle group may represent a greater relative external stimulus than the bigger and strong muscle groups of the knee. Regarding dynamic strength, the lower body also revealed greater declines, but in this case the muscle groups of the ankle displayed later breakpoints in comparison to the muscle groups of the elbow. This was expected as the dynamic contractions for the plantar- and dorsiflexors were similar to that

encountered during normal ambulation, thus the greater pattern of use may have resulted in the active, older age groups displaying similar values as their younger counterparts. For the three low isotonic conditions (UL, 20%, and 40%), the knee extensors and flexors displayed greater declines than the elbow extensor and flexors, but all four groups were similar at 60% maximal strength. Interestingly, during the endurance tasks, all muscle groups displayed similar relationships across both contraction velocities. During the slow velocity, older age groups were less fatigable to around the late-60s and then became more fatigable, whereas during the fast velocity the middle-aged age groups represented periods of critical changes in muscular endurance.

In contrast to our hypothesis, the elbow extensors displayed a smaller decline for isometric strength when compared to plantar flexors, which was also observed during the dynamic strength tasks. Of note, the plantar flexors displayed the smallest decline during the 240deg/s endurance task, which was expected since it is considered a muscle composed of type 1 fibers (Jennekens, Tomlinson and Walton, 1971). Although the elbow extensors were expected to show larger declines, it is possible that the amount of daily inclusion of the upper body (grip strength, elbow extensors, and elbow flexors) resulted in an attenuated decline with increasing age. Further, these data also suggest that the anterior muscle groups (elbow flexors, knee extensors, and dorsiflexors) experience greater age-related declines than the posterior muscle groups.

Biomarker Analyses

Interest has grown for determining biomarkers capable of identifying individual individuals at risk for age-related conditions but more specifically, sarcopenia, dynapenia, and frailty (Calvani *et al.*, 2018; Saedi *et al.*, 2019). In comparison to previous literature

analyzing serum myostatin via ELISA, it must be noted that the current values are both similar to previous observations (Ratkevicius *et al.*, 2011; Hofmann *et al.*, 2015; Arrieta *et al.*, 2019) and were much lower than alternative observations (Fife *et al.*, 2018; Peng *et al.*, 2018; Chew *et al.*, 2019; Moriwaki *et al.*, 2019). These differences are likely a function of differences in participant characteristics given that the current study included recreationally active women, none of which meeting previously suggested criteria for sarcopenia, whereas others sought to identify relationships with sarcopenia.

We observed a significant relationship between age and serum myostatin ($p<0.001$) as well as significant group differences between the two oldest age groups (75 to 79 and above 80 years, both $p<0.003$) in comparison to the age group with the lowest levels of myostatin (30 to 34 years). The increase with age supports previous observations (Yarasheski *et al.*, 2002; Egerman *et al.*, 2015; Parker *et al.*, 2017; Shibaguchi *et al.*, 2018), while conflicting with additional observations where no changes or decreases with increasing age were reported (Sandri *et al.*, 2013; Olson *et al.*, 2015; Poggioli *et al.*, 2016; Schafer *et al.*, 2016; Semba *et al.*, 2019). A concern regarding the conflicting evidence to date is that many of these age-related observations are derived from animal models. Moreover, a key potential explanation regarding the conflicting observations could be attributed to the analytical techniques used to quantify myostatin, as the homology is nearly identical to an additional member of the TGFβ family (90% shared). For example, some techniques may lack the specificity to correctly identify GDF-8 compared to its circulating antagonists, which have been reported to increase with age (Semba *et al.*, 2019).

Interesting to note, in addition to increasing levels with age, myostatin also displayed two critical changes in the age groups of 45 to 49 years and 65 to 59 years (both $p \leq 0.04$). The current results support the initial cross-sectional observations of Yarasheski *et al.* observing an increase with age and relationships between myostatin and muscle mass (Yarasheski *et al.*, 2002). Although agreeing with those observations, it must be mentioned that the oldest age group of participants in the aforementioned study were 76 to 92-year-old frail women, whereas our oldest group was similar in age (80 to 89 years) but were not frail and still engaged in recreational exercise. These observations suggest that physical activity may influence the relationship between myostatin and skeletal muscle characteristics in older participants. Moreover, by only including a young group (19 to 35 year-old women) and a group of 60 to 72-year old women, in addition to the older group mentioned above, their study design limited the capacity to determine when these increases occur, however differences between the two older groups were observed. Therefore, the first critical age period that the current observations suggest (48.5 years) could not be compared to their observations, since this age group was not included. However, when considering the second critical age period (69.4 years) in relation to their observations between the two older groups, collectively the observations provide support for the late 60s as a potentially critical age period for increases in myostatin (Yarasheski *et al.*, 2002). Unfortunately, the only strength measure was used in the classification of frailty, thus no correlations independent of frailty or for the younger groups were provided.

More recently, Semba *et al.* performed a similar investigation in 160 men and women (80 per sex) between the ages of 20 to 93 years assessing the quantity of GDF8

and GDF11 and their antagonists (Semba *et al.*, 2019). The current observations of a relationship between myostatin and age conflicts with their observations where no relationships were observed for men, women, or across the entire cohort for the pro-domain or mature protein ($p \geq 0.39$ and $p \geq 0.29$, respectively), suggestive of no changes with age. Potential reasons for the differences could be due to differences in sample size and/or the ages of their participants since they were not specifically disclosed, thus values could be easily influenced by a certain age group or range, whereas we included a larger number of women separated evenly across the lifespan. Alternatively, differences could be explained by methodological differences since Semba et al. used liquid chromatography-tandem mass spectrometry (SRM) and ELISA (but separate analyses), whereas the current results were obtained via ELISA. In fact, the associate between myostatin quantification methods (SRM and ELISA) were trivial ($p \geq 0.11$) (Semba *et al.*, 2019). However, our observations support theirs regarding the lack of association between myostatin and muscle strength when adjusting for age, which may again be a function of differences in physical activity influencing the relationship between myostatin and muscle performance, since their cohort appeared to have similar inclusion criteria.

Important to note, we observed the anticipated inverse relationships between both skeletal muscle mass and performance characteristics; however, when these relationships were adjusted for age, the number of relationships was reduced from 109/126 to 10/126. Nonetheless, recent cross-sectional observations have failed to distinguish the relationships between aging, myostatin, and muscle. Some report no differences between young and old men and women, in addition to no relationships with muscle mass and strength (Ratkevicius *et al.*, 2011; Hofmann *et al.*, 2015). When including both men and

women conflicting results continue to be observed between young and older participants, as well as just older cohorts in regard to relationships between myostatin and muscle mass and performance (Bergen *et al.*, 2015; Fife *et al.*, 2018; Peng *et al.*, 2018; Chew *et al.*, 2019; Moriwaki *et al.*, 2019). The conflicting observations may be due to the difficulty in specifically measuring myostatin, the methodology used to measure myostatin, the physical activity levels and sex of the participants, the methodology used to quantify muscle mass (DXA versus BIA) or the performance measure employed (grip strength versus functional parameters versus dynamometry).

Nonetheless, some potential explanations regarding the increases in myostatin in the current study could be explained by a few factors. First, it has been suggested that myostatin may be a part of antagonistic pleiotropy adaptations with increased age (Bergen *et al.*, 2015). In this regard, lower myostatin levels at a younger age may be beneficial for reproduction, in which the myometrium growth is a vital part of reproduction. Interesting to note, this postulation is bolstered by the detection of the first critical age period which has been associated with the menopausal transition and postmenopausal status. This observation would suggest a potential relationship between myostatin and female sex hormones. In fact, postmenopausal women supplementing with hormone replacement therapy have been observed to displayed lower levels of myostatin (Dieli-Conwright *et al.*, 2009, 2012). An alternative proposition could be the accelerator-brake hypothesis (Fife *et al.*, 2018). In this case, myostatin would be restrictive to excessive amounts of muscle growth during normal aging or in healthy individuals, whereas in those with altered homeostatic environments myostatin may decrease to provide a compensatory mechanism in attempt to return the body back to homeostasis. Since we had healthy,

recreationally active individuals across all age groups, the increases with age, especially in the older age groups would support this suggestion, however future research is needed to confirm this postulation. Last, an additional hypothesis for the critical age periods may be related to the timing of denervation-reinnervation with increasing age. The observations of Kelly *et al.* suggest that the denervation-reinnervation process does not occur fully and that many of the type 2 fibers that become reinnervated display characteristics of both type 1 (e.g. early recruitment) and type 2 fibers (e.g. hypertrophic adaptation) (Kelly, Hammond, Stec, *et al.*, 2018). With this in mind, the 'transitional fibers' (type 2 to type 1) would be recruited at a lower threshold and would result in greater expression of myostatin. Since myostatin is expressed in greater degrees in type 2 muscle, the transitional stages of the innervation process could potentially result in a greater serum concentration of myostatin. Nonetheless, future research should explore these potential mechanisms in their role for inducing increases in myostatin with age.

High levels of inflammatory markers have been suggested to play a role in the development of functional decline with aging. In fact, the chronic low-grade inflammatory status has been referred to as "inflammaging" (Ferrucci and Fabbri, 2018). The current observations support previous revealing a significant positive relationship with age (p=0.003) (Wei *et al.*, 1992; Ahluwalia *et al.*, 2001; Ferrucci *et al.*, 2005). Despite this relationship, there were no differences between groups, which conflicts with previous reports (Wei *et al.*, 1992; Ahluwalia *et al.*, 2001; Ferrucci *et al.*, 2005). Of note, our values are consistent with previous literature, and tend to be lower than previously established thresholds for elevated IL-6 levels representing potential current or forthcoming skeletal muscle mass and/or performance declines (Ferrucci *et al.*, 1999,

2002; Barbieri *et al.*, 2003; Penninx *et al.*, 2004; Alemán *et al.*, 2011; Newman *et al.*, 2016; Mikó *et al.*, 2018). This was expected as the current participants were recreationally active and tended to display normal body mass index levels.

Of note, upon removal of outliers, the current observations revealed a critical age in the rate of increase for serum IL-6 levels with the 65 to 69-year age group. A potential explanation for the increase within this age group and thereafter may have been the elevated fat mass levels, however, this relationship what not evident when performing age adjusted correlations for percent body fat and total fat mass (both $p>0.05$). Like myostatin, an alternative hypothesis regarding the age-related changes in IL-6 may be attributed to antagonistic pleiotropy, whereas inflammation during younger years has the ability to negate harmful effects at a younger age, but the persistent accumulation of inflammatory mediators with age inevitable results in consequences (Franceschi *et al.*, 2017).

A unique observation was that initially IL-6 displayed inverse relationships between both skeletal muscle mass and performance characteristics; however, when these relationships were adjusted for age, the number of relationships was reduced from 81/126 to 14/126. Closely resembling the current study, Blain et *al.* measured IL-6 and muscle performance among 220 asymptomatic women between the ages of 20 and 72 years, and also reported no relationships between IL-6 and knee extension or grip strength (Blain *et al.*, 2012). Giving that the levels of IL-6 between the current study and those of Blain et al. were nearly identical, this lends support to the need in determining IL-6 value thresholds that are associated with reduced muscle mass and performance as mentioned above.

Currently there appears to be associations between increased inflammatory markers and worsening physical function (functional performance or muscle strength) and muscle mass. For example, many longitudinal studies have suggested that elevated markers are associated with losses in muscle mass and/or muscle strength (Payette *et al.*, 2003; Alemán *et al.*, 2011; Sanders *et al.*, 2014; Newman *et al.*, 2016). In contrast to those observations, some longitudinal evidence suggests that IL-6 is not associated, or does not contribute to the declines observed in skeletal muscle (Ferrucci *et al.*, 2002; Westbury *et al.*, 2018). On the other hand, cross-sectional evidence in middle-aged to older individuals lends support for relationships between elevated inflammatory markers and muscle mass and performance (M. Visser *et al.*, 2002; Cesari *et al.*, 2004; Oliveira *et al.*, 2008; Pereira *et al.*, 2009, 2011; Tiainen *et al.*, 2010; Felicio *et al.*, 2014; Bian *et al.*, 2017; Dutra *et al.*, 2017), whereas other evidence does not support this relationship (Pereira *et al.*, 2011; Silva *et al.*, 2011; Lustosa *et al.*, 2017). Of note, the cross-sectional studies reporting no differences included both a muscular endurance tasks and traditional dynamometer strength testing, thereby providing a greater representation of skeletal muscle performance (Pereira *et al.*, 2011; Silva *et al.*, 2011). Additionally, the observations from Lustosa *et al.* divided their participants into sarcopenic and non-sarcopenic groups observing no differences in IL-6, despite observing differences in strength parameters, thereby questioning the influence of IL-6 on muscle performance (Lustosa *et al.*, 2017)

Another factor that must be mentioned regarding the lack of relationships between skeletal muscle and IL-6 observed in the current investigation could be attributed to the level of physical activity that was currently being completed by the participants. The

present cohort consisted of recreationally active exercisers completing resistance and/or aerobic training as well as additional physical activity (i.e. gardening, walking, etc.). The participants generally had been active over their entire lifespan, but do not reflect the same exercise levels of those classified as lifelong exercisers (Mikkelsen *et al.*, 2013; Chambers *et al.*, 2020; Lavin *et al.*, 2020). Further, the levels of IL-6 observed for participants of similar age, in comparison to a recent study evaluating the influence of lifelong exercise in basal and exercise-induced inflammation in young and older women were very similar (Lavin *et al.*, 2020). Therefore, it could be speculated that the exercise levels of the current cohort were sufficient in mitigating the age-related increase in IL-6. Exercise serves as a substantial countermeasure for inflammation (Nicklas and Brinkley, 2009). During exercise, skeletal muscle secretes several cytokines (notably, IL-6), which contribute to a number of metabolic changes, such as in times of low glycogen, IL-6 secretion is increased (Febbraio and Pederson, 2002; Muñoz-Cánoves *et al.*, 2013). Increased IL-6 also results in an increased level of anti-inflammatory cytokines, thereby resulting in reductions of TNFα (Addison *et al.*, 2012). Of note, Starkie *et al.* demonstrated the capacity for increased IL-6 levels observed with exercise can inhibit TNFα production (Starkie *et al.*, 2003). Additionally, chronic exercise may result in adaptive mechanisms that enhance the inflammatory defense mechanism by upregulating antioxidant enzymes and heat shock proteins (Scheele, Nielsen and Pedersen, 2009). For example, exercise results in increased nitric oxide and reactive oxygen species, which can impart negative consequences on contractile function and gene expression (Nicklas and Brinkley, 2009; Jo *et al.*, 2012; Muñoz-Cánoves *et al.*, 2013). Further, since reactive oxygen species are known to induce catabolic effects on skeletal muscle, the current

physical activity levels of the current cohort may have been sufficient to provide a more effective inflammatory defense mechanism, thereby resulting in lower IL-6 levels.

Altogether, the current study suggests that the relationships between myostatin and IL-6 with skeletal muscle are primarily drive by aging. Of note, when controlling for age, many of the relationships are no longer present. The observations do confirm previous reports of age-related increases, but the ability to ascertain the effects of the current biomarkers and their effects on skeletal muscle is limited. Further, it should be noted that we are looking at the change of these biomarkers with advanced age and not the reciprocal. In the context of aging research specifically, the included biomarkers and their respective functions like change and may do so in parallel given the observed relationships. Further, including additional TGFβ family members and inflammatory mediators may provide better context on the mechanisms behind their role in age-related changes in skeletal muscle.

Chapter V: Conclusions

Purpose

The primary purpose of this investigation was to determine if critical age periods where changes in quantitative and qualitative skeletal muscle parameters can be identified in recreationally active women. Further, we sought to determine if these parameters are influenced by muscle characteristics (e.g. fiber type, location, and size) and their relationships with circulating myostatin and interleukin 6.

Research Question

Are there critical ages that can be identified in recreationally active women when significant decreases in muscular strength, muscular power, muscular endurance, and muscle quality occur?

Research Question Hypotheses

It was hypothesized that women between 25 to 29 years of age will display the greatest amount muscular strength for each muscle observed. Additionally, muscular strength would remain relatively stable among women within the 30 to 49 years of age intervals, with a more apparent decline beginning for women in the 50s, which has been suggested by previous literature (Kallman, Plato, & Tobin, 1990; Lindle *et al.*, 1997). When transitioning into the sixth decade, muscle quality reductions will appear to become evident for women (Lynch *et al.*, 1999; Metter *et al.*, 1999). Further, it was hypothesized that women 25 to 29 years of age will display the greatest amount of muscular power with significant reductions occurring thereafter (>29 years) (Metter *et al.*, 1997; Dietzel *et al.*, 2013; Siglinsky *et al.*, 2015). In contrast to the hypothesized reductions in muscle

strength, power, and quality, it was hypothesized that muscular endurance was maintained with age until the >80-year group, which may be due to the selective decrease in fast-twitch muscle fibers resulting in slow-twitch muscle fibers becoming the dominant fiber type.

Research Question Conclusion

The current study was able to identify critical ages (breakpoints) at which skeletal muscle force parameters change across the lifespan in recreationally active women. In contrast to our hypotheses, when averaging maximal isometric strength, the 40s seem to be a critical period for upper leg muscle groups, while the 60s appear to influence the remaining muscle groups. When assessing dynamic strength, the slower contractions velocities, on average, resulted in a critical age period of 49 years, whereas faster contraction velocities resulted in a cumulative breakpoint of 41 years. In contrast to our hypotheses, across the body, various muscle groups, except for the elbow flexors (late 50s) reveal initial power declines during the late 30s to early 40s (35 to 42 years). Partly supporting our hypotheses, local muscular endurance was maintained until mid to late 60s for the slow contraction velocity (60 deg/s) while the faster contraction velocity resulted in earlier breakpoints (35 to 56 years). Partly supporting our hypotheses, muscle quality was greatly influence by contraction type, but in the attempt to make the muscle function relative to the amount of muscle mass, higher contraction velocities results in breakpoints between 35 to 49 years while slower or isometric contractions did not display critical ages.

Research Subquestion 1

Do age-related changes in muscle strength, power, endurance, and quality depend on muscle fiber type (type I versus type II), muscle location (upper versus lower body, proximal versus distal) or muscle size (large versus small)?

Research Subquestion 1 Hypotheses

It was hypothesized that muscles predominantly containing a type I fiber (soleus) composition was less affected with age when compared to a muscle predominantly composed of type II fibers (triceps). This is supported by the selective alterations in fiber type accompanied with aging and that the number and requirement of powerful contractions are greatly reduced with age (Mitchell *et al.*, 2012; Tieland, Trouwborst and Clark, 2018). Additionally, it was hypothesized that the declines in the lower body muscle function was greater and occur sooner than the observed in the upper body, which has been reported previously (Frontera *et al.*, 1991, 2000; Hughes *et al.*, 2001). However, with age, the use of the upper extremities remains relatively unchanged given the habitual use during activities of daily living, which may lessen the age-related changes. Additionally, the lower body possesses greater muscle mass and greater force production capabilities; therefore, a greater reduction is possible. Further, it was hypothesized that muscle function in muscle groups located distally will undergo greater reductions with age when compared to those that are located proximally, given the previous observations of the preferential reduction in motor units (Campbell, McComas and Petito, 1973; Lexell *et al.*, 1983; Tieland, Trouwborst and Clark, 2018).

Research Subquestion 1 Conclusion

Our hypotheses were partially supported as some of the differences with aging, such as the changes in soleus versus triceps [type I vs type II fibers], greater changes in the knee extensor and flexor groups, as well as earlier decreases, when compared to the upper body. However, our hypotheses regarding locations (e.g. distal vs proximal) was not supported as the plantar- and dorsiflexors revealed equal to or greater changes than the elbow extensors and flexors. Further, grip strength was maintained to the late 60s, whereas upper arm isometric strength decreases during the early 60s. Partly supporting our hypotheses, some of the greater declines were observed within the knee flexors and extensors, but for some contractions, the plantar- and dorsiflexors revealed comparable declines.

Research Subquestion 2

Are age-related changes in muscle mass and muscle function accompanied by changes in serum myostatin and interleukin 6?

Research Subquestion 2 Hypotheses

It was hypothesized that decreases in skeletal muscle mass was accompanied by increased myostatin and interleukin 6 levels, suggested by previous research. The age of initial increase was hypothesized to be approximately 50 years where noticeable reductions in skeletal muscle mass have been reported (Schaap *et al.*, 2006; Ryall, Schertzer and Lynch, 2008; Beyer, Mets and Bautmans, 2012; White and Lebrasseur, 2014).

Research Subquestion 2 Conclusion

Our hypotheses of inverse relationships were not supported in the present cohort. At first, these relationships existed, but after controlling for age, these relationships completely diminished. Interestingly, myostatin displayed two critical age periods (late 40s and late 60s) whereas IL-6 displayed a critical age during the late 60s.

Strengths and Limitations

Though we provide novel insight regarding age-related changes in muscle mass and function, the current study is not without limitations. First, the cross-sectional design limits our ability to infer causal relationships with age. Nevertheless, we sought to recruit female participants representing each five-year interval (20 to 24, 25 to 29, etc.) in order to provide a more thorough representing of "aging" rather than "age" per se. Strict physical activity guidelines needed to be met prior to participant enrollment, however, the physical activity was not measured outside of the study. Further, the participants enrolled in the current study may not provide an accurate representation of the entire female population, since they are likely more active and interested in their body composition and physical function than the general population. Another potential limitation with any aging study, is that the current study may have been influenced by refusal and/or survival effect bias, such as those subjects showing a poor health or decreased muscle function being less likely to accept participation or live to older years. Further, our 75 to 79 and 80 to 89-year groups had a total of 16 participants (8 each), however our primary modelling analysis would have been less affected than traditional ANOVA approaches, though both were performed. Regrettably we did not include

measures of physical function, such as the timed up and go or stair climb test, thus the ability to determine which age-related change amongst these parameters is most prudent for physical function is limited. Nonetheless, we provide novel insight for these estimates since we included measures of strength, power, endurance, and quality, which all contribute to an individual's physical function.

Significance of Study

To date, it has not been tested whether the slope of the relationship between muscle function measures and age is subjected to change at different age intervals throughout the lifespan in women. These results provide novel evidence regarding the existence of critical age periods in life in which muscle function is lost at an accelerated rate, how these changes differ between muscle groups (e.g. arms versus legs), and how they differ based up muscle function measure and contraction type (e.g. strength versus power and isometric versus dynamic). Further, women have been vastly underrepresented in health and exercise science research, which limits the ability to effectively implement exercise strategies towards combatting muscle function declines with increasing age. Further, since women are at a greater risk for experiencing physical limitations with advanced age, these observations are important for the maintenance of physical function with increasing age in women. Therefore, the current study offers a unique opportunity to specifically fill the void in the marginalized interests of women by contributing to the development of intervention strategies to target temporal phases across the lifespan (e.g. before changes have occurred or during critical periods in which severe changes happen)

in order to most effectively maintain muscle function with increasing age, thereby ensuring quality of life with increasing age in women.

Future Research Directions

The current study provided ages where changes and the prospective rate of change for each parameter of muscle function across recreationally active women. The logical next step is to support these observations with larger scale data and attempt to identify certain critical age periods within larger scale studies and then try to support those observations with longitudinal methodology. Similar efforts should be made in both sexes that determine the role of lifestyle (i.e. sedentary, recreationally active, highly active) and its effects on critical ages. Of note, it would be interesting to determine minimal effective exercise volumes for mitigating age-related losing among the included parameters. Following future confirmation, performing biological research to identify mechanisms contributing the critical age periods could improve tailoring of exercise interventions toward maintaining neuromuscular performance with advanced age. Alternative biomarkers, perhaps irisin, c-terminal agrin fragment, GDF11, among others, could be investigated to identify the relationships between changes in muscle mass and function.

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Appendix

Appendix A: DXA and pQCT Precision Values

Table 42. DXA and pQCT Precision Values

	Young women (18-25 years)	Older Women (60-85 years)
Percent Body Fat	2.35%	1.56%
Total Fat Mass (kg)	2.53%	1.74%
Bone Free Lean Body Mass (kg)	2.01%	1.21%
Fat Free Mass (kg)	1.77%	
Arms BFLBM (kg)		3.97%
Legs BFLBM (kg)		2.29%
Appendicular Skeletal Muscle Mass (kg)		2.08%
Muscle Cross-Sectional Area (mm^2)		
Femur	2.92%	
Calf	1.4%	1.73%

Note: Values obtained from previous research in the Bone Density Laboratory
Abbreviations: DXA- dual energy x-ray absorptiometry, pQCT- peripheral quantitative computed tomography, kg- kilograms, mm^2- millimeters squared.

Appendix B: Reliability of Neuromuscular Parameters

Table 43. Functional Measures Testing Reliability

Measure	ICC	SEM_{abs}	SEM_{rel}	$MDCR_{abs}$	$MDCR_{rel}$	CV (%)
Grip Strength	0.92-0.99	1.2-2.1	1.3-2.3	2.1-3.4	1.7-2.9	2.5-4.1
Jump Power	0.90-0.95	20.9-47.5	2.8-7.9	58.1-120.0	7.9-21.9	3.2-10.1
Jump Velocity	0.88-0.97	0.01-0.04	1.3-4.9	0.05-0.12	3.6-13.8	2.5-9.2

Abbreviations: ICC- intraclass correlation coefficient, SEM_{abs}- absolute standard error of the measure, SEM_{rel}- relative standard error of the measure, $MDCR_{abs}$- absolute minimum difference to be considered real, $MDCR_{rel}$- relative minimum difference to be considered real, CV- coefficient of variation.

Table 44. Elbow Extension Testing Reliability

Measure	ICC	SEM_{abs}	SEM_{rel}	$MDCR_{abs}$	$MDCR_{rel}$	CV (%)
Isometric						
MVIC	0.87-0.97	1.03-2.27	2.36-7.09	2.79-6.31	6.54-19.6	6.1-9.4
RTD	0.85-0.93	4.3-8.1	1.76-5.1	11.9-22.5	4.9-14.1	7.6-11.7
Isotonic						
1 Nm						
PP	0.79-0.95	2.4-3.9	4.6-8.8	6.5-10.9	12.3-24.2	3.1-9.1
PV	0.82-0.97	4.9-17.9	2.1-7.3	13.5-49.6	5.8-20.3	3.2-9.1
TTPP	0.81-0.96	0.01-0.02	2.7-6.0	0.02-0.05	7.35-16.6	3.2-9.1
TTPV	0.64-0.91	0.01-0.03	3.1-8.6	0.03-0.09	8.6-23.9	5.1-14.5
$MVIC_{20}$						
PP	0.85-0.95	1.9-3.9	3.0-7.5	5.8-10.8	8.5-18.4	4.1-9.2
PV	0.81-0.97	4.6-13.1	2.6-10.5	20.6-64.0	7.3-21.6	3.2-8.1
TTPP	0.84-0.96	0.01-0.02	2.8-7.6	0.03-0.06	7.7-21.2	4.1-8.2
TTPV	0.72-0.96	0.01-0.03	2.6-6.9	0.02-0.08	7.3-19.3	3.1-12.3
$MVIC_{40}$						
PP	0.84-0.95	1.9-3.2	2.7-8.2	4.9-9.0	7.6-22.6	3.1-8.2
PV	0.75-0.94	9.0-14.2	4.2-9.9	25.0-22.4	11.5-27.6	4.1-7.2
TTPP	0.87-0.94	0.01-0.02	2.7-4.9	0.02-0.05	7.5-13.5	2.9-7.4
TTPV	0.91-0.96	0.01-0.02	2.4-3.5	0.02-0.04	5.7-11.4	3.1-10.2
$MVIC_{60}$						
PP	0.89-0.96	1.1-2.8	4.3-8.7	3.2-7.9	11.8-24.1	3.1-6.7
PV	0.83-0.95	4.8-9.4	3.9-7.8	13.3-25.9	9.9-21.7	2.9-8.4
TTPP	0.88-0.95	0.01-0.02	2.1-4.9	0.01-0.04	5.9-13.5	3.1-5.4
TTPV	0.86-0.95	0.01-0.02	2.3-5.0	0.02-0.05	6.8-13.8	4.1-10.1
Isokinetic						
240 deg/s						
PT	0.78-0.88	1.9-3.6	2.1-5.4	2.3-9.3	5.3-12.3	4.7-11.3
TTPT	0.87-0.98	0.03-0.07	5.4-14.1	0.08-0.12	3.6-12.4	3.5-6.7
WF	0.81-0.98	0.74-8.2	4.0-16.5	2.1-22.6	7.9-27.1	2.9-10.4
60 deg/s						
PT	0.81-0.89	2.1-4.5	3.1-8.6	4.2-5.1	6.1-10.1	5.4-9.1
TTPT	0.87-0.95	0.02-0.06	4.7-12.1	0.06-0.11	23.6-10.4	1.5-5.7
WF	0.75-0.97	3.6-9.7	10.2-15.2	1.04-2.7	2.8-7.9	3.0-10.5

Abbreviations: ICC- intraclass correlation coefficient, SEM_{abs}- absolute standard error of the measure, SEM_{rel}- relative standard error of the measure, $MDCR_{abs}$- absolute minimum difference to be considered real, $MDCR_{rel}$- relative minimum difference to be considered real, CV- coefficient of variation, MVIC-maximal voluntary isometric contraction, RTD- rate of torque development, PP- peak power, PV- peak velocity, TTPP- time to peak power, TTPV- time to peak velocity, PT- peak torque, TTPT- time to peak torque, WF- work fatigue.

Table 45. Elbow Flexion Testing Reliability

Measure	ICC	SEM_{abs}	SEM_{rel}	$MDCR_{abs.}$	$MDCR_{rel.}$	CV (%)
Isometric						
MVIC	0.82-0.97	0.97-3.27	2.7-12.1	2.7-9.1	7.7-33.3	3.1-4.4
RTD	0.83-0.98	2.0-6.0	1.0-3.8	5.7-16.6	2.8-10.4	7.5-11.7
Isotonic						
1 Nm						
PP	0.87-0.98	1.2-2.4	3.6-8.5	3.5-7.1	9.9-17.8	2.8-9.5
PV	0.81-0.96	4.5-13.8	2.2-6.7	12.6-18.5	12.1-28.4	3.4-9.2
TTPP	0.82-0.97	0.01-0.02	1.5-6.6	0.02-0.05	4.3-18.3	2.3-7.1
TTPV	0.87-0.95	0.01-0.02	1.7-3.9	0.02-0.04	4.9-13.4	3.1-12.4
$MVIC_{20}$						
PP	0.87-0.98	0.84-2.7	1.9-6.7	2.3-7.6	5.2-20.2	5.1-7.2
PV	0.65-0.95	5.3-12.5	5.3-12.6	14.8-25.1	10.8-25.6	4.1-7.1
TTPP	0.87-0.93	0.01-0.02	3.3-4.7	0.03-0.05	9.2-13.0	2.1-6.1
TTPV	0.82-0.95	0.01-0.02	2.0-4.5	0.01-0.05	5.6-12.5	4.5-9.1
$MVIC_{40}$						
PP	0.86-0.96	2.3-5.1	3.2-6.1	1.5-3.5	6.6-17.7	3.1-8.1
PV	0.73-0.94	5.5-18.0	4.7-12.5	11.4-19.9	8.7-12.1	2.9-8.1
TTPP	0.77-0.97	0.01-0.03	1.7-7.3	0.02-0.08	4.6-20.1	5.1-8.7
TTPV	0.81-0.97	0.01-0.02	1.5-4.0	0.02-0.05	4.1-12.5	4.1-10.3
$MVIC_{60}$						
PP	0.84-0.97	0.9-2.1	1.9-7.1	1.6-3.9	6.9-18.8	5.1-8.2
PV	0.74-0.94	3.3-8.1	2.9-8.0	9.2-22.5	8.2-12.2	4.5-9.1
TTPP	0.76-0.97	0.01-0.03	1.9-5.1	0.02-0.07	5.2-14.2	2.7-10.1
TTPV	0.77-0.96	0.01-0.02	1.6-4.2	0.01-0.06	4.4-11.7	5.1-9.4
Isokinetic						
240 deg/s						
PT	0.74-0.96	0.09-2.8	2.7-6.3	2.5-7.7	6.2-17.4	3.1-7.1
TTPT	0.87-94	0.03-0.06	5.9-13.7	0.09-0.18	3.1-9.2	2.8-11.1
WF	0.86-0.96	0.85-2.4	1.7-5.9	2.3-5.9	4.8-16.5	3.2-12.6
60 deg/s						
PT	0.81-0.96	2.8-4.2	1.7-4.3	1.5-4.7	3.2-11.4	2.1-4.1
TTPT	0.85-0.97	0.04-0.07	4.2-8.3	0.06-0.12	4.5-8.9	2.5-7.1
WF	0.74-0.91	2.3-6.7	1.4-4.2	1.8-5.9	3.0-10.9	4.7-11.8

Abbreviations: ICC- intraclass correlation coefficient, SEM_{abs-} absolute standard error of the measure, SEM_{rel}- relative standard error of the measure, $MDCR_{abs}$- absolute minimum difference to be considered real, $MDCR_{rel}$- relative minimum difference to be considered real, CV- coefficient of variation, MVIC-maximal voluntary isometric contraction, RTD- rate of torque development, PP- peak power, PV- peak velocity, TTPP- time to peak power, TTPV- time to peak velocity, PT- peak torque, TTPT- time to peak torque, WF- work fatigue.

Table 46. Knee Extension Testing Reliability

Measure	ICC	SEM_{abs}	SEM_{rel}	$MDCR_{abs}$	$MDCR_{rel}$	CV (%)
Isometric						
MVIC	0.76-0.96	4.3-15.7	1.8-9.6	12.0-43.6	5.0-26.7	1.3-5.2
RTD	0.78-0.97	34.1-82.6	2.9-10.1	94.9-228.9	8.0-27.9	5.1-12.2
Isotonic						
1Newton						
PP	0.71-0.95	8.2-23.6	2.6-9.4	22.9-65.5	7.1-26.1	9.6-12.5
PV	0.72-0.98	8.14-22.3	3.4-6.6	22.6-64.9	6.7-18.4	5.9-14.2
TTPP	0.74-0.96	0.001-0.004	1.7-3.8	0.01-0.02	0.01-0.02	4.9-10.1
TTPV	0.75-0.92	0.002-0.003	1.3-2.6	0.008-0.02	3.7-7.2	3.3-11.9
$MVIC_{20}$						
PP	0.85-0.97	9.3-17.3	2.3-8.2	23.3-46.7	6.2-14.4	8.1-13.3
PV	0.81-0.95	8.9-20.1	3.1-5.6	24.7-55.6	8.6-15.4	9.1-10.1
TTPP	0.78-0.97	0.003-0.007	1.6-3.5	0.01-0.02	4.6-9.9	5.2-12.9
TTPV	0.81-0.97	0.003-0.007	1.4-3.1	0.008-0.02	3.2-8.8	4.6-11.7
$MVIC_{40}$						
PP	0.86-0.95	3.6-8.8	1.3-3.2	10.1-24.5	3.7-8.8	3.2-8.9
PV	0.85-0.96	9.2-18.4	4.4-11.1	25.6-52.4	11.7-30.9	7.7-10.4
TTPP	0.83-0.91	0.01-0.02	2.7-4.9	0.02-0.05	7.5-13.5	2.9-7.4
TTPV	0.87-0.95	0.01-0.02	3.6-6.7	0.02-0.04	9.9-17.9	3.4-11.1
$MVIC_{60}$						
PP	0.84-0.97	2.2-7.5	0.91-3.3	6.2-20.6	2.5-9.2	6.8-14.2
PV	0.80-0.97	6.8-20.3	2.4-9.6	18.9-56.3	6.6-26.8	9.0-12.1
TTPP	0.79-0.82	0.003-0.005	2.2-4.1	0.01-0.02	3.9-6.5	4.1-11.6
TTPV	0.74-0.97	0.01-0.02	2.8-8.3	0.02-0.05	9.4-23.0	4.9-10.5
Isokinetic						
240 deg/s						
PT	0.80-0.98	1.9-10.6	1.9-10.5	2.3-9.3	5.3-29.3	3.3-8.7
TTPT	0.83-0.96	0.01-0.03	2.3-7.9	0.04-0.09	6.5-12.3	4.7-9.1
WF	0.66-0.91	3.6-8.7	1.5-5.2	1.0-6.9	2.9-14.5	2.9-9.1
60 deg/s						
PT	0.91-0.97	2.6-7.8	2.3-5.4	7.2-21.6	7.2-21.6	5.4-9.2
TTPT	0.85-0.96	0.01-0.03	1.7-4.1	0.03-0.08	4.8-11.3	4.7-11.6
WF	0.79-0.92	3.5-9.2	4.6-12.1	4.5-9.2	5.2-18.6	3.5-8.9

Abbreviations: ICC- intraclass correlation coefficient, SEM_{abs-} absolute standard error of the measure, SEM_{rel}- relative standard error of the measure, $MDCR_{abs}$- absolute minimum difference to be considered real, $MDCR_{rel}$- relative minimum difference to be considered real, CV- coefficient of variation, MVIC-maximal voluntary isometric contraction, RTD- rate of torque development, PP- peak power, PV- peak velocity, TTPP- time to peak power, TTPV- time to peak velocity, PT- peak torque, TTPT- time to peak torque, WF- work fatigue.

Table 47. Knee Flexion Testing Reliability

Measure	ICC	SEM_{abs}	SEM_{rel}	$MDCR_{abs}$	$MDCR_{rel}$	CV (%)
Isometric						
MVIC	0.78-0.97	1.4-7.4	1.4-11.3	3.9-20.5	3.9-31.5	2.8-6.1
RTD	0.74-0.96	12.3-69.0	12.9-18.2	34.2-191.3	8.1-50.4	1.2-5.9
Isotonic						
1Newton						
PP	0.73-0.94	7.1-14.5	3.6-7.2	19.6-40.1	9.9-19.9	2.1-7.8
PV	0.89-0.97	7.3-19.5	2.3-7.9	27.5-52.8	6.2-22.0	4.2-12.1
TTPP	0.80-0.97	0.01-0.02	2.4-6.3	0.01-0.05	6.7-20.1	4.2-8.1
TTPV	0.77-0.97	0.01-0.02	2.3-6.1	0.02-0.05	6.4-16.9	5.1-8.9
$MVIC_{20}$						
PP	0.86-0.93	6.9-10.3	3.6-5.6	19.2-26.0	9.7-15.5	2.7-6.7
PV	0.82-0.95	7.5-20.1	3.6-8.6	20.8-53.5	9.9-14.1	3.9-8.1
TTPP	0.84-0.94	0.01-0.02	3.3-6.0	0.02-0.05	9.1-16.4	3.2-9.1
TTPV	0.74-0.92	0.01-0.02	2.2-5.1	0.02-0.04	6.8-14.0	2.1-7.5
$MVIC_{40}$						
PP	0.77-0.96	5.9-13.6	2.7-8.9	16.6-30.2	7.5-17.6	3.1-8.2
PV	0.73-0.93	10.4-24.1	5.6-11.4	28.7-66.9	5.3-16.2	4.1-9.3
TTPP	0.82-0.97	0.01-0.02	2.7-5.2	0.02-0.04	7.5-12.5	3.5-10.1
TTPV	0.81-0.96	0.01-0.02	2.9-6.5	0.02-0.05	7.8-17.9	4.1-9.3
$MVIC_{60}$						
PP	0.79-0.95	5.7-16.1	3.8-9.4	15.9-24.8	10.2-13.5	4.1-6.7
PV	0.81-0.95	6.9-13.8	3.4-8.6	19.2-38.3	9.5-15.4	5.2-8.1
TTPP	0.85-0.96	0.01-0.02	3.1-6.3	0.02-0.05	8.6-17.5	4.1-9.2
TTPV	0.65-0.92	0.01-0.02	3.3-6.6	0.03-0.06	9.1-23.4	4.3-12.1
Isokinetic						
240 deg/s						
PT	0.68-0.97	1.7-4.9	2.1-9.2	4.7-13.6	5.9-22.2	3.2-6.5
TTPT	0.68-0.97	0.01-0.06	6.9-14.2	0.04-0.13	8.1-13.4	4.2-7.1
WF	0.76-0.97	0.9-2.4	2.5-4.5	2.7-12.4	6.9-12.5	3.1-9.5
60 deg/s						
PT	0.87-0.96	1.8-3.0	1.9-3.5	4.9-8.4	5.1-9.1	2.1-4.9
TTPT	0.79-0.93	0.02-0.04	4.7-12.5	0.06-0.11	4.3-11.2	4.1-8.7
WF	0.87-0.97	1.1-2.1	2.9-4.9	2.9-5.7	8.2-13.5	3.9-10.2

Abbreviations: ICC- intraclass correlation coefficient, SEM_{abs-} absolute standard error of the measure, SEM_{rel}- relative standard error of the measure, $MDCR_{abs}$- absolute minimum difference to be considered real, $MDCR_{rel}$- relative minimum difference to be considered real, CV- coefficient of variation, MVIC-maximal voluntary isometric contraction, RTD- rate of torque development, PP- peak power, PV- peak velocity, TTPP- time to peak power, TTPV- time to peak velocity, PT- peak torque, TTPT- time to peak torque, WF- work fatigue.

Table 48. Plantarflexion Testing Reliability

Measure	ICC	SEM_{abs}	SEM_{rel}	$MDCR_{abs}$	$MDCR_{rel}$	CV (%)
Isometric						
MVIC	0.77-0.96	0.90-2.8	2.4-8.7	2.5-7.7	6.6-24.2	2.0-7.1
RTD	0.78-0.96	4.8-11.6	2.6-7.1	13.3-32.3	6.9-19.8	3.1-12.3
Isokinetic						
240 deg/s						
PT	0.78-0.94	0.96-2.7	2.9-8.3	2.7-7.5	8.2-22.9	3.1-6.1
TTPT	0.78-0.97	0.02-0.04	4.7-9.8	0.04-0.11	4.1-12.1	3.1-8.1
WF	0.81-0.98	0.92-3.64	3.6-7.9	2.6-10.1	9.9-21.8	4.2-9.7
60 deg/s						
PT	0.78-0.94	0.96-1.99	2.9-8.3	2.6-7.5	8.2-22.9	2.1-7.2
TTPT	0.90-0.96	0.01-0.03	6.8-11.8	0.03-0.09	4.5-12.1	4.1-8.1
WF	0.88-0.95	0.71-2.1	3.2-10.2	1.9-5.9	8.8-28.2	3.5-8.3

Abbreviations: ICC- intraclass correlation coefficient, SEM_{abs-} absolute standard error of the measure, SEM_{rel}- relative standard error of the measure, $MDCR_{abs}$- absolute minimum difference to be considered real, $MDCR_{rel}$- relative minimum difference to be considered real, CV- coefficient of variation, MVIC-maximal voluntary isometric contraction, RTD- rate of torque development, PT- peak torque, TTPT- time to peak torque, WF- work fatigue.

Table 49. Dorsiflexion Testing Reliability

Measure	ICC	SEM_{abs}	SEM_{rel}	$MDCR_{abs}$	$MDCR_{rel}$	CV (%)
Isometric						
MVIC	0.68-0.95	1.1-2.1	3.5-12.5	3.0-5.9	9.9-14.6	4.2-8.1
RTD	0.80-0.97	1.7-6.4	1.7-6.9	4.6-17.6	4.6-19.1	4.9-15.4
Isokinetic						
240 deg/s						
PT	0.84-0.96	0.69-1.3	3.5-14.6	1.9-3.9	4.2-16.7	4.5-11.1
TTPT	0.73-0.97	0.02-0.06	3.6-11.2	0.04-0.13	3.1-7.1	2.9-6.7
WF	0.69-0.94	1.6-5.0	3.0-7.9	4.3-13.9	8.5-21.9	2.9-9.7
60 deg/s						
PT	0.85-0.96	0.82-2.2	4.0-10.1	2.3-6.2	5.6-11.2	3.2-5.6
TTPT	0.75-0.97	0.01-0.05	2.5-8.2	0.03-0.14	7.6-22.7	2.1-8.7
WF	0.71-0.96	0.81-1.55	1.8-3.1	2.3-4.3	5.1-8.7	3.1-7.4

Abbreviations: ICC- intraclass correlation coefficient, SEM_{abs-} absolute standard error of the measure, SEM_{rel}- relative standard error of the measure, $MDCR_{abs}$- absolute minimum difference to be considered real, $MDCR_{rel}$- relative minimum difference to be considered real, CV- coefficient of variation, MVIC-maximal voluntary isometric contraction, RTD- rate of torque development, PT- peak torque, TTPT- time to peak torque, WF- work fatigue.

Appendix C: Additional Menstrual Information

Table 50. Supplementary Menstrual Information

	Premenopausal	Perimenopausal$^{\phi}$	Postmenopausal $^{\Delta}$
Sample (n)	75	19	58
Age (years)	33.9 (20.7, 48.0)	46.7 (42.5, 51.3)	67.6 (55.0, 89.0)
Height (cm)	165.3 (149.0, 182.0)	169.8 (151.3, 179.8)	163.2 (143.5, 177.0)
Weight (kg)	68.4 (48.9, 83.4)	65.9 (50.9, 82.3)	65.5 (50.0, 93.0)
Physical Activity (mm/w)	2348.2 (1738, 2984)	2407.8 (1909, 2953)	2291.9 (1722, 2960)
Exogenous hormone use	52/75	6/18	12/58

Note: Values are expressed as mean (minimum, maximum), ϕ: cycle irregularity and a period of ≥60 days absence of menstruation, Δ: absence of menstruation for 12 months

Abbreviations: mm/w- met minutes per week (derived from International Physical Activity Questionnaire)

Appendix D: Correlations with Biomarkers and Muscle Parameters

Table 51. Biomarker and Muscle Performance Correlations

Parameter	IL-6	$\rho_{12.Age}$	Myostatin	$\rho_{12.Age}$
Functional Measures				
Right Grip	-.154*	-.002	-.224**	.051
Left Grip	-.221**	-.004	-.231**	-.004
Vertical Jump Power	-.131	-.054	-.191*	-.021
Vertical Jump Velocity	-.171*	-.091	-.241**	-.013
Isometric Strength	IL-6	$\rho_{12.Age}$	Myostatin	$\rho_{12.Age}$
Elbow Extension (MVIC)	-.178*	-.031	-.257**	.063
RTD	-.134	.024	-.285**	.015
Elbow Flexion (MVIC)	-.163	-.007	-.321**	-.022
RTD	-.189*	.038	-.368**	.082
Knee Extension (MVIC)	-.260**	-.098	-.335**	0.143
RTD	-.253**	-.076	-.400**	.052
Knee Flexion (MVIC)	-.317**	-.202*	-.314**	.128
RTD	-.159	-.093	-.140	.001
Plantarflexion (MVIC)	-.213*	-.099	-.199*	.077
RTD	-.197*	.021	-.328**	.164
Dorsiflexion (MVIC)	-.190*	-.050	-.377**	-.118
RTD	-.189*	.010	-.423**	-.079
Dynamic Strength	IL-6	$\rho_{12.Age}$	Myostatin	$\rho_{12.Age}$
Elbow Extension				
PT60deg/s	-.158	.053	-.335**	.067
TTPT	.143	-.072	.294**	-.127
PT240deg/s	-.247**	-.093	-.294**	.124
TTPT	.226**	.086	.340**	.034
Elbow Flexion				
PT60deg/s	-.183*	-.073	-.403**	-.219**
TTPT	.121	.111	.107	.093
PT240deg/s	-.215*	-.507	-.397**	-.087
TTPT	.194*	.076	.195*	-.083
Knee Extension				
PT60deg/s	-.161	.083	-.355**	.092
TTPT	.223**	.013	.364**	-.137
PT240deg/s	-.184*	.008	-.283**	.147
TTPT	.303**	.195*	.395**	-.153
Knee Flexion				
PT60deg/s	-.270**	-.110	-.399**	.070
TTPT	.262**	.108	.281**	-.194*
PT240deg/s	-.298**	-.170*	-.434**	-.017
TTPT	.207*	-.025	.405**	-.051
Plantarflexion				
PT60deg/s	-.256**	-.141	-.287**	-.004
TTPT	.205*	.044	.322**	-.025
PT240deg/s	-.039	.212*	-.249**	.169
TTPT	.131	-.040	.161*	-.228
Dorsiflexion				
PT60deg/s	-.203*	-.037	-.279**	.111
TTPT	.207*	.044	.339*	-.010
PT240deg/s	-.290**	-.205*	-.301**	-.103
TTPT	.321**	.212*	.448**	.088
Isotonic	IL-6	$\rho_{12.Age}$	Myostatin	$\rho_{12.Age}$
Elbow Extension				
1 Nm				
PP	-.107	.094	-.336**	-.001
PV	-.168*	.054	-.390**	-.002

Isotonic continued	IL-6	$\rho_{12.Age}$	Myostatin	$\rho_{12.Age}$
TTPP	.084	-.140	.366**	.030
TTPV	.305**	.185*	.394**	-.069
$MVIC_{20}$				
PP	-.182*	.017	-.281**	.169
PV	-.236**	-.094	-.322**	.010
TTPP	.321**	.212*	.314**	-.038
TTPV	.271**	.119	.373**	-.062
$MVIC_{40}$				
PP	-.103	.034	-.240**	.022
PV	-.157	.068	-.333**	.097
TTPP	.142	-.040	.227**	-.164
TTPV	.246**	.079	.375**	-.024
$MVIC_{60}$				
PP	-.214*	-.069	-.263**	.080
PV	-.125	-.102	-.301**	-.002
TTPP	.179**	.143	.300**	.021
TTPV	.150	.138	.280**	.003
Elbow Flexion				
1 Nm				
PP	-.248**	-.142	-.271**	-.024
PV	-.158	-.011	-.406**	-.166*
TTPP	.214*	.062	.283**	-.076
TTPV	.219**	.047	.264**	-.184*
$MVIC_{20}$				
PP	-.211*	-.074	-.289**	.019
PV	-.138	.037	-.372**	-.078
TTPP	.117	-.073	.341**	.019
TTPV	.198*	.099	.128	-.115
$MVIC_{40}$				
PP	-.093	.032	-.245**	-.014
PV	-.181*	-.038	-.342**	-.067
TTPP	.189*	.040	.341**	.048
TTPV	.118	.040	.160*	.002
$MVIC_{60}$				
PP	-.069	.051	-.261**	-.050
PV	-.235**	-.102	-.302**	.011
TTPP	.220**	.143	.239**	.078
TTPV	.237**	.138	.349**	.152
Knee Extension				
1 Nm				
PP	-.222**	-.055	-.249**	.194*
PV		.027	-.366**	.030
TTPP	-.180*	.115	.352**	-.025
TTPV	.261**	.016	.286**	-.197*
$MVIC_{20}$				
PP	-.243**	-.035	-.345**	.110
PV	-.202*	-.043	-.365**	-.048
TTPP	.204*	.020	.307**	-.118
TTPV	.154	-.042	.317**	-.064
$MVIC_{40}$				
PP	-.393**	-.315**	-.342**	-.002
PV	-.195*	-.031	-.277**	.094
TTPP	.211*	-.046	.265**	-.164*
TTPV	.220**	.151	.344**	.024
$MVIC_{60}$				
PP	-.209*	-.035	-.295**	.119
PV	-.249**	-.073	-.367**	.090
TTPP	.211*	-.041	.384**	.041

Isotonic Continued	IL-6	$\rho_{12.Age}$	Myostatin	$\rho_{12.Age}$
TTPV	.220**	-.089	.374**	.115
Knee Flexion				
1 Nm				
PP	-.179*	.051	-.384**	.038
PV	-.272**	-.120	-.380**	.056
TTPP	.099	-.134	.277**	-.145
TTPV	.163	-.028	.340**	-.023
$MVIC_{20}$				
PP	-.193*	-.014	-.350**	.013
PV	-.344**	-.255*	-.323**	.172*
TTPP	.194*	.012	.383**	.037
TTPV	.194*	.040	.237**	-.128
$MVIC_{40}$				
PP	-.323**	-.213*	-.295**	.103
PV	-.208*	-.025	-.370**	.009
TTPP	.193*	.013	.267**	-.156
TTPV	.229**	.103	.316**	.036
$MVIC_{60}$				
PP	-.131	.023	-.347**	-.081
PV	-.163	.034	-.306**	.092
TTPP	.209*	.117	.274**	.085
TTPV	.229**	.115	.257**	-.010
Work Fatigue				
Elbow Extension				
60deg/s	.172*	.159	.045	.011
240deg/s	.275**	.130	.288**	-.185*
Elbow Flexion				
60deg/s	-.036	.015	.047	.170*
240deg/s	.150	-.017	.316**	-.001
Knee Extension				
60deg/s	-.243**	-.135	-.179**	.107
240deg/s	.158	-.110	.443**	.060
Knee Flexion				
60deg/s	-.182*	-.110	-.134	.031
240deg/s	.157	-.022	.242**	-.147
Plantarflexion				
60deg/s	.076	.036	.013	-.079
240deg/s	-.073	-.199*	.111	-.112
Dorsiflexion				
60deg/s	.185*	.116	.151	-.002
240deg/s	.297**	.182*	.302**	-.026

Note: Partial correlation controlling for age; MVC_{20}- 20% of maximal voluntary isometric contraction

Abbreviations: MVIC-maximal voluntary isometric contraction, RTD- rate of torque development, PP- peak power, PV- peak velocity, TTPP- time to peak power, TTPV- time to peak velocity, PT- peak torque, TTPT- time to peak torque, WF- work fatigue.

Table 52. Biomarker and Muscle Mass Correlations

Parameters	IL-6	$\rho_{12.Age}$	Myostatin	$\rho_{12.Age}$
DXA Parameters				
Total BFLBM (kg)	-.155	.028	-.114	-.018
Arm BFLBM (kg)	-.110	.025	-.117	-.003
Leg BFLBM (kg)	-.123	.026	-.090	.035
ASM (kg)	-.124	.027	-.094	.026
FFMI (kg/m^2)	-.081	.018	-.069	.028
SMI (ASM/m^2)	-.058	.024	-.062	.064
pQCT Parameters				
Upper leg				
Muscle density (mg/cm^3)	-.052	.134	-.221**	-.092
Muscle area (cm^2)	-.086	-.067	-.026	.085
Lower leg				
Muscle density (mg/cm^3)	-.061	.121	-.191*	-.084
Muscle area (cm^2)	-.092	-.054	-.031	.052

Note: Partial correlation controlling for age; "Upper" and "lower leg" values obtained from DXA and pQCT.
Abbreviations: DXA- dual energy x-ray absorptiometry, pQCT- peripheral quantitative computed tomography, BFLBM- bone free lean body mass, kg- kilograms, m^2- meters squared, ASM- appendicular skeletal muscle mass, FFMI- fat free mass index, SMI- skeletal muscle index.

Appendix E: Customized Analysis Strategy

```
####read the data file in####
library(readxl)
DISSERTATION_EXAM <-
read_excel("C:/Users/Ryan/Desktop/DISSERTATION_EXAM.xlsx") ####this is set to my desktop
View(DISSERTATION_EXAM)
attach(DISSERTATION_EXAM) ###attach the data
names(DISSERTATION_EXAM) ###check the names in file

as.data.frame(DISSERTATION_EXAM)

Trial_Mean <- (DISSERTATION_EXAM$Trial_Four +
DISSERTATION_EXAM$Trial_Five +
DISSERTATION_EXAM$Trial_Six +
DISSERTATION_EXAM$Trial_Seven +
DISSERTATION_EXAM$Trial_Eight +
DISSERTATION_EXAM$Trial_Nine) / 6
DISSERTATION_EXAM <-
cbind(DISSERTATION_EXAM, Trial_Mean) ####this is how we will set up the data to be pulled for graphing later
SD_pop <- sd(Trial_Mean)
Total_MEAN <- mean(Trial_Mean)


####below we create subsets of the grant table by Age_Group####
Group_one<- subset(DISSERTATION_EXAM,
Age_Group == "20-24") ####allows you to grab values for a 20-24 interval####
Group_two<- subset(DISSERTATION_EXAM,
Age_Group == "25-29") ####allows you to grab values for a 25-29 interval####
Group_three<- subset(DISSERTATION_EXAM,
Age_Group == "30-34") ####allows you to grab values for a 30-34 interval####
Group_four<- subset(DISSERTATION_EXAM,
Age_Group == "35-39") ####allows you to grab values for a 35-39 interval####
Group_five<- subset(DISSERTATION_EXAM,
Age_Group == "40-44") ####allows you to grab values for a 40-44 interval####
Group_six<- subset(DISSERTATION_EXAM, Age_Group == "45-49") ####allows you to grab values for a 45-49 interval####
Group_seven<- subset(DISSERTATION_EXAM,
Age_Group == "50-54") ####allows you to grab values for a 50-54 interval####
Group_eight<- subset(DISSERTATION_EXAM,
Age_Group == "55-59") ####allows you to grab values for a 55-59 interval####
Group_nine<- subset(DISSERTATION_EXAM,
Age_Group == "60-64") ####allows you to grab values for a 60-64 interval####
Group_ten<- subset(DISSERTATION_EXAM, Age_Group == "65-69") ####allows you to grab values for a 65-69 interval####
Group_eleven<- subset(DISSERTATION_EXAM,
Age_Group == "70-74") ####allows you to grab values for a 70-74 interval####
Group_twelve<- subset(DISSERTATION_EXAM,
Age_Group == "75-79") ####allows you to grab values for a 75-79 interval####
Group_thirteen<- subset(DISSERTATION_EXAM,
Age_Group == "80-89") ####allows you to grab values for a 80+ interval####

####Group_one#####
Group_one_averageTRIALSday2 <-
(Group_one$Trial_Four + Group_one$Trial_Five +
Group_one$Trial_Six) / 3 ##mean day 2
as.vector(Group_one_averageTRIALSday2)
G1D2<- sort(Group_one_averageTRIALSday2)
Group_one_averageTRIALSday3 <-
(Group_one$Trial_Seven + Group_one$Trial_Eight +
Group_one$Trial_Nine) / 3 ##mean day 3
as.vector(Group_one_averageTRIALSday3)
G1D3<- sort(Group_one_averageTRIALSday3)
Group_one_averageTRIALSd2_3 <-
(Group_one$Trial_Four + Group_one$Trial_Five +
Group_one$Trial_Six + Group_one$Trial_Seven +
Group_one$Trial_Eight + Group_one$Trial_Nine) / 6
##grand mean
G1_mean <- mean(Group_one_averageTRIALSd2_3)
##mean of means
SD_row_G1 <- apply(Group_one[,1:6],1,sd) ##SD for each participant
Group_one_SD <- mean(SD_row_G1) ###group SD
Group_one_means <- cbind(G1D2, G1D3) ###use this to run ICCs
Age_G1 <- mean(Group_one$Years) ####this will give us the mean age for the group
####Group_two
Group_two_averageTRIALSday2 <-
(Group_two$Trial_Four + Group_two$Trial_Five +
Group_two$Trial_Six) / 3
Group_two_averageTRIALSday3 <-
(Group_two$Trial_Seven + Group_two$Trial_Eight +
Group_two$Trial_Nine) / 3
Group_two_averageTRIALSd2_3 <-
(Group_two$Trial_Four + Group_two$Trial_Five +
Group_two$Trial_Six + Group_two$Trial_Seven +
Group_two$Trial_Eight + Group_two$Trial_Nine) / 6
G2_mean <- mean(Group_two_averageTRIALSd2_3)
SD_row_G2 <- apply(Group_two[,1:6],1,sd)
Group_two_SD <- mean(SD_row_G2)
as.vector(Group_two_averageTRIALSday2)
G2D2<- sort(Group_two_averageTRIALSday2)
as.vector(Group_two_averageTRIALSday3)
G2D3<- sort(Group_two_averageTRIALSday3)
Group_two_means <- cbind(G2D2, G2D3) ###use this to run ICCs
Age_G2 <- mean(Group_two$Years)
####Group_three
Group_three_averageTRIALSday2 <-
(Group_three$Trial_Four + Group_three$Trial_Five +
Group_three$Trial_Six) / 3
Group_three_averageTRIALSday3 <-
(Group_three$Trial_Seven + Group_three$Trial_Eight +
Group_three$Trial_Nine) / 3
Group_three_averageTRIALSd2_3 <-
(Group_three$Trial_Four + Group_three$Trial_Five +
Group_three$Trial_Six + Group_three$Trial_Seven +
Group_three$Trial_Eight + Group_three$Trial_Nine) / 6
G3_mean <- mean(Group_three_averageTRIALSd2_3)
SD_row_G3 <- apply(Group_three[,1:6],1,sd)
Group_three_SD <- mean(SD_row_G3)
as.vector(Group_three_averageTRIALSday2)
```

```
G3D2<- sort(Group_three_averageTRIALSday2)
as.vector(Group_three_averageTRIALSday3)
G3D3<- sort(Group_three_averageTRIALSday3)
Group_three_means <- cbind(G3D2, G3D3) ###use this to
run ICCs
Age_G3 <- mean(Group_three$Years)
####Group_four
Group_four_averageTRIALSday2 <-
(Group_four$Trial_Four + Group_four$Trial_Five +
Group_four$Trial_Six) / 3
Group_four_averageTRIALSday3 <-
(Group_four$Trial_Seven + Group_four$Trial_Eight +
Group_four$Trial_Nine) / 3
Group_four_averageTRIALSd2_3 <-
(Group_four$Trial_Four + Group_four$Trial_Five +
Group_four$Trial_Six + Group_four$Trial_Seven +
Group_four$Trial_Eight + Group_four$Trial_Nine) / 6
G4_mean <- mean(Group_four_averageTRIALSd2_3)
SD_row_G4 <- apply(Group_four[,1:6],1,sd)
Group_four_SD <- mean(SD_row_G4)
as.vector(Group_four_averageTRIALSday2)
G4D2<- sort(Group_four_averageTRIALSday2)
as.vector(Group_four_averageTRIALSday3)
G4D3<- sort(Group_four_averageTRIALSday3)
Group_four_means <- cbind(G4D2, G4D3) ###use this to
run ICCs
Age_G4 <- mean(Group_four$Years)
####Group_five
Group_five_averageTRIALSday2 <-
(Group_five$Trial_Four + Group_five$Trial_Five +
Group_five$Trial_Six) / 3
Group_five_averageTRIALSday3 <-
(Group_five$Trial_Seven + Group_five$Trial_Eight +
Group_five$Trial_Nine) / 3
Group_five_averageTRIALSd2_3 <-
(Group_five$Trial_Four + Group_five$Trial_Five +
Group_five$Trial_Six + Group_five$Trial_Seven +
Group_five$Trial_Eight + Group_five$Trial_Nine) / 6
G5_mean <- mean(Group_five_averageTRIALSd2_3)
SD_row_G5 <- apply(Group_five[,1:6],1,sd)
Group_five_SD <- mean(SD_row_G5)
as.vector(Group_five_averageTRIALSday2)
G5D2<- sort(Group_five_averageTRIALSday2)
as.vector(Group_five_averageTRIALSday3)
G5D3<- sort(Group_five_averageTRIALSday3)
Group_five_means <- cbind(G5D2, G5D3) ###use this to
run ICCs
Age_G5 <- mean(Group_five$Years)
####Group_six
Group_six_averageTRIALSday2 <-(Group_six$Trial_Four
+ Group_six$Trial_Five + Group_six$Trial_Six) / 3
Group_six_averageTRIALSday3 <-
(Group_six$Trial_Seven + Group_six$Trial_Eight +
Group_six$Trial_Nine) / 3
Group_six_averageTRIALSd2_3 <-(Group_six$Trial_Four
+ Group_six$Trial_Five + Group_six$Trial_Six +
Group_six$Trial_Seven + Group_six$Trial_Eight +
Group_six$Trial_Nine) / 6
G6_mean <- mean(Group_six_averageTRIALSd2_3)
SD_row_G6 <- apply(Group_six[,1:6],1,sd)
Group_six_SD <- mean(SD_row_G6)
as.vector(Group_six_averageTRIALSday2)
G6D2<- sort(Group_six_averageTRIALSday2)
as.vector(Group_six_averageTRIALSday3)
G6D3<- sort(Group_six_averageTRIALSday3)
Group_six_means <- cbind(G6D2, G6D3) ###use this to
run ICCs
Age_G6 <- mean(Group_six$Years)
####Group_seven
Group_seven_averageTRIALSday2 <-
(Group_seven$Trial_Four + Group_seven$Trial_Five +
Group_seven$Trial_Six) / 3
Group_seven_averageTRIALSday3 <-
(Group_seven$Trial_Seven + Group_seven$Trial_Eight +
Group_seven$Trial_Nine) / 3
Group_seven_averageTRIALSd2_3 <-
(Group_seven$Trial_Four + Group_seven$Trial_Five +
Group_seven$Trial_Six + Group_seven$Trial_Seven +
Group_seven$Trial_Eight + Group_seven$Trial_Nine) / 6
SD_row_G7 <- apply(Group_seven[,1:6],1,sd)
Group_seven_SD <- mean(SD_row_G7)
G7_mean <- mean(Group_seven_averageTRIALSd2_3)
as.vector(Group_seven_averageTRIALSday2)
G7D2<- sort(Group_seven_averageTRIALSday2)
as.vector(Group_seven_averageTRIALSday3)
G7D3<- sort(Group_seven_averageTRIALSday3)
Group_seven_means <- cbind(G7D2, G7D3) ###use this to
run ICCs
Age_G7 <- mean(Group_seven$Years)
####Group_eight
Group_eight_averageTRIALSday2 <-
(Group_eight$Trial_Four + Group_eight$Trial_Five +
Group_eight$Trial_Six) / 3
Group_eight_averageTRIALSday3 <-
(Group_eight$Trial_Seven + Group_eight$Trial_Eight +
Group_eight$Trial_Nine) / 3
Group_eight_averageTRIALSd2_3 <-
(Group_eight$Trial_Four + Group_eight$Trial_Five +
Group_eight$Trial_Six + Group_eight$Trial_Seven +
Group_eight$Trial_Eight + Group_eight$Trial_Nine) / 6
SD_row_G8 <- apply(Group_eight[,1:6],1,sd)
Group_eight_SD <- mean(SD_row_G8)
G8_mean <- mean(Group_eight_averageTRIALSd2_3)
as.vector(Group_one_averageTRIALSday2)
G8D2<- sort(Group_eight_averageTRIALSday2)
as.vector(Group_eight_averageTRIALSday3)
G8D3<- sort(Group_eight_averageTRIALSday3)
Group_eight_means <- cbind(G8D2, G8D3) ###use this to
run ICCs
Age_G8 <- mean(Group_eight$Years)
####Group_nine
Group_nine_averageTRIALSday2 <-
(Group_nine$Trial_Four + Group_nine$Trial_Five +
Group_nine$Trial_Six) / 3
Group_nine_averageTRIALSday3 <-
(Group_nine$Trial_Seven + Group_nine$Trial_Eight +
Group_nine$Trial_Nine) / 3
Group_nine_averageTRIALSd2_3 <-
(Group_nine$Trial_Four + Group_nine$Trial_Five +
Group_nine$Trial_Six + Group_nine$Trial_Seven +
Group_nine$Trial_Eight + Group_nine$Trial_Nine) / 6
SD_row_G9 <- apply(Group_nine[,1:6],1,sd)
Group_nine_SD <- mean(SD_row_G9)
G9_mean <- mean(Group_nine_averageTRIALSd2_3)
as.vector(Group_nine_averageTRIALSday2)
G9D2<- sort(Group_nine_averageTRIALSday2)
as.vector(Group_nine_averageTRIALSday3)
G9D3<- sort(Group_nine_averageTRIALSday3)
Group_nine_means <- cbind(G9D2, G9D3) ###use this to
run ICCs
Age_G9 <- mean(Group_nine$Years)
####Group_ten
Group_ten_averageTRIALSday2 <-(Group_ten$Trial_Four
+ Group_ten$Trial_Five + Group_ten$Trial_Six) / 3
```

```
Group_ten_averageTRIALSday3 <-
(Group_ten$Trial_Seven + Group_ten$Trial_Eight +
Group_ten$Trial_Nine) / 3
Group_ten_averageTRIALSd2_3 <-(Group_ten$Trial_Four
+ Group_ten$Trial_Five + Group_ten$Trial_Six +
Group_ten$Trial_Seven + Group_ten$Trial_Eight +
Group_ten$Trial_Nine) / 6
SD_row_G10 <- apply(Group_ten[,1:6],1,sd)
Group_ten_SD <- mean(SD_row_G10)
G10_mean <- mean(Group_ten_averageTRIALSd2_3)
as.vector(Group_ten_averageTRIALSday2)
G10D2<- sort(Group_ten_averageTRIALSday2)
as.vector(Group_ten_averageTRIALSday3)
G10D3<- sort(Group_ten_averageTRIALSday3)
Group_ten_means <- cbind(G10D2, G10D3) ###use this to
run ICCs
Age_G10 <- mean(Group_ten$Years)
####Group_eleven
Group_eleven_averageTRIALSday2 <-
(Group_eleven$Trial_Four + Group_eleven$Trial_Five +
Group_eleven$Trial_Six) / 3
Group_eleven_averageTRIALSday3 <-
(Group_eleven$Trial_Seven + Group_eleven$Trial_Eight +
Group_eleven$Trial_Nine) / 3
Group_eleven_averageTRIALSd2_3 <-
(Group_eleven$Trial_Four + Group_eleven$Trial_Five +
Group_eleven$Trial_Six + Group_eleven$Trial_Seven +
Group_eleven$Trial_Eight + Group_eleven$Trial_Nine) / 6
SD_row_G11 <- apply(Group_eleven[,1:6],1,sd)
Group_eleven_SD <- mean(SD_row_G11)
G11_mean <- mean(Group_eleven_averageTRIALSd2_3)
as.vector(Group_eleven_averageTRIALSday2)
G11D2<- sort(Group_eleven_averageTRIALSday2)
as.vector(Group_eleven_averageTRIALSday3)
G11D3<- sort(Group_eleven_averageTRIALSday3)
Group_eleven_means <- cbind(G11D2, G11D3)###use this
to run ICCs
Age_G11 <- mean(Group_eleven$Years)
####Group_twelve
Group_twelve_averageTRIALSday2 <-
(Group_twelve$Trial_Four + Group_twelve$Trial_Five +
Group_twelve$Trial_Six) / 3
Group_twelve_averageTRIALSday3 <-
(Group_twelve$Trial_Seven + Group_twelve$Trial_Eight +
Group_twelve$Trial_Nine) / 3
Group_twelve_averageTRIALSd2_3 <-
(Group_twelve$Trial_Four + Group_twelve$Trial_Five +
Group_twelve$Trial_Six + Group_twelve$Trial_Seven +
Group_twelve$Trial_Eight + Group_twelve$Trial_Nine) / 6
SD_row_G12 <- apply(Group_twelve[,1:6],1,sd)
Group_twelve_SD <- mean(SD_row_G12)
G12_mean <- mean(Group_twelve_averageTRIALSd2_3)
as.vector(Group_twelve_averageTRIALSday2)
G12D2<- sort(Group_twelve_averageTRIALSday2)
as.vector(Group_twelve_averageTRIALSday3)
G12D3<- sort(Group_twelve_averageTRIALSday3)
Group_twelve_means <- cbind(G12D2, G12D3) ###use this
to run ICCs
Age_G12 <- mean(Group_twelve$Years)
####Group_thirteen
Group_thirteen_averageTRIALSday2 <-
(Group_thirteen$Trial_Four + Group_thirteen$Trial_Five +
Group_thirteen$Trial_Six) / 3
Group_thirteen_averageTRIALSday3 <-
(Group_thirteen$Trial_Seven + Group_thirteen$Trial_Eight
+ Group_thirteen$Trial_Nine) / 3
Group_thirteen_averageTRIALSd2_3 <-
(Group_thirteen$Trial_Four + Group_thirteen$Trial_Five +
Group_thirteen$Trial_Six + Group_thirteen$Trial_Seven +
Group_thirteen$Trial_Eight + Group_thirteen$Trial_Nine) /
6
G13_mean <- mean(Group_thirteen_averageTRIALSd2_3)
SD_row_G13 <- apply(Group_thirteen[,1:6],1,sd)
Group_thirteen_SD <- mean(SD_row_G13)
as.vector(Group_thirteen_averageTRIALSday2)
G13D2<- sort(Group_thirteen_averageTRIALSday2)
as.vector(Group_thirteen_averageTRIALSday3)
G13D3<- sort(Group_thirteen_averageTRIALSday3)
Group_thirteen_means <- cbind(G13D2, G13D3) ###use
this to run ICCs
Age_G13 <- mean(Group_thirteen$Years)

Group_2_1 <-(G2_mean-G1_mean)
Group_3_2 <-(G3_mean-G2_mean)
Group_4_3 <-(G4_mean-G3_mean)
Group_5_4 <-(G5_mean-G4_mean)
Group_6_5 <-(G6_mean-G5_mean)
Group_7_6 <-(G7_mean-G6_mean)
Group_8_7 <-(G8_mean-G7_mean)
Group_9_8 <-(G9_mean-G8_mean)
Group_10_9 <-(G10_mean-G9_mean)
Group_11_10 <-(G11_mean-G10_mean)
Group_12_11 <-(G12_mean-G11_mean)
Group_13_12 <-(G13_mean-G12_mean)

Miller_ICC_DISS <- function (DATA, NULL_HYP = 0,
conf.level = 0.95) ####made the function for the ICC
{
DATA <- as.matrix(na.omit(DATA))
alpha <- 1 - conf.level
NUM_SUBS <- nrow(DATA)
NUM_RATERS <- ncol(DATA)
SStotal <- var(as.numeric(DATA)) * (NUM_SUBS *
NUM_RATERS - 1)
MSr <- var(apply(DATA, 1, mean)) * NUM_RATERS
MSw <- sum(apply(DATA, 1, var)/NUM_SUBS)
MSc <- var(apply(DATA, 2, mean)) * NUM_SUBS
MSe <- (SStotal - MSr * (NUM_SUBS - 1) - MSc *
(NUM_RATERS - 1))/((NUM_SUBS - 1) *
(NUM_RATERS - 1))
   coeff <- (MSr - MSe)/(MSr + (MSc - MSe)/NUM_SUBS)
   a <- NULL_HYP/(NUM_SUBS * (1 - NULL_HYP))
   b <- 1 + (NULL_HYP * (NUM_SUBS -
1))/(NUM_SUBS * (1 - NULL_HYP))
   Fvalue <- MSr/(a * MSc + b * MSe)
   a <- (NUM_RATERS * coeff)/(NUM_SUBS * (1 -
coeff))
   b <- 1 + (NUM_RATERS * coeff * (NUM_SUBS -
1))/(NUM_SUBS * (1 - coeff))
   v <- (a * MSc + b * MSe)^2/((a *
MSc)^2/(NUM_RATERS - 1) + (b *
MSe)^2/((NUM_SUBS - 1) * (NUM_RATERS - 1)))
   df1 <- NUM_SUBS - 1
   df2 <- v
   p.value <- pf(Fvalue, df1, df2, lower.tail = FALSE)
   FL <- qf(1 - alpha/2, NUM_SUBS - 1, v)
   FU <- qf(1 - alpha/2, v, NUM_SUBS - 1)
   LOWER_CI <- (NUM_SUBS * (MSr - FL * MSe))/(FL
* (MSc - MSe) + NUM_SUBS * MSr)
   UPPER_CI <- (NUM_SUBS * (FU * MSr - MSe))/(MSc
- MSe + NUM_SUBS * FU * MSr)

DETAILS <- structure(list(value = coeff, Fvalue = Fvalue,
p.value = p.value, LOWER_CI = LOWER_CI, UPPER_CI
= UPPER_CI, subjects = NUM_SUBS, raters =
NUM_RATERS, df1 = df1, df2 = df2))return(DETAILS)}
```

```
Group_one_Group_two<- rbind(Group_one_means,
Group_two_means)
Group_two_Group_three<- rbind(Group_two_means,
Group_three_means)
Group_three_Group_four<- rbind(Group_three_means,
Group_four_means)
Group_four_Group_five<- rbind(Group_four_means,
Group_five_means)
Group_five_Group_six<- rbind(Group_five_means,
Group_six_means)
Group_six_Group_seven<- rbind(Group_six_means,
Group_seven_means)
Group_seven_Group_eight<- rbind(Group_seven_means,
Group_eight_means)
Group_eight_Group_nine<- rbind(Group_eight_means,
Group_nine_means)
Group_nine_Group_ten<- rbind(Group_nine_means,
Group_ten_means)
Group_ten_Group_eleven<- rbind(Group_ten_means,
Group_eleven_means)
Group_eleven_Group_twelve<-
rbind(Group_eleven_means, Group_twelve_means)
Group_twelve_Group_thirteen<-
rbind(Group_twelve_means, Group_thirteen_means)

G1G2SD<-sd(Group_one_Group_two)
G2G3SD<-sd(Group_two_Group_three)
G3G4SD<-sd(Group_three_Group_four)
G4G5SD<-sd(Group_four_Group_five)
G5G6SD<-sd(Group_five_Group_six)
G6G7SD<-sd(Group_six_Group_seven)
G7G8SD<-sd(Group_seven_Group_eight)
G8G9SD<-sd(Group_eight_Group_nine)
G9G10SD<-sd(Group_nine_Group_ten)
G10G11SD<-sd(Group_ten_Group_eleven)
G11G12SD<-sd(Group_eleven_Group_twelve)
G12G13SD<-sd(Group_twelve_Group_thirteen)

CompICC_1<-Miller_ICC_DISS(Group_one_Group_two)
CompICC_2<-Miller_ICC_DISS(Group_two_Group_three)
CompICC_3<-Miller_ICC_DISS(Group_three_Group_four)
CompICC_4<-Miller_ICC_DISS(Group_four_Group_five)
CompICC_5<-Miller_ICC_DISS(Group_five_Group_six)
CompICC_6<-Miller_ICC_DISS(Group_six_Group_seven)
CompICC_7<-
Miller_ICC_DISS(Group_seven_Group_eight)
CompICC_8<-
Miller_ICC_DISS(Group_eight_Group_nine)
CompICC_9<-Miller_ICC_DISS(Group_nine_Group_ten)
CompICC_10<-
Miller_ICC_DISS(Group_ten_Group_eleven)
CompICC_11<-
Miller_ICC_DISS(Group_eleven_Group_twelve)
CompICC_12<-
Miller_ICC_DISS(Group_twelve_Group_thirteen)

ICC_1<-Miller_ICC_DISS(Group_one_means)
ICC_2<-Miller_ICC_DISS(Group_two_means)
ICC_3<-Miller_ICC_DISS(Group_three_means)
ICC_4<-Miller_ICC_DISS(Group_four_means)
ICC_5<-Miller_ICC_DISS(Group_five_means)
ICC_6<-Miller_ICC_DISS(Group_six_means)
ICC_7<-Miller_ICC_DISS(Group_seven_means)
ICC_8<-Miller_ICC_DISS(Group_eight_means)
ICC_9<-Miller_ICC_DISS(Group_nine_means)
ICC_10<-Miller_ICC_DISS(Group_ten_means)
ICC_11<-Miller_ICC_DISS(Group_eleven_means)
ICC_12<-Miller_ICC_DISS(Group_twelve_means)
ICC_13<-Miller_ICC_DISS(Group_thirteen_means)

ICC_1_R<-CompICC_1$value
ICC_2_R<-CompICC_2$value
ICC_3_R<-CompICC_3$value
ICC_4_R<-CompICC_4$value
ICC_5_R<-CompICC_5$value
ICC_6_R<-CompICC_6$value
ICC_7_R<-CompICC_7$value
ICC_8_R<-CompICC_8$value
ICC_9_R<-CompICC_9$value
ICC_10_R<-CompICC_10$value
ICC_11_R<-CompICC_11$value
ICC_12_R<-CompICC_12$value

SEM_1_R<- G1G2SD*sqrt(1-ICC_1_R)
SEM_2_R<- G2G3SD*sqrt(1-ICC_2_R)
SEM_3_R<- G3G4SD*sqrt(1-ICC_3_R)
SEM_4_R<- G4G5SD*sqrt(1-ICC_4_R)
SEM_5_R<- G5G6SD*sqrt(1-ICC_5_R)
SEM_6_R<- G6G7SD*sqrt(1-ICC_6_R)
SEM_7_R<- G7G8SD*sqrt(1-ICC_7_R)
SEM_8_R<- G8G9SD*sqrt(1-ICC_8_R)
SEM_9_R<- G9G10SD*sqrt(1-ICC_9_R)
SEM_10_R<-  G10G11SD*sqrt(1-ICC_10_R)
SEM_11_R<-  G11G12SD*sqrt(1-ICC_11_R)
SEM_12_R<-  G12G13SD*sqrt(1-ICC_12_R)

RSEM_1_R<-
(SEM_1_R/(mean(Group_one_Group_two))*100)
RSEM_2_R<-
(SEM_2_R/(mean(Group_two_Group_three))*100)
RSEM_3_R<-
(SEM_3_R/(mean(Group_three_Group_four))*100)
RSEM_4_R<-
(SEM_4_R/(mean(Group_four_Group_five))*100)
RSEM_5_R<-
(SEM_5_R/(mean(Group_five_Group_six))*100)
RSEM_6_R<-
(SEM_6_R/(mean(Group_six_Group_seven))*100)
RSEM_7_R<-
(SEM_7_R/(mean(Group_seven_Group_eight))*100)
RSEM_8_R<-
(SEM_8_R/(mean(Group_eight_Group_nine))*100)
RSEM_9_R<-
(SEM_9_R/(mean(Group_nine_Group_ten))*100)
RSEM_10_R<-
(SEM_10_R/(mean(Group_ten_Group_eleven))*100)
RSEM_11_R<-
(SEM_11_R/(mean(Group_eleven_Group_twelve))*100)
RSEM_12_R<-
(SEM_12_R/(mean(Group_twelve_Group_thirteen))*100)

MRD_1 <-SEM_1_R*1.96*sqrt(2)
MRD_2 <-SEM_2_R*1.96*sqrt(2)
MRD_3 <-SEM_3_R*1.96*sqrt(2)
MRD_4 <-SEM_4_R*1.96*sqrt(2)
MRD_5 <-SEM_5_R*1.96*sqrt(2)
MRD_6 <-SEM_6_R*1.96*sqrt(2)
MRD_7 <-SEM_7_R*1.96*sqrt(2)
MRD_8 <-SEM_8_R*1.96*sqrt(2)
MRD_9 <-SEM_9_R*1.96*sqrt(2)
MRD_10 <-SEM_10_R*1.96*sqrt(2)
MRD_11 <-SEM_11_R*1.96*sqrt(2)
MRD_12 <-SEM_12_R*1.96*sqrt(2)
```

```
MRD_1_R<-
(MRD_1/(mean(Group_one_Group_two))*100)
MRD_2_R<-
(MRD_2/(mean(Group_two_Group_three))*100)
MRD_3_R<-
(MRD_3/(mean(Group_three_Group_four))*100)
MRD_4_R<-
(MRD_4/(mean(Group_four_Group_five))*100)
MRD_5_R<-
(MRD_5/(mean(Group_five_Group_six))*100)
MRD_6_R<-
(MRD_6/(mean(Group_six_Group_seven))*100)
MRD_7_R<-
(MRD_7/(mean(Group_seven_Group_eight))*100)
MRD_8_R<-
(MRD_8/(mean(Group_eight_Group_nine))*100)
MRD_9_R<-
(MRD_9/(mean(Group_nine_Group_ten))*100)
MRD_10_R<-
(MRD_10/(mean(Group_ten_Group_eleven))*100)
MRD_11_R<-
(MRD_11/(mean(Group_eleven_Group_twelve))*100)
MRD_12_R<-
(MRD_12/(mean(Group_twelve_Group_thirteen))*100)

CV_1 <- (Group_one_SD/G1_mean)*100
CV_2 <- (Group_two_SD/G2_mean)*100
CV_3 <- (Group_three_SD/G3_mean)*100
CV_4 <- (Group_four_SD/G4_mean)*100
CV_5 <- (Group_five_SD/G5_mean)*100
CV_6 <- (Group_six_SD/G6_mean)*100
CV_7 <- (Group_seven_SD/G7_mean)*100
CV_8 <- (Group_eight_SD/G8_mean)*100
CV_9 <- (Group_nine_SD/G9_mean)*100
CV_10 <- (Group_ten_SD/G10_mean)*100
CV_11 <- (Group_eleven_SD/G11_mean)*100
CV_12 <- (Group_twelve_SD/G12_mean)*100
CV_13 <- (Group_thirteen_SD/G13_mean)*100

PC3 <-100 - ((G3_mean/mean12) * 100)
PC4 <-100 - ((G4_mean/mean12) * 100)
PC5 <-100 - ((G5_mean/mean12) * 100)
PC6 <-100 - ((G6_mean/mean12) * 100)
PC7 <-100 - ((G7_mean/mean12) * 100)
PC8 <-100 - ((G8_mean/mean12) * 100)
PC9 <-100 - ((G9_mean/mean12) * 100)
PC10 <-100 - ((G10_mean/mean12) * 100)
PC11 <-100 - ((G11_mean/mean12) * 100)
PC12 <-100 - ((G12_mean/mean12) * 100)
PC13 <-100 - ((G13_mean/mean12) * 100)

PC5_3 <- PC3/5
PC5_4 <- PC4/5
PC5_5 <- PC5/5
PC5_6 <- PC6/5
PC5_7 <- PC7/5
PC5_8 <- PC8/5
PC5_9 <- PC9/5
PC5_10 <- PC10/5
PC5_11 <- PC11/5
PC5_12 <- PC12/5
PC5_13 <- PC13/5

TS3<-(50 + 10 *((Group_three_means-
Total_MEAN)/SD_pop))
TS4<-(50 + 10 *((Group_four_means-
Total_MEAN)/SD_pop))
TS5<-(50 + 10 *((Group_five_means-
Total_MEAN)/SD_pop))
TS6<-(50 + 10 *((Group_six_means-
Total_MEAN)/SD_pop))
TS7<-(50 + 10 *((Group_seven_means-
Total_MEAN)/SD_pop))
TS8<-(50 + 10 *((Group_eight_means-
Total_MEAN)/SD_pop))
TS9<-(50 + 10 *((Group_nine_means-
Total_MEAN)/SD_pop))
TS10<-(50 + 10 *((Group_ten_means-
Total_MEAN)/SD_pop))
TS11<-(50 + 10 *((Group_eleven_means-
Total_MEAN)/SD_pop))
TS12<-(50 + 10 *((Group_twelve_means-
Total_MEAN)/SD_pop))
TS13<-(50 + 10 *((Group_thirteen_means-
Total_MEAN)/SD_pop))

MTS3 <- mean(TS3)-50
MTS4 <- mean(TS4)-50
MTS5 <- mean(TS5)-50
MTS6 <- mean(TS6)-50
MTS7 <- mean(TS7)-50
MTS8 <- mean(TS8)-50
MTS9 <- mean(TS9)-50
MTS10 <- mean(TS10)-50
MTS11 <- mean(TS11)-50
MTS12 <- mean(TS12)-50
MTS13<- mean(TS13)-50

AnCHG1<- (Group_2_1 /5)*100
AnCHG2<- (Group_3_2 /5)*100
AnCHG3<-(Group_4_3 /5)*100
AnCHG4<-(Group_5_4 /5)*100
AnCHG5<-(Group_6_5 /5)*100
AnCHG6<-(Group_7_6 /5)*100
AnCHG7<-(Group_8_7 /5)*100
AnCHG8<-(Group_9_8 /5)*100
AnCHG9<-(Group_10_9 /5)*100
AnCHG10<-(Group_11_10 /5)*100
AnCHG11<-(Group_12_11 /5)*100
AnCHG12<-(Group_13_12 /9)*100

SEG1<- (Group_one_SD/sqrt(15))
SEG2<- (Group_two_SD/sqrt(13))
SEG3<- (Group_three_SD/sqrt(11))
SEG4<- (Group_four_SD/sqrt(13))
SEG5<- (Group_five_SD/sqrt(13))
SEG6<- (Group_six_SD/sqrt(12))
SEG7<- (Group_seven_SD/sqrt(13))
SEG8<- (Group_eight_SD/sqrt(14))
SEG9<- (Group_nine_SD/sqrt(11))
SEG10<- (Group_ten_SD/sqrt(11))
SEG11<- (Group_eleven_SD/sqrt(10))
SEG12<- (Group_twelve_SD/sqrt(8))
SEG13<- (Group_thirteen_SD/sqrt(8))

Group = c("20-24", "25-29", "30-34", "35-39", "40-44",
"45-49", "50-54", "55-59", "60-64", "65-69", "70-74", "75-
79", "80<")
Age   = as.numeric(c(Age_G1, Age_G2, Age_G3, Age_G4,
Age_G5, Age_G6, Age_G7, Age_G8, Age_G9, Age_G10,
Age_G11, Age_G12, Age_G13))
Force = as.numeric(c(G1_mean, G2_mean, G3_mean,
G4_mean, G5_mean, G6_mean, G7_mean, G8_mean,
G9_mean, G10_mean, G11_mean, G12_mean, G13_mean))
```

```
SE = as.numeric(c(SEG1, SEG2, SEG3, SEG4, SEG5,
SEG6, SEG7, SEG8, SEG9, SEG10, SEG11, SEG12,
SEG13))
SD = as.numeric(c(Group_one_SD, Group_two_SD,
Group_three_SD, Group_four_SD, Group_five_SD,
Group_six_SD, Group_seven_SD, Group_eight_SD,
Group_nine_SD, Group_ten_SD, Group_eleven_SD,
Group_twelve_SD, Group_thirteen_SD))
DIFF = abs(c(0, Group_2_1, Group_3_2, Group_4_3,
Group_5_4, Group_6_5, Group_7_6, Group_8_7,
Group_9_8, Group_10_9, Group_11_10, Group_12_11,
Group_13_12))
PerCHG = abs(c(NA, NA, PC3, PC4, PC5, PC6, PC7, PC8,
PC9, PC10, PC11, PC12, PC13))
AbsCHG = as.numeric(c(NA, NA, NA, NA, NA, NA, NA,
NA, NA, NA, NA, NA, CHG))
AnCHG = abs(c(NA, AnCHG1, AnCHG2, AnCHG3,
AnCHG4, AnCHG5, AnCHG6, AnCHG7, AnCHG8,
AnCHG9, AnCHG10, AnCHG11, AnCHG12))
ICC = as.numeric(c(NA, ICC_1_R, ICC_2_R, ICC_3_R,
ICC_4_R, ICC_5_R, ICC_6_R, ICC_7_R, ICC_8_R,
ICC_9_R, ICC_10_R, ICC_11_R, ICC_12_R))
SEm = as.numeric(c(NA, SEM_1_R, SEM_2_R,
SEM_3_R, SEM_4_R, SEM_5_R, SEM_6_R, SEM_7_R,
SEM_8_R, SEM_9_R, SEM_10_R, SEM_11_R,
SEM_12_R))
RSEm = as.numeric(c(NA, RSEM_1_R, RSEM_2_R,
RSEM_3_R, RSEM_4_R, RSEM_5_R, RSEM_6_R,
RSEM_7_R, RSEM_8_R, RSEM_9_R, RSEM_10_R,
RSEM_11_R, RSEM_12_R))
MDCR = as.numeric(c(NA, MRD_1, MRD_2, MRD_3,
MRD_4, MRD_5, MRD_6, MRD_7, MRD_8, MRD_9,
MRD_10, MRD_11, MRD_12))
RMDCR = as.numeric(c(NA, MRD_1_R, MRD_2_R,
MRD_3_R, MRD_4_R, MRD_5_R, MRD_6_R,
MRD_7_R, MRD_8_R, MRD_9_R, MRD_10_R,
MRD_11_R, MRD_12_R))
CV = as.numeric(c(CV_1, CV_2, CV_3, CV_4, CV_5,
CV_6, CV_7, CV_8, CV_9, CV_10, CV_11, CV_12,
CV_13))
T.Score = as.numeric(c(NA, NA, MTS3, MTS4, MTS5,
MTS6, MTS7, MTS8, MTS9, MTS10, MTS11, MTS12,
MTS13))

Table_of_Values<-data.frame(Group, Age, Force, SE, SD,
DIFF, PerCHG, AbsCHG, AnCHG, ICC, SEm, RSEm,
MDCR, RMDCR, CV, T.Score)

install.packages("formattable")
library(formattable)

#formattable(Table_of_Values, a
   #align =c("l","c","c","c","c","c","c","c","c"),
   #list(`Group` = formatter("span", style = ~ style(color =
#"gray",font.weight = "bold"))))

PROJECT <- formatter("span", style = ~ ifelse(DIFF > SEm
& DIFF > MDCR, "color:red", NA))
formattable(Table_of_Values, list(Group = PROJECT))

library(tidyverse)

####this will provide an initial figure of strength x age

FIGURE.1<- ggplot(DISSERTATION_EXAM, aes(Age,
Trial_Mean)) +
    stat_summary(geom = "point", fun.y = mean, size=1) +
    stat_summary(geom = "linerange", fun.data = mean_se)+
theme_classic()

FIGURE.2 <- FIGURE.1+scale_x_continuous(name= "Age
Group",
breaks=as.numeric(c("1","2","3","4","5","6","7","8","9","10
","11","12","13")), labels = factor(c("20-24", "25-29", "30-
34", "35-39", "40-44", "45-49","50-54", "55-59", "60-64",
"65-69", "70-74",  "75-79", "80<")))+
scale_y_continuous(name="name.parameter)",
limits=c(ymin, ymax))


FIGURE.3

####the above figure doesnt look great, since the SE are
tiny from the grip tests. There will be a better figure
later####

library(segmented)

####We will make a few models here
linear.model <- lm(Trial_Mean ~ Years,
data=DISSERTATION_EXAM)
segmented.model <- segmented(linear.model, seg.z=~
Years)
quadratic.model <- lm(Trial_Mean ~ Years + Y2,
DISSERTATION_EXAM)

PP <- ggplot(DISSERTATION_EXAM, aes(Years,
Trial_Mean))
QQ <- PP + geom_point(aes(color=factor(Age_Group)),
size=5)+theme_bw() +
theme(panel.grid=element_blank())+theme_classic() +
labs(color = "Age Group") + labs(title = "Mean Participant
Grip Strength (kg) by Age",(hjust=0.5))
RR <- QQ + geom_point(aes(color=factor(Age_Group)),
size=5)+theme_bw() +
theme(panel.grid=element_blank())+theme_classic() +
labs(color = "Age Group")
SS <- RR + labs(title = "Mean Participant Grip Strength
(kg) by Age")
TT <- SS + theme(plot.title = element_text(hjust=0.5))
TT + ylab("Mean Strength (kg)") + xlab("Age (years)")

summary(linear.model)
summary(quadratic.model)
summary(segmented.model)

anova(linear.model, quadratic.model, segmented.model,
test="Chi")

confint(linear.model)
confint(quadratic.model)
confint.segmented(segmented.model)
slope(segmented.model, conf.level=0.95)

davies.test(segmented.model, ~Years)
pscore.test(segmented.model)
```

Appendix F: Institutional Review Board Approval

The UNIVERSITY of OKLAHOMA

Institutional Review Board for the Protection of Human Subjects

Initial Submission – Board Approval

Date: November 13, 2018

To: Michael G Bemben, PhD

IRB#: 9838
Meeting Date: 11/05/2018
Approval Date: 11/12/2018
Expiration Date: 10/31/2019

Study Title: Age-Related Changes in Muscular Strength, Power, Endurance and Quality in Women

Reference Number: 683848

Study Status: Active - Open

At its regularly scheduled meeting the IRB reviewed the above-referenced research study. Study documents associated with this submission are listed on page 2 of this letter. To review and/or access the submission forms as well as the study documents approved for this submission, open this study from the *My Studies* option, click to open this study, look under Protocol Items to click on the current *Application*, *Informed Consent* and *Other Study Documents*.

If this study required routing through the Office of Research Administration (ORA), you may *not begin your study yet*, as per OUHSC Institutional policy, until the contract through ORA is finalized and signed.

As principal investigator of this research study, it is your responsibility to:

- Conduct the research study in a manner consistent with the requirements of the IRB and federal regulations at 45 CFR 46 and/or 21 CFR 50 and 56.
- Request approval from the IRB prior to implementing any/all modifications.
- Promptly report to the IRB any harm experienced by a participant that is both unanticipated and related per IRB Policy.
- Maintain accurate and complete study records for evaluation by the HRPP quality improvement program and if applicable, inspection by regulatory agencies and/or the study sponsor.
- Promptly submit continuing review documents to the IRB upon notification approximately 60 days prior to the expiration date indicated above.

In addition, it is your responsibility to obtain informed consent and research privacy authorization using the currently approved, stamped forms and retain all original, signed forms, if applicable.

If you have questions about this notification or using iRIS, contact the IRB at 405-271-2045 or irb@ouhsc.edu.

Sincerely,

Karen Beckman, MD, Chair
Institutional Review Board

1105 N. Stonewall Avenue, Oklahoma City, OK 73117 (FWA0007961)

Study documents associated with this submission:

Study Documents			
Title	**Version #**	**Version Date**	**Outcome**
Disclaimer Statement	Version 1.0	11/09/2018	Approved
Kaur_Japneet_CITI	Version 1.0	10/04/2018	Noted
Medical Clearance Form	Version 1.0	09/26/2018	Approved
Telephone Script	Version 1.0	09/26/2018	Approved
Flyer	Version 1.0	09/26/2018	Approved
Screening Checklist	Version 1.0	09/26/2018	Approved
Physical Activity Readiness Questionnaire	Version 1.0	09/26/2018	Approved
International Physical Activity Questionnaire	Version 1.0	09/26/2018	Approved
Menstrual Status Questionnaire	Version 1.0	09/26/2018	Approved
Health Status Questionnaire	Version 1.0	09/26/2018	Approved
Calcium Intake Questionnaire	Version 1.0	09/26/2018	Approved
Bone-Specific Physical Activity Questionnaire	Version 1.0	09/26/2018	Approved
Verbal Script	Version 1.1	09/26/2018	Approved
Social Media Script	Version 1.1	09/26/2018	Approved
Message Board Script	Version 1.1	09/26/2018	Approved
Email Script	Version 1.1	09/26/2018	Approved
HIPAA Authorization 1	Version 1.1	09/26/2018	Approved
Protocol	Version 1.2	09/26/2018	Approved

Study Consent Form			
Title	**Version #**	**Version Date**	**Outcome**
Consent Form	Version 1.3	09/26/2018	Approved

Information for Industry Sponsors: the columns titled Version Number and Version Date are specific to the electronic submission system (iRIS) and should not to be confused with information included in the Document and/or Consent title(s).

Appendix G: Study Documentation

Screening Checklist

The Age-Related Changes in Muscular Strength, Power, Endurance and Quality in Women

Name: _____ Date: _____ Time:_____

Does participant meet the inclusion criteria for the study?

	Yes	No
Women 20 – 100 years of age	_____	_____
Independent living and recreationally active (i.e. performs activities of daily living, and instrumental activities of daily living independently)	_____	_____

Does participant have any exclusion criteria for the study?

Actively training for a competitive event (power lifting, Body building, extended length races, etc.)	_____	_____
Engages in >7 hours exercise per week	_____	_____
Has degenerative neuromuscular conditions (i.e. Parkinsons)	_____	_____
Is cognitively impaired	_____	_____
Is pregnant, planning to become pregnant or is breast feeding	_____	_____
Has diabetes, cancer or uncontrolled hypertension	_____	_____
Does not fit DXA table (>75" and/or 136kg)	_____	_____
Suffered a musculoskeletal injury in the previous 12 months	_____	_____
Has metal implants or joint replacement at hip, spine leg	_____	_____
Restrictions to perform functional performance or tests, e.g. myocardial infarction/congestive heart failure/ strokes/back surgery within the past 6 months	_____	_____

PI approval _____ Date _____

IRB NUMBER: 9838
IRB APPROVAL DATE: 11/12/2018

Consent Form
University of Oklahoma Health Sciences Center (OUHSC)
University of Oklahoma – Norman Campus (OU)

The Age-Related Changes in Muscular Strength, Power, Endurance, and Quality in Women
Sponsor: OU Department of Health and Exercise Science
Principal Investigator: Michael G. Bemben, PhD

This is a research study. Research studies include only patients who choose to take part in them. Please take your time to make your decision. Discuss this with your family and friends.

Why Have I Been Asked To Participate In This Study?
You are being asked to take part in this trial/study because you are a recreationally active, independent living woman between the ages of 20 to 100 years.

Why Is This Study Being Done?
The purpose of this study is to identify the critical ages when reductions in muscular performance occur in women. Additionally, this study will examine the relationships between body composition and muscle function.

How Many People Will Take Part In The Study?
About 300 women will take part in this study, all on the University of Oklahoma, Norman campus.

What Is Involved In The Study?
If you decide to take part in this study, a total of five visits will be needed.
The first visit consists of consent, blood pressure, questionnaires, and familiarization, which will take approximately one and half hours.

- You will sign and date the informed consent and privacy forms and complete the Health Status Questionnaire, International Physical Activity Questionnaire, Bone-Specific Physical Activity Questionnaire, Calcium Intake Questionnaire, and Menstrual History Questionnaire.
- Blood pressure measurement- Blood pressure will be measured at least twice.
- Depending on your age you will receive one of two forms:
    - If you are 44 years of age or younger you will complete the Physical Activity Readiness Questionnaire.
    - If you are 45 years of age or older and meet all the inclusion and exclusion criteria, you will be given a medical clearance form to take to your personal physician for approval to participate in this study.
- If you are eligible for this study, you will be familiarized via instruction and demonstrations of the testing equipment. After the instruction, you will be allowed to perform each test (hand grip strength, vertical jump, and other strength testing). For example, you will perform a submaximal hand grip test to become familiar with the test.

The second visit consists of a blood draw (approximately 30 minutes).

- The blood draw (about 7.5 ml) will be performed by a registered nurse or phlebotomist at the OU Goddard Student Health Center in the early morning after an overnight fast.

The third visit consists of a series of tests to evaluate body composition as well as the completion of additional familiarization trials for the muscle performance testing (approximately one and half hours).

- Height and Weight will be measured.
- Dual-energy x-ray absorptiometry (DXA) scans- Radiation procedures will be used to measure the bone density your whole body, lower back and both hips and your body fat and lean tissue values. You will be lying on your back on the DXA table for the scans and you will be required to remain still during the procedures.
- Peripheral quantitative computed tomography (pQCT) scans- The pQCT scan is a another radiation procedure to study your bones. You will sit as still as possible in a chair with your right leg in a leg support during the scan.
- Familiarization- We will instruct you on correct techniques for the handgrip, jump test and strength testing procedures. After the instruction, you will be supervised while practicing these tests at light intensities to become accustomed to the movements.

The fourth and fifth visits (approximately 2 hours each), which will be separated by 7 days, will consist of muscle performance testing in the following order:

- Handgrip Test– Grip strength will be measured with a handgrip dynamometer while in a seated position with the back supported. Starting with your right hand, you will squeeze the dynamometer as hard as possible for a maximum of 3 seconds. A rest period of 30 seconds will be given and then the procedure will be repeated on your left hand. This will occur for a total of 3 trials on each hand.
- Jump Test– Muscle power will be assessed by a jump test. You will stand in the center of the jump mat. crouch while swinging their arms, and jump up as high as possible, landing in the center of the mat. One minute of rest will be provided between jumps with a total of 3 successful attempts recorded and averaged. Staff will standby during the jumps to help you avoid falling.
- Biodex Dynamometer testing- You will perform muscular strength and endurance testing at the elbow, knee and ankle joint. The elbow and knee will consist of three protocols while the ankle will consist of two, these protocols are briefly outlined below. All tests will be conducted at the elbow, followed by the knee and ending with the ankle.
    - Isometric contractions: contract as fast and hard as possible against a stationary Biodex attachment.
    - Isotonic contractions: contract as fast and hard as possible against a load-dependent attachment at intensities of 20%, 40% and 60% of maximal isometric strength.
    - Isokinetic contractions: contract as fast and hard as possible against a speed-dependent attachment at a fast and slow speed.

How Long Will I Be In The Study?
We think that you will be in the study for 5 visits lasting for approximately 8 hours over the course of 15-20 days.

There may be unanticipated circumstances under which your participation may be terminated by the investigator without regard to your consent; for example, your participation may be terminated if you become pregnant.

You can stop participating in this study at any time. However, if you decide to stop participating in the study, we encourage you to talk to the researcher first.

What Are The Risks of The Study?
While in the study, you are at risk for these side effects. You should discuss these with the researcher prior to providing your consent. There may also be unforeseeable risks with participation.

Risks and side effects related to having pQCT and DXA scans: This study involves radiation exposure from the four DXA scans and four pQCT scans, which are types of x-ray procedures. These procedures are for research only and not needed for your medical care. The amount of additional radiation to which you will be exposed is approximately 1% of the amount of radiation to which we are exposed annually from background sources such as the Earth and Sun. In addition to any radiographic procedures that are being done as part of this research, you may also be exposed to radiation from procedures that are part of your normal care. The risk from radiation exposure increases over your lifetime as you receive additional exposure to radiation.

Risks and side effects related to functional performance tests: There is slight possibility of mild soreness due to muscle strength and power testing. Additionally, there is a slight risk of injury/fall during jumping tests.

Risks and side effects of blood draws: There may be temporary minor discomfort from needle puncture and also a potential for slight bruising.

Reproductive Risks for females: You must not be and should not become pregnant nor breast-feed an infant while on this study. Participating in the bone scans (DXA scans) while you are pregnant, or breastfeeding may involve risks to an embryo, fetus, or infant, including birth defects which are currently unforeseeable. In order to reduce your risk of pregnancy, you or your partner should use one or more of the acceptable methods of birth control listed below, regularly and consistently, while you are in this study. Acceptable methods of birth control (continuing throughout the study) include:

- An approved oral contraceptive (birth control pill)
- Intra-uterine device (IUD)
- Hormone implants
- Contraceptive injection (Depo-Provera)
- Barrier methods (diaphragm with spermicidal gel or condoms)
- Transdermal contraceptives (birth control patch)
- Vaginal contraception ring (birth control ring)
- Sterilization (tubal ligation, hysterectomy or vasectomy)

If you become pregnant or suspect that you are pregnant during this study, you should immediately inform the study personnel. A pregnancy test will be done. If pregnancy is confirmed, you will be withdrawn from the study.

Are There Benefits to Taking Part in The Study?
There are no direct benefits from participating in this study.

What Other Options Are There?
Your alternative is to not participate.

What about Confidentiality?
Efforts will be made to keep your personal information confidential. You will not be identifiable by name or description in any reports or publications about this study. We cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law. You will be asked to sign a separate authorization form for use or sharing of your protected health information.

There are organizations outside the OUHSC that may inspect and/or copy your research records for quality assurance and data analysis. These organizations include the US Food & Drug Administration and other regulatory agencies, and the OU Department of Health & Exercise Science and its representatives. The OUHSC Human Research Participant Program office, the OUHSC Institutional Review Board, and the OUHSC Office of Compliance may also inspect and/or copy your research records for these purposes.

What Are the Costs?
There is no cost to you if you participate in this study.

Will I Be Paid For Participating in This Study?
There will be no compensation for participating in this study.

What if I am Injured or Become ill while Participating in this Study?
In the case of injury or illness resulting from this study, emergency medical treatment is available. However, you or your insurance company may be expected to pay the usual charge for this treatment. No funds have been set aside by the University of Oklahoma or the University of Oklahoma Health Sciences Center to compensate you in the event of injury.

What Are My Rights As a Participant?
Taking part in this study is voluntary. You may choose not to participate. Refusal to participate will involve no penalty or loss of benefits to which you are otherwise entitled.

If you agree to participate and then decide against it, you can withdraw for any reason and leave the study at any time. Please be sure to discuss leaving the study with the principal investigator or your regular doctor. You may discontinue your participation at any time without penalty or loss of benefits to which you are otherwise entitled.

We will provide you with any significant new findings developed during the course of the research that may affect your health, welfare, or willingness to continue your participation in this study.

You have the right to access the medical information that has been collected about you as a part of this research study. However, you may not have access to this medical information until the entire research study has completely finished. You consent to this temporary restriction.

Whom Do I Call If I have Questions or Problems?
If you have questions, concerns, or complaints about the study or have a research-related injury, contact Dr. Michael G. Bemben at 405-325-2717 or mgbemben@ou.edu.

If you cannot reach the Investigator or wish to speak to someone other than the investigator, contact the OUHSC Director, Office of Human Research Participant Protection, at 405-271-2045.

For questions about your rights as a research participant, contact the OUHSC Director, Office of Human Research Participant Protection at 405-271-2045.

Future Communications
The researcher would like to contact you again to recruit you into future studies or to gather additional information.
_____I give my permission for the researcher to contact me in the future.
_____I do not wish to be contacted by the researcher again.

Signature:

By signing this form, you are agreeing to participate in this research study under the conditions described. You have not given up any of your legal rights or released any individual or entity from liability for negligence. You have been given an opportunity to ask questions. You will be given a copy of this consent document.

I agree to participate in this study:

PARTICIPANT SIGNATURE (age ≥18) (*Or Legally Authorized Representative)*	Printed Name	Date
SIGNATURE OF PERSON OBTAINING CONSENT	Printed Name	Date

AUTHORIZATION TO USE or SHARE
HEALTH INFORMATION[1] THAT IDENTIFIES YOU FOR RESEARCH
An Informed Consent Document for Research Participation may also be required.
Form 2 must be used for research involving psychotherapy notes.

Title of Research Project: **Age-Related Changes in Muscular Strength, Power, Endurance and Quality in Women.**

Leader of Research Team: **Michael G. Bemben, PhD**

Address: **1401 Asp Ave., Room 104, Norman, Oklahoma 73019**

Phone Number**: 405-325-2717**

If you decide to sign this document, University of Oklahoma Health Sciences Center (OUHSC) researchers may use or share information that identifies you (protected health information) for their research. Protected health information will be called PHI in this document.

PHI To Be Used or Shared. Federal law requires that researchers get your permission (authorization) to use or share your PHI. If you give permission, the researchers may use or share with the people identified in this Authorization any PHI related to this research from your medical records and from any test results. Information used or shared may include all information relating to any tests, procedures, surveys, or interviews as outlined in the consent form; medical records and charts; name, address, telephone number, date of birth, race, government-issued identification numbers, and answers to questionnaires and DXA and pQCT results.

Purposes for Using or Sharing PHI. If you give permission, the researchers may use your PHI to investigate the age-related changes in muscle function in women aged 20 to 100 years.

Other Use and Sharing of PHI. If you give permission, the researchers may also use your PHI to develop new procedures or commercial products. They may share your PHI with other researchers, the research sponsor and its agents, the OUHSC Institutional Review Board, auditors and inspectors who check the research, and government agencies such as the Food and Drug Administration (FDA) and the Department of Health and Human Services (HHS), and when required by law. The researchers may also share your PHI with no one else.

Confidentiality. Although the researchers may report their findings in scientific journals or meetings, they will not identify you in their reports. The researchers will try to keep your information confidential, but confidentiality is not guaranteed. The law does not require everyone receiving the

[1] **Protected Health Information includes all identifiable information relating to any aspect of an individual's health whether past, present or future, created or maintained by a Covered Entity.**

information covered by this document to keep it confidential, so they could release it to others, and federal law may no longer protect it.

YOU UNDERSTAND THAT YOUR PROTECTED HEALTH INFORMATION MAY INCLUDE INFORMATION REGARDING A COMMUNICABLE OR NONCOMMUNICABLE DISEASE.

Voluntary Choice. The choice to give OUHSC researchers permission to use or share your PHI for their research is voluntary. It is completely up to you. No one can force you to give permission. However, you must give permission for OUHSC researchers to use or share your PHI if you want to participate in the research and, if you cancel your authorization, you can no longer participate in this study.

Refusing to give permission will not affect your ability to get routine treatment or health care unrelated to this study from OUHSC.

Canceling Permission. If you give the OUHSC researchers permission to use or share your PHI, you have a right to cancel your permission whenever you want. However, canceling your permission will not apply to information that the researchers have already used, relied on, or shared or to information necessary to maintain the reliability or integrity of this research.

End of Permission. Unless you cancel it, permission for OUHSC researchers to use or share your PHI for their research will never end.

Contacting OUHSC: You may find out if your PHI has been shared, get a copy of your PHI, or cancel your permission at any time by writing to:

Privacy Official University of Oklahoma Health Sciences Center PO Box 26901 Oklahoma City, OK 73190	or	Privacy Board University of Oklahoma Health Sciences Center PO Box 26901 Oklahoma City, OK 73190

If you have questions, call: (405) 271-2511 or (405) 271-2045.

Access to Information. You have the right to access the medical information that has been collected about you as a part of this research study. However, you may not have access to this medical information until the entire research study is completely finished. You consent to this temporary restriction.

Giving Permission. By signing this form, you give OUHSC and OUHSC's researchers led by the Research Team Leader permission to share your PHI for the research project listed at the top of this form.

Patient/Participant Name (Print): _____

Signature of Patient-Participant or Parent if Participant is a minor	Date

Or

Signature of Legal Representative**	Date

**If signed by a Legal Representative of the Patient-Participant, provide a description of the relationship to the Patient-Participant and the authority to act as Legal Representative:

OUHSC may ask you to produce evidence of your relationship.

A signed copy of this form must be given to the Patient-Participant or the Legal Representative at the time this signed form is provided to the researcher or his representative.

Neuromuscular Research Laboratory
OU Department of Health and Exercise Science
Health Status Questionnaire

Instructions: Complete each question accurately. All information provided is confidential.
(NOTE: The following codes are for office use only: RF; MC)

Part 1. Information about the individual

1._____
Date

2. _____
Legal name Ethnicity

3._____
Mailing address

_____
Home phone Business/cell phone

4. Sex (circle one): Female Male (RF)

5. Year of birth: _____ Age: _____

6. Number of hours worked per week:
NA (retired) Less than 20 20-40 41-60 Over 60

If not retired, more than 25% of time spent on job (circle all that apply)

Sitting at desk Lifting or carrying loads Standing Walking Driving

Part 2. Medical history
7. (RF) Circle any who died of heart attack before age 50:

Father Mother Brother Sister Grandparent

8.Date of: Last medical physical exam: _____Last physical fitness test: _____
Year Year

9. Circle operations you have had:

Back Heart (MC) Kidney Eyes Joint Neck

Ears Hernia Lung Other _____

NONE

IRB NUMBER: 9838
IRB APPROVAL DATE: 11/12/2018

10. Please circle any of the following for which you have been diagnosed or treated by a physician or health professional:

Alcoholism	Diabetes	Kidney problem (MC)
Anemia, sickle cell	Emphysema	Mental illness
Anemia, other	Epilepsy	Neck strain
Asthma	Eye problems	Obesity (RF)
Back strain	Gout	Osteoporosis
Bleeding trait	Hearing loss	Phlebitis (MC)
Bronchitis, chronic	Heart problems	Rheumatoid arthritis
Cancer	High blood pressure (RF)	Stroke (MC)
Cirrhosis, liver (MC)	Hypoglycemia	Thyroid problem
Concussion (MC)	Hyperlipidemia (RF)	Ulcer
Congenital defect	Infectious mononucleosis (MC)	Other _____

NONE

11. Circle all medicine taken in last 6 months:

Asthma (list type)	High-blood-pressure medication	
Type: _____	*Type:* _____	Thyroid
Blood thinner (MC)	Epilepsy medication	Diuretic (MC)
Corticosteroids	Estrogen	Other_____
Depression	Heart-rhythm medication (MC)	
Diabetic pill	Insulin (MC)	**NONE**
Digitalis (MC)	Nitroglycerin (MC)	

12. Any of these health symptoms that occurs frequently is the basis for medical attention. Circle the number indicating how often you have each of the following:

1 = Practically never 2 = Infrequently 3 = Sometimes 4 = Fairly often 5 = Very often

a. Cough up blood (MC) 1 2 3 4 5

b. Abdominal pain (MC) 1 2 3 4 5

c. Low back pain (SLA) 1 2 3 4 5

d. Leg pain (MC) 1 2 3 4 5

e. Arm or shoulder pain (MC) 1 2 3 4 5

f. Chest pain (RF) (MC) 1 2 3 4 5

g. Swollen joints (MC) 1 2 3 4 5

h. Feel faint (MC) 1 2 3 4 5

I. Dizziness (MC) 1 2 3 4 5

j. Breathless with slight exertion (MC) 1 2 3 4 5

Part 3. Health-related behavior

13. (RF) Do you smoke? Yes No

14. If you are a smoker, indicate number smoked per day:

Cigarettes:	40 or more	20-39	10-19	1-9
Cigars or pipes only:	5 or more or any inhaled			Less than 5, none inhaled

15. Weight now: _____lb. One year ago: _____lb. Age 21 (if applicable): _____lb.

16. Do you regularly engage in strenuous exercise or hard physical labor? YES NO

17. On average how many days per week are you physically active? _____

About how long have you been this physically active? _____

Specific Exercise Questions

Do you engage in resistance training? _____Yes _____No

Type of exercise _____

Frequency per week_____ Duration per session _____Intensity (Sets/Reps) _____

Perceived exertion during resistance training _____

Do you engage in cardiovascular training? _____Yes _____No

Type of exercise _____

Frequency per week_____ Duration per session _____Intensity _____

Perceived exertion during cardiovascular training _____

Do you engage in group fitness classes? _____Yes _____No

Type of exercise _____

Frequency per week_____ Duration per session _____Intensity _____

Please use the space below to describe any other physical activity you regularly engage in.

Has this medication affected your menstrual cycle (regularity, length and amount of flow)?
If yes, indicate changes.

9. Have you taken hormonal contraceptives in the past?
If no, skip to SECTION B.
If yes, what was the brand name and dosage?
Brand:_____
Dosage:_____

10. When did you start taking the hormonal contraceptive; how long have you been taking it; and when did you stop taking it?
Started:_____
Time administered:_____
Time stopped:_____

If you answered yes to 9 or 10, did you experience any weight gain and/or a change in appetite as a result of oral contraceptive use? If so, please indicate amount of weight gained. _____lbs.

SECTION A2: CURRENT MENSTRUAL STATUS (Postmenopausal Women)

1. At what age did you experience your final menstrual period?

_____ years
_____ years postmenopausal

2. Have you had a hysterectomy (surgical removal of the uterus)? If yes, at what age did you have this surgery?

YES NO
Age of hysterectomy: _____ years

3. Have you had your ovaries removed? If yes, at what age did you have this surgery?

YES NO
Age of ovariectomy: _____ years

4. Are you currently on estrogen and/or progesterone replacement therapy? If no, skip to question 5.
If yes, how long have you been on hormone replacement therapy?

_____ years

Subject ID:_____ Date:_____

Neuromuscular Research Laboratory
Department of Health and Exercise Science University of Oklahoma
MENSTRUAL HISTORY QUESTIONNAIRE

We are asking you to give us as complete a menstrual history as possible. All information is strictly confidential.

Are you pregnant (circle your response)

YES- Do not complete the rest of this form
NO- Continue to section A.

SECTION A1: CURRENT MENSTRUAL STATUS (Premenopausal Women)

1. Approximately how many menstrual periods have you had during the past 12 months? (please circle what months you have had a period. This means from this time last year to the present month)

Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec

2. What is the usual length of your menstrual cycle (first day of your period to the next onset of your period)?

_____days. Today is day _____ of your present menstrual cycle.

3. What was the date of the onset of your last period?

4. When do you expect you next period?

5. What is the average length (number of days) of your menstrual flow? _____ days

How many of these days do you consider "heavy"? _____days

6. Do you experience cramps during menstruation (dysmenorrheal)? If yes, how many days does this last?

7. Do you experience symptoms of premenstrual syndrome (i.e., weight gain, increased eating, depression, headaches, anxiety, breast tenderness)? If yes, please list the symptoms.

8. Do you take oral contraceptives or any other medication that includes estrogen and/or progesterone?

If yes, how long have you been taking this medication?_____
What is the brand name and dosage of this mediation?_____

What is/are the brand name(s), dosage(s), and type(s) (e. g., pills, cream, patch) of hormone medication you are taking?

5. Have you taken estrogen and/or progesterone replacement in the past? If no, skip to SECTION B.

If yes, what was the type (e.g., pills, cream, patch) and dosage of the medication?

At what age did you start taking hormone replacement?

_____ years

How long did you continue taking the hormone replacement?

At what age and why did you stop taking hormone replacement?

6. If you answered yes to questions 4 or 5, did you experience any side effects (e.g., weight gain, mood swings, headaches) while taking hormone replacement? If yes, please list the side effects.

SECTION B: PAST MENSTRUAL HISTORY

1. At what age did you experience your first menstrual period?

_____ years

2. Were your periods regular (occurring monthly) during the first two years after menstruation began? If not, at what age did your period become regular?

YES NO
_____ years

3. Has there been any time in the past where your periods were irregular or absent? If no, skip to question 4. If yes, did these periods coincide with unusual bouts of training, or with a period of stress?

4. If you have had an irregular period due to training please describe (i.e., you have a period in the offseason but only irregular menstruation during preseason and season)?

5. Have you ever consulted a doctor about menstrual problems (specifically, about irregular or missing periods)? If no, skip to question 6. Have you ever been diagnosed as having a shortened luteal phase (the time in between periods)?

6. Have you ever consulted a doctor about any problems relating to your hormonal system? If so, please explain.

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE (October 2002)

LONG LAST 7 DAYS SELF-ADMINISTERED FORMAT

FOR USE WITH YOUNG AND MIDDLE-AGED ADULTS (15-69 years)

The International Physical Activity Questionnaires (IPAQ) comprises a set of 4 questionnaires. Long (5 activity domains asked independently) and short (4 generic items) versions for use by either telephone or self-administered methods are available. The purpose of the questionnaires is to provide common instruments that can be used to obtain internationally comparable data on health–related physical activity.

Background on IPAQ
The development of an international measure for physical activity commenced in Geneva in 1998 and was followed by extensive reliability and validity testing undertaken across 12 countries (14 sites) during 2000. The final results suggest that these measures have acceptable measurement properties for use in many settings and in different languages, and are suitable for national population-based prevalence studies of participation in physical activity.

Using IPAQ
Use of the IPAQ instruments for monitoring and research purposes is encouraged. It is recommended that no changes be made to the order or wording of the questions as this will affect the psychometric properties of the instruments.

Translation from English and Cultural Adaptation
Translation from English is encouraged to facilitate worldwide use of IPAQ. Information on the availability of IPAQ in different languages can be obtained at www.ipaq.ki.se. If a new translation is undertaken we highly recommend using the prescribed back translation methods available on the IPAQ website. If possible please consider making your translated version of IPAQ available to others by contributing it to the IPAQ website. Further details on translation and cultural adaptation can be downloaded from the website.

Further Developments of IPAQ
International collaboration on IPAQ is on-going and an ***International Physical Activity Prevalence Study*** is in progress. For further information see the IPAQ website.

More Information
More detailed information on the IPAQ process and the research methods used in the development of IPAQ instruments is available at www.ipaq.ki.se and Booth, M.L. (2000). *Assessment of Physical Activity: An International Perspective.* Research Quarterly for Exercise and Sport, 71 (2): s114-20. Other scientific publications and presentations on the use of IPAQ are summarized on the website.

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE

We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. The questions will ask you about the time you spent being physically active in the **last 7 days**. Please answer each question even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport.

Think about all the **vigorous** and **moderate** activities that you did in the **last 7 days**. **Vigorous** physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. **Moderate** activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal.

PART 1: JOB-RELATED PHYSICAL ACTIVITY

The first section is about your work. This includes paid jobs, farming, volunteer work, course work, and any other unpaid work that you did outside your home. Do not include unpaid work you might do around your home, like housework, yard work, general maintenance, and caring for your family. These are asked in Part 3.

1. Do you currently have a job or do any unpaid work outside your home?

   ☐ Yes

   ☐ No → ***Skip to PART 2: TRANSPORTATION***

The next questions are about all the physical activity you did in the **last 7 days** as part of your paid or unpaid work. This does not include traveling to and from work.

2. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, digging, heavy construction, or climbing up stairs **as part of your work**? Think about only those physical activities that you did for at least 10 minutes at a time.

   _____ **days per week**

   ☐ No vigorous job-related physical activity → ***Skip to question 4***

3. How much time did you usually spend on one of those days doing **vigorous** physical activities as part of your work?

   _____ **hours per day**
   _____ **minutes per day**

4. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** physical activities like carrying light loads **as part of your work**? Please do not include walking.

   _____ **days per week**

   ☐ No moderate job-related physical activity → ***Skip to question 6***

5. How much time did you usually spend on one of those days doing **moderate** physical activities as part of your work?

_____ **hours per day**
_____ **minutes per day**

6. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time **as part of your work**? Please do not count any walking you did to travel to or from work.

_____ **days per week**

☐ No job-related walking → ***Skip to PART 2: TRANSPORTATION***

7. How much time did you usually spend on one of those days **walking** as part of your work?

_____ **hours per day**
_____ **minutes per day**

PART 2: TRANSPORTATION PHYSICAL ACTIVITY

These questions are about how you traveled from place to place, including to places like work, stores, movies, and so on.

8. During the **last 7 days**, on how many days did you **travel in a motor vehicle** like a train, bus, car, or tram?

_____ **days per week**

☐ No traveling in a motor vehicle → ***Skip to question 10***

9. How much time did you usually spend on one of those days **traveling** in a train, bus, car, tram, or other kind of motor vehicle?

_____ **hours per day**
_____ **minutes per day**

Now think only about the **bicycling** and **walking** you might have done to travel to and from work, to do errands, or to go from place to place.

10. During the **last 7 days**, on how many days did you **bicycle** for at least 10 minutes at a time to go **from place to place**?

_____ **days per week**

☐ No bicycling from place to place → ***Skip to question 12***

11. How much time did you usually spend on one of those days to **bicycle** from place to place?

_____ **hours per day**
_____ **minutes per day**

12. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time to go **from place to place**?

_____ **days per week**

☐ No walking from place to place → ***Skip to PART 3: HOUSEWORK, HOUSE MAINTENANCE, AND CARING FOR FAMILY***

13. How much time did you usually spend on one of those days **walking** from place to place?

_____ **hours per day**
_____ **minutes per day**

PART 3: HOUSEWORK, HOUSE MAINTENANCE, AND CARING FOR FAMILY

This section is about some of the physical activities you might have done in the **last 7 days** in and around your home, like housework, gardening, yard work, general maintenance work, and caring for your family.

14. Think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, chopping wood, shoveling snow, or digging **in the garden or yard**?

_____ **days per week**

☐ No vigorous activity in garden or yard → ***Skip to question 16***

15. How much time did you usually spend on one of those days doing **vigorous** physical activities in the garden or yard?

_____ **hours per day**
_____ **minutes per day**

16. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** activities like carrying light loads, sweeping, washing windows, and raking **in the garden or yard**?

_____ **days per week**

☐ No moderate activity in garden or yard → ***Skip to question 18***

17. How much time did you usually spend on one of those days doing **moderate** physical activities in the garden or yard?

_____ **hours per day**
_____ **minutes per day**

18. Once again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** activities like carrying light loads, washing windows, scrubbing floors and sweeping **inside your home**?

_____ **days per week**

☐ No moderate activity inside home → ***Skip to PART 4: RECREATION, SPORT AND LEISURE-TIME PHYSICAL ACTIVITY***

19. How much time did you usually spend on one of those days doing **moderate** physical activities inside your home?

_____ **hours per day**
_____ **minutes per day**

PART 4: RECREATION, SPORT, AND LEISURE-TIME PHYSICAL ACTIVITY

This section is about all the physical activities that you did in the **last 7 days** solely for recreation, sport, exercise or leisure. Please do not include any activities you have already mentioned.

20. Not counting any walking you have already mentioned, during the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time **in your leisure time**?

_____ **days per week**

☐ No walking in leisure time → ***Skip to question 22***

21. How much time did you usually spend on one of those days **walking** in your leisure time?

_____ **hours per day**
_____ **minutes per day**

22. Think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **vigorous** physical activities like aerobics, running, fast bicycling, or fast swimming **in your leisure time**?

_____ **days per week**

☐ No vigorous activity in leisure time → ***Skip to question 24***

23. How much time did you usually spend on one of those days doing **vigorous** physical activities in your leisure time?

_____ **hours per day**
_____ **minutes per day**

24. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** physical activities like bicycling at a regular pace, swimming at a regular pace, and doubles tennis **in your leisure time**?

_____ **days per week**

☐ No moderate activity in leisure time → ***Skip to PART 5: TIME SPENT SITTING***

25. How much time did you usually spend on one of those days doing **moderate** physical activities in your leisure time?
_____ **hours per day**
_____ **minutes per day**

PART 5: TIME SPENT SITTING

The last questions are about the time you spend sitting while at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading or sitting or lying down to watch television. Do not include any time spent sitting in a motor vehicle that you have already told me about.

26. During the **last 7 days**, how much time did you usually spend **sitting** on a **weekday**?

_____ **hours per day**
_____ **minutes per day**

27. During the **last 7 days**, how much time did you usually spend **sitting** on a **weekend day**?

_____ **hours per day**
_____ **minutes per day**

This is the end of the questionnaire, thank you for participating.

Physical Activity Readiness
Questionnaire - PAR-Q
(revised 2002)

PAR-Q & YOU

(A Questionnaire for People Aged 15 to 69)

Regular physical activity is fun and healthy, and increasingly more people are starting to become more active every day. Being more active is very safe for most people. However, some people should check with their doctor before they start becoming much more physically active.

If you are planning to become much more physically active than you are now, start by answering the seven questions in the box below. If you are between the ages of 15 and 69, the PAR-Q will tell you if you should check with your doctor before you start. If you are over 69 years of age, and you are not used to being very active, check with your doctor.

Common sense is your best guide when you answer these questions. Please read the questions carefully and answer each one honestly: check YES or NO.

YES	NO		
☐	☐	1.	**Has your doctor ever said that you have a heart condition and that you should only do physical activity recommended by a doctor?**
☐	☐	2.	**Do you feel pain in your chest when you do physical activity?**
☐	☐	3.	**In the past month, have you had chest pain when you were not doing physical activity?**
☐	☐	4.	**Do you lose your balance because of dizziness or do you ever lose consciousness?**
☐	☐	5.	**Do you have a bone or joint problem (for example, back, knee or hip) that could be made worse by a change in your physical activity?**
☐	☐	6.	**Is your doctor currently prescribing drugs (for example, water pills) for your blood pressure or heart condition?**
☐	☐	7.	**Do you know of any other reason why you should not do physical activity?**

If you answered

YES to one or more questions

Talk with your doctor by phone or in person BEFORE you start becoming much more physically active or BEFORE you have a fitness appraisal. Tell your doctor about the PAR-Q and which questions you answered YES.

- You may be able to do any activity you want — as long as you start slowly and build up gradually. Or, you may need to restrict your activities to those which are safe for you. Talk with your doctor about the kinds of activities you wish to participate in and follow his/her advice.
- Find out which community programs are safe and helpful for you.

NO to all questions

If you answered NO honestly to all PAR-Q questions, you can be reasonably sure that you can:

- start becoming much more physically active – begin slowly and build up gradually. This is the safest and easiest way to go.
- take part in a fitness appraisal – this is an excellent way to determine your basic fitness so that you can plan the best way for you to live actively. It is also highly recommended that you have your blood pressure evaluated. If your reading is over 144/94, talk with your doctor before you start becoming much more physically active.

DELAY BECOMING MUCH MORE ACTIVE:

- if you are not feeling well because of a temporary illness such as a cold or a fever – wait until you feel better; or
- if you are or may be pregnant – talk to your doctor before you start becoming more active.

PLEASE NOTE: If your health changes so that you then answer YES to any of the above questions, tell your fitness or health professional. Ask whether you should change your physical activity plan.

Informed Use of the PAR-Q: The Canadian Society for Exercise Physiology, Health Canada, and their agents assume no liability for persons who undertake physical activity, and if in doubt after completing this questionnaire, consult your doctor prior to physical activity.

No changes permitted. You are encouraged to photocopy the PAR-Q but only if you use the entire form.

NOTE: If the PAR-Q is being given to a person before he or she participates in a physical activity program or a fitness appraisal, this section may be used for legal or administrative purposes.

"I have read, understood and completed this questionnaire. Any questions I had were answered to my full satisfaction."

NAME _____

SIGNATURE _____ DATE _____

SIGNATURE OF PARENT or GUARDIAN (for participants under the age of majority) _____ WITNESS _____

Note: This physical activity clearance is valid for a maximum of 12 months from the date it is completed and becomes invalid if your condition changes so that you would answer YES to any of the seven questions.

Supported by: Health Canada Santé Canada

continued on other side...

Age-Related Changes in Muscular Strength, Power, Endurance and Quality in Women

BONE DENSITY RESEARCH LABORATORY
DEPARTMENT OF HEALTH AND EXERCISE SCIENCE
UNIVERSITY OF OKLAHOMA

CALCIUM INTAKE ESTIMATION

NAME:_____ TODAY'S DATE:_____

Complete this form (where indicated) to represent your dietary intake in the past year.

				I EAT THIS FOOD: EVERY WEEK	EVERY DAY
Tally	**Score**	**Food Type**	**serving size**	**servings/week**	**servings/day**
	300	Milk- whole, 2%, skim	1 cup		
	150	Cheese food or spread	1 oz		
	150	Cheese sauce	1/4 cup		
	150	American cheese	1 slice		
	150	Cottage cheese	1 cup		
	250	Ricotta cheese	1 oz		
	150	Blue cheese	½ cup		
	200	Natural cheese (except cream cheese) includes cheddar, Swiss, mozzarella, etc.	1 oz		
	285	Buttermilk	1 cup		
	300	Yogurt, flavored or plain	1 cup		
	450	Fast Food Milkshake	12 oz		
	165	Cocoa from mix	1 packet		
	330	Eggnog	1 cup		
	280	Chocolate milk	1 cup		
	250	Macaroni and cheese, cheese souffle, lasagna, quiche, cannelloni, pizza	1 serving		
	180	Cream soup or chowder with milk	1 cup		
	115	Almonds	1/3 cup		
	180	Broccoli	1 cup		
	85	Beet greens, spinach	½ cup		
	160	Baked beans	1 cup		
	100	Figs	5 dried		
	140	Scalloped potatoes	1 cup		
	150	Soybeans	1 cup		
	150	Tofu	½ cup		
Tally	**Score**	**Food Type**	**serving size**	**servings/week**	**servings/day**

PLEASE TURN OVER

	30	Bread, white or whole grain	1 slice		
	120	Waffle or pancake	1 large		
	50	Muffin, biscuit, cornbread	1 medium		
	40	Rolls, buns	½		
	225	Egg McMuffin	1		
	130	Fast food cheeseburger or hamburger	1		
	110	Enchilada or bean burrito	1		
	125	Creamed fish and meats	1 cup		
	130	Shellfish, cooked	4 oz		
	200	Canned salmon with bones	½ cup		
	200	Sardines, smelts, herring	½ cup		
	100	Fudgesicle	1		
	125	Custard pie	1 slice		
	175	Ice cream or ice milk	1 cup		
	190	Pudding with milk	½ cup		
	200	Frozen yogurt	1 cup		

Please list below any dietary supplements (single and multi-vitamins, calcium, herbal etc.) you take daily/weekly, including the brand name, amount (mg) per dose and total number of doses per day (or per week if not taken daily).

1. _____

2. _____

3. _____

4. _____

5. _____

Bone-Specific Physical Activity Questionnaire (BPAQ)
OU Bone Density Research Laboratory

Participant ID: _____ Date: _____

1. Please list any sports or other physical activities you have participated in regularly. Please tick the boxes to indicate how old you were for each sport/activity and how many years you participated.

Sport/Activity	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30

Sport/Activity	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60

IRB NUMBER: 9838
IRB APPROVAL DATE: 11/12/2018

Sport/Activity	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90

Sport/Activity	91	92	93	94	95	96	97	98	99	100

2. Please list the sports or other physical activities (be as specific as possible) you participated in regularly in the past 12 months and indicate the average frequency (sessions per week)? On the back of this page is a list of activities you may use as a reference.

Activity: _____ Frequency (per week):_____

Activity: _____ Frequency (per week):_____

Activity: _____ Frequency (per week):_____

Activity: _____ Frequency (per week):_____

Activity: _____ Frequency (per week):_____

BONE-SPECIFIC PHYSICAL ACTIVITY QUESTIONNAIRE
Developed by B.K. Weeks and B.R. Beck 2018
Griffith University, QLD, Australia

Activity: _____ Frequency (per week):_____

Bone-Specific Physical Activity Questionnaire (BPAQ)
OU Bone Density Research Laboratory

Sport/Activity	Sport/Activity	Sport/Activity
Aerobics (low impact)	Resistance Training	* Other Low impact
Aerobics (high impact)	Rollerblading	* Other Moderate Impact
Badminton	Rowing	* Other High Impact
Ballet	Rugby	* CrossFit
Baseball	Scuba Diving	
Basketball	Shot Put/Discus	
Cheerleading	Skate Boarding	
Cricket	Skiing/Snowboarding	
Cross-Country	Soccer	
Cycling	Softball	
Dancing	Squash	
Diving	Stairmaster	
Field Hockey	Surfing	
Football	Swimming	
Golf	T-ball	
Gymnastics	Table tennis	
Horse-Riding	Tennis	
Ice Hockey	Track-Sprint	
Ice-Skating	Track-Distance	
Judo	Triathlon	
Jump Rope	Ultimate Frisbee	
Kung Fu	Volleyball	
Lacrosse	Walking/Hiking	
Pickle Ball	Waterskiing	
Power Lifting	Wind Surfing	
Racquet Ball	Yoga/Pilates	

BONE-SPECIFIC PHYSICAL ACTIVITY QUESTIONNAIRE
Developed by B.K. Weeks and B.R. Beck
Griffith University, QLD, Australia

Participant Medical Clearance Form

University of Oklahoma Neuromuscular Laboratory

Dear Doctor,

Your patient, _____, has indicated that she wishes to participate in a research study investigating the age-related changes in muscular strength, power, endurance and quality in women. This study involves 5 required visits: (1) consenting, blood pressure, questionnaires and muscle function testing familiarization; (2) fasted blood draw at the Goddard Health Center on the OU Norman Campus; (3) four scans for DXA (total body, lumbar spine, dual femur and four pQCT scans (1 femur and 3 tibia); (4 and 5) muscle function testing consisting of hand grip dynamometry, vertical jump testing, and Biodex dynamometer testing. The hand grip and vertical jump testing will consist of 3 maximal trials (3 each hand during grip testing, 6 total). Biodex dynamometer testing will consist of three contraction modes (isometric, isotonic, isokinetic). Participants will perform maximal contractions at the elbow, knee, and ankle joints. Participants will perform 6 maximal isometric contractions at each joint and 3 trials of 6 repetitions of isotonic testing with submaximal loads. The isokinetic testing consists of 2 total trials of 30 repetitions at a fast speed (240 degrees per second) and slow speed (60 degrees per second). All muscle function testing will be performed and monitored by certified strength and conditioning specialists and participant will receive verbal encouragement to ensure they are exerting maximal effort. Proper safety precautions will be taken during the entire protocol. Prior to participation, participant is required to obtain medical clearance from her personal physician(s). Specific inclusion and exclusion criteria apply to the participants recruited for this study. Below are the exclusion criteria:

- Women who are actively training for a competitive event (i.e. body building, power lifting, extended length races);
- Women that engage in more than 1 hour of exercise per day or >7 hours per week;
- Women who are or are planning to become pregnant or that are currently breastfeeding;
- Current smokers;
- Women currently smoking, have diabetes, cancer, or uncontrolled hypertension;
- Individuals outside of limits of the DXA table (height over 6'4", weight over 350 lbs);
- Individuals who had a musculoskeletal injury within the previous 12 months;
- Individuals with metal implants or joint replacement at the hip, spine, or leg;
- Restrictions to perform muscle function tests (i.e. myocardial infarction/congestive heart failure/ strokes/back surgery within the past 6 months);
- Has degenerative neuromuscular conditions (i.e. Parkinson's disease);
- Women that are cognitively impaired.

☐ I recommend that the above-named individual be allowed to participate in the study.

☐ I do not recommend that the above-named individual be allowed to participate in the study.

MEDICATIONS/NOTES: _____

Physician Name: _____ Contact Number: _____
(please print)

Physician Signature: _____ Date: _____

This form can be faxed to (405) 325-0594 or emailed to ryanmiller1@ou.edu. Thank you!
This study has been approved by the University of Oklahoma Institutional Review Board.
For questions, please contact Michael G. Bemben, Ph.D. at (405) 325-2717 or mgbemben@ou.edu.

IRB NUMBER: 9838
IRB APPROVAL DATE: 11/12/2018

Age-Related Changes in Muscular Strength, Power, Endurance and Quality in Women

FEMALE PARTICIPANTS NEEDED

To study the influence of aging on muscle function and body composition.

To Participate

- 20 years of age or older
- Recreationally active
- Non-smoker

Included Testing

- 5 visits (8 total hours)
- Body, muscle, and bone composition scans (DXA & pQCT)
- Muscular strength, power, and endurance testing at the elbow, knee, and ankle
- Handgrip and vertical jump test
- 1 blood draw

If you are eligible and interested, please contact:

Ryan Miller at 913-526-2997 or ryanmiller1@ou.edu
Department of Health and Exercise Science
Michael Bemben, PhD, Principal Investigator

Visits will take place on the OU Norman Campus

Appendix H: Sample Data Sheet

Visit 3

Participant ID: _____ **Date: _____**

Height:	
Weight (no shoes):	
Weight (shoes):	

Tester: _____

USG:	
Pregnancy Test:	
Tibia Length:	
Femur Length:	

Tester: _____

Position	**Elbow**	**Knee**	**Ankle**
Chair angle (below seat)	15	45	70
Seat tilt (side of seat)	80	80	60
Dynamometer angle (circle below dyna.)	15	45	65
Dynamometer height		0	
Specific attachments	Elbow att.:	Foot att.:	Ankle att.:
	Hand att.:		Leg att.:
Comments: 3-5 minutes between joints, 1 min between contraction types, 5 min between 240 & 60deg/s, ask about reliability after visit 4.			

Tester: _____

Visit 4

Participant ID: _____ **Date**: _____

Grip Strength Position: _____

Grip Strength	**Trial 1**	**Trial 2**	**Trail 3**
Right (kg)			
Left (kg)			
Comments: 30s rest between trials (R, L, R, L, R, L)			

Tester: _____

Proceed to jump testing

Insert weight (kg) in TENDO unit

Vertical Jump	**Trial 1**	**Trial 2**	**Trial 3**
Power (W)			
Velocity (m/s)			
Height (in)			
Time in air (s)			
Comments: 60s rest between trials; adjust weight in tendo			

Tester: _____

Proceed to Biodex testing

Biodex Position (data retrieved following participant visit)

Position	**Elbow**	**Knee**	**Ankle**
Chair angle (below seat)	15	45	70
Seat tilt (side of seat)	80	80	60
Dynamometer angle (circle below dyna.)	15	45	65
Dynamometer height		0	
Specific attachments	Elbow att.:	Foot att.:	Ankle att.:
	Hand att.:		Leg att.:
Comments: 3-5 minutes between joints, 1 min between contraction types, 5 min between 240 & 60deg/s, ask about reliability after visit.			

Tester: _____

Visit 5

Participant ID: _____ **Date**: _____

Grip Strength Position: _____

Grip Strength	**Trial 1**	**Trial 2**	**Trail 3**
Right (kg)			
Left (kg)			
Comments: 30s rest between trials (R, L, R, L, R, L)			

Tester: _____

Proceed to jump testing

Insert weight (kg) in TENDO unit

Vertical Jump	**Trial 1**	**Trial 2**	**Trial 3**
Power (W)			
Velocity (m/s)			
Height (in)			
Time in air (s)			
Comments: 60s rest between trials; adjust weight in tendo			

Tester: _____

Proceed to Biodex testing

Biodex Position (data retrieved following participant visit)

Position	**Elbow**	**Knee**	**Ankle**
Chair angle (below seat)	15	45	70
Seat tilt (side of seat)	80	80	60
Dynamometer angle (circle below dyna.)	15	45	65
Dynamometer height		0	
Specific attachments	Elbow att.:	Foot att.:	Ankle att.:
	Hand att.:		Leg att.:
Comments: 3-5 minutes between joints, 1 min between contraction types, 5 min between 240 & 60deg/s.			

Tester: _____

Appendix I: ELISA Assay Procedures

Human Myostatin (MSTN) ELISA Kit

Cat No: **MBS779358**

Standard Curve Range: 0.2ng/ml -8ng/ml

Sensitivity: 0.1ng/ml

Expiration date: six months .

Storage: 2-8°C.

For samples: Serum, plasma, cell culture supernatants, body fluid and tissue homogenate

When stored at 2 -8 °C unopened reagents will retain reactivity until expiration date.

Opened reagents must be stored at 2 -8 °C.

Read this manual carefully before using. The ELISA kit is based on the principle of double antibody sandwich technology.

And the ELISA kits only be used for research purposes, not for medical diagnosis.

Reagent preparation: Bring all reagents to room temperature before using.

FOR RESEARCH USE ONLY; NOT FOR THERAPEUTIC OR DIAGNOSTIC APPLICATIONS!
PLEASE READ THROUGH ENTIRE PROCEDURE BEFORE BEGINNING!

Intended Use

For the quantitative determination of Human Myostatin(MSTN) concentrations in serum, plasma, saliva, urine, tissue homogenate, cell culture supernates and other biological fluids.

Test Principle

The kit was used to test the level of Human Myostatin(MSTN), based on the principle of double antibody sandwich technology enzyme linked immunosorbent assay (ELISA).

Add Standard and Sample to the wells that pre-coated with objective antibody, then add HRP-Conjugate reagent to form an immune complex, incubation, by incubation and washing, removal of unbound enzyme, and then add the substrate A and B, then the solution will turn blue and finally change into yellow at the effect of acid. The color depth or light was positively correlated with the concentration of Myostatin (MSTN).

MATERIALS PROVIDED WITH THE KIT

All reagents provided are stored at 2-8°C. Refer to the expiration date on the label.

Reagents components		96 determinations	48 determinations
1.	Microelisa stripplate	12*8strips	12*4strips
2.	Standard A	0ng/ml	0ng/ml
3.	Standard B	0.5ng/ml	0.5ng/ml
4.	Standard C	1ng/ml	1ng/ml
5.	Standard D	2ng/ml	2ng/ml
6.	Standard E	4ng/ml	4ng/ml
7.	Standard F	8ng/ml	8ng/ml
8.	Sample Diluent	6.0ml	3.0ml
9.	HRP-Conjugate reagent	10.0ml	5.0ml
10.	20X Wash solution	25ml	15ml
11.	Chromogen Solution A	6.0ml	3.0ml
12.	Chromogen Solution B	6.0ml	3.0ml
13.	Stop Solution	6.0ml	3.0ml
14.	Closure plate membrane	2	2
15.	User manual	1	1
16.	Sealed bags	1	1

Note: Standard (A→F) concentration was followed by: 0ng/ml ,0.5ng/ml ,1ng/ml , 2ng/ml ,4ng/ml ,8ng/ml.

Materials required but not supplied

1.37 °C incubator

2.Microplate reader capable of measuring absorbance at 450 nm.

3.Precision pipettes to deliver 2 ml to 1 ml volumes.

4.100 ml and 1 liter graduated cylinders.

5. Distilled water,

6. Disposable test tube

7. Absorbent paper

8. Precision pipettes and disposable tip

Precautions

1.Do not substitute reagents from one kit lot to another. Standard, conjugate and microtiter plates are matched for optimal performance. Use only the reagents supplied by manufacturer.

2.It is highly recommended to use the remaining reagents within 1 month before the deadline. For the expiration date, please refer to the label on the kit box. All components are stable before this expiration date.Do not use kit components beyond their expiration date.

3.Remove all kit reagents from refrigerator and allow them to reach room temperature (20-25°C) before use. Do not use water baths to thaw samples or reagents.

4.Use only deionized or distilled water to dilute reagents.

5.Each steps add sample, should use sampler, and often proofread the accuracy to avoid the test error. Use fresh disposable pipette tips for each transfer to avoid contamination.

6.Test should strict accordance with the instructions of the operation, the test results must be determined by the microplate reader.

7.Do not remove microtiter plate from the storage bag until needed. Unused strips should be stored at 2-8°C in their pouch with the desiccant provided.

8.Do not mix acid and sodium hypochlorite solutions.

9.Serum and plasma should be handled as potentially hazardous and capable of transmitting disease. Disposable gloves must be worn during the assay procedure, since no known test method can offer complete assurance that products derived from Rat blood will not transmit infectious agents. Therefore, all blood derivatives should be considered potentially infectious and good laboratory practices should be followed.

10.All samples should be disposed of in a manner that will inactivate viruses.

11.Liquid Waste: Add sodium hypochlorite to a final concentration of 1.0%. The waste should be allowed to stand for a minimum of 30 minutes to inactivate the viruses before disposal.

12.Substrate Solution is easily contaminated. If bluish prior to use, do not use. Substrate B is sensitive to light and avoid prolonged exposure to light.

Specimen Requirements

1.**Serum:** Allow the serum to clot for 10-20 minutes at room temperature. Centrifuge (at 2000-3000 RPM) for 20 minutes. Collect the supernatants carefully. When sediments occurred during storage, centrifugation should be performed again.

2.**Blood plasma**: In accordance with the requirements of sample collection, EDTA or sodium citrate should be used as anti coagulation. Add EDTA or sodium citrate and mix them for 10-20 minutes. Centrifuge (at 2000-3000 RPM) for approximately 20 minutes. Collect the supernatants carefully. When sediments occurred during storage, centrifugation should be performed again.

3.**Urine**: Collect by sterile tube. Centrifuge (at 2000-3000 RPM) for approximately 20 minutes. Collect the supernatants carefully. When sediments occurred during storage, centrifugation should be performed again. When collecting pleuroperitoneal fluid and cerebrospinal fluid, please follow the procedures above-mentioned.

4.**Cell culture supernatant**: Collect by sterile tubes when examining secrete components. Centrifuge (at 2000-3000 RPM) for approximately 20 minutes. Collect the supernatants carefully. When examining the components within the cell, use PBS (PH 7.2-7.4) to dilute cell suspension to the cell concentration of approximately 1 million/ml. Damage cells through repeated freeze-thaw cycles to let out the inside components. Centrifuge (at 2000-3000 RPM) for approximately 20 minutes. Collect the supernatants carefully. When sediments occurred during storage, centrifugation should be performed again.

5.**Tissue sample**: Incise sample and weigh up. Add a certain amount of PBS (PH 7.4). Freeze with liquid nitrogen immediately for later use. Thaw the sample and keep it at 2-8°C. Add a certain amount of PBS (PH 7.4) and then homogenize the sample thoroughly by hand or homogenizer. Centrifuge (at 2000-3000 RPM) for approximately 20 minutes. Collect the supernatants carefully. Aliquot and keep one for examination and freeze the others for later use.

Note: 1.Samples to be used within 5 days may be stored at 2-8°C, otherwise samples must be stored at -20°C (≤1month) or -80°C (≤2 months) to avoid loss of bioactivity and avoid contamination.

2.Sample hemolysis will influence the result, so the samples should be centrifuged adequately and no hemolysis or granule was allowed.

3.When performing the assay, bring samples to room temperature.

Samples containing NaN3 can't be tested as it inhibits the activity of Horse Radish Peroxidase (HRP).

4.After collecting the sample, extraction should be immediately carried out in accordance with related documents. After extraction, experiment should be conducted immediately as well. Otherwise, keep the sample at -20°C. Avoid repeated freeze-thaw cycles.

Washed plate method

1.Hand-washed plate method: get rid of the liquid within the ELISA plate; in the experimental bench paved a few layers of absorbent paper, pat hard the ELISA plate several times downward; the diluted washing solution at least 0.35ml inject into the well, soaking 1-2 minutes. Repeat this process several times as needed.

2. Automatic plate washing: If you have automatic washing machine, Should be skilled use, and then used in the formal experiment process.

Assay procedure

1. Prepare all reagents before starting assay procedure. It is recommended that all Standards and Samples be added in duplicate to the Microelisa Stripplate.

2. Add standard: Set Standard wells, testing sample wells. Add standard 50μl to standard well.

3. Add Sample: ①Add Sample 10μl to testing sample well, then add sample diluent 40μl to testing sample well; Blank well doesn't add anything.

② Add 100μl of HRP-conjugate reagent to each well(Standard wells and testing sample wells), then cover it with seal plate membrane, gently shake and mix for 60 minutes at 37 ° C incubation.

4.Preparation of washing solution: Dilute the washing concentration (20X) with distilled or deionized water for later use.

5.Washing by hand: carefully remove the sealing film, drain the liquid, dried up, each well filled with washing solution, put it aside for 1 min then drain the liquid, so repeat 5 times, pat dry. (Automatic washing: Each wells inject into the wash solution 350μL, soak 1min, wash plate 5 times.)

6. Color developing: firstly add 50μl chromogen solution A to each wells, then add 50μl chromogen solution B to each well as well. Shake gently to mix up. Incubate for 15 minutes at 37°C,away from light for color developing.

7.Stop: Add 50μl Stop Solution to each well to stop the reaction (the blue color changes into yellow immediately at that moment). If the color in the wells is green or the color change does not appear uniform, gently tap the plate to ensure thorough mixing.

8.Assay: Take blank well as zero, measure the absorbance (OD) of each well one by one under 450nm wavelength, which should be carried out within the 15 minutes after having added the stop solution.

9.According to standards' concentrations and the corresponding OD values, to calculate the linear regression equation of the standard curve. Then according to the OD value of samples, calculate the concentration of the corresponding sample.

Also can use related application software.

Summary of operating procedures

Prepare reagents, samples and standards

⇩

Add prepared samples and standards,and HRP, 37°C incubation for 60 minutes

⇩

Wash the plate 5 times, add chromogen solution A, B, 37°C developing color for 15 minutes

⇩

Add the stop solution

⇩

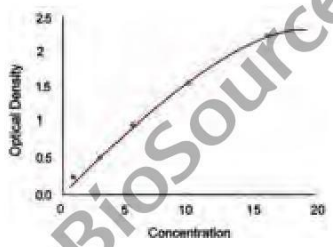
Read the OD value within 15 minutes

⇩

Calculate

Calculation of results

1. This standard curve is used to determine the amount in an unknown sample. The standard curve is generated by plotting the average O.D. (450 nm) obtained for each of the six standard concentrations on the vertical (Y) axis versus the corresponding concentration on the horizontal (X) axis.
2. First, calculate the mean O.D. value for each standard and sample. All O.D. values, are subtracted by the mean value of the zero standard before result interpretation. Construct the standard curve using graph paper or statistical software.
3. To determine the amount in each sample, first locate the O.D. value on the Y-axis and extend a horizontal line to the standard curve. At the point of intersection, draw a vertical line to the X-axis and read the corresponding concentration.
4. Any variation in operator, pipetting and washing technique, incubation time or temperature, and kit age can cause variation in result. Each user should obtain their own standard curve.
5. Intra-assay CV(%) is less than 10% and Inter-assay CV(%) is less than 15%.
6. Standard curve : The following standard curve only for demonstration purposes, each standard curve should be generated with each assay.



1.Any variation in operator, pipetting and washing technique, incubation time or temperature, and kit age can cause variation in result. Each user should obtain their own standard curve.

2.If samples have been diluted, the concentration read from the standard curve must be multiplied by the dilution factor.

3.If specimens generate values higher than the highest standard, dilute the specimens and repeat the assay.

Quantikine® HS ELISA

Human IL-6 Immunoassay

Catalog Number HS600C
SS600C
PHS600C

For the quantitative determination of human Interleukin 6 (IL-6) concentrations in serum, plasma, and urine.

This package insert must be read in its entirety before using this product.
For research use only. Not for use in diagnostic procedures.

TABLE OF CONTENTS

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INTRODUCTION

Interleukin 6 (IL-6) is a pleiotropic, α-helical, 22-28 kDa phosphorylated and variably glycosylated cytokine that plays important roles in the acute phase reaction, inflammation, hematopoiesis, bone metabolism, and cancer progression (1-5). Mature human IL-6 is 183 amino acids (aa) in length and shares 39% aa sequence identity with mouse and rat IL-6 (6). Alternative splicing generates several isoforms with internal deletions, some of which exhibit antagonistic properties (7-10). Cells known to express IL-6 include $CD8^+$ T cells, fibroblasts, synoviocytes, adipocytes, osteoblasts, megakaryocytes, endothelial cells (under the influence of endothelins), sympathetic neurons, cerebral cortex neurons, adrenal medulla chromaffin cells, retinal pigment cells, mast cells, keratinocytes, Langerhans cells, fetal and adult astrocytes, neutrophils, monocytes, eosinophils, colonic epithelial cells, B1 B cells and pancreatic islet beta cells (2, 11-33). IL-6 production is generally correlated with cell activation and is normally kept in control by glucocorticoids, catecholamines, and secondary sex steroids (2). Normal human circulating IL-6 is in the 1 pg/mL range, with slight elevations during the menstrual cycle, modest elevations in certain cancers, and large elevations after surgery (34-38).

IL-6 induces signaling through a cell surface heterodimeric receptor complex composed of a ligand binding subunit (IL-6 R alpha) and a signal transducing subunit (gp130). IL-6 binds to IL-6 Rα, triggering IL-6 Rα association with gp130 and gp130 dimerization (39). gp130 is also a component of the receptors for CLC, CNTF, CT-1, IL-11, IL-27, LIF, and OSM (40). Soluble forms of IL-6 Rα are generated by both alternative splicing and proteolytic cleavage (5). In a mechanism known as trans-signaling, complexes of soluble IL-6 and IL-6 Rα elicit responses from gp130-expressing cells that lack cell surface IL-6 Rα (5). Trans-signaling enables a wider range of cell types to respond to IL-6, as the expression of gp130 is ubiquitous, while that of IL-6 Rα is predominantly restricted to hepatocytes, monocytes, and resting lymphocytes (2, 5). Soluble splice forms of gp130 block trans-signaling from IL-6/IL-6 Rα but not from other cytokines that use gp130 as a co-receptor (5, 41).

IL-6, along with TNF-α and IL-1, drives the acute inflammatory response. IL-6 is almost solely responsible for fever and the acute phase response in the liver, and it is important in the transition from acute inflammation to either acquired immunity or chronic inflammatory disease (1-5). When dysregulated, it contributes to chronic inflammation in conditions such as obesity, insulin resistance, inflammatory bowel disease, arthritis, and sepsis (2, 5). IL-6 modulates bone resorption and is a major effector of inflammatory joint destruction in rheumatoid arthritis through its promotion of Th17 cell development and activity (1). It contributes to atherosclerotic plaque development and destabilization as well as the development of inflammation-associated carcinogenesis (1, 2). IL-6 can also function as an anti-inflammatory molecule, as in skeletal muscle where it is secreted in response to exercise (2). In addition, it enhances hematopoietic stem cell proliferation and the differentiation of memory B cells and plasma cells (42).

The Quantikine® HS Human IL-6 Immunoassay is a 4.0 hour solid-phase ELISA designed to measure human IL-6 in serum, plasma, and urine. It contains *E. coli*-expressed recombinant human IL-6 and has been shown to accurately quantitate the recombinant factor. Results obtained using natural human IL-6 showed linear curves that were parallel to the standard curves obtained using the Quantikine® HS kit standards. These results indicate that this kit can be used to determine relative mass values for natural human IL-6.

PRINCIPLE OF THE ASSAY

This assay employs the quantitative sandwich enzyme immunoassay technique. A monoclonal antibody specific for human IL-6 has been pre-coated onto a microplate. Standards and samples are pipetted into the wells and any IL-6 present is bound by the immobilized antibody. After washing away any unbound substances, a biotinylated polyclonal antibody specific for human IL-6 is added to the wells. Following a wash to remove any unbound antibody-biotin reagent, an enzyme-linked streptavidin is added to the wells. After washing away any unbound streptavidin-enzyme reagent, a substrate solution is added to the wells and color develops in proportion to the amount of IL-6 bound in the initial step. The color development is stopped and the intensity of the color is measured.

LIMITATIONS OF THE PROCEDURE

- FOR RESEARCH USE ONLY. NOT FOR USE IN DIAGNOSTIC PROCEDURES.
- The kit should not be used beyond the expiration date on the kit label.
- Do not mix or substitute reagents with those from other lots or sources.
- Any variation in diluent, operator, pipetting technique, washing technique, incubation time or temperature, and kit age can cause variation in binding.
- Variations in sample collection, processing, and storage may cause sample value differences.
- This assay is designed to eliminate interference by other factors present in biological samples. Until all factors have been tested in the Quantikine® Immunoassay, the possibility of interference cannot be excluded.

TECHNICAL HINTS

- To ensure accurate results, bring liquids to room temperature and mix to homogeneity prior to pipetting or aliquoting.
- When mixing protein solutions, always avoid foaming.
- To ensure accurate results, proper adhesion of plate sealers during incubation steps is necessary.
- When using an automated plate washer, adding a 30 second soak period following the addition of Wash Buffer, and/or rotating the plate 180 degrees between wash steps may improve assay precision.
- Substrate Solution should remain colorless until added to the plate. Keep Substrate Solution protected from light. Substrate Solution should change from colorless to gradations of blue.
- Stop Solution should be added to the plate in the same order as the Substrate Solution. The color developed in the wells will turn from blue to yellow upon addition of the Stop Solution. Wells that are green in color indicate that the Stop Solution has not mixed thoroughly with the Substrate Solution.
- Assay precision for serum and plasma samples can be further improved with additional centrifugation of the samples. A two minute centrifugation at 13,000 RPM is recommended for serum and plasma samples.

MATERIALS PROVIDED & STORAGE CONDITIONS

Store the unopened kit at 2-8 °C. Do not use past kit expiration date.

PART	PART #	CATALOG # HS600C	CATALOG # SS600C	DESCRIPTION	STORAGE OF OPENED/ RECONSTITUTED MATERIAL
Human IL-6 HS Microplate	898933	1 plate	6 plates	96 well polystyrene microplate (12 strips of 8 wells) coated with a monoclonal antibody specific for human IL-6.	Return unused wells to the foil pouch containing the desiccant pack. Reseal along entire edge of zip-seal. May be stored for up to 1 month at 2-8 °C.*
Human IL-6 HS Standard	898935	2 vials	12 vials	Recombinant human IL-6 in a buffered protein base with preservatives; lyophilized. *Refer to vial label for reconstitution volume.*	Use a fresh standard for each assay. Discard after use.
Human IL-6 HS Conjugate	898934	1 vial	6 vials	21 mL/vial of a polyclonal antibody specific for human IL-6 conjugated to biotin with preservatives.	May be stored for up to 1 month at 2-8 °C.*
Assay Diluent RD1W	895117	1 vial	6 vials	11 mL/vial of a buffered protein base with preservatives.	
Calibrator Diluent RD5-4	895435	1 vial	6 vials	21 mL/vial of animal serum with preservatives.	
Wash Buffer Concentrate	895003	2 vials	12 vials	21 mL/vial of a 25-fold concentrated solution of buffered surfactant with preservative. *May turn yellow over time.*	
Stop Solution	895032	1 vial	6 vials	6 mL/vial of 2 N sulfuric acid.	
Color Reagent A	895000	1 vial	6 vials	12 mL/vial of stabilized hydrogen peroxide.	
Color Reagent B	895001	1 vial	6 vials	12 mL/vial of stabilized chromogen (tetramethylbenzidine).	
Streptavidin Polymer-HRP Diluent	898387	1 vial	6 vials	21 mL/vial of a solution with preservatives.	
Streptavidin Polymer-HRP (100X)	898350	1 vial	6 vials	0.3 mL/vial of Streptavidin Polymer-HRP in a buffer with preservative.	
Plate Sealers	N/A	8 strips	48 strips	Adhesive strips.	

* Provided this is within the expiration date of the kit.

HS600C contains sufficient materials to run an ELISA on one 96 well plate.
SS600C (SixPak) contains sufficient materials to run ELISAs on six 96 well plates.

This kit is also available in a PharmPak (R&D Systems®, Catalog # PHS600C). Specific vial counts of each component may vary. Refer to the PharmPak Contents section for specific vial counts.

PHARMPAK CONTENTS

Each PharmPak contains reagents sufficient for the assay of 50 microplates (96 wells/plate). The package inserts supplied are the same as those supplied in the single kit packs and because of this, a few minor differences related to the number of reagents and their container sizes should be noted.

- Sufficient material is supplied to perform at least 50 standard curves; reuse of each vial may be required. The number of vials, and the number of standard curves obtained per vial will vary with the analyte.
- Wash Buffer 25X Concentrate is bulk packed in 125 mL bottles containing 100 mL.
  Note: *Additional wash buffer is available for purchase (R&D Systems®, Catalog # WA126).*

The reagents provided in this PharmPak are detailed below.

PART	PART #	QUANTITY
Human IL-6 HS Microplate	898933	50 plates
Human IL-6 HS Standard	898935	25 vials
Human IL-6 HS Conjugate	898934	50 vials
Assay Diluent RD1W	895117	50 vials
Calibrator Diluent RD5-4	895435	50 vials
Wash Buffer Concentrate	895126	12 bottles
Stop Solution	895032	50 vials
Color Reagent A	895000	50 vials
Color Reagent B	895001	50 vials
Streptavidin Polymer-HRP Diluent	898387	50 vials
Streptavidin Polymer-HRP (100X)	898350	50 vials
Plate Sealers	N/A	200 sheets
Package Inserts	753296	2 booklets

OTHER SUPPLIES REQUIRED

- Microplate reader capable of measuring absorbance at 450 nm, with the correction wavelength set at 540 nm or 570 nm.
- Pipettes and pipette tips.
- Deionized or distilled water.
- Squirt bottle, manifold dispenser, or automated microplate washer.
- 1000 mL graduated cylinder.
- Horizontal orbital microplate shaker (0.12" orbit) capable of maintaining a speed of 500 ± 50 rpm.
- Test tubes for dilution of standards.
- Human IL-6 HS Controls (optional; R&D Systems®, Catalog # QC41).

PRECAUTIONS

IL-6 is detectable in saliva. Take precautionary measures to prevent contamination of kit reagents while running this assay.

The Stop Solution provided with this kit is an acid solution.

Some components in this kit contain a preservative which may cause an allergic skin reaction. Avoid breathing mist.

Color Reagent B may cause skin, eye, and respiratory irritation. Avoid breathing fumes.

Wear protective gloves, clothing, eye, and face protection. Wash hands thoroughly after handling. Refer to the SDS on our website prior to use.

SAMPLE COLLECTION & STORAGE

Serum - Use a serum separator tube (SST) and allow samples to clot for 30 minutes at room temperature before centrifugation for 15 minutes at 1000 x g. Remove serum and assay immediately or aliquot and store samples at ≤ -20 °C. Avoid repeated freeze-thaw cycles.

Plasma - Collect plasma using EDTA or heparin as an anticoagulant. Centrifuge for 15 minutes at 1000 x g within 30 minutes of collection. Assay immediately or aliquot and store samples at ≤ -20 °C. Avoid repeated freeze-thaw cycles.

Note: *Citrate plasma is not validated for use in this assay.*
Grossly hemolyzed samples are not suitable for use in this assay.

Urine - Aseptically collect the first urine of the day (mid-stream), voided directly into a sterile container. Centrifuge to remove particulate matter. Assay immediately or aliquot and store samples at ≤ -20 °C. Avoid repeated freeze-thaw cycles.

REAGENT PREPARATION

Bring all reagents to room temperature before use.

Note: *High concentrations of IL-6 are found in saliva. It is recommended that a face mask and gloves be used to protect kit reagents from contamination.*

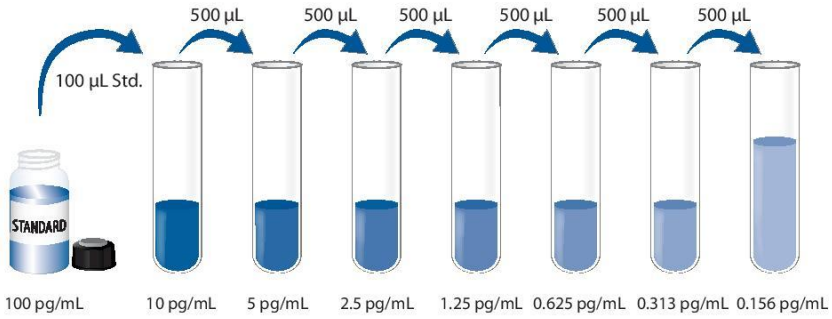
Wash Buffer - If crystals have formed in the concentrate, warm to room temperature and mix gently until the crystals have completely dissolved. Add 40 mL of Wash Buffer Concentrate to 960 mL of deionized or distilled water to prepare 1000 mL of Wash Buffer.

Substrate Solution - Color Reagents A and B should be mixed together in equal volumes within 15 minutes of use. Protect from light. 200 µL of the resultant mixture is required per well.

Streptavidin Polymer-HRP (1X) - Add 0.215 mL of Streptavidin Polymer-HRP (100X) directly to the Streptavidin Polymer-HRP Diluent. Mix well.

Human IL-6 HS Standard - **Refer to the vial label for reconstitution volume.** Reconstitute the Human IL-6 HS Standard with deionized or distilled water. This reconstitution produces a stock solution of 100 pg/mL. Allow the standard to sit for a minimum of 15 minutes with gentle agitation prior to making dilutions.

Pipette 900 µL of Calibrator Diluent RD5-4 into the 10 pg/mL tube. Pipette 500 µL into the remaining tubes. Use the stock solution to produce a dilution series (below). Mix each tube thoroughly before the next transfer. The 10 pg/mL standard serves as the high standard. Calibrator Diluent RD5-4 serves as the zero standard (0 pg/mL).



ASSAY PROCEDURE

Bring all reagents and samples to room temperature before use. It is recommended that all standards, controls, and samples be assayed in duplicate.

Note: *High concentrations of IL-6 are found in saliva. It is recommended that a face mask and gloves be used to protect kit reagents from contamination.*

1. Prepare all reagents and working standards as directed in the previous sections.
2. Remove excess microplate strips from the plate frame, return them to the foil pouch containing the desiccant pack, and reseal.
3. Add 100 µL of Assay Diluent RD1W to each well.
4. Add 100 µL of standard, control, or sample per well. Cover with the adhesive strip provided. Incubate for **2 hours** at room temperature on a horizontal orbital microplate shaker (0.12" orbit) set at 500 ± 50 rpm. A plate layout is provided to record standards and samples assayed.
5. Aspirate each well and wash, repeating the process three times for a total of four washes. Wash by filling each well with Wash Buffer (400 µL) using a squirt bottle, manifold dispenser, or autowasher. Complete removal of liquid at each step is essential to good performance. After the last wash, remove any remaining Wash Buffer by aspirating or decanting. Invert the plate and blot it against clean paper towels.
6. Add 200 µL of Human IL-6 HS Conjugate to each well. Cover with a new adhesive strip. Incubate for **1 hour** at room temperature on the shaker.
7. Repeat the wash as in step 5.
8. Add 200 µL of Streptavidin Polymer-HRP (1X) to each well. Cover with a new adhesive strip. Incubate for 30 minutes at room temperature on the shaker.
9. Repeat the wash as in step 5.
10. Add 200 µL of Substrate Solution to each well. Incubate for 30 minutes at room temperature **on the benchtop. Protect from light.**
11. Add 50 µL of Stop Solution to each well. The color in the wells should change from blue to yellow. If the color in the wells is green or the color change does not appear uniform, gently tap the plate to ensure thorough mixing.
12. Determine the optical density of each well within 30 minutes, using a microplate reader set to 450 nm. If wavelength correction is available, set to 540 nm or 570 nm. If wavelength correction is not available, subtract readings at 540 nm or 570 nm from the readings at 450 nm. This subtraction will correct for optical imperfections in the plate. Readings made directly at 450 nm without correction may be higher and less accurate.

CALCULATION OF RESULTS

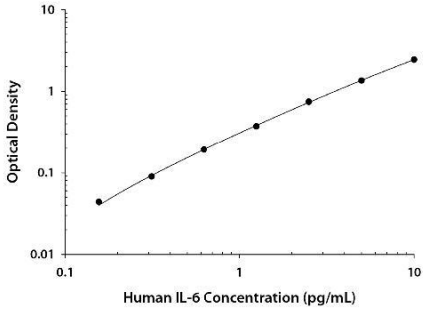
Average the duplicate readings for each standard, control, and sample and subtract the average zero standard optical density (O.D.).

Create a standard curve by reducing the data using computer software capable of generating a four parameter logistic (4-PL) curve-fit. As an alternative, construct a standard curve by plotting the mean absorbance for each standard on the y-axis against the concentration on the x-axis and draw a best fit curve through the points on the graph. The data may be linearized by plotting the log of the human IL-6 concentrations versus the log of the O.D. and the best fit line can be determined by regression analysis. This procedure will produce an adequate but less precise fit of the data.

If samples have been diluted, the concentration read from the standard curve must be multiplied by the dilution factor.

TYPICAL DATA

This standard curve is provided for demonstration only. A standard curve should be generated for each set of samples assayed.



(pg/mL)	O.D.	Average	Corrected
0	0.051 0.067	0.059	—
0.156	0.101 0.105	0.103	0.044
0.313	0.148 0.149	0.149	0.090
0.625	0.246 0.255	0.251	0.192
1.25	0.431 0.433	0.432	0.373
2.5	0.798 0.809	0.804	0.745
5	1.407 1.429	1.418	1.359
10	2.485 2.510	2.498	2.439

PRECISION

Intra-Assay Precision (Precision within an assay)
Three samples of known concentration were tested twenty times on one plate to assess intra-assay precision.

Inter-Assay Precision (Precision between assays)
Three samples of known concentration were tested in separate assays to assess inter-assay precision. Assays were performed by at least three technicians using two lots of components.

	Intra-Assay Precision			Inter-Assay Precision		
Sample	**1**	**2**	**3**	**1**	**2**	**3**
n	20	20	20	20	20	20
Mean (pg/mL)	0.527	2.75	5.38	0.528	2.75	5.58
Standard deviation	0.025	0.100	0.223	0.057	0.135	0.220
CV (%)	4.7	3.6	4.1	10.8	4.9	3.9

RECOVERY

The recovery of human IL-6 spiked to levels throughout the range of the assay in various matrices was evaluated.

Sample Type	Average % Recovery	Range
Serum (n=4)	95	80-119%
EDTA plasma (n=4)	94	83-108%
Heparin plasma (n=4)	94	83-117%
Urine (n=4)	97	90-103%

LINEARITY

To assess the linearity of the assay, samples spiked with high concentrations of human IL-6 were serially diluted with the calibrator diluent to produce samples with values within the dynamic range of the assay.

		Serum (n=4)	EDTA plasma (n=4)	Heparin plasma (n=4)	Urine (n=4)
1:2	Average % of Expected	101	102	99	106
	Range (%)	97-107	95-106	95-104	96-115
1:4	Average % of Expected	104	103	101	108
	Range (%)	102-107	90-108	96-105	97-116
1:8	Average % of Expected	106	108	105	108
	Range (%)	101-113	93-117	101-109	100-117
1:16	Average % of Expected	110	109	112	108
	Range (%)	102-121	89-116	94-125	103-117

SENSITIVITY

Twenty-five assays were evaluated and the minimum detectable dose (MDD) of human IL-6 ranged from 0.007-0.090 pg/mL. The mean MDD was 0.031 pg/mL.

The MDD was determined by adding two standard deviations to the mean O.D. value of twenty zero standard replicates and calculating the corresponding concentration.

CALIBRATION

This immunoassay is calibrated against a highly purified *E. coli*-expressed recombinant human IL-6 produced at R&D Systems®.

The NIBSC/WHO IL-6 (Human rDNA derived) 1st International Standard 89/548, which was intended as a potency standard, was evaluated in this kit. This standard is a CHO cell-derived recombinant human IL-6. Each ampoule contains a nominal 1.0 µg of glycosylated recombinant human IL-6 and was assigned a unitage of 100,000 International Units/ampuole.

The dose response curve of this 1st International Standard parallels the Quantikine® HS standard curve. To convert sample values obtained with the Quantikine® HS Human IL-6 kit to approximate NIBSC 89/548 mass values, use the equation below.

NIBSC (89/548) approximate value (IU/mL) = 0.087 x Quantikine® HS Human IL-6 value (pg/mL)

Note: *Based on data generated in December 2017.*

SAMPLE VALUES

Serum/Plasma/Urine - Samples from apparently healthy volunteers were evaluated for the presence of human IL-6 in this assay. No medical histories were available for the donors used in this study.

Sample Type	Mean (pg/mL)	Range (pg/mL)	Standard Deviation (pg/mL)
Serum (n=30)	1.46	0.495-3.92	0.848
EDTA plasma (n=30)	1.45	0.351-3.48	0.826
Heparin plasma (n=30)	1.51	0.414-3.97	0.876

Sample Type	Mean of Detectable (pg/mL)	% Detectable	Range (pg/mL)
Urine (n=24)	1.04	83	ND-3.48

ND=Non-detectable

SPECIFICITY

This assay recognizes natural and recombinant human IL-6.

The factors listed below were prepared at 50 ng/mL in calibrator diluent and assayed for cross-reactivity. Preparations of the following factors at 50 ng/mL in a mid-range recombinant human IL-6 control were assayed for interference. No significant cross-reactivity or interference was observed.

Recombinant human:

Cardiotrophin-1
CLC
CLC/CNTF Rα
CLF-1
CLF-1/CLC Complex
CNTF
CNTF R
CNTF Rα
Epo
Fas
gp130
G-CSF
G-CSF R
GDNF
GITR
GITR Ligand
IFN-γ
IL-4
IL-6 R
IL-6 Rα/gp130
IL-11
IL-11 Rα
IL-31
Leptin
Leptin R
LIF
LIF Rα
Oncostatin M
Oncostatin M Rβ

Other recombinants:

canine IL-6
mouse IL-6
rat IL-6

Recombinant porcine IL-6 does not interfere but does cross-react approximately 0.022% in this assay.

Recombinant human IL-6/IL-6 Rα Chimera does not interfere but does cross-react approximately 24% in this assay.

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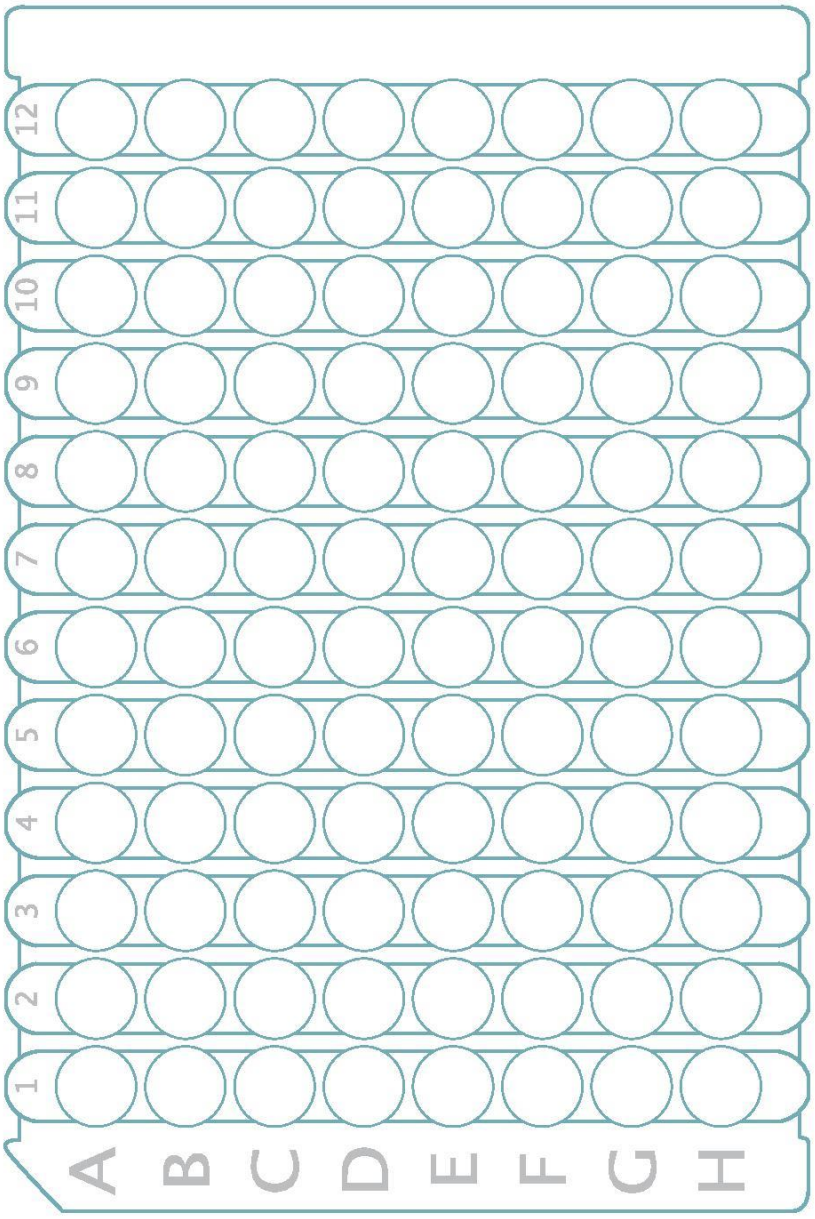
PLATE LAYOUT

Use this plate layout to record standards and samples assayed.



NOTES

Appendix J: Data

[redacted]	Group	WT	HT	BMI	IL6	MYO	EH	Diagnoses	hoursworked	IPAQ	Day_wo	REPRE	AERPE	Meds	Legs_RegionFat	TOT_RegionFat
	1	68.0	177.0	21.71	6.100	0.340	3	2	2	2576.92	7	7	8	1	41.3	35.5
	8	55.4	167.0	19.86	1.607	0.410	7	1	0	2095.00	3	4	8	1	28.3	22.4
	4	54.9	157.5	22.13	0.410	0.440	2	2	3	2570.42	7	8	5	3	39.0	31.9
	1	66.0	168.5	23.25	3.088	0.450	3	0	1	2393.72	3	4	5	5	38.7	41.9
	8	60.4	162.0	23.01	0.696	0.480	6	3	1	2878.99	4	6	5	3	37.0	30.4
	4	78.2	172.5	26.28	0.695	0.500	3	5	0	2149.10	7	4	7	3	33.0	27.6
	8	67.1	165.0	24.65	0.853	0.510	7	0	1	2234.49	4	4	8	6	37.0	35.9
	2	55.2	164.0	20.52	1.859	0.520	1	3	0	2884.30	4	4	9	4	35.8	33.2
	6	54.2	160.5	21.04	0.818	0.520	1	0	3	1878.95	3	4	9	7	25.6	21.8
	7	66.5	165.0	24.43	0.483	0.530	4	0	1	2310.23	6	4	6	0	38.3	34.0
	7	70.8	163.5	26.48	0.636	0.530	4	4	0	2758.17	7	6	7	4	25.6	28.2
	3	61.9	162.0	23.59	0.543	0.540	2	3	1	1862.11	3	4	6	2	38.3	31.5
	2	64.8	166.0	23.52	0.735	0.550	1	0	3	2587.88	3	5	3	0	38.3	33.2
	7	51.9	164.0	19.30	1.326	0.560	4	2	1	1959.22	5	6	6	6	31.4	25.5
	3	75.4	156.0	30.98	0.974	0.570	1	3	2	2155.30	6	5	7	0	44.9	43.0
	4	69.3	162.5	26.24	1.328	0.580	3	5	0	2626.52	3	7	3	6	30.3	22.6
	3	63.3	155.0	26.35	1.538	0.600	3	2	3	2055.18	7	7	7	5	37.0	31.4
	4	71.3	162.5	27.00	0.703	0.600	1	4	3	2404.00	3	5	9	1	36.5	35.7
	1	52.7	158.0	21.11	1.573	0.610	3	0	2	2309.01	4	8	3	1	33.2	26.3
	1	56.1	157.0	22.76	5.440	0.610	2	1	0	2883.52	7	8	8	0	33.0	34.6
	4	58.4	179.0	18.23	1.160	0.610	2	0	1	1814.57	3	4	8	7	26.2	21.6
	4	79.0	164.5	29.19	0.967	0.610	1	3	1	2316.65	4	4	5	5	35.9	37.2
	5	75.6	171.5	25.70	1.776	0.610	2	4	0	2305.79	3	5	6	7	44.0	40.8
	3	95.4	155.5	39.45	1.221	0.620	3	1	2	2411.01	3	6	4	3	45.0	42.0
	10	71.3	165.6	26.00	2.451	0.620	7	0	2	1849.34	5	5	4	3	47.1	46.4
	3	71.2	173.5	23.65	0.492	0.640	1	3	3	2515.41	6	8	4	2	31.2	26.7
	2	68.0	166.9	22.20	1.270	0.650	2	2	0	2118.00	5	6	7	3	36.7	25.6
	2	69.4	176.0	22.40	5.430	0.660	3	0	1	2276.39	5	7	3	2	21.8	18.1
	2	76.4	167.5	27.23	0.627	0.660	1	2	3	2642.54	5	7	7	1	39.5	38.0
	6	61.4	162.5	23.25	1.074	0.660	2	3	1	1742.82	6	5	7	3	29.1	27.7
	9	50.5	153.5	21.43	1.634	0.660	6	4	1	2418.49	3	8	9	7	26.3	35.1
	4	59.5	169.0	20.83	1.018	0.670	3	0	1	2953.37	3	8	5	5	31.7	24.2
	10	73.2	172.5	24.60	1.359	0.670	7	4	1	2544.34	7	4	6	3	42.2	39.7
	3	66.6	167.0	23.88	0.681	0.680	3	0	3	2419.53	7	6	7	4	37.4	33.0
	2	78.1	172.0	26.40	0.564	0.690	1	1	3	2612.27	6	4	6	3	35.7	33.4
	3	86.7	174.0	28.64	0.613	0.690	3	1	3	1757.64	3	5	8	0	39.3	37.8
	5	71.8	165.0	26.37	0.500	0.690	2	3	1	2576.49	7	8	7	2	38.2	37.5
	10	69.4	168.5	24.44	0.883	0.690	7	3	1	2891.34	3	4	5	0	31.0	29.6
	1	55.2	158.0	22.11	1.253	0.700	2	4	3	2783.55	7	7	5	2	30.1	27.9
	6	74.4	182.0	22.46	1.884	0.720	3	3	3	2467.08	5	7	7	7	31.0	26.7
	2	73.3	171.0	25.07	0.570	0.730	2	0	1	2339.36	3	8	6	2	32.1	31.6
	9	83.6	162.5	31.66	1.914	0.730	7	3	0	2768.91	7	6	6	6	41.9	42.0
	1	64.0	167.5	22.81	1.070	0.740	1	2	2	2584.88	6	8	9	0	28.0	26.4
	1	58.3	159.5	22.92	1.420	0.740	3	1	2	2073.84	7	6	6	6	37.7	33.8
	2	84.3	162.5	31.92	0.608	0.740	2	2	1	1793.32	6	7	8	1	39.6	37.6
	11	66.2	177.0	21.13	1.913	0.740	7	3	0	1913.06	3	8	4	7	33.2	33.8
	1	67.0	153.5	28.44		0.750	1	0	1	2140.35	6	4	7	2	44.3	41.8
	1	68.0	169.5	23.67	2.117	0.750	1	2	1	2483.19	4	8	3	0	25.7	24.4
	6	48.9	158.0	19.59	2.228	0.750	3	3	0	2451.14	4	6	7	7	32.3	29.3
	2	53.9	166.0	19.56	2.106	0.760	3	2	2	2524.57	6	4	6	1	33.1	28.4
	6	53.2	153.5	22.58	1.798	0.760	4	1	0	2873.70	6	7	3	3	40.7	37.3
	4	63.0	159.0	24.92	1.001	0.770	3	4	3	1995.64	4	4	6	2	32.8	35.4
	6	103.4	167.5	36.85	0.727	0.770	4	2	3	2176.50	6	4	6	3	53.3	50.0
	7	53.1	160.5	20.61	4.451	0.770	4	2	1	2775.07	5	6	8	7	26.2	22.1
	6	54.0	160.5	20.96	2.241	0.770	1	1	2	2088.52	3	5	3	7	32.6	25.3
	9	67.6	154.0	28.50	2.798	0.770	6	1	2	2005.44	7	5	9	3	37.0	39.4
	11	59.2	161.0	22.84	7.642	0.770	6	4	0	2381.25	5	4	5	2	30.9	26.7
	4	64.3	166.5	23.19	0.619	0.780	3	4	3	2957.64	4	8	6	4	38.7	35.7
	3	60.1	168.0	21.29	1.436	0.790	2	3	0	2024.40	5	5	8	4	37.6	33.0
	5	66.2	158.5	26.35	1.350	0.800	1	3	3	2133.32	3	6	8	5	37.2	35.0
	8	73.2	160.5	28.42	0.610	0.800	7	2	1	2021.21	6	3	7	5	50.9	46.0
	7	57.7	156.5	23.56	1.406	0.800	4	3	1	1956.52	4	6	4	1	37.8	39.3
	1	74.2	174.0	24.51	2.063	0.810	1	1	1	2752.07	5	5	4	2	42.1	37.8

[redacted]	3	57.6	159.0	22.78	1.212	0.810	1	1	1	2881.59	6	5	8	4	32.3	27.9
	4	54.9	166.0	19.92	0.993	0.820	2	1	2	1797.89	4	5	6	4	29.1	21.3
	9	60.1	173.0	20.08	3.597	0.830	6	4	2	1722.84	4	5	6	0	33.5	28.3
	7	52.0	166.5	18.76	0.305	0.840	4	3	1	2899.77	4	5	4	2	27.8	22.0
	2	67.2	165.0	26.20	1.070	0.850	1	2	0	2518.00	5	6	7	3	30.7	35.6
	5	68.0	156.0	26.20	0.970	0.850	2	4	2	2227.00	5	5	8	5	36.6	33.7
	2	62.4	162.5	23.63	1.500	0.850	3	3	1	1757.79	5	6	9	2	32.8	30.8
	8	68.6	170.5	23.60	0.719	0.850	7	1	2	2561.71	3	8	6	2	42.1	39.3
	8	73.8	175.0	24.10	0.679	0.890	7	1	0	2676.78	6	8	9	0	33.0	25.3
	8	68.3	166.0	25.30	1.680	0.899	7	3	0	2628.00	5	5	7	3	41.7	36.5
	8	70.8	168.0	25.20	1.483	0.900	4	3	3	2228.00	5	4	7	4	40.7	36.0
	7	50.8	167.5	18.11	0.656	0.900	4	1	2	1917.35	5	4	8	4	28.5	23.5
	1	57.7	159.5	22.68	0.891	0.910	3	0	0	2280.92	5	6	3	2	33.8	29.3
	8	65.0	165.0	24.80	1.280	0.911	7	3	1	1828.00	5	3	7	4	39.7	35.0
	2	69.5	173.0	23.22	0.444	0.930	2	3	3	2248.26	7	5	9	6	36.5	31.3
	3	76.1	167.7	27.06	1.321	0.930	3	3	1	2984.99	4	4	6	5	37.8	35.8
	5	71.3	160.5	27.68	0.518	0.930	1	2	3	2893.86	3	7	4	1	39.8	35.6
	6	70.9	168.5	24.97	1.685	0.940	3	3	0	2871.36	7	5	6	0	43.9	38.1
	6	79.5	158.5	31.65	0.482	0.940	2	3	2	1798.66	4	4	8	0	43.6	43.2
	8	74.4	164.0	27.66	2.234	0.940	7	1	1	1773.85	3	8	4	8	41.6	39.3
	4	72.4	167.5	25.81	1.860	0.950	2	3	3	2960.68	3	8	8	1	33.7	28.2
	7	62.1	176.5	19.93	6.513	0.960	4	1	2	2104.22	3	7	5	6	32.6	28.1
	5	71.8	167.5	25.59	0.850	0.970	3	2	1	1889.29	4	4	3	0	36.8	36.5
	6	73.4	168.5	25.85	0.942	0.970	4	4	1	2054.52	4	7	5	6	42.5	37.8
	9	67.5	173.5	22.42	0.752	0.970	7	1	2	2683.36	5	4	9	0	36.7	30.3
	1	95.4	167.0	34.21	1.816	0.990	1	0	2	2039.40	4	7	5	6	31.0	37.6
	7	80.6	170.0	27.89	7.692	1.000	4	2	2	2622.64	5	4	7	1	41.8	40.9
	5	88.6	167.5	31.58	1.903	1.010	1	3	3	2622.85	7	8	8	2	47.9	46.3
	5	70.5	177.5	22.38	0.572	1.010	3	0	1	1927.95	5	8	3	3	38.9	34.3
	10	67.5	168.0	23.92	0.496	1.020	7	2	0	2058.22	4	5	6	5	41.1	43.2
	5	69.8	173.5	23.19	2.389	1.040	2	4	1	2469.25	3	8	4	3	23.5	19.3
	11	74.5	168.0	26.40	0.393	1.040	7	2	2	2032.44	3	6	7	4	31.5	35.4
	5	70.0	165.0	26.10	1.090	1.050	2	4	2	2267.00	5	4	7	4	40.6	37.7
	5	65.5	158.0	26.24	0.636	1.050	1	0	0	1814.25	7	8	5	3	38.3	32.5
	10	63.9	168.0	22.64	3.051	1.050	7	0	2	2052.25	5	5	7	3	41.3	38.9
	6	66.8	166.5	24.10	1.496	1.060	4	1	1	2841.74	3	7	6	7	33.8	32.4
	6	74.6	164.0	27.74	0.732	1.060	1	3	2	2488.83	5	6	4	5	40.9	37.9
	7	64.3	172.0	21.73	2.326	1.060	4	2	0	2360.71	3	5	4	3	35.1	29.5
	9	60.4	168.0	21.40	1.512	1.070	7	1	1	2117.25	3	4	8	5	27.0	26.6
	4	54.6	155.0	22.73	1.342	1.090	3	2	2	1738.93	7	4	9	5	30.4	30.4
	7	60.3	159.0	23.85	3.203	1.090	4	5	0	2774.31	3	7	6	5	33.3	31.1
	9	52.1	157.0	21.14	5.330	1.090	7	0	2	2650.28	3	6	7	1	24.9	22.2
	3	74.4	169.5	25.90	2.024	1.100	1	0	1	2358.31	3	8	3	5	32.2	34.3
	10	64.9	163.5	24.28	1.089	1.100	6	4	2	2960.49	6	5	8	0	41.9	38.8
	11	70.9	165.0	26.04	2.128	1.100	7	3	1	2698.46	5	4	9	10	48.5	46.6
	4	97.7	167.5	34.82	2.564	1.110	1	5	3	2933.12	4	6	8	6	40.9	44.8
	10	65.2	171.5	22.17	2.650	1.110	6	3	1	2224.08	4	6	3	7	28.5	30.1
	8	83.7	153.5	35.52	1.805	1.130	7	2	3	1798.99	7	5	6	0	56.8	52.1
	10	72.9	174.0	24.08	0.504	1.130	6	2	1	1828.89	6	8	9	4	40.8	44.3
	11	70.7	159.0	27.97	1.850	1.160	7	4	0	2788.78	5	7	6	5	44.1	40.7
	8	59.8	165.6	21.81	4.839	1.190	7	0	3	2421.42	6	6	6	5	43.0	37.0
	2	51.1	149.0	23.02	1.157	1.200	3	0	2	1837.08	6	8	9	6	26.2	21.8
	5	74.8	181.5	22.71	0.536	1.220	3	4	0	1752.46	7	4	5	4	35.3	34.0
	5	75.7	160.5	29.39	0.306	1.220	1	0	2	2340.67	6	8	4	7	44.3	41.3
	12	50.9	162.0	19.39	0.709	1.220	6	3	1	2874.22	5	8	6	7	29.8	24.6
	1	75.6	154.4	31.71	1.446	1.230	2	3	1	2767.63	4	7	7	6	42.2	44.4
	8	65.4	173.5	21.73	1.415	1.230	7	3	2	1985.54	5	8	8	0	37.9	33.6
	9	69.0	167.0	24.74	1.037	1.230	7	5	3	1749.26	5	4	5	0	38.3	32.4
	10	93.3	169.5	32.47	1.533	1.230	7	0	1	2366.75	5	4	8	1	49.2	45.3
	10	64.6	160.5	25.08	2.072	1.270	7	1	0	2024.76	3	8	3	6	40.9	36.7
	11	72.2	159.5	28.38	2.293	1.270	7	1	3	2276.95	4	7	7	3	49.0	45.8
	10	68.9	164.0	25.62	3.048	1.280	7	3	3	2684.06	3	6	7	4	46.0	44.0
	12	55.9	151.0	24.52	2.431	1.310	7	4	1	1915.26	5	8	6	6	33.9	32.6
	7	74.9	152.0	32.42	2.310	1.320	4	4	0	2953.02	5	5	6	7	43.8	42.2

11	57.2	154.5	23.96	1.475	1.390	7	1	0	2305.85	6	7	5	1	38.8	39.6
13	67.5	168.5	23.77	1.450	1.400	7	2	0	2228.51	7	4	6	4	39.7	34.3
13	63.4	162.7	24.90	1.990	1.420	7	0	3	2213.00	6	5	7	2	40.8	45.6
13	53.2	154.0	22.43	2.878	1.430	7	3	1	2642.34	4	4	9	9	32.6	40.6
12	68.6	160.0	24.70	1.970	1.470	7	3	3	2005.00	6	8	6	6	37.1	34.3
12	90.4	165.0	33.20	3.750	1.470	7	0	1	2740.46	7	5	6	2	50.8	49.3
8	69.9	166.0	25.37	0.862	1.480	6	5	0	2066.41	4	3	4	1	40.8	40.9
1	51.7	167.5	18.43	4.560	1.500	3	0	2	1882.84	7	6	4	4	26.4	23.3
13	66.8	156.5	27.27	1.869	1.500	7	3	0	2593.10	6	8	5	3	45.7	41.7
10	67.0	160.0	26.17	2.239	1.530	7	3	1	2600.99	4	7	9	0	36.4	34.6
9	50.0	158.5	19.90	0.749	1.560	7	4	0	2733.34	4	4	8	7	27.8	33.7
13	59.4	150.7	25.30	1.990	1.630	7	2	3	2413.00	6	5	7	4	42.9	39.5
9	51.3	152.0	22.20	0.840	1.640	6	2	2	2444.31	5	6	6	5	38.6	35.0
11	51.8	168.0	18.35	1.465	1.650	7	3	1	1807.72	7	8	6	5	26.4	23.3
11	74.7	162.5	28.29	1.608	1.650	7	3	1	2521.02	7	8	6	4	45.9	41.5
9	53.8	164.0	20.00	0.742	1.660	7	2	1	2117.11	7	6	4	2	34.2	31.1
12	64.6	164.0	25.30	2.070	1.680	7	3	3	2205.00	6	8	6	6	40.9	36.3
11	66.2	155.5	27.38	1.187	1.780	7	2	1	2277.96	6	6	8	1	39.1	39.4
13	66.5	156.0	27.33	0.822	1.820	7	0	1	2342.36	5	4	9	2	46.5	42.1
13	61.4	155.7	25.60	2.540	1.820	7	4	3	2613.00	6	5	7	6	44.8	35.6
1	65.2	175.0	21.29	0.527	1.850	2	2	1	2858.10	4	6	4	5	33.1	28.2
7	76.2	170.0	26.37	0.645	1.870	4	1	3	1909.98	5	5	5	0	36.4	34.4
12	66.6	162.0	25.70	2.170	1.870	7	3	0	2405.00	6	7	6	5	41.1	38.3
13	53.0	143.5	25.74	3.733	1.960	7	2	1	2258.87	7	5	3	2	49.9	42.4
12	70.1	166.5	25.29	2.666	2.030	7	4	1	1739.14	7	5	8	2	39.0	35.7
12	65.9	165.5	24.06	0.801	2.320	7	4	1	1759.79	4	7	4	6	45.9	39.5

ARMS_BFLBM_kg	arms_fat_kg	TB_BFLBM_KG	LEGS_BFLBM_kg	APSMkg	Arms_RegionFat	legs_fat_kg	tot_fat_kg	SMI	FFMI	EE60degTTPT
4.04	2.70	38.44	13.27	17.31	36.20	10.69	24.08	5.52	12.27	0.645
3.68	1.06	38.66	12.00	15.68	20.10	5.43	12.40	5.62	13.86	0.859
3.16	2.25	33.04	10.18	13.33	37.90	7.45	17.57	5.37	13.32	0.788
3.51	2.49	33.99	11.85	15.36	38.20	8.42	27.69	5.41	11.97	0.664
3.52	1.92	37.62	11.49	15.01	32.00	7.64	18.34	5.72	14.33	0.802
5.89	2.26	51.32	18.52	24.41	25.70	10.05	21.49	8.20	17.25	0.630
4.16	2.63	38.02	12.78	16.94	35.50	8.54	24.08	6.22	13.97	1.162
3.46	1.77	31.95	10.26	13.72	30.40	6.57	18.32	5.10	11.88	0.632
4.01	1.30	37.76	11.38	15.38	22.20	4.43	11.79	5.97	14.66	0.846
3.83	2.34	38.92	11.78	15.61	34.70	8.33	22.64	5.73	14.29	0.933
5.74	2.51	46.03	15.72	21.46	28.00	6.01	19.99	8.03	17.22	0.784
3.45	1.76	37.78	12.33	15.77	30.40	8.65	19.50	6.01	14.39	0.795
3.19	2.23	37.94	13.20	16.39	37.30	9.19	21.44	5.95	13.77	0.693
3.59	1.30	34.24	10.45	14.04	23.70	5.50	13.25	5.22	12.73	0.681
4.55	3.24	38.61	14.18	18.73	38.90	12.82	32.41	7.70	15.87	0.868
5.97	1.74	48.65	13.94	19.91	20.60	6.77	15.66	7.54	18.42	0.837
4.37	2.11	39.25	13.44	17.81	29.90	8.79	19.82	7.41	16.34	0.701
4.33	2.92	39.97	12.12	16.44	36.70	8.05	25.45	6.23	15.14	0.682
3.34	1.47	34.83	11.20	14.54	27.60	6.31	13.90	5.82	13.95	0.620
3.24	2.02	32.08	11.20	14.43	34.90	6.28	19.37	5.86	13.01	0.662
4.12	1.28	40.80	13.37	17.48	21.10	5.45	12.64	5.46	12.73	0.683
5.04	3.71	44.75	15.62	20.66	39.50	9.69	29.44	7.63	16.54	0.780
3.88	3.42	39.83	13.66	17.54	43.00	12.12	30.90	5.96	13.54	0.805
5.67	4.72	50.24	15.50	21.17	43.30	13.86	39.75	8.75	18.00	0.600
3.40	3.78	33.89	11.95	15.36	49.00	12.05	33.07	5.60	12.36	0.904
5.20	1.72	46.85	17.02	22.21	22.80	8.59	19.09	7.38	15.56	0.667
4.12	1.20	42.10	13.40	18.02	32.30	7.09	15.80	6.33	14.75	0.612
5.49	1.07	51.92	17.04	22.53	15.00	5.29	12.61	7.27	16.76	0.577
4.54	3.27	41.69	14.05	18.59	38.30	10.40	29.02	6.63	14.86	0.659
4.13	1.90	40.48	12.58	16.71	29.30	5.76	17.09	6.33	15.33	0.793
3.32	1.96	29.81	8.89	12.21	34.80	3.50	17.76	5.18	12.65	0.837
4.51	1.44	39.60	13.12	17.64	21.40	7.01	14.46	6.17	13.86	0.605
3.66	2.59	39.76	14.25	17.91	38.10	11.69	29.09	6.02	13.36	0.838
4.65	2.57	39.71	13.98	18.63	32.90	9.41	22.03	6.68	14.24	0.722
4.62	2.67	46.27	15.80	20.42	33.40	9.90	26.10	6.90	15.64	0.627
4.82	3.19	47.46	18.40	23.22	36.40	13.42	32.79	7.67	15.68	0.809
4.23	2.77	40.21	12.68	16.91	36.60	8.83	26.87	6.21	14.77	0.726
4.68	2.57	44.58	13.69	18.37	32.70	6.90	20.56	6.47	15.70	0.801
3.41	1.53	34.92	11.93	15.34	28.20	5.78	15.29	6.14	13.99	0.549
5.99	2.35	49.01	17.25	23.25	25.90	8.66	19.96	7.02	14.80	0.812
4.74	2.58	44.21	14.49	19.22	32.10	7.85	23.13	6.57	15.12	0.703
4.39	3.54	43.11	14.05	18.43	41.90	11.29	34.84	6.98	16.32	0.953
4.57	1.94	41.88	14.99	19.56	26.90	6.55	16.92	6.97	14.93	0.641
3.29	2.19	34.26	11.31	14.60	36.30	7.69	19.69	5.74	13.47	0.649
5.05	3.79	47.46	16.15	21.20	39.80	11.83	31.69	8.03	17.97	0.694
3.95	2.56	37.96	12.62	16.57	35.30	7.31	22.38	5.29	12.12	0.917
3.63	3.18	34.02	11.75	15.38	43.80	10.39	27.19	6.53	14.44	0.492
5.14	1.81	46.77	15.68	20.82	24.00	6.01	16.63	7.25	16.28	0.549
3.03	1.53	30.94	9.89	12.91	30.40	5.35	14.23	5.17	12.39	0.716
3.10	1.30	34.06	11.99	15.09	26.50	6.69	15.36	5.48	12.36	0.642
2.81	1.99	29.90	10.32	13.13	38.10	7.81	19.76	5.57	12.69	0.800
3.95	2.65	35.96	12.03	15.98	36.90	6.72	22.31	6.32	14.23	0.624
4.41	4.23	46.69	16.52	20.93	45.90	20.95	51.72	7.46	16.64	0.728
4.55	1.36	37.08	12.42	16.98	20.80	5.01	11.75	6.59	14.39	0.983
3.49	1.31	36.18	11.62	15.11	24.70	6.32	13.71	5.86	14.04	0.758
3.89	3.17	36.62	12.97	16.86	41.80	8.47	26.66	7.11	15.44	0.871
4.15	1.77	39.96	12.91	17.06	27.80	6.37	15.82	6.58	15.42	0.903
3.77	2.32	36.38	11.86	15.63	34.60	8.53	22.77	5.64	13.12	0.631
3.22	2.03	35.63	12.51	15.73	34.80	8.60	19.87	5.57	12.63	0.837
4.16	2.23	38.56	13.41	17.56	32.00	8.84	23.14	6.99	15.35	0.624
3.33	4.04	34.89	10.87	14.20	51.10	12.87	33.60	5.51	13.55	0.718
3.44	2.84	31.73	9.22	12.66	42.60	6.26	22.61	5.17	12.96	0.942
4.22	2.72	39.77	12.66	16.88	35.90	10.53	27.29	5.58	13.14	0.761

4.04	1.73	36.63	11.86	15.89	27.10	6.55	16.05	6.29	14.49	0.742
4.05	1.38	38.63	13.01	17.05	22.80	6.05	11.73	6.19	14.02	0.781
4.19	1.62	38.16	11.51	15.70	24.90	6.76	17.06	5.25	12.75	0.830
3.65	1.14	36.20	11.80	15.45	21.30	5.17	11.52	5.57	13.06	0.817
4.21	3.20	41.20	13.80	18.10	31.10	9.09	25.80	6.73	14.95	0.550
4.51	2.61	39.60	13.98	18.24	33.40	9.92	22.20	6.60	14.86	0.619
3.72	2.12	38.04	12.06	15.78	32.90	6.72	19.11	5.98	14.40	0.714
3.54	2.89	36.79	11.16	14.70	41.00	9.36	26.90	5.06	12.65	0.863
5.90	1.89	49.32	16.49	22.38	22.10	9.23	18.72	7.31	16.11	1.070
3.96	2.83	38.50	12.75	16.64	36.46	10.30	27.40	6.19	14.13	0.929
3.89	2.63	38.40	12.50	16.44	36.20	10.11	25.40	5.99	13.93	0.922
3.38	1.69	34.45	11.30	14.68	29.80	5.19	11.97	5.23	12.28	0.937
4.23	1.96	36.59	11.98	16.21	29.40	6.79	16.74	6.37	14.38	0.645
3.91	2.43	37.80	12.25	16.24	36.06	9.80	23.40	5.79	13.73	0.885
4.33	2.35	42.66	14.47	18.80	32.20	9.43	21.74	6.28	14.25	0.760
3.85	2.79	43.59	15.57	19.42	38.40	10.63	27.11	6.90	15.50	0.756
3.61	2.36	41.43	14.27	17.88	36.70	10.46	25.36	6.94	16.08	0.632
4.46	3.14	38.85	12.78	17.25	37.80	11.31	26.88	6.07	13.68	0.788
4.10	3.23	40.12	13.62	17.72	40.90	11.74	34.35	7.05	15.97	0.664
4.35	2.75	40.82	13.76	18.11	36.10	10.89	29.19	6.73	15.18	0.957
4.63	2.23	46.56	16.44	21.07	29.60	9.44	20.47	7.51	16.60	0.645
3.54	1.53	40.05	12.37	15.90	26.80	6.91	17.54	5.11	12.86	0.899
4.42	2.77	40.95	13.66	18.07	35.60	8.91	26.20	6.44	14.59	0.675
4.25	3.04	40.12	14.01	18.26	38.20	11.72	27.71	6.43	14.13	0.686
3.66	2.11	42.77	14.65	18.31	33.90	9.36	20.32	6.08	14.21	0.890
7.17	4.15	54.13	17.69	24.86	34.50	8.71	35.91	8.91	16.00	0.690
3.97	2.62	42.29	14.88	18.85	36.50	12.02	32.97	6.52	14.63	0.892
4.75	4.22	42.40	14.07	18.82	44.10	14.57	41.00	6.71	15.11	0.700
4.21	2.43	41.69	15.18	19.39	33.70	10.81	24.14	6.16	13.23	0.594
3.99	3.13	34.07	9.96	13.95	40.60	7.98	28.94	4.94	12.07	0.718
6.28	1.34	49.89	16.59	22.87	15.80	5.81	13.42	7.60	16.57	0.640
4.21	2.52	43.85	13.74	17.95	35.00	7.01	26.28	6.36	15.54	0.762
4.49	3.01	42.60	14.01	18.64	37.40	10.10	30.20	6.70	14.89	0.780
4.48	2.27	39.28	12.40	16.88	30.80	8.76	21.30	6.76	15.74	0.740
3.79	2.36	34.73	11.41	15.20	35.30	9.16	24.73	5.39	12.30	0.881
4.96	2.21	40.36	12.58	17.53	28.50	7.26	21.70	6.32	14.56	0.673
4.03	2.21	41.27	13.75	17.77	32.40	10.80	28.28	6.61	15.34	0.818
3.90	2.28	40.22	12.20	16.10	33.20	7.59	18.94	5.44	13.59	0.900
4.10	1.87	40.30	12.78	16.88	28.70	5.28	16.11	5.98	14.28	0.809
3.36	1.64	33.83	11.01	14.38	30.00	5.42	16.53	5.98	14.08	0.745
3.46	1.85	37.03	11.71	15.17	31.40	6.64	18.82	6.00	14.65	0.938
3.51	1.17	36.62	12.24	15.76	22.70	4.55	11.58	6.39	14.85	0.936
5.13	3.02	43.46	15.54	20.67	34.10	8.30	25.48	7.20	15.13	0.631
3.64	2.24	35.56	12.56	16.20	35.30	10.15	25.08	6.06	13.30	0.902
3.18	3.39	33.65	11.04	14.21	48.20	11.74	32.95	5.22	12.36	0.849
6.01	5.61	49.38	17.19	23.20	46.00	13.13	43.94	8.27	17.60	0.765
4.92	2.08	41.45	12.45	17.37	27.60	5.55	19.66	5.91	14.09	1.003
3.86	3.91	36.12	13.43	17.29	47.30	19.42	43.77	7.34	15.33	0.832
3.71	2.94	36.40	12.40	16.11	41.10	9.57	32.15	5.32	12.02	0.849
3.95	3.24	37.63	12.66	16.61	42.00	11.21	28.61	6.57	14.89	0.934
3.09	2.38	33.31	10.95	14.04	39.20	9.46	22.07	5.12	12.14	1.004
3.73	1.31	36.50	13.23	16.95	23.80	5.20	11.13	7.64	16.44	0.781
4.77	3.25	42.96	14.43	19.20	36.80	9.11	25.39	5.83	13.04	0.785
4.34	3.85	39.98	13.39	17.74	43.80	11.92	31.24	6.88	15.52	0.666
2.72	1.49	34.52	10.54	13.26	31.70	5.11	12.51	5.05	13.15	1.045
4.43	4.33	38.05	12.31	16.73	46.60	10.01	33.56	7.02	15.96	0.597
3.80	2.24	38.72	13.35	17.15	33.60	9.30	21.90	5.70	12.86	0.828
4.11	2.39	42.53	15.37	19.49	33.80	10.50	22.42	6.99	15.25	0.761
4.43	4.13	46.42	17.16	21.59	45.00	18.37	42.62	7.51	16.16	0.830
3.90	2.50	36.26	10.83	14.73	35.80	8.59	23.62	5.72	14.08	0.824
3.38	3.28	35.36	12.03	15.41	46.00	12.90	33.23	6.06	13.90	0.906
3.52	2.93	34.65	11.70	15.22	42.60	11.00	30.20	5.66	12.88	0.929
3.46	2.08	34.01	9.52	12.98	34.70	5.52	18.30	5.69	14.92	0.985
5.30	4.35	39.21	12.73	18.03	42.70	11.07	31.72	7.81	16.97	0.751

3.48	2.25	30.27	9.97	13.45	36.00	7.17	22.64	5.64	12.68	0.892
4.14	3.25	40.06	14.50	18.64	40.80	10.55	23.17	6.57	14.11	1.379
2.98	3.24	31.10	10.99	14.17	43.50	9.30	22.50	5.66	13.39	1.202
2.65	1.97	28.55	8.75	11.39	39.20	4.69	21.57	4.80	12.04	1.230
3.33	2.37	35.20	11.33	15.24	55.60	6.90	23.30	5.67	13.96	1.002
4.36	4.67	41.78	15.47	19.82	48.80	17.41	44.50	7.28	15.35	0.896
4.13	3.26	36.53	11.26	15.39	40.90	9.05	28.52	5.59	13.26	0.892
3.52	1.32	35.90	12.70	16.21	24.90	5.11	12.11	5.78	12.80	0.538
3.36	3.45	34.97	12.35	15.71	47.60	11.64	27.79	6.41	14.28	1.236
4.37	2.52	39.21	12.64	17.00	34.10	8.03	23.23	6.64	15.31	0.784
3.42	2.05	30.34	9.27	12.70	34.50	3.98	17.17	5.05	12.08	0.816
3.08	2.65	33.10	11.29	14.37	44.40	9.60	24.50	5.89	13.59	1.207
2.97	2.02	29.85	9.04	12.01	37.50	6.38	17.90	5.20	12.92	0.814
3.23	1.46	35.27	11.51	14.74	28.00	4.69	12.06	5.22	12.50	0.632
3.59	3.37	39.78	14.48	18.07	45.50	13.48	31.02	6.84	15.07	0.884
3.49	1.72	33.73	10.98	14.47	30.90	6.32	16.81	5.38	12.54	0.789
3.52	2.58	37.20	12.20	15.47	50.20	5.40	25.30	5.86	14.17	0.777
3.67	3.19	35.46	10.68	14.35	43.00	7.83	26.04	5.94	14.67	0.905
3.02	3.33	34.49	12.17	15.19	49.00	11.86	27.90	6.24	14.17	1.150
3.18	2.64	35.10	11.59	14.57	45.50	9.90	26.50	6.06	13.79	1.300
4.72	1.71	41.38	13.95	18.67	24.20	7.82	18.33	6.09	13.51	0.584
4.53	2.87	44.63	16.25	20.77	35.30	10.38	26.21	7.19	15.44	0.856
3.73	2.77	39.20	12.23	15.64	50.20	8.90	27.30	6.07	14.36	1.022
2.26	2.22	27.48	8.68	10.93	45.50	9.67	22.43	5.31	13.35	1.177
4.04	2.23	40.23	13.57	17.61	45.30	9.86	24.92	6.35	14.51	0.850
3.13	2.42	35.35	10.57	13.70	39.40	10.33	26.02	5.00	12.91	1.040

EF60degTTPT	EE240TTPT	EF240degTTPT	KE60degTTPT	KE240degTTPT	KF60degTTPT	KF240degTTPT	PF60TTPT	PF240PT	PFTTPT240
0.824	0.402	0.487	0.450	0.250	0.236	0.181	0.245	19.718	0.235
0.886	0.428	0.563	0.660	0.481	0.493	0.206	0.332	15.175	0.300
0.981	0.638	0.524	0.590	0.279	0.239	0.163	0.328	29.970	0.157
0.969	0.306	0.681	0.530	0.297	0.328	0.094	0.331	22.849	0.146
0.891	0.682	0.357	0.690	0.477	0.446	0.279	0.318	16.294	0.330
1.033	0.389	0.613	0.540	0.309	0.293	0.144	0.316	19.327	0.133
0.899	0.479	0.608	0.700	0.431	0.455	0.256	0.207	23.859	0.301
0.773	0.490	0.465	0.460	0.059	0.346	0.143	0.253	21.785	0.266
0.685	0.560	0.337	0.580	0.234	0.298	0.218	0.238	21.595	0.348
0.897	0.510	0.645	0.650	0.477	0.367	0.209	0.323	17.377	0.244
1.041	0.626	0.717	0.610	0.530	0.373	0.216	0.196	17.316	0.238
1.206	0.510	0.372	0.580	0.215	0.209	0.211	0.263	25.403	0.226
0.828	0.481	0.553	0.520	0.308	0.323	0.053	0.198	21.875	0.108
0.699	0.375	0.341	0.450	0.291	0.287	0.200	0.216	25.309	0.213
1.020	0.372	0.323	0.610	0.239	0.311	0.181	0.257	21.599	0.238
0.972	0.280	0.490	0.700	0.320	0.391	0.115	0.214	28.134	0.240
0.889	0.309	0.574	0.640	0.272	0.333	0.132	0.213	26.964	0.302
0.846	0.447	0.244	0.540	0.335	0.308	0.144	0.217	25.117	0.268
0.681	0.449	0.490	0.470	0.261	0.354	0.123	0.201	25.713	0.161
0.817	0.345	0.489	0.490	0.257	0.268	0.141	0.238	27.079	0.142
0.709	0.435	0.446	0.590	0.293	0.275	0.246	0.287	18.428	0.242
0.886	0.497	0.679	0.470	0.363	0.425	0.193	0.350	23.962	0.189
0.917	0.383	0.462	0.530	0.274	0.243	0.270	0.274	23.525	0.265
0.974	0.483	0.458	0.470	0.133	0.325	0.160	0.229	23.370	0.160
0.778	0.718	0.873	0.740	0.686	0.649	0.400	0.333	17.249	0.366
0.990	0.485	0.638	0.560	0.222	0.308	0.184	0.207	14.888	0.236
0.598	0.495	0.608	0.580	0.304	0.294	0.145	0.267	23.471	0.193
0.921	0.689	0.431	0.490	0.150	0.274	0.122	0.278	27.576	0.293
0.728	0.116	0.637	0.580	0.185	0.389	0.219	0.299	23.283	0.190
0.690	0.371	0.372	0.580	0.244	0.385	0.227	0.303	19.563	0.221
0.941	0.864	0.818	0.730	0.445	0.329	0.311	0.317	17.081	0.416
0.999	0.598	0.432	0.680	0.274	0.308	0.168	0.286	17.076	0.209
1.004	0.949	0.747	0.720	0.738	0.505	0.439	0.523	19.158	0.313
1.013	0.374	0.452	0.590	0.239	0.335	0.128	0.176	20.668	0.140
0.957	0.646	0.532	0.450	0.142	0.231	0.162	0.306	24.611	0.272
0.963	0.363	0.422	0.610	0.164	0.263	0.139	0.259	18.359	0.154
1.053	0.438	0.444	0.580	0.316	0.329	0.384	0.308	19.974	0.209
0.952	0.608	0.854	0.810	0.607	0.532	0.342	0.419	20.585	0.281
1.095	0.460	0.354	0.520	0.285	0.273	0.155	0.180	21.807	0.273
0.958	0.257	0.621	0.670	0.392	0.233	0.282	0.294	27.046	0.224
0.927	0.466	0.364	0.510	0.283	0.294	0.204	0.350	26.122	0.129
0.721	0.768	0.787	0.710	0.549	0.628	0.389	0.400	17.115	0.243
0.941	0.526	0.319	0.450	0.144	0.295	0.114	0.334	22.134	0.227
0.971	0.232	0.434	0.560	0.169	0.303	0.162	0.360	26.302	0.174
0.904	0.237	0.596	0.540	0.258	0.380	0.200	0.321	19.295	0.196
1.048	0.807	0.285	0.890	0.806	0.650	0.419	0.518	14.646	0.356
0.801	0.535	0.647	0.560	0.217	0.344	0.150	0.170	22.188	0.136
0.995	0.254	0.546	0.400	0.151	0.282	0.126	0.308	26.150	0.205
0.809	0.455	0.397	0.610	0.382	0.344	0.286	0.261	17.563	0.267
0.599	0.488	0.493	0.470	0.191	0.370	0.150	0.217	25.346	0.157
0.662	0.505	0.433	0.610	0.261	0.280	0.356	0.225	22.971	0.205
1.018	0.534	0.514	0.630	0.191	0.360	0.142	0.420	25.824	0.184
0.909	0.451	0.597	0.660	0.348	0.264	0.399	0.255	18.782	0.275
0.797	0.562	0.652	0.710	0.570	0.326	0.266	0.306	21.901	0.215
1.133	0.332	0.388	0.610	0.229	0.279	0.230	0.299	18.797	0.244
0.932	0.627	0.617	0.810	0.502	0.529	0.332	0.354	17.997	0.182
1.147	0.781	0.673	0.860	0.652	0.677	0.433	0.409	17.154	0.315
1.032	0.660	0.496	0.550	0.270	0.252	0.091	0.342	17.942	0.222
1.002	0.420	0.507	0.560	0.139	0.278	0.086	0.227	26.823	0.267
0.838	0.571	0.636	0.600	0.214	0.317	0.263	0.263	21.109	0.277
0.779	0.493	0.529	0.540	0.427	0.497	0.225	0.330	14.899	0.350
1.157	0.400	0.575	0.620	0.421	0.270	0.308	0.235	24.504	0.331
0.957	0.496	0.477	0.560	0.211	0.273	0.072	0.257	25.641	0.219

0.948	0.401	0.335	0.610	0.308	0.369	0.215	0.261	22.648	0.277
1.038	0.346	0.518	0.590	0.279	0.252	0.136	0.250	21.282	0.260
0.877	0.558	0.583	0.690	0.525	0.490	0.381	0.312	13.085	0.323
0.987	0.451	0.644	0.710	0.468	0.382	0.305	0.345	18.761	0.185
1.165	0.618	0.461	0.520	0.253	0.218	0.098	0.242	19.365	0.126
0.993	0.186	0.652	0.530	0.264	0.414	0.043	0.365	21.676	0.238
1.012	0.337	0.427	0.600	0.316	0.310	0.141	0.259	20.391	0.265
0.709	0.492	0.570	0.600	0.540	0.472	0.277	0.302	19.590	0.361
0.867	0.506	0.472	0.670	0.513	0.413	0.341	0.327	20.033	0.322
0.766	0.603	0.451	0.650	0.544	0.505	0.369	0.302	20.955	0.178
1.029	0.512	0.485	0.660	0.429	0.267	0.280	0.364	22.485	0.198
0.757	0.468	0.378	0.730	0.441	0.426	0.361	0.351	24.811	0.200
0.824	0.402	0.487	0.450	0.250	0.236	0.181	0.245	19.718	0.235
0.832	0.528	0.522	0.790	0.512	0.508	0.317	0.357	17.664	0.223
1.104	0.455	0.486	0.460	0.164	0.249	0.192	0.301	28.525	0.215
1.059	0.305	0.361	0.550	0.265	0.300	0.150	0.332	26.408	0.201
1.143	0.440	0.602	0.560	0.323	0.326	0.309	0.311	22.447	0.282
0.819	0.303	0.587	0.570	0.389	0.206	0.169	0.341	21.384	0.150
1.012	0.630	0.534	0.550	0.331	0.282	0.256	0.388	23.708	0.170
0.839	0.815	0.562	0.700	0.440	0.387	0.324	0.370	17.161	0.254
0.749	0.553	0.487	0.540	0.198	0.315	0.077	0.447	15.723	0.204
0.890	0.412	0.382	0.710	0.545	0.413	0.213	0.296	23.629	0.112
0.803	0.239	0.325	0.650	0.418	0.345	0.223	0.221	22.457	0.255
0.669	0.493	0.349	0.690	0.306	0.378	0.325	0.232	22.569	0.231
0.753	0.469	0.800	0.830	0.529	0.387	0.401	0.293	8.716	0.257
1.137	0.525	0.409	0.620	0.235	0.217	0.152	0.246	24.933	0.187
1.043	0.468	0.445	0.610	0.552	0.415	0.221	0.172	21.996	0.175
0.658	0.481	0.528	0.690	0.348	0.316	0.227	0.189	21.035	0.170
0.695	0.281	0.685	0.570	0.347	0.275	0.216	0.152	21.869	0.171
0.899	0.582	0.505	0.720	0.610	0.549	0.351	0.508	16.826	0.275
0.963	0.376	0.361	0.650	0.292	0.311	0.271	0.350	23.763	0.203
0.917	0.808	0.564	0.880	0.764	0.561	0.521	0.517	15.041	0.379
0.953	0.317	0.675	0.600	0.308	0.410	0.161	0.318	24.970	0.273
0.996	0.316	0.454	0.540	0.153	0.304	0.227	0.383	15.151	0.236
0.746	0.706	0.569	0.810	0.593	0.470	0.266	0.379	16.532	0.213
0.981	0.054	0.297	0.680	0.326	0.260	0.274	0.188	19.939	0.167
0.777	0.488	0.472	0.680	0.283	0.291	0.319	0.342	26.329	0.213
0.859	0.396	0.476	0.720	0.465	0.434	0.333	0.270	22.715	0.151
0.812	0.343	0.753	0.600	0.629	0.597	0.248	0.275	17.502	0.293
0.987	0.562	0.523	0.710	0.221	0.354	0.116	0.267	21.522	0.238
0.879	0.598	0.430	0.690	0.442	0.285	0.290	0.432	22.725	0.254
0.943	0.296	0.695	0.840	0.603	0.502	0.465	0.211	18.582	0.461
0.918	0.561	0.587	0.530	0.191	0.301	0.080	0.347	17.438	0.197
0.819	0.676	0.599	0.750	0.733	0.525	0.419	0.444	15.258	0.321
0.647	1.055	0.604	0.760	0.712	0.653	0.365	0.429	13.221	0.325
0.774	0.091	0.057	0.460	0.109	0.304	0.177	0.295	22.526	0.205
0.710	0.775	0.465	0.660	0.446	0.535	0.334	0.353	16.510	0.341
0.798	0.468	0.473	0.620	0.403	0.390	0.191	0.331	17.939	0.312
1.145	0.673	0.833	0.850	0.646	0.503	0.491	0.466	18.930	0.259
0.758	0.882	0.657	0.820	0.821	0.688	0.424	0.476	15.772	0.449
0.676	0.600	0.509	0.680	0.493	0.310	0.221	0.355	11.564	0.339
0.812	0.630	0.205	0.500	0.306	0.280	0.139	0.120	19.502	0.184
1.193	0.631	0.476	0.520	0.380	0.284	0.213	0.340	22.098	0.273
1.071	0.599	0.502	0.530	0.330	0.303	0.194	0.224	22.035	0.214
1.355	0.931	1.009	0.860	0.780	0.619	0.385	0.499	14.522	0.383
0.943	0.130	0.326	0.520	0.147	0.231	0.152	0.191	17.486	0.153
0.953	0.502	0.624	0.610	0.518	0.440	0.365	0.441	19.837	0.229
0.647	0.485	0.832	0.740	0.535	0.532	0.280	0.248	17.795	0.335
0.968	0.804	0.962	0.800	0.755	0.553	0.352	0.391	12.683	0.224
1.144	0.594	0.604	0.770	0.676	0.540	0.441	0.472	12.056	0.201
0.758	0.925	0.763	0.870	0.647	0.504	0.505	0.481	13.454	0.521
0.930	0.710	0.877	0.760	0.692	0.456	0.281	0.397	10.770	0.211
0.945	0.738	0.736	0.870	0.682	0.613	0.526	0.542	16.455	0.292
0.853	0.339	0.476	0.560	0.483	0.367	0.265	0.383	29.947	0.196

0.881	0.629	0.844	0.860	0.676	0.410	0.429	0.537	13.806	0.209
1.224	0.796	0.553	0.820	0.821	0.592	0.568	0.644	10.646	0.488
1.021	0.742	0.583	0.850	0.723	0.544	0.507	0.616	8.383	0.349
1.202	0.925	0.804	0.970	0.900	0.615	0.500	0.719	9.466	0.420
1.179	0.638	0.666	0.890	0.830	0.681	0.370	0.497	13.985	0.334
1.297	1.126	0.568	0.740	0.807	0.718	0.469	0.539	13.848	0.334
0.737	0.466	0.526	0.680	0.464	0.489	0.286	0.370	19.506	0.281
0.931	0.426	0.746	0.570	0.132	0.285	0.158	0.262	28.556	0.194
1.215	0.820	0.555	0.930	0.849	0.628	0.310	0.681	10.579	0.405
0.663	0.639	0.644	0.780	0.518	0.616	0.359	0.496	16.517	0.372
0.754	0.624	0.610	0.650	0.546	0.440	0.326	0.394	15.877	0.267
1.328	0.763	0.808	0.870	0.683	0.652	0.611	0.592	11.228	0.480
0.536	0.526	0.931	0.680	0.541	0.527	0.302	0.325	21.381	0.267
0.669	0.722	0.817	0.930	0.776	0.610	0.550	0.506	17.184	0.330
0.831	0.838	0.679	0.850	0.619	0.703	0.351	0.487	16.592	0.434
0.845	0.359	0.590	0.640	0.499	0.573	0.426	0.297	16.211	0.248
0.947	0.838	0.649	0.770	0.692	0.486	0.487	0.454	13.098	0.496
0.916	0.974	0.719	0.820	0.753	0.624	0.458	0.550	14.240	0.318
0.997	0.938	0.546	0.870	0.826	0.688	0.454	0.612	8.148	0.382
1.406	0.806	0.709	0.890	1.021	0.724	0.588	0.675	8.473	0.424
0.947	0.434	0.333	0.600	0.199	0.275	0.109	0.260	30.794	0.237
1.061	0.534	0.353	0.540	0.482	0.299	0.194	0.180	22.108	0.215
1.031	0.839	0.539	0.870	0.776	0.596	0.490	0.628	13.541	0.318
1.173	1.152	0.814	0.750	0.932	0.454	0.407	0.542	8.737	0.474
1.007	0.864	0.668	0.830	0.660	0.581	0.446	0.532	12.810	0.351
0.983	0.984	0.754	0.820	0.650	0.632	0.644	0.536	17.408	0.356

DF60PT	DF60TTPT	DF240TTPT	EETTPPUL	EETTPVUL	eettpp20	eettpv20	eettpp40	eettpv40	eettpp60	eettpv60	efttppul	efttpvul	efttpp20	efttpv20
23.800	0.325	0.282	0.287	0.261	0.241	0.281	0.291	0.386	0.284	0.290	0.322	0.336	0.355	0.365
15.538	0.382	0.318	0.362	0.397	0.329	0.307	0.321	0.361	0.317	0.394	0.296	0.321	0.393	0.397
18.951	0.432	0.297	0.236	0.333	0.392	0.231	0.307	0.385	0.277	0.335	0.285	0.388	0.404	0.388
19.275	0.353	0.299	0.274	0.307	0.302	0.312	0.291	0.293	0.321	0.345	0.365	0.319	0.327	0.319
12.412	0.447	0.431	0.318	0.415	0.399	0.340	0.337	0.421	0.312	0.315	0.339	0.368	0.302	0.440
24.110	0.357	0.329	0.348	0.317	0.308	0.321	0.331	0.361	0.361	0.335	0.320	0.375	0.411	0.420
12.300	0.451	0.497	0.329	0.439	0.380	0.433	0.347	0.385	0.358	0.329	0.365	0.411	0.340	0.373
23.443	0.350	0.328	0.294	0.292	0.300	0.314	0.280	0.351	0.313	0.284	0.344	0.393	0.373	0.391
22.742	0.348	0.314	0.325	0.354	0.285	0.359	0.281	0.357	0.316	0.298	0.352	0.380	0.399	0.327
20.261	0.494	0.401	0.278	0.364	0.294	0.347	0.297	0.361	0.353	0.335	0.317	0.430	0.399	0.337
24.037	0.385	0.427	0.343	0.352	0.322	0.413	0.292	0.354	0.312	0.349	0.339	0.371	0.378	0.403
23.578	0.450	0.296	0.242	0.339	0.250	0.298	0.253	0.345	0.256	0.313	0.316	0.378	0.326	0.377
25.955	0.356	0.248	0.297	0.317	0.232	0.325	0.271	0.372	0.328	0.344	0.348	0.312	0.360	0.410
16.899	0.317	0.384	0.348	0.329	0.299	0.333	0.333	0.297	0.288	0.359	0.345	0.305	0.406	0.422
18.563	0.402	0.322	0.313	0.274	0.236	0.303	0.319	0.312	0.296	0.368	0.303	0.396	0.328	0.359
23.787	0.427	0.309	0.303	0.330	0.257	0.347	0.278	0.361	0.352	0.348	0.324	0.312	0.331	0.419
22.633	0.370	0.308	0.310	0.270	0.281	0.289	0.303	0.347	0.320	0.329	0.303	0.388	0.397	0.378
27.033	0.425	0.315	0.288	0.251	0.264	0.370	0.323	0.367	0.316	0.381	0.270	0.411	0.378	0.389
22.657	0.357	0.341	0.253	0.308	0.288	0.362	0.279	0.299	0.269	0.364	0.323	0.333	0.343	0.359
28.203	0.412	0.336	0.274	0.270	0.231	0.317	0.288	0.353	0.307	0.349	0.299	0.335	0.302	0.369
23.279	0.359	0.243	0.284	0.314	0.238	0.302	0.299	0.346	0.277	0.350	0.289	0.384	0.396	0.385
28.648	0.402	0.321	0.289	0.369	0.264	0.340	0.305	0.358	0.339	0.407	0.301	0.324	0.386	0.399
23.853	0.398	0.310	0.309	0.277	0.239	0.363	0.276	0.362	0.323	0.354	0.302	0.432	0.357	0.346
28.917	0.375	0.383	0.354	0.343	0.351	0.336	0.317	0.361	0.354	0.431	0.332	0.422	0.361	0.343
12.878	0.566	0.576	0.369	0.469	0.323	0.450	0.384	0.473	0.338	0.398	0.350	0.547	0.411	0.450
18.124	0.402	0.302	0.354	0.319	0.302	0.315	0.301	0.335	0.330	0.356	0.320	0.384	0.402	0.382
32.778	0.343	0.321	0.258	0.312	0.253	0.315	0.334	0.327	0.372	0.366	0.283	0.357	0.351	0.371
17.284	0.393	0.411	0.227	0.301	0.320	0.330	0.282	0.344	0.334	0.312	0.350	0.335	0.321	0.378
27.351	0.337	0.314	0.271	0.272	0.329	0.317	0.288	0.305	0.322	0.386	0.347	0.403	0.337	0.427
24.063	0.401	0.335	0.310	0.333	0.332	0.304	0.276	0.380	0.363	0.393	0.272	0.350	0.318	0.388
14.518	0.399	0.489	0.350	0.468	0.324	0.456	0.324	0.464	0.312	0.345	0.361	0.522	0.375	0.412
17.793	0.423	0.391	0.283	0.338	0.253	0.306	0.304	0.420	0.280	0.292	0.277	0.293	0.395	0.377
15.872	0.633	0.490	0.317	0.475	0.401	0.515	0.333	0.393	0.447	0.373	0.335	0.474	0.460	0.386
21.812	0.309	0.301	0.278	0.232	0.267	0.391	0.301	0.320	0.299	0.372	0.335	0.378	0.382	0.361
16.711	0.391	0.305	0.301	0.411	0.228	0.301	0.289	0.367	0.344	0.332	0.315	0.361	0.334	0.388
25.280	0.295	0.361	0.276	0.369	0.294	0.358	0.316	0.320	0.306	0.343	0.362	0.366	0.281	0.342
28.540	0.388	0.272	0.308	0.316	0.257	0.344	0.335	0.370	0.346	0.329	0.335	0.362	0.343	0.400
11.008	0.536	0.439	0.350	0.478	0.268	0.491	0.395	0.366	0.338	0.383	0.397	0.443	0.432	0.414
27.864	0.388	0.292	0.293	0.304	0.243	0.348	0.243	0.330	0.342	0.362	0.338	0.382	0.330	0.408
22.693	0.365	0.388	0.357	0.320	0.322	0.367	0.324	0.372	0.335	0.267	0.352	0.429	0.400	0.366
22.257	0.374	0.301	0.282	0.346	0.341	0.310	0.287	0.349	0.279	0.370	0.332	0.411	0.305	0.305
18.949	0.356	0.480	0.391	0.462	0.383	0.439	0.295	0.437	0.346	0.311	0.396	0.419	0.348	0.426
24.320	0.355	0.297	0.272	0.298	0.245	0.285	0.311	0.343	0.256	0.341	0.315	0.362	0.310	0.386
23.104	0.332	0.380	0.293	0.254	0.264	0.280	0.271	0.394	0.347	0.346	0.313	0.282	0.356	0.378
14.254	0.327	0.243	0.276	0.364	0.237	0.377	0.261	0.349	0.277	0.278	0.323	0.305	0.309	0.309
17.278	0.582	0.457	0.368	0.433	0.363	0.509	0.409	0.478	0.461	0.388	0.455	0.538	0.442	0.506
25.091	0.380	0.251	0.238	0.266	0.264	0.276	0.327	0.315	0.297	0.327	0.332	0.357	0.396	0.347
21.334	0.316	0.493	0.263	0.280	0.293	0.327	0.275	0.322	0.285	0.337	0.330	0.359	0.343	0.388
19.386	0.375	0.349	0.283	0.325	0.290	0.345	0.288	0.387	0.299	0.289	0.335	0.356	0.416	0.377
18.370	0.385	0.235	0.295	0.294	0.294	0.322	0.333	0.339	0.339	0.314	0.326	0.333	0.300	0.400
26.252	0.343	0.350	0.321	0.342	0.269	0.306	0.252	0.326	0.342	0.370	0.319	0.414	0.352	0.378
24.010	0.393	0.360	0.252	0.279	0.235	0.312	0.318	0.369	0.375	0.291	0.219	0.397	0.411	0.397
23.185	0.281	0.353	0.318	0.339	0.310	0.366	0.335	0.311	0.325	0.321	0.308	0.350	0.379	0.384
15.980	0.468	0.394	0.255	0.401	0.329	0.413	0.316	0.388	0.352	0.375	0.309	0.393	0.364	0.326
17.001	0.446	0.311	0.275	0.297	0.318	0.271	0.260	0.430	0.276	0.329	0.288	0.350	0.318	0.358
14.051	0.543	0.561	0.375	0.442	0.327	0.422	0.412	0.402	0.320	0.306	0.359	0.462	0.364	0.346
14.644	0.686	0.412	0.359	0.502	0.388	0.499	0.397	0.462	0.466	0.523	0.407	0.601	0.388	0.402
22.428	0.344	0.270	0.286	0.309	0.257	0.344	0.317	0.317	0.312	0.337	0.253	0.396	0.382	0.412
21.723	0.342	0.342	0.258	0.337	0.301	0.308	0.311	0.383	0.313	0.415	0.302	0.420	0.376	0.346
19.320	0.476	0.303	0.303	0.293	0.221	0.346	0.336	0.299	0.248	0.360	0.344	0.373	0.399	0.353
15.198	0.456	0.324	0.340	0.389	0.285	0.326	0.366	0.392	0.321	0.435	0.272	0.410	0.421	0.387
21.490	0.448	0.459	0.247	0.360	0.334	0.429	0.273	0.342	0.325	0.391	0.255	0.426	0.385	0.438
21.118	0.360	0.321	0.247	0.321	0.271	0.324	0.250	0.352	0.332	0.368	0.328	0.426	0.309	0.388

23.129	0.386	0.284	0.353	0.300	0.294	0.295	0.331	0.288	0.278	0.340	0.353	0.373	0.332	0.382
22.202	0.306	0.334	0.274	0.297	0.241	0.318	0.335	0.355	0.322	0.345	0.341	0.357	0.313	0.396
14.248	0.401	0.517	0.334	0.472	0.302	0.437	0.372	0.459	0.312	0.333	0.335	0.518	0.383	0.420
23.656	0.409	0.454	0.333	0.342	0.336	0.392	0.343	0.384	0.278	0.376	0.333	0.362	0.387	0.397
29.348	0.363	0.333	0.280	0.326	0.238	0.235	0.307	0.368	0.347	0.318	0.312	0.365	0.354	0.397
17.303	0.456	0.320	0.271	0.352	0.264	0.342	0.318	0.268	0.289	0.301	0.255	0.399	0.357	0.429
23.297	0.350	0.228	0.281	0.274	0.246	0.258	0.268	0.346	0.318	0.371	0.294	0.349	0.313	0.372
16.458	0.294	0.455	0.320	0.428	0.347	0.401	0.310	0.407	0.261	0.438	0.364	0.415	0.351	0.375
18.061	0.405	0.451	0.325	0.469	0.364	0.371	0.322	0.420	0.384	0.427	0.345	0.339	0.296	0.359
17.722	0.409	0.547	0.286	0.350	0.298	0.384	0.321	0.408	0.347	0.345	0.335	0.423	0.329	0.395
25.019	0.362	0.384	0.354	0.401	0.353	0.339	0.316	0.365	0.293	0.361	0.348	0.361	0.413	0.367
19.200	0.442	0.419	0.321	0.385	0.307	0.425	0.299	0.357	0.302	0.357	0.300	0.395	0.370	0.357
23.800	0.325	0.282	0.287	0.261	0.241	0.281	0.291	0.386	0.284	0.290	0.322	0.336	0.355	0.365
20.461	0.412	0.335	0.370	0.370	0.383	0.409	0.312	0.387	0.341	0.394	0.275	0.413	0.381	0.363
25.794	0.385	0.244	0.367	0.353	0.268	0.336	0.291	0.386	0.313	0.321	0.329	0.338	0.331	0.389
16.777	0.361	0.318	0.327	0.319	0.275	0.300	0.303	0.283	0.340	0.320	0.309	0.405	0.352	0.404
25.053	0.347	0.302	0.287	0.340	0.299	0.355	0.304	0.351	0.294	0.326	0.354	0.448	0.333	0.338
19.913	0.329	0.413	0.273	0.332	0.298	0.409	0.225	0.369	0.369	0.371	0.352	0.332	0.365	0.381
16.419	0.333	0.338	0.344	0.351	0.256	0.296	0.346	0.318	0.281	0.321	0.283	0.434	0.362	0.394
18.585	0.443	0.461	0.385	0.395	0.298	0.391	0.319	0.369	0.336	0.363	0.318	0.388	0.389	0.404
18.555	0.396	0.306	0.301	0.303	0.279	0.340	0.384	0.308	0.322	0.347	0.279	0.365	0.433	0.346
20.336	0.314	0.404	0.350	0.401	0.376	0.402	0.273	0.382	0.344	0.342	0.303	0.392	0.382	0.396
11.785	0.383	0.449	0.299	0.285	0.249	0.334	0.287	0.310	0.266	0.416	0.279	0.358	0.379	0.407
19.141	0.428	0.353	0.345	0.323	0.325	0.404	0.305	0.372	0.388	0.342	0.363	0.341	0.341	0.414
14.327	0.369	0.524	0.346	0.465	0.282	0.442	0.383	0.433	0.363	0.401	0.399	0.473	0.355	0.390
23.343	0.326	0.341	0.307	0.306	0.243	0.295	0.271	0.317	0.281	0.354	0.287	0.362	0.358	0.351
18.646	0.414	0.496	0.358	0.336	0.378	0.381	0.328	0.402	0.343	0.384	0.294	0.365	0.415	0.366
25.854	0.400	0.352	0.229	0.311	0.298	0.335	0.291	0.357	0.279	0.394	0.308	0.337	0.346	0.386
16.871	0.473	0.263	0.239	0.309	0.270	0.335	0.284	0.324	0.327	0.351	0.332	0.385	0.394	0.348
18.380	0.432	0.538	0.324	0.472	0.399	0.469	0.318	0.407	0.363	0.452	0.325	0.573	0.434	0.366
23.194	0.384	0.448	0.258	0.303	0.315	0.323	0.329	0.345	0.322	0.360	0.354	0.357	0.304	0.386
12.786	0.580	0.527	0.287	0.500	0.355	0.539	0.383	0.521	0.328	0.456	0.388	0.545	0.427	0.416
25.372	0.413	0.362	0.271	0.337	0.286	0.361	0.339	0.407	0.326	0.324	0.332	0.378	0.305	0.332
22.905	0.357	0.312	0.279	0.346	0.319	0.283	0.318	0.322	0.343	0.352	0.345	0.405	0.321	0.377
11.778	0.518	0.496	0.391	0.429	0.353	0.509	0.372	0.457	0.357	0.288	0.338	0.376	0.466	0.443
19.617	0.317	0.444	0.294	0.338	0.284	0.341	0.260	0.337	0.361	0.377	0.333	0.371	0.394	0.332
22.774	0.332	0.354	0.310	0.334	0.342	0.347	0.302	0.309	0.378	0.416	0.334	0.374	0.388	0.438
24.701	0.405	0.399	0.385	0.441	0.299	0.344	0.307	0.409	0.315	0.394	0.348	0.439	0.374	0.355
19.576	0.374	0.524	0.434	0.528	0.316	0.443	0.334	0.388	0.293	0.268	0.435	0.469	0.485	0.400
20.196	0.373	0.325	0.261	0.313	0.267	0.335	0.315	0.316	0.340	0.342	0.307	0.376	0.339	0.394
17.843	0.335	0.523	0.375	0.327	0.238	0.410	0.342	0.357	0.373	0.295	0.313	0.396	0.296	0.349
17.667	0.485	0.344	0.340	0.392	0.399	0.471	0.361	0.415	0.304	0.313	0.439	0.493	0.442	0.361
26.154	0.401	0.303	0.211	0.298	0.233	0.332	0.301	0.346	0.327	0.274	0.279	0.406	0.330	0.402
15.095	0.564	0.506	0.320	0.427	0.300	0.470	0.447	0.430	0.362	0.305	0.383	0.567	0.454	0.273
14.589	0.696	0.433	0.406	0.445	0.359	0.483	0.387	0.464	0.452	0.412	0.417	0.573	0.430	0.490
20.337	0.358	0.330	0.285	0.305	0.225	0.290	0.324	0.312	0.346	0.308	0.265	0.419	0.334	0.371
18.558	0.451	0.397	0.336	0.382	0.296	0.400	0.370	0.473	0.301	0.393	0.402	0.423	0.378	0.361
21.262	0.458	0.482	0.392	0.402	0.357	0.303	0.308	0.410	0.353	0.294	0.386	0.415	0.330	0.381
14.188	0.463	0.555	0.385	0.473	0.336	0.461	0.408	0.544	0.347	0.425	0.342	0.526	0.426	0.412
13.607	0.679	0.459	0.339	0.468	0.331	0.447	0.308	0.483	0.391	0.453	0.445	0.578	0.471	0.495
20.184	0.360	0.515	0.411	0.390	0.246	0.392	0.402	0.383	0.350	0.493	0.328	0.404	0.383	0.378
20.959	0.312	0.361	0.330	0.365	0.276	0.345	0.290	0.273	0.300	0.364	0.268	0.370	0.322	0.424
20.427	0.392	0.336	0.329	0.335	0.278	0.352	0.329	0.317	0.341	0.327	0.331	0.400	0.379	0.384
18.595	0.364	0.379	0.293	0.332	0.321	0.315	0.362	0.356	0.274	0.332	0.284	0.373	0.370	0.348
11.345	0.682	0.660	0.358	0.500	0.401	0.471	0.387	0.505	0.455	0.543	0.412	0.637	0.461	0.374
20.839	0.360	0.339	0.256	0.283	0.239	0.343	0.331	0.352	0.331	0.387	0.269	0.362	0.344	0.386
20.983	0.350	0.435	0.286	0.419	0.292	0.378	0.290	0.384	0.315	0.312	0.348	0.385	0.313	0.333
9.329	0.364	0.360	0.424	0.475	0.330	0.395	0.360	0.338	0.343	0.396	0.354	0.433	0.395	0.454
12.325	0.555	0.480	0.274	0.406	0.341	0.430	0.351	0.455	0.390	0.426	0.404	0.523	0.423	0.424
16.753	0.599	0.538	0.323	0.463	0.381	0.435	0.440	0.474	0.378	0.365	0.366	0.506	0.371	0.413
11.841	0.587	0.515	0.385	0.460	0.412	0.518	0.366	0.508	0.354	0.451	0.439	0.521	0.362	0.445
15.229	0.491	0.489	0.377	0.480	0.364	0.413	0.353	0.407	0.385	0.357	0.408	0.537	0.392	0.419
15.056	0.522	0.560	0.350	0.524	0.331	0.560	0.440	0.516	0.399	0.534	0.458	0.687	0.522	0.482
21.681	0.384	0.397	0.273	0.361	0.299	0.285	0.361	0.410	0.343	0.371	0.359	0.386	0.406	0.369

14.722	0.448	0.451	0.368	0.475	0.368	0.413	0.320	0.444	0.388	0.449	0.379	0.617	0.444	0.385
14.005	0.863	0.666	0.380	0.480	0.398	0.444	0.458	0.561	0.494	0.539	0.476	0.662	0.543	0.430
12.371	0.791	0.542	0.453	0.485	0.467	0.475	0.473	0.536	0.476	0.578	0.462	0.651	0.526	0.393
12.166	0.815	0.579	0.413	0.512	0.371	0.523	0.359	0.514	0.526	0.477	0.521	0.638	0.545	0.465
12.851	0.666	0.622	0.393	0.488	0.394	0.482	0.346	0.557	0.475	0.527	0.448	0.652	0.479	0.429
14.197	0.677	0.662	0.414	0.460	0.311	0.525	0.361	0.462	0.454	0.561	0.425	0.626	0.513	0.551
20.965	0.406	0.370	0.336	0.432	0.336	0.439	0.312	0.327	0.284	0.328	0.319	0.462	0.329	0.430
26.729	0.350	0.287	0.282	0.297	0.237	0.396	0.328	0.349	0.324	0.337	0.322	0.341	0.364	0.389
14.764	0.690	0.663	0.405	0.512	0.374	0.500	0.375	0.584	0.474	0.490	0.504	0.555	0.509	0.569
10.370	0.632	0.444	0.408	0.459	0.320	0.514	0.337	0.461	0.310	0.384	0.417	0.480	0.399	0.410
13.873	0.344	0.522	0.332	0.427	0.294	0.347	0.267	0.421	0.333	0.365	0.337	0.395	0.349	0.389
14.023	0.776	0.695	0.500	0.515	0.411	0.506	0.355	0.554	0.460	0.524	0.462	0.646	0.539	0.446
18.066	0.414	0.499	0.378	0.423	0.383	0.370	0.442	0.351	0.307	0.436	0.373	0.472	0.393	0.389
12.310	0.679	0.496	0.407	0.516	0.307	0.587	0.429	0.508	0.384	0.415	0.409	0.518	0.428	0.497
11.884	0.538	0.546	0.412	0.515	0.346	0.476	0.437	0.463	0.409	0.391	0.439	0.680	0.450	0.468
15.801	0.499	0.467	0.353	0.431	0.366	0.453	0.346	0.358	0.317	0.366	0.321	0.435	0.402	0.336
11.924	0.641	0.536	0.394	0.461	0.411	0.561	0.391	0.475	0.506	0.492	0.449	0.572	0.533	0.495
13.404	0.639	0.469	0.341	0.445	0.318	0.388	0.391	0.501	0.445	0.430	0.446	0.649	0.481	0.434
12.472	0.822	0.650	0.435	0.521	0.423	0.544	0.347	0.525	0.516	0.501	0.478	0.682	0.525	0.442
15.105	0.762	0.701	0.416	0.473	0.444	0.467	0.369	0.592	0.468	0.484	0.527	0.700	0.549	0.504
23.472	0.381	0.248	0.291	0.342	0.227	0.317	0.332	0.347	0.256	0.365	0.351	0.365	0.293	0.364
23.790	0.354	0.435	0.365	0.413	0.366	0.384	0.323	0.370	0.349	0.415	0.313	0.356	0.336	0.422
14.743	0.586	0.687	0.383	0.491	0.352	0.575	0.390	0.560	0.535	0.495	0.478	0.683	0.507	0.464
13.829	0.695	0.627	0.409	0.481	0.402	0.568	0.422	0.473	0.586	0.556	0.453	0.650	0.541	0.467
12.829	0.708	0.556	0.369	0.517	0.366	0.475	0.450	0.540	0.490	0.491	0.502	0.540	0.452	0.359
17.577	0.766	0.570	0.407	0.485	0.340	0.572	0.366	0.429	0.444	0.522	0.416	0.598	0.508	0.477

efpp40	efttpp40	efttpv40	efpp60	efttpp60	efttpv60	kettppul	kettpvul	kettpp20	kettpv20	kettpp40	kettpv40	kettpp60	kettpv60	kfttppul	kfttpvul	kfttpp20
24.951	0.332	0.385	26.047	0.346	0.443	0.168	0.230	0.170	0.214	0.181	0.182	0.190	0.229	0.230	0.255	0.236
23.364	0.374	0.458	25.100	0.390	0.419	0.187	0.258	0.210	0.226	0.202	0.240	0.248	0.250	0.254	0.248	0.235
24.855	0.338	0.433	21.856	0.377	0.490	0.170	0.245	0.189	0.234	0.219	0.224	0.206	0.254	0.192	0.244	0.219
25.782	0.400	0.376	22.231	0.321	0.375	0.237	0.218	0.206	0.206	0.170	0.271	0.161	0.196	0.210	0.217	0.233
28.458	0.352	0.443	19.326	0.364	0.514	0.217	0.257	0.203	0.252	0.248	0.291	0.241	0.249	0.285	0.292	0.224
23.630	0.297	0.386	20.177	0.350	0.385	0.182	0.262	0.158	0.220	0.186	0.244	0.220	0.255	0.259	0.284	0.203
26.039	0.371	0.368	19.893	0.412	0.408	0.231	0.293	0.208	0.234	0.237	0.262	0.274	0.223	0.245	0.216	0.216
25.619	0.394	0.347	21.668	0.385	0.442	0.172	0.223	0.164	0.223	0.186	0.213	0.242	0.207	0.218	0.223	0.195
23.442	0.373	0.376	28.159	0.393	0.432	0.169	0.257	0.168	0.198	0.273	0.220	0.252	0.218	0.217	0.216	0.237
27.823	0.299	0.394	24.988	0.295	0.428	0.198	0.268	0.215	0.239	0.209	0.246	0.219	0.287	0.250	0.280	0.221
23.032	0.348	0.427	19.914	0.363	0.453	0.183	0.262	0.190	0.234	0.224	0.282	0.196	0.227	0.243	0.264	0.236
24.254	0.395	0.370	21.776	0.370	0.433	0.183	0.245	0.204	0.190	0.214	0.270	0.222	0.220	0.180	0.238	0.204
28.374	0.346	0.464	20.932	0.382	0.404	0.143	0.250	0.182	0.221	0.211	0.254	0.240	0.256	0.254	0.240	0.212
27.462	0.333	0.420	27.231	0.302	0.412	0.161	0.265	0.220	0.218	0.221	0.237	0.221	0.237	0.195	0.255	0.205
27.651	0.398	0.380	17.758	0.354	0.425	0.179	0.243	0.180	0.204	0.186	0.238	0.176	0.243	0.224	0.224	0.224
23.904	0.369	0.384	22.926	0.351	0.385	0.176	0.268	0.168	0.190	0.202	0.256	0.191	0.276	0.233	0.235	0.214
26.621	0.350	0.356	22.134	0.359	0.369	0.183	0.237	0.179	0.202	0.196	0.249	0.154	0.258	0.258	0.279	0.177
23.142	0.367	0.393	19.807	0.379	0.394	0.182	0.233	0.177	0.218	0.241	0.237	0.211	0.221	0.237	0.209	0.264
23.463	0.362	0.405	21.795	0.383	0.444	0.181	0.247	0.173	0.197	0.175	0.285	0.179	0.204	0.209	0.260	0.168
37.663	0.371	0.366	23.678	0.346	0.461	0.183	0.253	0.166	0.195	0.212	0.229	0.230	0.266	0.228	0.212	0.257
24.647	0.341	0.390	21.200	0.354	0.447	0.158	0.210	0.188	0.225	0.238	0.248	0.146	0.232	0.269	0.267	0.245
18.916	0.361	0.388	18.853	0.334	0.407	0.191	0.250	0.167	0.200	0.236	0.263	0.237	0.253	0.210	0.271	0.221
29.487	0.404	0.419	22.360	0.387	0.424	0.155	0.218	0.180	0.240	0.230	0.216	0.222	0.226	0.247	0.254	0.244
27.277	0.397	0.358	21.849	0.398	0.355	0.183	0.232	0.167	0.219	0.192	0.226	0.194	0.256	0.208	0.205	0.212
22.004	0.485	0.466	22.547	0.386	0.382	0.222	0.275	0.223	0.243	0.238	0.320	0.235	0.269	0.250	0.292	0.279
22.723	0.323	0.382	19.205	0.392	0.461	0.186	0.237	0.182	0.212	0.202	0.227	0.193	0.239	0.224	0.244	0.248
23.801	0.340	0.385	19.279	0.381	0.388	0.168	0.223	0.184	0.199	0.214	0.164	0.158	0.200	0.225	0.253	0.202
26.785	0.313	0.405	22.794	0.378	0.497	0.163	0.198	0.167	0.180	0.198	0.243	0.212	0.215	0.194	0.254	0.222
28.945	0.383	0.390	26.185	0.404	0.383	0.200	0.248	0.166	0.215	0.222	0.206	0.212	0.245	0.200	0.190	0.184
29.880	0.345	0.366	18.785	0.360	0.466	0.167	0.285	0.179	0.247	0.237	0.253	0.254	0.227	0.205	0.236	0.240
25.270	0.333	0.366	25.666	0.355	0.415	0.197	0.272	0.170	0.230	0.282	0.243	0.289	0.261	0.250	0.273	0.260
21.686	0.378	0.413	20.307	0.377	0.432	0.197	0.240	0.178	0.205	0.253	0.252	0.235	0.231	0.251	0.226	0.247
20.591	0.456	0.394	23.777	0.395	0.436	0.240	0.310	0.225	0.236	0.301	0.323	0.273	0.280	0.234	0.295	0.272
22.991	0.379	0.379	24.881	0.411	0.449	0.155	0.257	0.186	0.195	0.174	0.263	0.216	0.185	0.191	0.226	0.224
25.793	0.345	0.433	28.104	0.346	0.443	0.161	0.235	0.179	0.225	0.202	0.261	0.259	0.271	0.223	0.236	0.237
26.907	0.291	0.436	22.930	0.431	0.441	0.191	0.200	0.174	0.204	0.233	0.237	0.193	0.251	0.247	0.236	0.167
21.833	0.332	0.392	23.300	0.286	0.404	0.173	0.230	0.185	0.190	0.246	0.269	0.251	0.204	0.208	0.249	0.211
23.396	0.442	0.353	19.121	0.343	0.466	0.222	0.295	0.226	0.242	0.254	0.346	0.290	0.292	0.258	0.275	0.291
25.054	0.355	0.382	21.110	0.353	0.416	0.191	0.248	0.190	0.191	0.228	0.220	0.222	0.230	0.227	0.215	0.221
23.195	0.373	0.357	22.673	0.352	0.404	0.154	0.225	0.170	0.200	0.202	0.214	0.235	0.229	0.222	0.296	0.210
23.568	0.353	0.428	23.656	0.405	0.454	0.167	0.237	0.161	0.214	0.180	0.191	0.197	0.220	0.183	0.212	0.209
21.622	0.370	0.420	19.256	0.382	0.472	0.201	0.260	0.222	0.203	0.306	0.289	0.212	0.245	0.251	0.346	0.322
27.479	0.342	0.384	25.372	0.363	0.379	0.171	0.212	0.159	0.206	0.217	0.265	0.238	0.229	0.234	0.254	0.167
23.061	0.346	0.315	26.668	0.381	0.364	0.218	0.195	0.157	0.192	0.164	0.213	0.196	0.193	0.176	0.248	0.213
21.534	0.357	0.415	21.603	0.379	0.456	0.175	0.238	0.168	0.215	0.163	0.247	0.205	0.206	0.192	0.241	0.257
21.181	0.466	0.452	15.378	0.561	0.426	0.222	0.267	0.272	0.250	0.230	0.324	0.226	0.281	0.279	0.292	0.243
25.467	0.293	0.366	26.411	0.399	0.428	0.179	0.232	0.173	0.206	0.167	0.241	0.252	0.202	0.206	0.268	0.236
24.120	0.375	0.421	24.508	0.339	0.382	0.168	0.245	0.164	0.193	0.216	0.217	0.216	0.260	0.164	0.245	0.218
21.362	0.365	0.368	21.060	0.325	0.426	0.208	0.257	0.190	0.200	0.251	0.212	0.239	0.215	0.199	0.227	0.200
25.014	0.373	0.422	20.366	0.362	0.396	0.178	0.243	0.158	0.191	0.212	0.210	0.176	0.236	0.226	0.206	0.207
19.480	0.377	0.379	24.653	0.419	0.441	0.165	0.253	0.167	0.203	0.248	0.293	0.169	0.255	0.207	0.280	0.271
27.140	0.395	0.420	22.680	0.441	0.437	0.171	0.260	0.171	0.190	0.238	0.225	0.200	0.257	0.232	0.226	0.308
26.630	0.388	0.437	22.364	0.362	0.388	0.170	0.253	0.167	0.222	0.192	0.213	0.249	0.202	0.207	0.229	0.212
29.246	0.335	0.406	21.843	0.406	0.419	0.173	0.258	0.174	0.196	0.196	0.320	0.208	0.235	0.208	0.212	0.266
28.178	0.382	0.392	27.762	0.378	0.384	0.181	0.270	0.181	0.200	0.174	0.254	0.229	0.229	0.191	0.223	0.252
19.398	0.388	0.398	18.355	0.357	0.401	0.199	0.280	0.238	0.263	0.318	0.304	0.192	0.288	0.269	0.296	0.277
16.146	0.420	0.459	16.639	0.376	0.503	0.235	0.313	0.260	0.270	0.363	0.274	0.358	0.272	0.276	0.252	0.305
28.648	0.397	0.380	25.907	0.357	0.400	0.180	0.232	0.168	0.207	0.193	0.242	0.211	0.200	0.157	0.252	0.195
27.691	0.314	0.462	21.928	0.413	0.417	0.177	0.240	0.182	0.177	0.171	0.187	0.196	0.258	0.231	0.202	0.234
22.507	0.360	0.435	18.215	0.342	0.464	0.178	0.203	0.197	0.210	0.246	0.259	0.201	0.231	0.239	0.245	0.221
15.726	0.406	0.395	23.470	0.336	0.465	0.215	0.267	0.196	0.233	0.227	0.217	0.218	0.290	0.214	0.252	0.277
22.412	0.337	0.374	25.031	0.397	0.382	0.211	0.280	0.184	0.242	0.247	0.243	0.192	0.252	0.249	0.250	0.217
25.679	0.358	0.423	20.317	0.364	0.414	0.153	0.247	0.177	0.179	0.190	0.203	0.189	0.226	0.238	0.201	0.213

26.440	0.359	0.413	19.826	0.354	0.418	0.182	0.225	0.152	0.208	0.206	0.247	0.229	0.234	0.185	0.278	0.201
25.505	0.372	0.418	20.442	0.333	0.410	0.173	0.237	0.217	0.183	0.166	0.217	0.165	0.192	0.186	0.228	0.207
25.763	0.423	0.440	19.283	0.334	0.391	0.203	0.268	0.192	0.241	0.277	0.298	0.264	0.273	0.267	0.310	0.317
25.079	0.417	0.397	22.927	0.330	0.452	0.216	0.272	0.198	0.196	0.218	0.266	0.202	0.230	0.283	0.308	0.232
22.757	0.340	0.406	20.927	0.393	0.420	0.148	0.255	0.173	0.209	0.176	0.201	0.197	0.229	0.196	0.250	0.210
32.701	0.338	0.383	22.888	0.375	0.450	0.178	0.213	0.190	0.236	0.207	0.230	0.248	0.279	0.248	0.258	0.166
21.715	0.348	0.369	25.742	0.385	0.403	0.168	0.247	0.159	0.201	0.208	0.233	0.191	0.183	0.206	0.250	0.221
23.067	0.290	0.451	28.283	0.352	0.389	0.219	0.260	0.215	0.250	0.278	0.274	0.260	0.260	0.261	0.284	0.236
26.175	0.412	0.363	19.747	0.358	0.438	0.216	0.278	0.210	0.247	0.287	0.238	0.273	0.287	0.221	0.276	0.277
26.636	0.470	0.434	23.661	0.340	0.349	0.193	0.253	0.213	0.250	0.259	0.263	0.242	0.279	0.235	0.258	0.257
26.083	0.409	0.381	24.628	0.346	0.381	0.209	0.273	0.187	0.210	0.226	0.303	0.213	0.247	0.279	0.243	0.246
26.945	0.355	0.388	23.564	0.455	0.492	0.184	0.262	0.180	0.229	0.201	0.250	0.238	0.284	0.233	0.292	0.224
24.951	0.332	0.385	26.047	0.346	0.443	0.168	0.230	0.170	0.214	0.181	0.182	0.190	0.229	0.230	0.255	0.236
23.746	0.384	0.367	18.495	0.379	0.435	0.204	0.267	0.208	0.260	0.233	0.265	0.242	0.249	0.243	0.266	0.229
22.292	0.361	0.411	20.427	0.380	0.388	0.163	0.247	0.161	0.202	0.210	0.210	0.242	0.276	0.243	0.275	0.251
25.583	0.392	0.397	22.465	0.392	0.445	0.180	0.240	0.156	0.194	0.199	0.231	0.214	0.237	0.181	0.222	0.221
25.368	0.326	0.384	23.099	0.394	0.436	0.146	0.217	0.202	0.212	0.209	0.252	0.245	0.256	0.196	0.268	0.221
27.931	0.397	0.353	25.716	0.381	0.441	0.200	0.240	0.169	0.237	0.273	0.242	0.227	0.246	0.256	0.289	0.242
25.457	0.386	0.378	22.048	0.322	0.430	0.166	0.247	0.165	0.199	0.247	0.233	0.254	0.215	0.240	0.258	0.322
22.270	0.343	0.409	25.010	0.342	0.455	0.198	0.273	0.210	0.249	0.284	0.248	0.258	0.227	0.247	0.285	0.302
22.586	0.364	0.356	21.693	0.380	0.427	0.150	0.233	0.181	0.232	0.199	0.238	0.196	0.226	0.237	0.271	0.219
31.761	0.372	0.457	26.740	0.342	0.486	0.248	0.255	0.173	0.201	0.230	0.250	0.200	0.265	0.221	0.281	0.232
21.404	0.371	0.379	20.741	0.361	0.424	0.178	0.230	0.184	0.208	0.239	0.238	0.189	0.256	0.202	0.238	0.242
32.271	0.361	0.328	21.298	0.363	0.374	0.172	0.213	0.176	0.180	0.158	0.272	0.220	0.250	0.239	0.269	0.215
24.869	0.456	0.427	23.680	0.394	0.463	0.221	0.243	0.185	0.232	0.329	0.259	0.254	0.251	0.252	0.253	0.273
22.069	0.341	0.380	23.773	0.316	0.403	0.173	0.242	0.173	0.189	0.192	0.211	0.212	0.263	0.237	0.226	0.242
23.693	0.394	0.408	23.000	0.304	0.437	0.223	0.272	0.183	0.190	0.187	0.273	0.213	0.203	0.244	0.255	0.239
28.041	0.381	0.423	22.029	0.327	0.417	0.187	0.228	0.185	0.195	0.224	0.234	0.195	0.256	0.156	0.291	0.203
20.271	0.327	0.356	21.627	0.395	0.447	0.188	0.230	0.179	0.249	0.188	0.217	0.191	0.217	0.218	0.241	0.215
17.741	0.398	0.355	22.477	0.361	0.490	0.199	0.267	0.218	0.266	0.299	0.211	0.337	0.210	0.316	0.359	0.294
21.054	0.389	0.392	19.646	0.387	0.424	0.203	0.258	0.184	0.186	0.211	0.220	0.201	0.237	0.180	0.259	0.231
18.932	0.419	0.452	14.293	0.384	0.433	0.202	0.297	0.215	0.248	0.233	0.274	0.313	0.273	0.347	0.256	0.256
19.870	0.415	0.395	21.677	0.381	0.463	0.183	0.213	0.182	0.195	0.173	0.234	0.240	0.226	0.226	0.242	0.189
26.382	0.353	0.379	24.895	0.421	0.401	0.177	0.260	0.185	0.238	0.201	0.227	0.186	0.223	0.234	0.247	0.203
19.363	0.377	0.409	16.183	0.373	0.405	0.258	0.297	0.272	0.251	0.266	0.263	0.327	0.286	0.264	0.289	0.248
28.601	0.377	0.337	21.319	0.367	0.413	0.177	0.238	0.175	0.180	0.200	0.225	0.177	0.191	0.209	0.245	0.281
32.689	0.440	0.407	22.715	0.355	0.410	0.183	0.240	0.170	0.230	0.211	0.188	0.176	0.221	0.264	0.259	0.274
25.805	0.349	0.445	25.329	0.404	0.377	0.186	0.298	0.173	0.209	0.221	0.231	0.216	0.244	0.265	0.243	0.229
25.302	0.343	0.377	18.551	0.422	0.473	0.174	0.283	0.207	0.238	0.261	0.336	0.295	0.272	0.286	0.290	0.249
20.158	0.365	0.414	20.086	0.376	0.381	0.146	0.218	0.176	0.188	0.219	0.244	0.188	0.240	0.210	0.243	0.272
24.015	0.359	0.374	22.619	0.361	0.437	0.173	0.307	0.179	0.241	0.217	0.223	0.208	0.275	0.235	0.229	0.242
23.414	0.375	0.382	20.400	0.357	0.434	0.237	0.238	0.256	0.229	0.319	0.238	0.260	0.269	0.260	0.281	0.265
25.743	0.386	0.438	19.911	0.400	0.407	0.177	0.210	0.193	0.219	0.226	0.262	0.186	0.213	0.214	0.260	0.211
26.979	0.425	0.445	17.204	0.425	0.490	0.225	0.312	0.217	0.245	0.299	0.288	0.261	0.248	0.302	0.280	0.238
19.741	0.405	0.397	16.162	0.431	0.559	0.206	0.283	0.206	0.259	0.325	0.329	0.322	0.319	0.315	0.308	0.243
30.016	0.328	0.410	19.460	0.380	0.390	0.160	0.278	0.183	0.190	0.205	0.227	0.216	0.195	0.239	0.239	0.226
26.011	0.410	0.411	21.192	0.401	0.429	0.204	0.272	0.194	0.249	0.246	0.281	0.270	0.354	0.299	0.268	0.311
22.847	0.359	0.443	21.765	0.343	0.446	0.214	0.253	0.182	0.249	0.216	0.254	0.244	0.217	0.235	0.322	0.253
25.199	0.416	0.341	20.078	0.438	0.460	0.220	0.290	0.251	0.213	0.231	0.336	0.286	0.349	0.259	0.374	0.273
14.444	0.407	0.408	12.711	0.441	0.436	0.213	0.318	0.208	0.258	0.352	0.287	0.265	0.217	0.283	0.395	0.317
19.060	0.377	0.385	21.341	0.371	0.423	0.212	0.282	0.233	0.221	0.241	0.200	0.245	0.267	0.261	0.255	0.277
23.996	0.381	0.381	25.758	0.269	0.432	0.190	0.213	0.196	0.216	0.197	0.217	0.202	0.203	0.190	0.189	0.249
25.754	0.344	0.400	21.676	0.387	0.379	0.178	0.215	0.193	0.195	0.205	0.247	0.215	0.237	0.201	0.204	0.226
28.406	0.400	0.440	28.845	0.347	0.454	0.185	0.220	0.167	0.205	0.200	0.252	0.196	0.257	0.228	0.255	0.243
20.761	0.461	0.407	13.977	0.439	0.437	0.244	0.285	0.220	0.270	0.250	0.249	0.343	0.291	0.302	0.341	0.288
25.459	0.361	0.408	19.167	0.311	0.414	0.175	0.240	0.220	0.205	0.203	0.222	0.219	0.214	0.231	0.268	0.200
20.300	0.406	0.416	28.862	0.371	0.433	0.221	0.263	0.200	0.242	0.270	0.279	0.259	0.236	0.272	0.248	0.240
26.618	0.337	0.353	21.625	0.364	0.458	0.197	0.258	0.184	0.209	0.243	0.248	0.183	0.222	0.241	0.298	0.256
22.685	0.411	0.415	22.623	0.378	0.442	0.225	0.287	0.212	0.242	0.261	0.307	0.256	0.263	0.218	0.352	0.328
25.605	0.434	0.362	23.120	0.393	0.449	0.228	0.333	0.222	0.236	0.261	0.295	0.282	0.297	0.330	0.324	0.320
20.423	0.408	0.481	15.391	0.509	0.540	0.253	0.303	0.207	0.266	0.307	0.326	0.298	0.296	0.281	0.345	0.289
24.348	0.459	0.420	19.596	0.377	0.412	0.217	0.292	0.218	0.245	0.298	0.297	0.306	0.226	0.321	0.347	0.264
15.920	0.493	0.388	18.901	0.567	0.532	0.243	0.290	0.225	0.259	0.254	0.308	0.318	0.321	0.270	0.359	0.337
25.985	0.323	0.413	22.149	0.398	0.423	0.196	0.260	0.183	0.212	0.236	0.293	0.250	0.242	0.214	0.266	0.248

17.079	0.438	0.472	20.499	0.420	0.427	0.223	0.303	0.216	0.240	0.359	0.318	0.305	0.284	0.346	0.311	0.288
17.212	0.482	0.493	8.445	0.455	0.468	0.283	0.283	0.230	0.266	0.257	0.366	0.305	0.296	0.291	0.344	0.354
16.747	0.488	0.527	10.463	0.502	0.518	0.230	0.328	0.271	0.262	0.311	0.324	0.312	0.348	0.273	0.331	0.387
18.244	0.511	0.455	12.111	0.474	0.500	0.214	0.307	0.283	0.260	0.317	0.347	0.324	0.284	0.360	0.286	0.325
12.030	0.456	0.431	9.362	0.377	0.448	0.223	0.298	0.244	0.236	0.207	0.256	0.270	0.325	0.338	0.369	0.293
19.401	0.440	0.407	13.553	0.467	0.491	0.216	0.303	0.231	0.207	0.299	0.312	0.430	0.278	0.285	0.281	0.294
27.410	0.361	0.442	19.875	0.364	0.418	0.198	0.280	0.196	0.246	0.284	0.270	0.250	0.267	0.244	0.259	0.290
26.676	0.363	0.336	21.963	0.372	0.407	0.148	0.202	0.154	0.203	0.225	0.233	0.221	0.216	0.232	0.242	0.219
9.447	0.470	0.405	11.592	0.426	0.577	0.226	0.293	0.226	0.275	0.346	0.272	0.340	0.370	0.273	0.342	0.336
17.277	0.450	0.421	20.653	0.375	0.445	0.250	0.287	0.221	0.239	0.277	0.269	0.290	0.247	0.360	0.313	0.292
29.213	0.385	0.367	20.183	0.406	0.445	0.192	0.272	0.225	0.245	0.230	0.274	0.239	0.239	0.215	0.265	0.262
17.365	0.511	0.546	9.012	0.507	0.530	0.222	0.308	0.239	0.271	0.348	0.335	0.291	0.313	0.305	0.261	0.387
28.047	0.391	0.386	22.550	0.393	0.414	0.197	0.305	0.245	0.236	0.250	0.282	0.253	0.267	0.269	0.295	0.292
23.660	0.413	0.429	12.418	0.528	0.403	0.198	0.297	0.196	0.236	0.228	0.295	0.326	0.311	0.326	0.302	0.374
22.891	0.433	0.390	16.382	0.396	0.469	0.218	0.303	0.203	0.248	0.248	0.246	0.311	0.231	0.234	0.261	0.310
24.708	0.425	0.424	22.681	0.371	0.432	0.235	0.257	0.195	0.256	0.326	0.310	0.204	0.270	0.278	0.305	0.230
10.893	0.444	0.452	21.160	0.418	0.467	0.233	0.325	0.236	0.246	0.283	0.303	0.316	0.271	0.360	0.332	0.355
18.855	0.415	0.446	20.831	0.463	0.487	0.215	0.317	0.220	0.259	0.284	0.342	0.263	0.252	0.304	0.253	0.210
16.417	0.559	0.418	9.749	0.511	0.577	0.233	0.302	0.236	0.282	0.349	0.293	0.270	0.336	0.380	0.319	0.311
10.009	0.516	0.472	9.883	0.529	0.499	0.233	0.292	0.214	0.279	0.267	0.415	0.371	0.370	0.259	0.331	0.408
25.449	0.300	0.401	27.951	0.386	0.416	0.187	0.217	0.163	0.194	0.205	0.241	0.218	0.263	0.214	0.237	0.203
18.369	0.367	0.442	27.186	0.349	0.443	0.186	0.258	0.205	0.205	0.257	0.267	0.175	0.244	0.224	0.263	0.272
17.707	0.486	0.449	10.858	0.425	0.475	0.228	0.285	0.239	0.266	0.309	0.322	0.301	0.262	0.308	0.301	0.290
15.346	0.441	0.438	7.804	0.490	0.508	0.247	0.280	0.232	0.279	0.283	0.311	0.378	0.248	0.318	0.331	0.383
11.507	0.492	0.453	12.450	0.334	0.450	0.228	0.313	0.207	0.269	0.304	0.281	0.290	0.288	0.352	0.361	0.351
12.484	0.477	0.483	12.123	0.517	0.601	0.224	0.298	0.222	0.242	0.278	0.348	0.333	0.265	0.299	0.362	0.334

kftpv20	kftpp40	kftppv40	kftpp60	kftpv60	EEMVC	EERTD	EFMVC	EFRTD	KEMVC	KERTD	KFMVC	KFRTD	PFMVC	PFRTD	DFMVC
0.248	0.260	0.277	0.295	0.278	85.382	253.326	73.210	#######	244.907	#######	138.807	435.185	42.712	202.734	24.777
0.267	0.274	0.251	0.233	0.257	100.259	220.633	67.122	#######	222.614	830.606	125.204	427.064	40.512	159.220	29.388
0.238	0.272	0.264	0.339	0.242	95.122	256.072	92.190	#######	240.355	#######	117.260	584.924	48.521	191.534	30.314
0.264	0.253	0.259	0.303	0.234	93.344	269.013	77.011	#######	228.693	#######	134.259	474.359	42.395	224.297	36.997
0.285	0.272	0.293	0.242	0.261	91.794	234.986	65.035	#######	201.966	716.602	118.486	436.710	33.296	151.584	32.648
0.270	0.228	0.328	0.323	0.253	93.681	244.663	79.552	#######	248.913	#######	148.370	504.856	38.692	187.013	27.773
0.292	0.257	0.273	0.245	0.256	95.896	241.141	73.586	#######	185.823	#######	120.290	433.535	35.978	133.712	27.849
0.203	0.267	0.259	0.258	0.272	87.639	250.622	75.998	#######	231.709	#######	130.871	418.968	36.967	180.417	28.392
0.233	0.226	0.215	0.291	0.263	93.109	231.552	72.207	#######	223.250	904.247	134.150	491.008	38.709	122.082	31.529
0.244	0.257	0.309	0.253	0.269	87.962	235.794	68.103	#######	220.651	#######	118.690	411.945	43.315	151.988	34.665
0.267	0.272	0.285	0.315	0.246	93.319	222.331	78.602	#######	239.808	860.573	129.983	345.070	38.581	165.076	28.244
0.229	0.279	0.249	0.274	0.302	95.895	229.925	67.322	#######	240.164	#######	129.933	343.542	40.987	203.461	27.690
0.229	0.206	0.211	0.292	0.265	91.370	243.630	69.604	#######	245.103	#######	131.783	411.420	33.621	220.446	33.966
0.279	0.191	0.270	0.352	0.240	93.801	254.244	70.329	#######	225.765	#######	139.271	347.862	42.851	146.048	26.896
0.277	0.265	0.236	0.306	0.291	89.205	236.595	67.564	#######	227.954	#######	147.619	410.756	39.484	198.040	30.716
0.240	0.278	0.275	0.279	0.262	86.284	273.475	82.367	#######	222.817	#######	135.870	391.051	42.329	213.166	28.951
0.230	0.245	0.200	0.256	0.262	93.415	235.570	71.407	#######	217.624	#######	146.665	375.673	36.170	195.815	34.909
0.251	0.229	0.283	0.285	0.304	93.394	262.716	77.135	#######	239.068	#######	131.555	635.570	44.284	217.775	32.360
0.259	0.251	0.261	0.332	0.220	96.270	237.563	69.847	#######	247.643	#######	126.612	404.184	37.326	233.419	31.085
0.240	0.205	0.272	0.282	0.237	95.819	211.688	77.913	#######	244.270	#######	134.279	425.058	44.746	194.200	33.981
0.287	0.203	0.287	0.367	0.275	88.870	225.613	83.099	#######	250.640	#######	130.541	343.646	40.850	216.261	31.500
0.231	0.260	0.235	0.255	0.219	97.245	244.967	72.005	#######	248.786	932.357	131.838	629.098	42.565	196.743	27.185
0.217	0.265	0.339	0.282	0.293	93.193	239.449	77.641	#######	255.920	#######	140.773	536.608	35.742	169.059	26.852
0.233	0.232	0.245	0.363	0.228	91.837	262.234	84.532	#######	240.130	#######	151.273	480.814	40.873	214.452	33.162
0.286	0.264	0.337	0.352	0.299	90.050	243.977	66.981	#######	152.707	650.914	101.814	439.755	30.600	138.052	26.323
0.250	0.256	0.259	0.306	0.278	97.557	244.891	73.323	#######	252.505	#######	157.714	444.336	41.507	189.479	29.909
0.203	0.207	0.265	0.270	0.223	92.916	255.551	75.554	#######	238.501	#######	128.400	462.503	33.911	184.034	27.442
0.285	0.254	0.226	0.279	0.264	97.605	235.291	77.100	#######	228.647	#######	107.925	450.970	40.724	145.553	33.689
0.244	0.260	0.265	0.224	0.286	94.554	224.002	73.407	#######	229.697	#######	122.904	369.720	40.160	216.393	32.567
0.267	0.210	0.346	0.282	0.219	92.479	233.793	71.294	#######	233.441	#######	130.594	438.552	38.351	162.704	25.259
0.202	0.317	0.278	0.243	0.294	95.270	275.744	67.196	#######	164.472	791.559	102.539	368.755	37.461	136.426	28.835
0.201	0.266	0.289	0.287	0.264	95.047	253.068	80.968	#######	244.230	#######	130.133	347.789	41.427	203.494	25.163
0.339	0.338	0.314	0.319	0.288	90.748	203.530	71.971	#######	174.739	636.324	93.260	388.816	36.936	129.056	14.370
0.244	0.260	0.303	0.234	0.259	96.040	255.265	69.288	#######	258.805	#######	139.007	423.789	42.399	190.534	26.265
0.250	0.209	0.283	0.221	0.281	86.361	254.195	82.192	#######	238.817	#######	133.294	416.948	42.750	180.261	25.913
0.236	0.260	0.228	0.239	0.235	94.817	257.246	79.068	#######	218.738	860.051	138.455	403.330	32.733	231.960	33.006
0.274	0.252	0.302	0.328	0.279	94.927	279.642	77.227	#######	208.978	#######	140.560	414.695	37.198	166.842	26.053
0.333	0.310	0.333	0.342	0.308	82.051	232.214	67.335	#######	167.602	727.017	98.765	373.420	40.978	133.804	22.638
0.257	0.249	0.261	0.230	0.235	103.590	250.856	66.087	#######	223.838	#######	140.979	452.859	33.261	198.660	33.614
0.240	0.241	0.299	0.276	0.247	101.087	252.103	78.541	#######	209.898	#######	141.431	512.596	39.719	162.614	30.605
0.227	0.239	0.238	0.311	0.285	94.094	265.768	81.719	#######	233.964	#######	126.798	412.738	35.621	210.405	28.683
0.297	0.304	0.286	0.274	0.254	92.690	256.895	73.860	#######	187.195	612.378	110.276	371.270	39.767	164.067	26.836
0.294	0.228	0.232	0.264	0.304	91.703	261.988	81.059	#######	242.361	#######	133.311	408.598	43.761	185.227	31.768
0.247	0.253	0.241	0.290	0.281	94.218	260.364	77.054	#######	236.719	#######	140.964	529.527	34.271	212.210	32.474
0.190	0.214	0.243	0.297	0.242	106.873	218.489	82.908	#######	237.329	#######	124.633	401.416	45.376	238.873	22.486
0.340	0.355	0.337	0.376	0.271	74.298	192.136	61.542	#######	162.881	747.559	94.023	412.468	33.264	137.336	23.155
0.240	0.233	0.243	0.320	0.213	95.756	268.194	71.469	#######	253.359	#######	121.343	505.547	39.524	186.821	34.939
0.228	0.249	0.226	0.270	0.214	92.022	260.350	71.267	#######	236.025	#######	130.172	432.722	36.857	190.273	35.039
0.261	0.240	0.275	0.302	0.268	87.137	247.734	71.886	#######	238.255	#######	124.602	656.642	39.196	219.283	26.878
0.209	0.234	0.252	0.284	0.276	93.068	260.653	70.190	#######	251.495	#######	131.139	441.307	35.177	202.500	30.408
0.290	0.231	0.285	0.350	0.297	93.518	254.725	76.074	#######	233.929	981.151	133.089	539.107	40.308	150.748	34.717
0.246	0.243	0.233	0.290	0.248	90.256	234.631	76.225	#######	249.387	#######	121.543	369.168	42.679	172.795	31.895
0.266	0.259	0.262	0.282	0.260	98.524	242.692	75.856	#######	237.893	#######	132.537	493.908	40.329	153.015	31.561
0.260	0.204	0.325	0.331	0.195	92.722	242.140	80.218	#######	213.787	880.131	114.888	456.325	39.313	160.567	21.039
0.282	0.241	0.285	0.245	0.301	94.394	274.189	76.161	#######	250.614	#######	130.975	401.913	38.964	175.188	28.391
0.300	0.328	0.296	0.286	0.296	90.127	231.918	69.298	#######	191.016	800.659	107.190	420.933	39.630	123.778	31.561
0.383	0.315	0.343	0.418	0.276	81.613	190.149	60.854	#######	157.687	562.475	92.685	493.111	34.435	138.111	22.725
0.238	0.275	0.258	0.274	0.289	83.672	254.706	67.235	#######	249.033	#######	131.071	440.561	36.859	179.520	28.960
0.254	0.209	0.266	0.299	0.273	96.564	245.056	78.105	#######	219.221	#######	133.966	436.232	34.523	170.321	26.744
0.244	0.277	0.241	0.360	0.337	95.275	246.675	72.914	#######	277.720	989.010	139.082	351.553	32.598	161.243	26.538
0.289	0.263	0.245	0.375	0.292	91.279	207.160	67.589	#######	183.395	686.310	121.921	425.925	34.227	123.798	22.202
0.217	0.228	0.282	0.321	0.261	93.235	230.834	74.457	#######	238.948	854.451	113.521	418.105	39.884	147.729	33.283
0.223	0.258	0.300	0.297	0.223	97.995	247.620	71.530	#######	258.325	#######	124.329	468.660	33.177	207.926	29.694

0.244	0.251	0.209	0.256	0.261	91.010	246.171	72.395	######	239.140	######	157.264	414.646	38.954	203.756	26.607
0.220	0.280	0.269	0.293	0.268	92.376	252.142	79.499	######	241.349	######	127.870	257.173	34.402	194.626	29.035
0.347	0.351	0.279	0.284	0.250	89.670	236.199	71.224	######	186.553	801.359	99.348	462.181	36.703	144.337	29.609
0.256	0.301	0.260	0.275	0.260	84.601	240.413	83.765	######	208.967	######	128.137	474.136	39.152	131.259	21.458
0.219	0.268	0.237	0.259	0.245	95.594	221.955	75.011	######	233.687	######	125.967	497.456	37.853	203.764	29.106
0.270	0.238	0.332	0.237	0.323	90.673	230.916	76.362	######	244.610	######	127.018	386.685	40.322	217.835	26.233
0.222	0.285	0.262	0.313	0.262	104.785	250.775	76.902	######	246.418	######	126.415	487.079	43.206	241.030	31.919
0.309	0.309	0.315	0.315	0.250	89.337	233.506	77.759	######	188.938	726.135	118.801	392.764	37.180	156.823	30.999
0.270	0.279	0.261	0.267	0.262	94.835	215.750	76.534	######	205.880	825.716	119.569	432.734	39.169	180.996	33.010
0.270	0.323	0.146	0.226	0.222	87.155	211.299	75.273	######	192.724	968.963	113.730	499.767	32.660	149.050	25.614
0.244	0.270	0.324	0.250	0.260	90.256	249.519	72.982	######	224.449	902.569	131.767	406.534	39.236	146.965	18.131
0.258	0.291	0.302	0.361	0.286	86.768	247.974	72.975	######	255.053	674.498	126.193	427.013	34.655	137.827	25.206
0.248	0.260	0.277	0.295	0.278	85.382	253.326	73.210	######	244.907	######	138.807	435.185	42.712	202.734	24.777
0.208	0.372	0.291	0.277	0.280	83.093	267.080	74.999	######	209.789	######	126.458	358.109	39.329	149.257	27.846
0.180	0.212	0.303	0.288	0.279	92.149	224.207	81.304	######	227.786	######	155.623	531.675	42.251	208.504	29.737
0.274	0.190	0.197	0.313	0.289	99.836	249.027	73.611	######	255.072	######	151.017	361.800	38.732	223.122	31.236
0.287	0.296	0.311	0.236	0.241	100.475	240.652	74.838	######	263.280	######	134.451	496.914	39.875	166.070	24.947
0.218	0.225	0.288	0.274	0.230	97.892	247.491	63.759	######	254.448	######	122.289	450.343	38.613	163.755	28.001
0.195	0.249	0.248	0.283	0.262	104.190	215.106	62.925	######	223.522	988.964	138.397	476.690	38.514	152.223	29.121
0.264	0.273	0.231	0.268	0.296	91.772	229.468	65.723	######	207.343	706.793	128.740	418.787	36.826	150.185	26.279
0.306	0.293	0.298	0.334	0.254	91.225	230.437	80.480	######	232.194	######	135.142	482.798	42.374	195.108	31.710
0.277	0.271	0.280	0.321	0.277	89.874	245.650	71.226	######	210.414	928.392	131.124	472.747	37.863	180.024	28.469
0.253	0.289	0.263	0.345	0.300	90.099	246.727	70.761	######	247.031	967.256	137.857	614.917	38.988	157.313	25.633
0.269	0.226	0.277	0.282	0.333	89.789	252.610	81.170	######	250.684	######	138.619	445.852	41.637	153.643	27.430
0.307	0.302	0.267	0.284	0.278	90.903	255.351	74.677	######	199.876	976.380	101.757	492.865	35.364	142.394	33.609
0.221	0.238	0.279	0.225	0.225	91.505	275.582	65.893	######	259.513	######	145.859	539.470	38.512	192.242	29.475
0.259	0.251	0.307	0.285	0.297	95.887	239.396	73.399	######	199.019	981.473	132.485	393.796	39.580	153.346	20.836
0.257	0.268	0.278	0.291	0.356	95.085	261.479	74.732	######	233.058	######	117.819	333.408	35.936	175.333	26.039
0.272	0.248	0.304	0.302	0.247	99.701	240.884	81.327	######	247.584	886.405	120.815	416.970	37.533	182.414	27.977
0.328	0.264	0.321	0.268	0.340	81.049	245.690	63.196	######	181.970	632.405	94.492	576.208	35.570	146.427	14.370
0.231	0.226	0.302	0.311	0.257	105.772	249.818	74.157	######	254.281	882.615	126.163	546.713	36.769	172.011	27.086
0.265	0.319	0.334	0.387	0.351	83.721	204.082	57.016	######	143.555	403.435	80.984	345.727	29.892	143.797	22.882
0.224	0.290	0.296	0.278	0.290	104.355	250.011	73.203	######	223.178	######	129.825	564.529	40.880	180.224	29.507
0.243	0.213	0.219	0.241	0.289	94.883	252.132	75.196	######	247.549	######	132.080	481.620	41.935	153.994	31.268
0.346	0.358	0.340	0.289	0.257	87.894	233.971	66.252	######	183.239	604.367	105.523	373.962	37.487	129.626	23.407
0.268	0.263	0.236	0.304	0.228	94.102	232.806	79.305	######	225.505	######	127.147	552.779	41.193	179.822	28.662
0.266	0.257	0.238	0.277	0.241	90.900	248.355	79.031	######	222.660	848.348	130.736	495.247	39.430	166.964	29.555
0.225	0.205	0.251	0.355	0.278	89.416	219.071	64.454	######	242.345	881.858	137.101	404.302	36.032	153.023	27.590
0.340	0.310	0.281	0.268	0.312	88.290	252.121	68.026	######	193.337	761.041	118.591	492.914	39.547	145.270	30.606
0.223	0.226	0.271	0.282	0.241	102.038	235.142	72.261	######	238.786	######	124.248	395.136	35.921	203.663	27.358
0.224	0.253	0.262	0.282	0.274	100.602	231.774	64.504	######	235.127	813.383	135.487	408.047	30.728	145.655	20.951
0.288	0.290	0.295	0.268	0.265	97.275	258.407	73.828	######	185.067	857.804	100.675	338.179	34.645	171.192	27.546
0.228	0.301	0.274	0.312	0.239	91.666	247.353	72.336	######	230.874	######	122.489	366.671	33.190	196.864	31.971
0.307	0.303	0.323	0.233	0.270	87.274	229.191	74.666	######	152.045	749.574	93.804	300.862	37.678	150.839	27.097
0.315	0.345	0.364	0.410	0.301	85.222	198.229	68.205	######	133.996	704.833	100.247	314.256	39.516	118.141	26.066
0.233	0.245	0.241	0.200	0.270	97.534	244.458	68.129	######	226.420	######	140.530	396.868	41.174	197.634	27.566
0.228	0.321	0.256	0.274	0.282	94.573	237.841	73.858	######	163.710	583.146	99.867	424.268	40.743	147.451	29.391
0.255	0.369	0.286	0.216	0.347	86.836	253.664	70.589	######	204.230	843.220	129.804	345.047	39.265	152.861	24.156
0.311	0.384	0.336	0.377	0.338	89.465	232.940	70.609	######	173.869	763.472	104.522	299.924	28.881	152.196	23.767
0.354	0.336	0.285	0.273	0.272	83.617	199.387	61.254	######	157.362	440.527	89.417	240.097	36.546	136.564	16.000
0.273	0.360	0.235	0.257	0.262	97.175	273.185	68.171	######	200.059	840.359	132.642	383.188	34.359	151.119	27.376
0.291	0.254	0.260	0.223	0.285	102.345	264.334	82.078	######	248.623	######	142.947	375.679	41.494	164.455	30.052
0.255	0.304	0.261	0.327	0.371	99.347	247.304	80.485	######	244.236	######	146.628	453.490	35.804	172.505	29.840
0.249	0.251	0.310	0.251	0.205	96.289	256.744	80.640	######	222.468	717.547	136.260	436.984	44.900	158.173	28.039
0.335	0.353	0.336	0.499	0.351	82.361	162.309	51.044	######	165.291	740.793	95.579	443.853	26.081	115.114	19.234
0.216	0.232	0.221	0.305	0.284	101.941	250.429	80.931	######	221.134	######	127.795	386.893	42.601	199.684	28.147
0.255	0.339	0.250	0.325	0.258	85.829	245.954	72.332	######	186.137	926.960	113.709	343.531	32.110	163.255	23.179
0.297	0.339	0.251	0.299	0.278	97.376	260.993	78.506	######	171.403	803.629	116.604	548.475	36.294	140.489	28.357
0.289	0.301	0.299	0.330	0.307	91.788	227.292	61.372	######	171.605	904.901	86.220	451.842	40.492	134.853	27.217
0.280	0.305	0.359	0.346	0.311	91.836	224.887	69.501	######	173.408	734.680	94.322	290.956	37.618	150.995	24.840
0.327	0.303	0.330	0.247	0.265	74.305	193.501	62.428	######	149.136	557.823	96.754	501.168	30.878	133.409	27.041
0.290	0.346	0.365	0.296	0.297	85.887	226.251	69.154	######	166.906	660.063	103.104	409.807	39.793	143.222	26.364
0.242	0.359	0.329	0.359	0.341	87.454	182.066	59.744	######	152.520	546.622	94.403	302.664	36.006	162.380	15.019
0.280	0.237	0.316	0.284	0.307	98.730	235.861	76.076	######	227.330	855.924	117.821	437.451	40.616	175.397	28.802

0.270	0.340	0.301	0.373	0.319	81.845	192.018	75.016	######	164.184	684.336	94.127	189.608	30.075	156.072	30.047
0.372	0.378	0.369	0.398	0.352	72.728	124.062	61.396	######	157.505	667.175	81.213	272.941	25.095	99.866	14.890
0.284	0.341	0.365	0.412	0.327	73.010	157.925	61.976	######	125.322	491.274	92.906	357.766	26.808	133.445	10.251
0.334	0.345	0.284	0.428	0.426	73.675	171.494	53.732	######	143.577	625.476	86.542	364.387	22.373	136.283	15.739
0.364	0.374	0.308	0.389	0.355	79.581	162.025	55.925	######	160.294	482.189	101.298	348.909	30.871	146.991	17.363
0.281	0.314	0.235	0.418	0.310	71.757	167.328	54.470	######	143.768	564.374	104.757	477.179	28.308	120.445	19.923
0.269	0.323	0.251	0.270	0.306	88.378	242.088	71.929	######	203.884	900.624	121.300	441.148	39.222	150.945	25.941
0.216	0.225	0.238	0.264	0.272	92.459	223.809	74.420	######	238.721	######	137.087	474.220	38.522	189.192	28.147
0.316	0.392	0.361	0.339	0.463	73.800	188.019	45.793	######	147.993	519.804	85.155	314.064	19.365	95.043	13.903
0.326	0.347	0.283	0.355	0.348	83.680	241.582	72.675	######	167.684	596.787	108.334	463.991	37.213	183.040	23.025
0.293	0.255	0.293	0.223	0.233	82.715	235.939	73.362	######	201.143	######	120.739	437.488	34.221	124.750	32.643
0.280	0.365	0.326	0.383	0.343	67.408	143.982	59.006	######	127.305	441.144	100.480	383.077	34.757	117.048	12.905
0.267	0.294	0.278	0.271	0.310	98.659	220.684	82.508	######	179.270	947.684	107.898	478.671	36.198	154.430	32.957
0.271	0.301	0.279	0.379	0.304	79.803	197.034	51.517	######	142.935	572.269	100.435	559.217	33.862	134.536	24.672
0.300	0.324	0.353	0.285	0.358	71.880	195.195	61.961	######	140.466	465.629	101.120	393.349	30.203	166.012	25.306
0.262	0.312	0.274	0.291	0.288	98.663	247.284	66.990	######	157.578	723.880	102.970	362.535	38.250	142.601	30.828
0.328	0.310	0.329	0.324	0.420	85.286	165.688	56.181	######	155.180	566.276	101.390	462.548	29.345	119.405	15.404
0.297	0.359	0.277	0.374	0.369	84.673	199.696	59.009	######	163.772	543.442	89.773	377.764	34.659	137.468	23.855
0.315	0.299	0.312	0.457	0.314	67.687	148.735	59.617	######	144.531	457.926	90.033	308.323	21.237	122.904	19.851
0.385	0.366	0.379	0.393	0.344	81.522	158.019	60.986	######	134.131	452.903	86.968	271.921	23.187	103.027	18.597
0.223	0.286	0.242	0.280	0.255	90.590	273.996	80.019	######	237.499	975.039	140.176	428.246	35.649	201.679	21.299
0.293	0.296	0.277	0.303	0.302	83.370	232.558	69.321	######	231.811	######	133.615	442.714	35.452	154.359	23.300
0.345	0.365	0.303	0.442	0.381	77.678	174.872	50.126	######	145.963	533.335	99.621	340.896	30.574	135.785	20.840
0.387	0.410	0.375	0.383	0.379	72.889	159.631	48.884	######	113.621	590.640	85.863	291.296	29.758	126.289	16.845
0.321	0.328	0.370	0.375	0.392	89.491	137.684	55.854	######	128.916	619.251	97.487	268.709	32.406	134.221	16.936
0.253	0.318	0.331	0.471	0.358	64.968	162.602	59.187	######	136.407	542.407	103.594	348.544	25.321	127.697	17.845

DFRTD	EE60degPT	EF60deg	EE240degPT	EF240degPT	KE60degPT	KE240degPT	KF60degpt	KF240degPT	PF60PT	DF240PT	EEPPUL	EEPVUL
118.962	83.698	59.659	64.710	48.050	156.452	108.261	115.277	97.990	30.532	26.740	48.385	247.561
109.475	75.998	60.477	38.873	38.318	129.575	74.185	94.101	69.546	29.801	23.040	38.785	204.370
99.154	79.431	66.288	69.679	48.015	147.990	111.687	109.077	85.100	27.837	17.570	60.422	263.724
119.890	87.002	53.838	49.641	45.423	152.565	102.313	115.654	96.905	31.370	17.870	70.323	244.274
105.346	80.831	58.744	48.965	43.966	142.948	61.527	102.021	65.697	33.783	24.100	42.444	224.151
117.800	74.183	54.790	62.131	47.357	149.787	113.623	111.721	83.112	40.589	25.000	49.057	192.806
99.737	88.151	61.405	48.694	41.436	144.333	77.132	100.399	78.284	30.188	20.200	30.795	217.974
117.397	81.248	57.834	53.293	44.846	154.052	103.276	115.706	89.518	29.810	19.180	59.374	237.856
102.828	67.857	57.534	45.757	43.788	127.850	104.194	116.465	62.461	38.046	21.280	61.251	217.604
103.642	69.710	66.080	49.873	41.165	125.713	88.290	90.704	78.266	32.889	22.950	59.259	257.643
94.928	70.458	61.664	56.270	41.343	133.200	77.338	98.610	69.153	30.654	20.720	51.909	238.016
98.283	89.639	56.140	58.777	50.185	138.614	88.787	123.919	85.121	38.405	24.350	54.355	276.561
123.530	74.123	59.127	55.932	46.904	148.999	127.490	125.171	98.648	36.616	21.690	54.676	258.491
99.881	74.767	52.902	52.270	46.007	119.173	112.251	115.123	64.568	32.031	18.360	58.228	252.767
134.885	78.276	59.994	47.867	45.767	152.277	129.800	113.545	95.003	38.138	23.200	63.325	249.804
96.674	84.877	57.437	63.132	44.521	141.518	115.330	120.616	96.781	41.089	22.240	65.114	257.300
112.154	85.526	59.430	62.239	45.298	131.604	119.309	112.133	88.176	37.628	20.930	69.326	273.336
111.742	70.836	65.582	62.865	44.355	145.865	134.088	107.742	82.041	33.869	18.600	56.808	216.508
107.743	82.883	54.900	53.918	41.028	161.034	127.810	114.126	92.922	36.110	19.830	75.193	290.351
117.244	82.227	57.538	54.888	43.742	134.893	121.119	108.256	92.501	35.382	27.170	49.588	290.078
106.970	80.391	66.030	61.981	46.316	172.357	115.244	114.912	83.189	38.886	22.480	49.707	206.885
101.234	84.468	61.155	57.003	48.246	137.263	114.145	111.117	93.396	38.366	19.860	65.849	238.346
108.541	76.517	62.007	64.463	48.074	126.173	106.519	107.529	63.390	33.679	24.890	60.689	270.630
113.590	72.117	55.423	54.259	43.819	144.460	106.137	122.982	96.653	34.843	17.540	57.335	243.486
90.695	53.681	50.623	30.128	41.101	119.286	76.148	88.083	62.198	26.237	20.650	45.362	186.031
129.686	77.225	63.795	71.568	49.492	135.577	124.672	120.750	95.658	36.038	22.760	63.789	205.664
118.906	80.894	60.135	57.367	44.460	166.927	128.770	116.675	94.059	35.483	26.450	58.016	289.430
129.667	78.792	58.621	59.083	47.210	164.453	131.335	113.671	83.991	32.751	17.040	60.805	256.469
112.084	78.907	59.622	64.705	49.042	148.536	134.134	111.366	91.019	33.051	18.640	70.498	282.904
75.476	83.357	51.444	41.596	37.357	132.168	119.679	104.654	65.048	35.814	23.080	57.086	191.376
100.782	66.663	55.658	48.485	40.903	128.102	81.196	96.261	49.620	39.400	19.340	50.900	218.318
118.932	83.728	62.193	60.664	42.677	165.932	108.977	113.718	93.570	32.349	23.030	78.135	271.284
102.776	62.970	52.574	39.973	36.206	105.525	80.719	84.317	58.862	29.764	14.690	33.560	200.932
108.166	69.110	53.792	52.551	41.484	141.510	102.311	112.212	102.255	33.217	25.650	54.088	249.054
119.056	84.421	42.832	52.964	44.838	165.461	98.302	110.449	92.912	34.241	18.680	71.268	300.038
98.437	83.321	59.768	52.989	39.547	146.099	126.733	107.180	80.447	33.370	23.950	54.272	237.135
116.993	71.008	60.549	53.608	50.371	124.788	101.294	107.135	80.923	35.302	19.910	68.830	248.452
94.836	60.983	56.959	33.776	36.558	105.578	100.378	85.082	60.728	35.963	18.550	39.701	191.982
118.578	85.909	58.953	47.917	36.701	139.112	129.000	121.596	92.399	31.200	20.380	45.592	271.061
105.571	81.746	56.402	45.251	45.417	138.267	125.830	108.130	68.132	32.847	19.180	57.298	247.324
109.062	83.386	47.837	48.523	46.724	174.333	132.062	103.994	94.674	42.775	14.940	60.559	236.830
97.333	67.178	57.692	35.798	40.475	122.815	83.454	102.928	59.766	38.695	18.920	40.291	176.205
113.672	78.894	68.552	52.974	40.736	121.975	121.808	117.774	80.067	36.271	17.420	76.959	258.955
108.032	78.327	61.340	59.686	47.608	136.138	112.123	110.930	89.143	37.096	25.410	48.026	291.408
120.855	73.310	55.259	47.667	42.431	172.061	97.926	111.905	94.098	36.521	16.100	65.147	266.348
68.362	56.958	51.571	36.619	35.430	98.210	102.000	78.772	60.398	25.534	20.270	35.043	163.856
111.669	74.106	70.929	59.368	35.697	159.029	124.840	114.508	88.619	40.585	16.810	68.227	247.541
114.629	82.814	62.480	52.728	38.623	156.829	119.418	120.273	84.306	32.489	22.870	55.239	287.785
104.456	76.286	59.879	62.093	43.811	140.011	117.362	105.741	66.462	32.380	17.310	59.324	275.359
112.682	85.294	52.410	62.786	40.171	135.588	124.361	115.051	89.634	36.474	20.500	57.613	309.416
90.070	83.442	54.384	48.234	38.946	145.112	127.000	104.535	62.538	33.082	18.070	67.524	256.489
109.800	84.165	63.808	54.678	45.820	147.698	105.756	108.900	81.642	38.100	24.590	62.515	244.615
94.387	78.224	63.990	51.900	45.046	110.180	92.016	114.145	71.111	32.424	21.680	57.429	241.351
103.283	68.702	61.242	45.585	43.560	126.812	82.702	94.975	67.881	28.760	21.830	68.220	239.603
115.052	79.777	51.780	57.649	47.207	139.088	94.721	103.469	61.157	31.243	16.680	69.001	294.312
97.524	71.453	59.629	54.737	37.738	101.064	110.271	98.027	49.951	32.306	21.990	39.810	180.297
89.528	55.526	59.359	39.838	39.830	94.960	88.536	86.309	52.989	30.667	16.890	46.564	189.761
105.457	82.313	62.687	57.395	44.304	157.563	111.322	116.885	89.026	34.826	24.790	62.804	257.333
118.344	77.254	59.934	54.823	47.261	139.315	114.114	110.969	87.864	34.288	25.580	55.054	244.721
99.929	79.158	54.274	54.280	50.972	179.370	79.379	100.725	72.912	36.144	21.110	54.996	238.429
98.314	79.597	58.132	39.816	36.551	93.927	70.416	95.893	74.560	29.518	18.850	47.430	242.656
117.429	82.185	59.070	46.916	43.567	130.283	71.270	96.643	73.693	33.590	23.280	62.239	242.097
107.063	84.814	61.192	61.884	49.382	169.525	136.612	108.091	94.091	26.063	16.500	58.434	309.104

113.509	75.499	56.915	54.741	46.428	150.174	89.680	113.735	96.975	37.206	23.800	50.613	255.810
102.714	70.151	65.478	47.785	54.345	136.192	125.830	110.821	84.544	39.731	23.670	52.081	232.574
94.405	63.816	62.540	42.532	43.480	94.839	87.929	96.768	73.309	33.013	19.860	45.252	195.550
109.790	68.163	55.982	42.897	48.013	150.501	74.882	90.092	85.305	34.307	18.590	64.289	249.256
121.889	77.984	51.924	58.154	43.823	147.449	73.207	104.094	85.069	25.089	21.500	56.019	253.385
109.693	76.555	72.733	62.202	45.707	168.267	109.279	111.278	92.272	35.757	18.000	62.653	262.480
112.605	81.683	52.147	54.594	43.763	125.029	111.930	110.294	90.207	29.159	25.650	57.919	251.608
108.233	69.274	67.572	47.568	39.894	120.529	68.987	100.363	70.533	31.918	15.610	52.322	238.037
99.351	85.621	64.249	48.391	44.324	125.860	71.638	98.197	73.989	31.450	18.480	42.318	219.330
114.649	72.352	52.130	46.000	41.023	125.669	80.091	98.921	68.104	34.243	24.620	42.048	220.517
105.169	74.448	56.884	57.186	43.463	115.714	108.617	96.749	69.099	36.045	18.120	70.081	216.399
108.277	71.947	60.569	51.114	43.693	128.113	80.782	87.980	68.378	32.700	24.140	56.828	212.571
118.962	83.698	59.659	64.710	48.050	156.452	108.261	115.277	97.990	30.532	26.740	48.385	247.561
101.700	71.742	57.478	43.025	45.517	102.093	110.000	89.715	81.343	31.933	14.580	34.091	211.672
125.082	90.740	64.117	65.682	43.127	107.338	144.911	119.867	94.768	30.445	21.380	62.414	267.584
105.873	86.191	57.781	59.649	49.706	160.158	111.420	115.353	80.420	36.081	21.220	57.350	248.505
108.099	83.007	59.992	50.874	50.234	109.100	130.675	120.023	82.589	30.206	16.850	55.564	280.765
91.160	76.910	57.727	56.473	36.401	140.396	103.608	106.328	82.907	36.795	20.770	64.069	240.407
103.310	81.633	60.169	43.282	46.730	128.132	109.188	107.110	61.749	34.211	17.400	59.299	261.113
104.953	68.581	57.527	50.256	42.303	125.056	70.590	95.863	65.044	35.297	22.440	47.794	162.882
110.967	76.288	63.871	48.022	45.235	139.379	119.588	111.699	91.397	38.811	19.300	60.001	226.723
101.205	72.422	63.800	42.794	45.720	130.190	87.538	88.081	55.483	29.457	18.260	58.027	262.867
70.758	88.141	53.936	60.844	45.293	141.898	113.442	91.928	73.023	32.891	18.440	59.335	233.447
108.141	84.070	64.755	56.494	43.638	158.403	102.146	108.140	65.857	29.643	16.970	61.668	222.144
98.263	64.891	54.076	40.394	48.491	122.168	80.858	97.698	72.306	33.081	20.210	42.921	209.578
111.175	80.796	63.607	65.706	42.201	158.316	100.225	118.407	89.998	33.287	21.480	41.468	273.437
109.719	86.673	56.226	51.522	43.323	120.644	90.734	99.296	67.046	28.970	18.170	57.543	226.029
107.933	90.839	62.858	54.415	47.052	144.794	111.819	110.111	77.294	35.135	16.350	65.212	259.429
107.787	76.320	60.399	61.785	43.931	168.760	86.753	106.274	74.988	32.094	17.070	64.244	269.524
81.908	63.863	57.632	42.666	36.507	101.105	91.506	88.096	67.963	35.100	18.620	50.516	190.404
112.423	75.213	57.525	56.184	40.598	126.907	115.191	104.241	80.212	29.081	19.180	64.159	230.464
86.442	69.031	48.028	47.186	31.151	107.674	76.450	91.579	55.280	23.849	16.410	40.990	212.491
100.452	75.147	55.619	60.503	42.716	160.453	117.658	109.250	64.315	40.101	18.040	65.445	176.423
102.584	83.556	64.849	51.652	44.654	153.842	107.630	115.394	73.457	31.207	21.610	59.726	252.262
95.321	62.230	52.679	31.930	34.988	134.407	87.601	92.755	52.750	31.324	19.160	42.950	186.636
108.456	81.943	55.407	56.584	43.462	147.994	111.607	109.632	67.504	39.065	21.830	60.732	266.077
101.077	84.022	57.507	43.639	45.026	143.182	131.000	114.356	65.190	31.626	18.360	49.536	270.466
109.979	72.812	57.492	54.740	41.215	115.766	85.588	94.452	69.491	28.566	18.750	65.269	228.767
101.181	65.361	48.481	42.153	38.155	128.268	66.214	86.617	57.578	41.396	18.500	53.808	186.327
112.831	79.382	60.837	50.148	47.234	151.755	125.088	108.828	81.690	35.478	19.550	59.408	264.409
120.940	76.969	62.694	58.666	48.389	133.495	84.090	98.659	62.603	28.396	18.870	61.878	236.529
87.626	68.799	55.532	39.302	46.193	126.195	70.908	94.547	67.976	33.033	21.540	54.119	200.058
117.033	74.797	65.373	53.022	51.545	162.665	98.293	104.648	95.274	28.033	25.080	49.462	269.709
97.275	66.212	52.523	49.351	38.958	116.452	77.493	87.932	55.927	24.583	20.720	47.680	168.195
90.202	55.177	55.401	33.817	36.913	105.334	94.674	86.301	60.877	26.253	16.910	45.505	199.868
87.194	75.993	61.442	69.093	42.114	153.199	118.208	99.058	91.836	37.924	21.820	68.867	273.667
108.186	67.113	59.704	39.466	41.682	112.962	90.041	87.508	61.819	36.634	25.000	47.522	189.296
87.569	86.502	54.436	48.221	40.319	95.554	79.436	106.243	65.171	36.333	25.160	38.605	206.757
94.518	54.208	62.035	42.860	34.398	118.717	106.718	107.547	60.163	33.096	16.360	38.630	182.406
89.705	54.137	48.907	38.978	23.976	103.622	78.041	87.084	57.266	26.682	14.860	45.886	199.147
95.976	68.593	49.120	49.341	40.874	95.925	69.225	94.089	77.839	30.832	22.300	38.502	201.900
124.819	82.533	62.212	60.733	43.140	166.861	122.454	113.133	81.136	33.807	16.500	61.762	259.135
121.441	69.458	54.161	58.916	40.977	116.870	130.841	122.675	75.939	35.818	21.420	61.081	226.389
127.996	79.607	57.831	48.142	49.478	131.485	116.814	106.024	80.348	32.890	18.310	62.923	233.999
83.182	53.287	50.108	41.100	23.981	82.115	80.127	80.000	45.023	24.248	18.170	50.848	186.017
106.786	84.290	62.244	69.641	48.811	156.877	82.239	114.905	84.923	32.007	16.950	81.507	279.368
93.484	71.947	51.950	45.570	41.292	101.031	115.000	87.620	48.913	29.350	16.940	41.710	228.392
107.146	69.655	57.292	44.206	38.544	138.228	85.700	92.973	75.997	35.407	16.300	46.722	222.635
96.587	57.877	44.802	34.550	40.373	123.398	84.372	95.505	53.919	28.156	21.060	32.179	150.789
107.510	73.051	61.630	26.471	38.722	113.102	78.517	83.243	58.995	27.305	22.360	49.706	214.130
86.793	58.289	57.776	50.657	29.394	98.106	70.207	90.986	63.715	25.052	15.240	40.484	123.873
99.723	62.260	53.993	48.961	37.993	101.520	79.795	100.433	51.225	30.363	17.000	61.370	171.279
80.542	56.942	46.267	34.457	27.683	87.828	77.160	65.895	38.289	21.816	15.180	35.919	152.999
103.819	78.362	57.133	54.112	50.860	134.030	97.833	107.125	64.490	32.337	23.160	77.418	252.711

91.341	64.755	55.466	47.015	32.611	97.544	72.532	78.948	57.894	20.962	13.760	38.648	188.232
84.670	57.912	46.417	40.501	18.621	80.757	64.875	65.352	47.263	19.464	16.790	28.269	194.637
76.221	64.390	39.374	29.934	22.250	67.215	65.004	60.430	45.210	22.804	12.270	44.118	163.427
86.416	51.655	48.311	35.529	24.479	68.178	56.089	67.894	45.775	18.426	13.100	49.704	140.147
75.065	62.386	45.451	34.124	21.976	91.673	73.155	79.489	53.967	29.032	14.670	57.543	152.776
80.145	51.283	48.569	31.698	28.147	79.746	61.814	76.521	55.983	23.766	16.990	40.067	186.032
110.513	71.094	54.063	56.679	39.426	123.065	83.466	89.870	80.813	28.932	20.940	35.036	168.676
117.463	76.637	57.359	66.318	47.911	181.779	120.000	105.156	98.237	36.474	19.780	57.938	247.111
64.990	58.070	46.463	35.099	22.568	78.236	61.784	63.191	44.280	15.353	13.080	41.490	143.635
97.566	76.590	47.531	43.039	37.159	100.887	80.304	88.759	57.246	29.959	19.240	38.689	185.689
98.022	73.035	57.013	42.798	37.450	123.068	83.718	97.143	65.673	32.759	21.130	39.370	185.723
59.995	42.254	42.266	34.443	25.042	74.459	61.668	64.759	46.804	22.540	10.940	42.833	162.002
92.008	67.998	56.675	35.242	38.053	115.100	93.333	90.397	68.976	37.427	17.420	33.658	234.116
84.903	39.920	51.593	41.325	32.670	87.189	76.787	79.193	59.434	26.119	17.550	51.508	210.182
85.688	63.129	52.593	36.400	31.862	94.869	66.136	78.288	58.939	27.736	16.500	44.370	134.491
87.276	69.798	56.393	46.242	42.089	118.244	119.000	99.320	68.896	25.666	17.890	45.329	238.635
69.254	56.646	53.292	28.387	23.898	96.682	63.158	78.949	54.354	25.647	14.980	38.931	170.599
81.947	48.299	50.774	47.777	33.986	98.070	77.540	80.697	44.957	27.608	21.000	41.156	205.479
75.982	48.895	43.178	38.348	20.155	88.192	55.459	62.712	40.304	19.232	11.180	43.382	202.209
77.417	54.586	44.408	32.154	22.732	91.469	58.283	65.201	52.886	17.869	15.230	40.751	153.251
111.761	91.648	55.652	61.895	47.566	125.516	130.719	115.771	90.900	35.291	19.560	66.528	245.423
108.003	71.208	59.847	43.720	38.621	130.771	91.065	94.431	84.427	30.566	23.280	60.405	242.639
80.473	54.666	48.842	41.929	29.964	99.215	62.563	72.518	47.870	23.773	13.350	41.512	172.246
69.607	68.206	48.104	26.828	25.933	89.334	53.596	71.269	44.091	20.823	11.510	37.869	179.908
73.557	48.798	47.398	40.631	27.876	79.667	70.726	77.229	43.812	25.393	13.200	30.802	161.516
85.220	47.457	48.192	44.355	26.614	83.088	70.750	65.939	52.921	25.025	15.350	36.062	176.256

EEpp20	eepv20	eepp40	eepv40	eepp60	eepv60	efppul	efpvul	efpp20	efpv20	efpv40	efpv60	keppul	kepvul	kepp20	kepv20	kepp40
77.610	276.601	54.472	239.374	27.384	138.498	26.550	226.480	40.811	176.369	152.756	130.535	356.292	476.085	392.643	380.057	237.810
58.462	216.665	63.748	211.946	38.403	136.583	35.818	225.419	41.074	171.946	164.289	114.497	230.559	417.581	286.281	390.052	257.843
83.067	248.864	59.959	223.182	31.124	134.221	31.554	250.066	45.585	173.474	146.938	146.068	344.903	480.931	381.685	402.151	326.253
70.522	217.832	63.770	251.575	36.999	114.337	25.771	237.136	43.179	178.301	184.103	117.750	319.229	590.192	359.595	438.070	298.687
64.993	277.203	56.887	221.528	31.976	117.797	40.965	235.959	46.083	142.695	150.496	137.511	225.863	390.555	256.088	332.556	273.377
72.653	233.530	57.065	206.634	38.798	145.558	28.312	218.990	41.844	180.019	158.825	116.939	315.869	411.668	389.238	401.723	340.618
57.396	254.347	51.135	236.040	27.914	146.426	37.476	211.961	46.190	179.657	157.424	119.789	305.023	538.701	277.118	358.203	319.343
73.595	185.842	57.920	229.658	34.631	143.959	38.886	294.694	41.068	174.511	161.348	118.558	297.489	603.169	354.091	473.593	284.572
71.535	210.914	54.804	178.285	31.570	154.009	33.710	249.114	42.549	158.635	127.867	100.316	277.713	450.257	391.446	367.377	293.584
63.992	148.542	54.491	201.366	38.451	134.331	20.857	177.556	49.338	182.513	148.449	114.261	238.185	415.843	279.618	386.617	304.160
65.772	238.439	58.795	203.084	31.633	121.347	33.921	252.259	38.176	193.202	155.097	108.775	235.155	448.658	293.794	378.713	234.814
71.097	260.386	61.534	246.813	34.940	118.930	39.693	188.873	48.830	172.900	185.753	125.277	359.519	485.086	354.030	330.106	321.833
58.983	272.582	70.297	208.393	35.602	155.998	38.741	201.894	41.658	193.847	159.689	131.764	386.686	550.799	336.382	405.087	351.711
74.366	221.053	62.505	202.104	33.934	107.450	30.651	173.638	42.603	184.256	135.027	94.215	281.316	517.484	346.733	382.701	318.570
71.376	259.898	50.762	220.196	34.817	131.868	30.787	243.094	50.570	171.550	146.494	113.580	297.748	514.753	353.272	372.913	377.029
68.272	291.029	57.029	240.354	38.854	115.326	30.688	239.286	46.262	176.376	167.983	137.565	292.632	487.004	316.455	382.598	325.297
68.487	230.348	58.985	237.179	32.302	156.503	38.479	160.589	38.511	166.742	166.146	126.170	332.675	507.190	385.209	466.054	246.997
62.317	264.545	67.893	196.081	34.341	136.910	38.599	189.676	44.569	194.582	152.999	131.952	312.739	606.208	381.955	410.715	306.596
71.503	248.863	60.286	236.361	32.689	112.289	34.009	186.444	50.422	196.550	157.210	133.414	320.884	502.597	402.723	437.037	319.290
67.337	224.751	57.153	233.941	39.492	144.079	37.717	185.562	40.863	159.251	138.964	141.720	339.474	499.465	335.117	459.119	309.604
68.986	289.190	54.144	226.207	34.840	149.327	22.961	228.814	36.686	163.331	145.793	155.323	323.221	631.500	302.578	387.800	297.500
69.501	184.396	61.612	239.064	32.890	128.389	27.124	214.576	44.440	188.221	161.643	148.508	400.546	470.601	356.419	429.316	288.503
67.561	239.954	51.942	206.665	32.859	146.443	32.996	226.404	47.350	203.714	125.585	133.216	364.916	523.967	388.488	458.078	384.518
72.831	233.159	46.993	202.408	36.532	155.837	37.097	218.646	50.143	203.942	159.286	134.556	329.240	530.373	368.429	422.329	275.336
48.399	124.842	50.073	145.293	32.378	121.773	27.729	180.008	38.432	167.947	123.836	84.939	330.333	279.590	174.429	321.777	263.190
72.743	272.574	64.130	217.735	34.476	127.648	36.590	189.646	44.760	192.217	148.284	125.277	316.755	516.984	337.972	370.759	315.358
62.279	257.488	51.791	229.017	35.686	135.062	33.438	236.237	45.452	202.084	169.250	128.143	278.088	501.915	352.932	414.451	280.707
61.378	234.653	48.614	222.326	35.730	117.376	39.618	225.608	43.970	164.682	165.987	136.471	336.766	426.333	413.745	416.148	315.750
62.997	264.570	66.414	222.670	40.597	119.659	36.606	220.572	43.858	183.846	170.746	112.774	299.033	643.040	362.056	387.518	221.454
73.117	234.051	71.656	231.717	32.640	119.577	34.214	195.996	42.421	154.988	146.497	130.215	336.298	447.142	328.401	384.076	331.883
50.329	123.354	50.314	185.173	40.651	122.101	33.718	184.250	37.305	207.470	180.941	135.647	263.424	463.363	221.320	321.758	258.362
67.003	206.909	59.212	236.731	33.884	138.181	32.064	212.295	43.905	174.642	147.609	121.574	331.785	532.821	339.545	415.504	232.633
54.212	123.480	58.854	172.648	26.564	117.259	14.597	202.962	31.068	125.038	126.188	102.654	214.904	274.264	205.287	338.946	215.571
65.327	221.959	59.969	198.726	30.379	130.627	37.516	238.928	43.049	211.161	177.288	119.658	286.118	610.450	348.691	396.067	353.733
72.150	282.077	52.261	239.126	36.152	131.114	30.597	187.742	34.091	179.842	150.029	122.852	338.637	612.476	335.338	496.766	311.296
70.442	255.187	65.963	232.014	40.542	147.748	33.463	201.613	49.429	207.978	156.179	140.073	322.042	637.667	357.554	369.735	309.455
64.139	193.883	62.167	191.738	38.627	102.467	38.840	205.259	38.824	184.093	177.978	144.696	366.190	510.622	364.717	392.971	334.430
50.748	190.344	52.866	166.796	33.741	92.606	20.544	160.438	33.294	144.565	156.222	100.969	334.667	443.600	291.974	309.412	255.568
66.223	271.869	49.001	247.539	35.488	158.419	33.650	236.202	44.353	168.826	152.294	126.431	267.772	550.627	299.004	390.350	286.244
63.652	231.498	49.537	226.165	38.845	128.510	40.830	192.337	37.820	163.699	141.068	133.217	295.214	543.146	374.320	415.743	329.013
62.915	266.764	73.514	236.039	34.857	136.446	37.410	242.269	46.185	160.539	192.139	112.063	317.771	591.032	396.433	367.012	325.936
54.113	186.912	57.282	186.993	38.482	127.713	46.419	207.385	46.617	151.790	158.566	106.636	191.441	456.167	270.978	347.122	289.457
71.077	210.499	60.578	221.631	31.669	146.451	31.903	193.994	39.102	197.930	132.815	116.104	294.259	631.000	368.758	440.669	330.852
70.994	237.632	58.173	219.539	40.802	130.895	42.637	189.712	47.853	189.592	170.133	155.590	320.967	533.230	375.725	363.838	322.220
68.497	236.520	66.074	205.965	37.305	136.769	41.943	252.472	43.918	180.441	177.847	146.053	309.904	469.700	438.277	412.983	361.188
44.371	205.656	56.695	156.828	26.935	88.623	27.637	185.532	27.414	150.994	106.849	111.462	207.752	293.580	192.072	371.125	229.757
64.315	246.104	55.906	203.949	34.008	120.708	35.573	241.846	37.335	163.980	165.834	142.852	256.796	517.328	326.291	384.211	334.063
72.075	266.070	46.703	236.109	38.509	150.777	31.919	235.312	42.678	179.393	155.453	115.342	320.676	548.692	372.623	408.750	307.148
84.842	243.707	50.745	207.343	33.184	117.275	40.715	226.788	46.399	200.782	165.801	122.805	233.060	421.883	298.345	426.425	329.312
64.459	304.038	49.345	241.732	36.803	137.896	33.826	190.720	58.934	188.643	156.950	133.355	331.404	525.842	412.608	403.345	255.176
64.316	157.100	61.101	232.011	28.912	122.845	31.462	219.763	43.330	177.332	158.491	121.193	227.957	439.208	369.095	429.170	309.579
67.604	206.036	50.828	238.108	31.795	164.220	35.308	212.860	44.078	185.979	155.202	120.164	381.165	597.173	444.183	437.281	320.349
63.542	263.110	48.138	214.024	28.753	152.293	28.026	204.156	47.347	168.672	157.742	121.633	276.389	498.876	372.901	341.201	348.921
64.429	198.494	60.806	199.050	31.741	120.332	34.838	250.163	49.058	181.568	175.487	102.876	282.141	488.894	321.456	458.434	296.465
77.839	213.164	54.315	215.495	31.555	158.623	36.754	226.617	45.428	157.310	179.613	137.075	354.729	519.273	424.854	428.755	375.564
56.702	184.850	51.662	202.098	25.956	142.824	40.475	207.217	45.726	193.741	155.203	138.347	258.118	339.992	240.545	379.921	366.441
52.141	165.297	30.875	153.322	21.598	116.840	21.491	185.381	30.161	156.228	107.082	101.246	296.333	230.252	169.066	293.848	257.220
59.084	255.006	55.624	232.268	29.228	142.404	34.773	241.432	44.340	157.676	177.647	145.973	316.272	533.353	389.740	432.865	389.169
72.849	277.807	59.853	217.803	43.137	110.949	43.272	231.845	40.157	155.053	159.087	142.315	325.228	510.264	417.831	404.491	368.124
68.483	241.690	52.635	213.820	38.080	141.729	42.488	224.536	46.149	175.610	183.851	131.712	308.484	601.500	328.112	395.598	334.247
59.888	242.538	54.767	219.082	38.100	140.267	39.062	251.140	44.392	165.464	173.371	107.671	222.293	388.953	255.712	401.449	313.768
63.492	192.763	56.262	230.031	36.239	132.849	32.469	213.092	35.352	193.617	142.375	114.205	265.845	499.838	321.358	392.705	342.126
72.429	203.103	56.654	243.493	31.314	133.191	30.761	272.962	39.377	176.844	150.597	122.242	307.458	509.870	365.338	386.716	306.669

71.212 184.318 56.828 213.693 31.461 154.123 34.459 196.046 44.813 172.744 191.847 130.549 328.957 556.486 314.801 405.783 287.320
72.924 237.288 57.809 193.920 30.677 122.071 32.172 244.079 42.871 206.119 156.900 107.237 291.848 622.629 330.221 375.578 370.489
52.197 186.052 48.591 175.113 33.965 112.540 31.609 224.520 42.630 160.655 131.573 138.443 231.279 375.240 255.428 241.333 197.810
62.951 252.963 48.363 197.811 32.981 117.563 38.090 232.130 46.536 184.580 159.945 115.171 251.622 453.511 232.072 434.958 302.127
69.389 158.135 56.816 219.916 41.709 137.887 37.032 242.936 44.498 193.418 190.745 124.000 296.249 626.041 371.560 377.500 309.530
76.216 284.998 60.343 214.114 35.901 161.099 31.853 236.893 47.468 176.916 152.872 155.249 302.481 651.409 365.008 373.299 356.325
70.045 213.299 51.736 230.954 40.293 158.263 34.767 206.852 47.011 173.052 190.364 132.295 344.799 554.770 339.043 333.303 343.081
74.701 336.045 66.340 198.617 28.042 141.034 33.437 251.841 40.519 196.419 167.986 143.382 236.480 304.174 348.730 438.609 254.154
62.190 190.899 63.012 231.025 35.488 128.610 34.152 233.596 49.496 185.852 154.090 106.228 260.805 384.003 322.120 414.360 215.228
63.839 244.866 57.765 204.719 30.318 144.128 34.881 211.479 35.633 174.538 163.009 135.853 204.022 401.005 311.413 367.047 259.824
70.134 188.719 58.609 212.253 34.062 111.653 40.022 206.102 41.743 167.227 162.506 104.929 264.553 485.393 322.974 332.811 259.420
66.847 198.398 57.174 206.505 32.787 145.597 37.081 176.176 42.945 181.217 156.353 117.327 300.216 618.099 339.180 430.757 229.678
77.610 276.601 54.472 239.374 27.384 138.498 26.550 226.480 40.811 176.369 152.756 130.535 356.292 476.085 392.643 380.057 237.810
62.590 231.660 66.235 203.510 33.527 141.583 44.708 180.674 41.590 146.306 164.870 128.506 215.382 506.000 299.780 415.977 260.308
66.998 327.302 55.228 257.986 38.388 149.680 36.100 205.340 43.741 184.961 195.290 124.279 367.253 462.606 336.637 380.597 278.456
78.073 237.414 65.539 238.737 35.709 131.831 38.237 246.835 37.724 155.265 148.095 140.172 336.395 432.411 365.367 354.821 335.639
73.641 222.461 58.589 224.249 31.043 132.839 34.854 255.391 44.813 167.751 176.454 128.931 300.755 421.401 372.460 374.651 329.104
80.462 290.873 60.786 209.495 40.064 163.975 39.042 185.276 49.782 162.267 128.084 121.816 248.560 398.652 312.422 394.360 312.287
68.897 243.735 53.130 225.776 33.140 118.032 33.816 204.706 44.222 176.640 136.200 118.942 283.215 573.368 342.204 386.438 299.728
64.018 236.571 53.996 197.243 26.174 127.722 32.120 195.436 29.922 167.359 168.851 118.882 279.409 362.051 240.111 413.292 271.641
65.982 236.067 60.851 213.271 33.384 138.170 35.786 265.543 42.103 177.549 144.356 112.171 347.053 457.987 381.505 453.980 277.352
69.386 276.240 62.247 207.598 36.460 136.002 36.993 161.867 46.272 154.700 149.145 117.059 275.199 442.111 305.837 411.087 315.425
83.384 243.628 62.221 238.159 38.152 129.773 41.095 215.540 39.851 160.692 172.687 129.283 336.294 503.213 351.614 437.346 369.548
68.617 228.595 52.559 234.174 32.601 140.562 38.517 216.084 45.788 176.096 165.659 128.520 301.718 554.044 371.722 314.919 340.318
46.005 221.592 46.493 178.911 37.875 100.735 39.428 206.768 46.418 171.138 163.797 127.878 215.654 327.445 272.854 336.119 256.981
73.068 264.056 49.490 228.655 36.873 225.866 31.421 218.572 42.067 183.315 170.742 113.110 324.099 628.164 348.543 423.785 252.762
66.831 237.877 62.826 240.346 35.275 147.138 35.046 199.644 35.730 164.221 168.739 122.706 334.864 375.687 385.131 415.718 272.761
75.055 245.915 49.757 245.468 34.383 160.152 31.386 239.854 48.800 200.145 156.995 117.101 320.401 321.500 368.788 379.395 284.566
63.013 246.113 53.127 206.131 31.541 112.513 29.652 260.270 45.883 180.519 181.405 113.971 321.528 423.256 399.157 418.978 281.376
50.211 154.374 50.928 175.277 27.777 121.630 26.255 154.277 39.974 158.289 127.598 106.101 227.270 433.116 272.806 356.235 210.020
86.158 208.329 68.012 203.131 31.331 132.760 36.925 217.951 33.732 167.057 168.767 126.569 303.288 588.854 334.016 350.940 324.525
47.118 163.886 36.002 186.384 26.256 86.858 22.386 181.346 38.791 124.007 113.362 92.928 230.312 314.250 170.213 276.749 195.084
64.232 217.887 58.967 202.951 33.579 127.594 35.942 241.407 46.729 190.350 178.783 109.757 308.324 471.597 351.449 388.921 306.475
70.712 225.105 57.884 225.734 33.819 118.218 40.427 218.407 42.984 166.064 175.858 140.035 291.906 619.833 345.105 421.730 396.764
58.011 202.943 53.574 170.467 28.714 135.963 23.509 163.608 32.123 158.889 125.416 114.515 218.736 368.661 175.302 323.739 175.833
59.630 196.575 51.057 226.843 33.727 151.982 40.559 217.072 49.823 142.205 181.962 132.949 302.507 492.364 382.255 377.216 299.106
76.650 278.254 58.494 234.008 31.237 150.225 29.501 172.284 43.811 182.588 139.516 103.403 347.713 417.998 385.325 432.643 304.968
62.828 219.654 60.650 208.495 33.266 121.059 34.554 228.642 42.006 213.212 155.292 103.742 270.493 454.809 364.181 397.991 327.593
50.224 222.584 50.850 180.574 31.737 112.240 31.718 189.736 30.597 179.532 184.488 97.264 266.711 489.667 243.061 399.201 280.622
65.598 266.410 58.372 223.027 33.273 158.272 43.353 217.828 41.269 173.121 177.784 107.033 286.948 546.181 340.039 381.035 346.310
67.050 189.198 45.138 218.046 33.841 133.546 35.291 192.477 43.524 183.773 172.337 121.886 246.986 533.828 297.107 349.046 321.217
45.416 204.656 49.448 192.721 30.632 162.423 30.890 215.064 31.003 156.288 170.304 101.144 209.089 352.899 288.539 456.736 321.021
73.321 232.151 54.167 212.047 31.580 156.328 37.589 231.650 48.711 190.375 123.948 127.497 286.469 588.434 329.248 410.735 322.884
45.717 193.422 51.877 182.193 30.851 97.346 21.809 197.488 35.856 134.821 121.721 98.785 249.390 324.897 266.563 276.032 175.708
45.992 178.192 37.808 152.468 20.810 119.838 20.052 165.118 30.440 130.788 121.632 116.994 244.617 383.552 190.107 298.623 206.923
70.175 235.484 56.440 214.850 35.202 106.617 24.742 218.986 48.285 192.023 159.950 131.138 311.175 594.845 396.250 387.391 372.808
60.804 197.198 46.175 186.765 35.786 119.208 33.739 223.052 39.967 164.757 158.156 128.792 199.397 384.267 266.416 366.319 279.973
53.834 190.958 55.012 232.771 31.543 129.260 40.987 193.918 41.503 163.819 155.891 131.004 254.109 401.300 313.345 320.814 275.545
54.598 188.738 53.845 146.847 29.221 120.555 19.507 163.367 35.644 157.842 133.159 97.358 234.125 272.149 190.859 281.259 227.246
47.278 166.366 31.230 149.922 26.157 102.692 24.596 165.651 35.958 165.645 120.807 104.445 194.131 236.121 161.117 294.373 207.647
64.496 135.332 58.025 197.266 32.887 131.985 36.929 245.823 39.795 160.180 148.707 109.554 255.086 585.833 182.784 386.096 300.180
66.600 258.244 47.251 233.492 35.001 141.376 37.456 256.033 42.841 211.375 164.547 117.962 345.439 401.167 305.650 432.672 311.085
73.332 167.890 63.491 187.539 33.778 151.116 29.454 198.628 37.954 181.715 136.470 138.343 359.800 571.492 369.642 440.594 335.513
71.305 203.408 48.643 215.036 34.800 151.323 31.878 237.304 32.219 176.909 176.705 122.654 298.381 330.167 339.859 400.994 297.157
43.975 140.980 44.883 154.488 24.975 116.736 18.738 163.322 26.959 129.432 131.475 104.634 195.977 330.649 133.645 246.225 217.951
67.366 271.627 55.866 241.560 31.428 103.606 30.263 235.333 48.777 202.209 161.027 130.833 287.666 461.070 371.526 461.352 370.555
66.547 205.272 63.355 203.917 32.797 144.725 32.809 224.290 31.408 175.707 148.202 103.874 215.014 541.996 346.622 258.161 308.756
51.222 185.570 52.048 195.744 35.898 118.974 38.848 217.929 39.177 158.317 158.243 110.509 289.978 277.122 301.275 355.591 242.109
52.238 195.851 52.985 157.651 22.992 100.480 26.661 201.423 42.067 152.646 129.818 107.812 226.963 240.542 231.447 370.017 255.426
59.541 192.584 52.032 202.330 26.681 114.140 26.934 211.433 33.260 151.844 128.059 90.495 232.614 279.745 276.067 274.965 197.553
45.665 224.017 36.842 160.087 31.179 105.118 22.683 134.763 33.214 143.844 107.247 102.108 241.762 364.333 179.236 278.699 210.609
49.667 188.171 54.454 170.555 29.819 95.216 33.358 203.819 32.956 175.860 146.158 122.261 212.910 320.188 169.962 394.425 253.346
41.411 145.491 42.788 165.989 21.817 70.126 28.170 152.715 25.714 149.950 95.939 86.425 224.123 227.854 228.849 250.827 187.773
69.774 212.549 62.023 221.247 39.286 152.226 35.511 225.955 42.031 211.540 178.265 97.527 267.420 462.438 231.022 387.131 298.995

48.968 104.039 37.988 175.915 24.156 111.172 18.310 174.220 36.959 129.183 107.376 89.493 231.384 174.000 177.701 284.685 259.574
48.373 151.223 37.901 154.588 18.164 97.761 23.625 131.455 28.052 95.771 115.444 55.394 157.983 277.282 177.223 209.375 121.935
50.618 173.364 42.066 173.330 18.611 77.170 19.321 139.317 28.446 112.298 85.274 96.502 142.969 198.673 205.975 198.670 110.451
40.001 196.774 29.692 136.487 18.187 100.576 18.932 157.333 23.029 112.511 105.305 63.766 126.875 211.625 133.412 185.777 147.936
46.006 130.244 40.070 183.120 21.438 55.409 25.265 135.918 33.289 125.097 76.756 57.240 327.067 310.115 192.823 240.197 172.022
35.262 138.545 38.791 148.183 23.952 91.946 20.510 162.697 28.252 138.328 130.222 89.755 187.699 204.574 148.079 289.037 182.050
58.284 202.698 62.089 202.224 31.803 128.558 38.022 219.883 42.977 152.695 156.989 133.901 325.035 260.829 268.297 286.832 253.830
65.228 215.136 62.424 213.298 38.644 135.847 41.036 189.203 41.645 206.180 140.051 119.189 336.793 414.790 366.704 347.805 311.254
52.868 166.012 44.746 155.046 18.056 89.932 27.970 173.123 31.489 131.842 112.311 94.573 144.189 285.499 171.855 234.314 203.487
59.135 165.634 54.388 212.751 25.636 116.638 16.363 175.267 34.667 140.720 156.018 110.413 243.873 231.172 210.006 318.453 239.179
68.560 231.998 59.906 206.073 28.964 121.227 30.790 251.406 50.063 177.723 132.611 117.475 277.389 314.006 272.919 391.722 293.137
50.612 156.028 42.989 109.289 22.253 56.720 19.843 152.831 26.826 128.142 71.533 71.570 107.350 270.640 114.413 238.602 169.360
57.319 186.073 56.303 189.891 34.081 146.449 34.757 212.630 40.446 192.038 171.856 108.285 279.691 543.833 237.150 383.849 213.446
50.192 146.114 26.780 115.115 23.639 89.382 21.999 167.014 38.203 156.029 122.259 105.715 228.059 250.161 242.327 280.719 215.145
48.639 177.283 43.365 171.936 28.593 73.837 29.828 144.066 33.331 136.833 117.960 107.865 254.297 249.564 227.140 277.218 175.881
57.203 213.458 53.544 196.252 37.595 98.537 37.900 216.543 33.553 157.830 118.146 122.128 314.174 419.318 306.382 357.345 209.269
47.798 138.716 48.385 165.059 13.199 103.539 19.953 162.172 37.545 136.161 128.345 85.866 241.647 188.638 221.251 239.837 242.547
48.029 191.840 40.250 135.628 25.292 104.782 13.368 186.623 26.499 152.411 97.051 90.641 226.351 199.574 240.235 294.280 181.238
39.954 170.755 43.239 128.501 21.872 54.836 16.883 167.903 21.496 115.632 102.058 80.525 127.049 225.085 201.084 224.894 124.032
41.889 145.991 33.653 144.968 16.229 63.952 22.545 172.007 25.823 117.841 114.911 90.927 114.598 159.003 187.945 258.901 162.114
77.133 263.172 63.631 268.730 30.057 128.230 30.897 243.659 44.862 175.978 188.210 109.576 315.963 503.060 374.977 419.338 328.034
54.345 200.790 57.212 204.807 36.268 110.032 36.690 199.835 48.146 156.389 131.593 120.302 271.828 416.807 319.224 350.830 249.959
42.487 146.666 41.881 158.828 17.324 95.089 25.708 176.340 28.565 110.147 101.120 94.427 177.574 314.597 212.158 249.944 206.276
45.222 162.688 41.947 184.372 15.874 77.274 22.107 124.097 32.312 101.548 101.173 73.458 110.852 188.934 154.712 259.380 123.488
44.548 151.882 41.460 140.365 19.890 84.023 21.949 162.815 34.683 126.645 98.046 78.229 217.084 177.782 227.022 233.341 238.966
39.528 138.765 44.092 136.144 22.633 87.680 18.542 177.281 37.141 138.333 104.630 79.336 191.527 256.667 196.961 254.920 181.352

kepv40	kepp60	kepv60	kfppul	kfpvul	kfpp20	kfpv20	kfpp40	kfpv40	kfpp60	kfpv60	EE60WF	EE240WF	EF60WF	EF240WF	KE60WF
360.489	290.510	188.806	183.327	491.769	264.714	354.034	264.847	379.621	237.399	173.794	36.530	26.590	34.970	21.060	41.140
287.667	276.051	193.966	185.738	319.805	205.843	329.127	219.444	202.157	231.236	200.995	40.650	25.940	28.090	28.350	39.870
247.537	266.800	215.416	225.507	412.024	245.368	420.365	238.200	336.242	199.545	204.444	34.120	22.240	27.860	19.870	34.100
315.464	297.584	222.814	218.944	447.133	229.621	405.290	207.276	276.890	204.045	187.822	44.590	29.830	33.200	17.240	47.290
250.419	228.499	203.432	170.420	403.273	263.198	298.255	184.068	242.577	214.132	176.634	37.130	29.440	26.010	32.060	40.170
325.818	243.822	234.591	211.272	474.691	266.162	407.588	230.636	332.150	247.352	193.716	32.830	28.460	33.700	20.680	34.930
340.250	233.475	187.193	175.566	273.109	223.694	214.553	203.196	280.561	207.571	202.873	37.690	37.480	23.870	32.370	34.860
363.639	261.339	208.304	206.848	352.909	234.736	322.421	223.787	326.640	192.408	234.749	37.730	29.830	33.110	20.030	40.650
268.579	230.995	238.653	201.676	347.130	261.669	365.137	246.043	369.841	191.133	191.982	38.470	32.320	28.270	31.710	38.320
315.545	305.192	213.819	185.492	314.815	226.094	331.900	218.776	220.821	224.347	211.500	38.910	28.690	25.510	19.090	35.530
338.630	283.459	180.614	213.391	330.199	300.534	311.903	222.141	295.124	214.056	197.289	40.190	27.850	29.530	26.820	40.770
286.816	311.978	216.285	216.273	427.763	231.955	334.170	213.095	266.195	234.046	207.023	37.950	21.850	27.840	24.670	45.520
302.696	269.598	207.399	206.648	559.509	251.552	387.306	220.806	301.590	189.292	217.528	37.640	26.080	32.640	17.890	38.780
291.190	275.491	205.218	195.536	317.609	240.772	398.283	242.084	300.277	235.645	163.983	36.190	27.980	32.020	23.390	40.480
281.838	261.795	202.063	240.171	339.106	277.795	474.699	232.639	310.604	214.582	200.847	38.110	27.060	34.100	26.570	44.200
260.842	280.198	234.342	208.796	459.996	229.071	338.454	209.729	212.149	253.657	189.138	38.910	21.040	25.170	20.390	35.150
253.517	255.305	213.589	192.923	426.621	190.626	387.792	237.695	391.205	247.974	206.084	39.260	28.670	26.610	21.090	41.790
228.955	240.822	194.517	256.505	486.304	264.924	279.020	234.603	361.314	188.321	183.385	31.850	22.480	29.350	19.290	39.790
369.268	262.091	265.231	220.004	440.406	250.000	413.526	265.853	311.685	247.747	228.729	34.570	29.020	39.610	22.340	41.320
326.539	258.487	251.024	204.437	400.514	278.340	489.527	240.834	321.570	235.823	193.496	39.390	28.720	34.360	24.690	43.080
265.985	293.727	242.501	218.488	381.758	278.559	329.373	268.987	352.255	210.956	215.818	34.110	23.490	32.670	21.200	46.820
302.987	262.520	250.893	214.202	340.610	269.389	373.296	248.407	280.687	226.091	185.853	33.060	25.940	32.160	20.630	39.840
294.697	300.262	247.368	228.009	348.582	233.451	361.147	196.505	281.250	230.554	213.551	36.290	25.330	30.270	19.250	43.380
360.481	255.362	219.945	216.004	503.557	207.243	395.789	262.986	279.757	222.769	212.875	38.730	21.850	35.970	26.030	38.980
275.988	240.375	151.689	153.228	282.966	187.773	268.877	205.573	141.320	191.548	175.810	27.790	36.460	24.710	25.740	38.800
248.265	260.875	220.924	221.460	443.191	241.340	422.808	206.610	266.180	215.377	164.440	35.580	25.130	29.100	22.510	45.100
272.925	227.579	215.275	208.154	384.478	256.739	441.684	210.935	362.317	240.380	220.863	39.400	24.320	33.990	22.000	43.920
395.892	306.150	223.354	219.916	422.220	203.220	359.381	232.809	347.969	222.631	211.316	37.130	25.290	31.140	25.700	39.370
316.874	267.730	246.570	251.240	488.914	277.704	355.131	247.441	367.790	225.096	230.366	33.140	28.480	31.460	18.360	36.210
280.152	255.277	213.408	192.937	414.100	214.654	456.432	255.016	304.163	210.450	197.557	41.750	21.320	27.560	18.280	35.120
250.419	218.324	161.161	146.124	397.221	207.045	233.907	211.560	169.230	235.211	166.118	35.500	35.610	32.780	25.930	37.870
305.186	292.013	230.848	221.766	449.505	253.240	381.608	235.593	283.306	209.011	201.837	33.020	24.010	33.670	24.130	40.320
257.999	220.623	142.797	159.146	282.357	183.299	240.380	192.852	167.008	172.763	171.964	33.470	34.390	27.310	25.160	33.560
311.236	296.539	231.364	213.350	507.276	219.858	402.096	222.672	334.914	230.934	214.618	33.110	21.820	31.890	25.230	41.970
368.007	283.102	235.047	240.805	567.587	288.487	441.227	244.197	222.273	223.330	167.353	33.140	21.750	28.960	21.540	47.530
336.536	291.180	214.643	240.793	465.038	219.947	347.231	230.515	296.129	236.782	219.945	32.860	27.010	28.770	21.580	42.810
272.447	285.392	207.623	218.820	425.313	264.835	420.008	246.693	324.770	253.044	191.639	37.800	32.630	31.860	22.920	41.200
216.922	195.394	162.894	172.608	234.027	191.629	249.867	214.101	175.050	201.339	194.744	39.610	35.140	25.150	25.720	31.670
290.934	285.039	247.086	247.544	416.714	232.861	420.571	251.579	342.184	236.023	203.252	31.320	25.590	33.340	16.330	40.610
238.597	261.408	189.646	201.550	414.777	218.781	356.212	219.275	327.036	226.933	207.365	38.510	25.890	29.640	19.330	46.250
367.691	294.717	180.505	264.793	393.730	223.403	368.709	221.198	312.988	245.159	237.200	38.440	30.460	32.980	21.490	42.950
299.973	226.811	196.317	170.642	301.438	193.619	238.352	186.116	223.271	186.095	151.871	35.380	40.060	30.740	27.720	31.700
335.933	289.516	247.109	253.386	363.470	239.745	478.482	247.055	256.935	246.895	213.917	35.240	20.100	27.180	25.150	40.710
345.070	307.108	235.566	244.783	457.806	228.193	376.385	231.964	332.022	210.919	213.116	38.170	19.810	33.090	20.860	42.560
359.592	268.667	225.311	207.751	420.498	201.573	359.788	220.513	375.562	245.431	218.273	33.550	29.750	29.690	20.750	45.460
220.725	194.394	144.429	159.894	189.930	199.033	245.607	181.057	133.576	173.978	124.881	36.180	38.550	21.170	28.130	34.850
323.599	292.209	204.942	220.133	551.845	258.045	397.190	223.422	322.314	215.251	203.994	39.130	29.120	29.600	21.600	42.760
290.821	274.729	227.554	229.484	456.774	267.856	444.743	230.770	316.476	201.968	212.520	40.480	22.250	28.380	24.070	41.910
287.434	263.666	214.250	210.967	383.809	266.982	311.691	241.642	269.661	223.496	164.812	27.290	28.790	28.800	25.860	37.680
284.090	275.548	244.304	186.870	468.635	223.315	337.123	228.454	338.796	218.220	221.612	32.070	26.050	33.950	18.040	43.780
260.312	268.826	228.145	180.179	446.922	211.608	333.857	254.617	389.133	220.463	209.371	32.160	24.930	23.830	23.090	39.430
276.810	305.484	213.944	237.065	475.482	224.421	320.198	276.716	286.964	222.402	206.508	33.980	27.840	25.470	19.590	39.010
309.734	275.615	211.120	186.475	334.833	206.916	331.730	228.331	305.514	177.657	200.978	35.820	24.810	24.420	19.840	38.340
285.896	252.253	185.499	200.422	310.567	236.243	326.902	209.363	223.051	225.671	216.025	32.950	27.350	25.720	19.930	33.050
313.955	259.211	202.502	222.788	496.809	221.075	385.630	203.873	319.640	217.652	202.034	38.350	26.810	33.480	20.720	42.610
297.982	244.816	148.719	149.119	350.982	180.138	276.262	197.142	235.063	180.708	180.893	31.040	35.740	27.410	28.360	33.930
208.389	186.585	154.863	142.397	192.446	152.250	204.745	195.746	226.900	181.550	148.237	36.790	41.030	34.030	32.190	30.290
280.179	254.913	192.376	196.210	482.182	225.041	376.935	236.442	215.015	190.656	194.164	33.480	25.710	31.230	20.120	42.770
295.162	238.005	236.487	194.856	498.738	204.845	365.588	211.659	328.359	208.862	216.190	36.290	33.060	33.030	26.650	41.440
288.853	286.752	196.746	234.863	467.490	207.268	353.564	233.369	339.736	193.194	194.044	38.780	26.340	33.580	22.910	35.820
235.494	212.643	189.813	172.973	303.810	209.134	334.351	201.752	165.425	217.297	197.016	35.560	34.950	24.950	27.530	36.370
281.723	281.750	200.251	243.003	377.212	219.658	234.364	191.138	295.655	243.469	198.801	36.300	26.220	25.440	31.650	39.550
370.479	284.586	227.556	234.538	475.212	239.277	384.152	239.530	334.972	232.808	193.465	37.430	28.350	32.610	18.650	42.700

298.742	245.899	266.846	233.154	518.347	265.802	482.213	211.275	449.708	227.082	183.508	36.420	25.220	32.140	28.070	43.570
301.880	241.030	207.753	232.258	456.160	229.872	428.405	219.737	341.424	252.787	240.422	32.710	24.920	32.340	20.030	40.530
185.265	220.080	218.055	196.903	235.343	185.541	300.450	206.479	251.372	229.480	188.816	37.050	37.220	25.010	27.260	35.830
272.125	236.495	193.041	171.575	423.527	237.564	335.356	230.495	235.665	225.738	183.835	43.720	29.450	24.120	22.230	42.910
249.433	277.017	225.812	207.907	417.952	231.925	418.857	249.830	278.175	198.897	220.114	32.360	23.560	28.040	22.210	47.480
369.268	282.927	209.951	209.269	417.105	265.732	392.418	188.648	363.739	243.683	170.690	35.180	24.320	29.070	23.750	44.510
323.838	295.273	204.591	225.546	486.238	200.707	378.252	229.262	280.712	230.737	201.958	39.720	28.120	30.100	18.620	37.190
286.086	276.812	174.955	170.931	322.117	198.788	299.833	224.999	276.712	226.889	190.067	33.740	38.540	26.810	32.570	37.410
364.554	217.813	170.951	176.845	355.266	211.607	324.248	208.868	265.316	199.564	182.514	37.490	32.670	25.140	22.370	38.910
327.153	262.482	210.538	178.848	339.440	192.705	358.620	234.529	271.758	215.567	172.215	31.670	31.990	25.070	24.900	37.140
354.725	295.507	186.348	189.469	377.257	223.374	392.610	225.482	276.559	192.722	223.191	38.010	25.290	32.350	18.570	48.700
299.488	293.905	229.814	204.759	310.437	239.730	342.246	224.095	306.450	213.673	182.904	37.670	31.250	21.390	24.120	46.990
360.489	290.510	188.806	183.327	491.769	264.714	354.034	264.847	379.621	237.399	173.794	36.530	26.590	34.970	21.060	41.140
316.151	227.717	159.053	203.610	408.943	242.505	269.345	219.833	270.659	213.446	204.666	37.810	32.860	25.710	25.390	35.720
305.852	296.935	230.295	225.787	427.427	253.691	394.965	259.358	309.150	212.527	228.256	35.960	22.350	29.720	20.400	48.550
322.246	264.378	225.858	216.717	302.855	219.929	403.504	229.025	300.201	207.216	233.724	35.440	31.440	29.150	19.880	43.900
291.555	252.604	218.611	236.903	456.455	262.046	391.445	236.639	311.648	199.558	184.512	39.460	29.760	36.090	23.300	43.970
236.833	260.316	210.413	170.027	376.330	248.500	496.637	230.400	220.692	224.208	185.296	37.360	26.400	28.990	21.220	36.010
294.797	283.676	220.539	216.965	354.776	246.087	413.710	241.162	348.908	228.391	194.229	33.040	25.410	27.290	26.910	37.170
279.885	264.831	163.422	137.679	306.262	206.659	223.950	220.297	217.717	229.742	188.057	36.170	32.370	25.630	25.350	37.310
313.078	290.249	191.419	210.219	427.024	210.182	403.796	224.679	372.954	202.456	203.880	34.950	27.130	32.120	20.090	42.560
245.628	288.196	155.717	189.129	343.510	253.609	356.597	207.179	321.721	217.010	200.774	40.110	23.750	30.120	27.590	37.540
261.904	261.004	229.118	216.362	403.720	225.851	328.560	251.173	287.637	217.860	180.428	35.510	28.850	32.000	21.010	44.000
320.485	257.340	210.849	200.008	386.996	192.921	276.896	207.017	397.908	202.454	212.719	36.540	23.520	22.610	20.220	36.350
168.396	233.021	181.107	185.140	297.449	169.496	264.511	229.877	248.434	205.794	199.461	37.150	33.690	30.210	24.930	38.940
301.896	289.929	219.953	229.517	438.253	231.696	426.084	260.621	316.568	269.626	210.514	36.480	24.300	26.950	20.330	41.560
234.603	288.275	200.182	200.370	275.266	208.926	298.239	223.371	189.372	204.255	212.531	36.610	32.940	26.140	17.330	40.820
273.059	261.169	250.235	225.539	431.095	212.578	411.373	198.818	364.797	190.198	200.871	37.360	27.750	31.840	22.020	38.300
282.550	262.040	224.518	226.457	429.601	271.234	412.626	219.205	349.620	205.105	182.995	37.860	26.150	32.760	21.970	38.090
244.286	219.715	159.345	174.176	204.776	182.083	211.434	162.014	168.977	161.257	193.779	35.620	38.740	27.540	27.870	30.100
272.555	249.813	201.074	205.415	463.241	247.905	318.784	215.646	351.321	237.926	187.539	37.160	30.360	34.040	21.440	44.030
141.819	182.355	147.325	170.197	307.841	146.229	245.778	224.385	135.268	179.179	170.297	38.420	42.790	29.050	21.090	38.470
284.488	251.889	195.249	237.490	393.101	258.082	402.318	270.182	299.530	220.276	199.070	36.780	28.700	26.400	25.680	36.980
317.825	260.763	231.290	227.502	347.574	259.071	421.504	229.679	334.393	187.432	221.370	35.430	26.450	30.160	21.930	35.440
252.227	213.665	179.843	134.304	257.943	197.438	300.162	195.223	191.444	214.329	173.230	37.430	35.840	30.430	27.740	28.910
255.950	268.008	198.239	244.688	433.314	236.249	374.762	247.815	308.479	258.167	211.184	36.860	27.370	21.220	28.220	38.420
241.335	267.385	217.223	195.089	398.631	234.933	465.086	236.569	414.253	254.441	204.209	38.990	24.880	26.740	19.010	40.900
269.960	269.180	199.256	158.288	359.261	208.953	441.084	220.654	326.002	232.242	201.928	38.530	31.320	28.900	26.420	45.130
207.333	229.554	165.013	194.631	327.260	211.691	290.113	200.726	225.643	194.879	175.688	32.510	33.210	25.730	26.470	33.970
205.541	255.958	207.992	234.446	373.897	222.838	375.307	242.832	288.421	242.130	233.194	36.790	23.510	31.610	21.760	43.770
258.156	270.321	207.011	161.221	322.160	229.667	308.401	196.371	304.554	239.570	170.641	41.990	27.040	27.110	19.020	33.700
207.439	219.578	177.436	167.460	300.869	177.123	273.575	217.528	211.305	210.188	176.659	38.660	33.220	23.330	24.340	38.760
348.410	275.971	210.868	200.291	380.184	250.609	366.582	215.021	275.953	207.882	202.481	39.560	30.590	33.910	23.460	39.470
257.829	219.644	142.363	180.500	277.021	151.061	253.391	189.921	163.954	179.651	129.238	30.050	39.640	22.300	24.970	39.640
145.497	227.534	105.887	144.016	225.421	166.503	214.508	182.891	194.797	210.304	161.812	39.160	37.020	29.070	30.150	28.560
266.568	271.221	229.119	252.462	394.390	236.642	410.410	239.682	367.505	182.734	185.159	39.000	29.550	31.830	21.010	45.010
278.184	244.692	188.377	135.498	288.868	201.226	178.562	190.491	220.472	219.761	185.174	31.730	32.280	21.790	31.040	34.960
211.860	254.286	193.278	222.712	307.750	232.128	269.241	202.646	236.168	217.478	176.682	34.970	35.000	26.900	27.920	35.600
245.136	235.212	165.613	143.875	268.431	205.302	261.453	202.356	180.890	187.612	183.111	38.760	34.870	26.330	26.190	36.620
234.006	217.413	158.080	160.957	312.678	170.438	158.072	179.568	175.733	174.875	147.056	35.730	37.700	31.670	27.660	34.570
347.292	258.271	191.689	179.625	350.130	209.635	364.708	228.015	277.312	217.378	171.088	37.060	29.040	27.020	27.960	34.690
345.205	307.057	209.712	224.460	460.660	252.797	370.884	237.745	261.276	236.812	222.989	37.210	23.910	31.950	29.830	42.600
317.650	266.618	220.267	234.900	418.248	224.501	426.385	237.357	323.004	198.723	193.940	42.320	27.330	35.660	20.400	35.440
343.402	276.040	229.814	205.638	508.920	237.728	309.382	214.583	360.809	204.165	211.867	35.650	28.990	32.970	28.010	35.420
160.674	184.576	142.110	167.333	246.507	158.563	190.403	161.339	195.031	127.948	110.643	42.230	41.960	42.350	32.230	39.280
323.454	310.988	213.795	232.267	427.273	233.096	336.296	227.413	244.319	231.500	230.331	40.870	30.380	34.150	22.570	48.650
282.868	270.417	162.728	187.677	334.324	207.686	319.693	209.235	273.528	235.641	189.825	40.130	32.660	22.670	27.710	38.150
310.171	243.241	193.407	203.483	255.096	209.950	244.627	200.045	210.405	227.183	202.379	35.520	37.050	26.770	22.280	35.430
283.978	203.771	159.773	174.468	218.325	177.369	254.013	185.113	175.966	181.386	195.980	35.890	33.830	20.660	29.290	28.940
226.366	174.398	146.860	194.112	327.609	181.238	178.769	178.641	163.255	186.268	160.376	29.900	37.880	24.710	27.010	38.140
220.422	195.958	150.464	152.215	171.188	181.629	253.716	198.812	142.799	127.885	140.886	31.530	38.470	35.530	35.190	36.460
191.635	244.800	177.693	149.450	389.708	182.041	252.422	203.128	199.116	197.271	191.593	34.170	34.990	21.710	35.320	36.320
165.949	202.334	146.697	136.805	230.545	167.732	196.675	146.469	193.701	124.750	101.603	38.630	42.120	27.490	31.000	33.690
296.037	255.963	215.665	172.511	316.628	225.535	374.171	213.734	293.648	231.828	195.073	39.980	28.180	23.040	25.610	39.180

182.650	179.800	128.591	135.073	249.035	169.478	190.867	207.568	193.904	181.330	190.197	32.630	44.810	30.570	27.340	32.740
188.449	156.750	110.937	112.178	180.530	144.602	198.643	165.298	177.476	98.105	85.485	36.190	36.920	41.150	31.590	38.080
170.110	148.767	129.356	109.446	260.333	162.850	143.730	134.799	202.864	135.091	78.466	39.600	34.000	31.300	33.730	37.990
186.170	146.444	76.975	141.593	193.255	142.917	158.687	160.941	138.439	137.446	124.503	33.990	34.030	34.980	29.380	41.860
131.957	224.124	92.613	121.394	282.843	149.865	221.282	210.888	183.979	177.809	129.508	42.520	41.400	26.930	25.400	39.440
174.698	198.062	146.397	130.607	247.494	159.928	222.659	166.008	182.476	118.730	116.750	41.990	37.500	33.150	29.800	35.400
235.426	201.710	181.234	169.077	325.815	201.122	297.085	212.753	255.296	230.566	186.718	31.120	33.650	24.390	28.430	34.180
375.359	302.343	218.567	227.973	433.146	275.775	421.908	240.395	212.582	208.083	220.018	34.100	25.120	37.640	17.520	36.940
123.611	171.735	70.629	129.043	210.706	110.187	173.267	155.718	174.807	130.318	91.117	36.590	36.110	35.390	32.570	40.570
228.109	189.804	146.256	159.345	274.497	191.946	269.899	188.527	241.091	170.483	185.934	30.390	34.840	28.630	25.160	34.850
267.212	264.928	205.612	213.320	326.429	204.415	257.265	188.454	231.970	188.140	197.824	38.740	32.090	24.920	23.990	32.620
219.507	174.845	112.231	114.100	219.480	156.273	182.883	146.593	147.298	127.174	132.019	43.880	40.800	33.440	36.220	33.500
282.872	232.265	167.914	195.819	368.343	253.128	301.440	172.071	152.771	219.426	147.753	37.750	40.230	26.200	21.820	35.910
202.041	194.181	112.721	167.654	270.606	207.894	180.643	187.819	166.161	163.727	155.259	33.380	39.290	29.000	33.340	30.560
175.775	197.179	134.438	154.998	216.592	147.944	186.067	186.088	201.933	215.772	172.258	31.830	33.200	28.010	27.770	35.380
240.813	210.962	171.097	171.850	338.284	193.756	199.983	227.838	262.924	196.220	189.597	30.340	32.230	30.020	25.270	33.540
187.614	199.707	147.065	163.604	250.871	155.944	241.612	173.226	178.422	159.176	117.224	37.990	34.390	29.970	32.050	33.000
199.956	211.004	128.709	198.958	284.769	201.477	220.628	216.895	223.201	167.959	149.182	38.760	37.870	28.110	25.610	37.900
154.081	180.651	120.641	82.455	189.352	140.020	162.501	169.921	141.035	113.092	109.751	38.820	38.560	37.390	35.570	42.400
161.141	161.423	72.235	138.442	202.893	135.286	236.742	149.271	166.279	125.855	100.606	39.160	46.550	31.440	30.370	45.140
335.041	296.637	255.137	212.660	394.021	269.214	444.340	258.082	349.817	185.271	192.217	41.030	21.270	30.450	25.470	43.280
289.803	302.510	217.141	195.113	443.176	252.026	353.566	228.116	286.011	198.589	211.460	41.270	24.380	24.000	23.330	38.950
143.691	185.506	127.795	134.003	237.253	145.637	171.064	164.219	158.974	156.343	150.626	35.430	43.290	30.790	32.170	40.030
105.193	151.410	108.945	105.032	198.061	137.115	170.564	147.993	161.253	128.651	98.392	40.640	39.770	33.960	37.390	37.750
150.537	234.104	126.084	138.349	245.717	140.994	237.345	154.592	178.339	187.657	116.066	40.650	47.240	32.870	31.590	39.950
212.236	201.980	144.685	178.676	243.855	141.214	198.447	186.643	138.305	163.835	122.693	35.400	44.270	28.420	26.030	36.440

KE240WF	KF60WF	KF240WF	PF60WF	PF240WF	DF60WF	DF240WF
30.830	37.580	29.570	29.250	16.210	27.260	22.070
40.210	35.250	35.650	16.090	19.870	24.500	29.630
31.660	37.290	27.100	20.170	16.550	26.130	32.130
27.680	31.930	27.670	16.420	20.390	24.030	20.070
34.740	33.990	30.680	23.730	17.780	29.940	25.030
39.180	39.660	25.600	20.850	24.160	29.760	16.190
43.560	33.440	32.450	19.110	20.950	28.670	24.200
35.040	43.690	25.120	17.940	19.340	27.270	26.050
41.140	39.810	34.950	23.900	23.300	21.650	25.940
41.310	34.370	34.440	21.370	23.050	26.560	25.970
34.590	40.090	32.970	16.430	22.390	28.260	23.310
32.280	35.390	25.440	21.860	20.750	26.540	25.380
38.780	37.350	26.200	17.320	22.010	22.910	25.380
33.320	38.670	32.640	23.210	27.340	24.770	21.030
33.780	36.660	28.930	20.260	17.850	29.120	18.270
29.150	33.980	27.950	31.560	18.540	25.470	31.650
27.130	35.690	27.590	19.510	18.910	25.040	22.600
33.740	38.790	30.520	22.880	16.360	23.960	23.070
28.570	35.660	23.680	22.920	12.020	22.380	19.780
36.420	38.550	28.350	25.750	20.000	30.730	22.330
27.570	38.830	27.460	20.920	22.290	39.550	25.960
28.690	33.630	27.800	22.560	21.600	23.330	28.750
34.730	43.750	29.290	17.940	19.340	28.250	19.490
28.280	40.000	25.350	24.550	21.070	30.060	21.220
44.880	31.870	30.350	21.330	18.390	27.020	30.860
35.910	38.780	29.860	22.220	22.440	29.680	20.510
27.870	44.940	26.980	19.560	17.650	23.610	22.360
29.350	39.150	18.310	21.520	15.560	22.940	26.340
33.680	40.170	28.330	13.460	14.060	21.160	24.040
36.670	36.030	28.800	22.850	22.740	25.500	27.350
36.650	34.750	28.420	24.280	16.870	36.750	33.160
25.960	32.390	25.420	25.070	24.820	34.940	27.640
48.590	33.080	36.670	18.330	15.130	26.800	32.110
34.590	39.520	26.540	20.160	20.960	25.960	20.360
32.750	33.820	25.380	20.820	16.710	21.200	24.960
30.130	32.790	26.980	26.170	15.590	29.080	23.740
33.190	42.700	24.690	14.700	19.180	30.110	19.070
46.890	37.760	41.820	18.220	27.670	24.220	36.110
31.260	46.310	25.360	18.410	16.640	27.910	19.790
34.490	37.140	29.000	16.740	21.490	32.380	22.850
38.140	40.460	27.500	18.670	17.920	25.330	23.700
39.720	32.740	28.230	24.860	25.560	27.520	26.040
31.950	37.190	24.600	18.440	14.640	21.140	19.660
29.160	37.670	22.220	22.570	15.120	25.140	16.800
37.680	38.650	26.890	20.570	13.540	28.700	23.910
46.400	33.250	34.120	22.310	19.990	30.630	32.080
34.290	36.950	28.080	20.140	16.470	25.510	19.150
30.350	41.210	25.660	24.110	17.640	24.400	20.540
46.140	34.210	29.660	23.760	15.490	24.210	24.800
32.360	39.430	25.300	20.500	17.230	30.460	21.580
28.400	32.400	28.660	19.680	19.210	28.250	26.130
24.440	34.650	28.570	30.520	18.190	33.160	25.660
36.930	41.380	27.120	12.820	18.250	20.640	24.550
40.580	34.580	28.920	19.660	26.580	35.260	24.760
36.030	38.270	32.170	22.530	20.610	31.490	24.160
41.280	32.940	38.880	23.280	18.600	23.590	23.730
51.950	30.420	40.780	17.600	14.550	32.890	29.860
31.660	41.330	30.860	21.950	23.330	26.860	28.260
34.780	32.940	28.520	19.320	18.760	25.560	21.650
39.130	34.680	28.890	22.130	21.430	25.410	26.160
33.990	34.310	26.140	29.170	25.300	23.480	26.490
37.340	36.740	27.350	16.090	25.060	28.020	28.410
32.820	37.740	29.410	22.810	20.080	30.470	21.460

34.290	38.880	32.220	20.460	17.710	25.850	24.040
33.820	43.050	27.600	29.140	23.520	30.570	24.650
40.080	32.600	42.780	23.660	21.070	22.210	25.780
37.620	35.790	28.870	24.780	24.640	31.670	21.070
33.770	40.810	33.320	16.820	19.710	28.460	22.030
39.020	39.310	28.240	23.260	12.830	25.050	25.700
36.940	37.300	31.100	19.760	17.360	29.060	27.830
33.950	40.530	27.800	19.650	24.870	22.940	25.470
41.480	39.970	31.950	17.130	26.290	26.780	29.570
35.680	32.960	36.850	17.060	23.170	28.400	26.620
46.410	29.040	26.400	25.790	25.470	29.080	24.930
36.790	30.080	31.790	19.510	7.780	31.040	25.930
30.830	37.580	29.570	29.250	16.210	27.260	22.070
42.490	37.510	29.780	23.530	21.910	30.710	28.360
38.440	40.610	26.240	23.370	15.820	25.980	16.640
32.590	36.140	28.770	22.720	16.650	26.410	21.400
34.670	36.830	31.780	19.520	21.660	20.060	16.540
33.730	33.880	29.880	14.290	19.360	22.900	22.300
45.370	37.780	35.020	22.440	18.530	23.370	30.810
39.600	40.100	28.960	23.460	22.540	25.310	22.430
30.620	46.180	35.910	25.030	25.080	23.340	20.090
38.830	38.590	32.760	29.640	13.810	24.970	19.170
31.050	34.150	26.900	17.370	21.660	28.250	23.030
39.540	37.980	30.930	29.620	16.590	23.690	21.570
42.890	33.330	35.060	15.860	23.910	26.670	23.930
35.030	34.600	31.310	19.220	16.760	22.580	22.640
39.680	32.190	24.990	22.480	20.160	25.700	28.400
35.100	36.900	26.560	20.010	19.880	32.500	31.200
33.770	35.910	29.110	24.180	18.190	28.410	17.680
43.500	33.480	22.910	12.010	31.190	27.230	35.500
35.800	41.620	34.950	23.920	17.300	26.520	22.940
52.740	36.250	31.790	20.200	22.600	24.030	36.570
36.010	33.220	28.280	25.020	19.660	21.320	27.460
34.510	40.240	23.270	21.440	14.730	30.820	21.070
48.210	31.300	37.770	19.240	20.080	25.930	28.190
34.920	32.240	22.390	19.040	23.370	27.080	24.110
39.030	32.920	32.760	21.970	22.070	26.750	26.230
35.680	43.260	23.390	28.510	18.440	31.570	24.340
41.270	31.420	32.000	16.200	18.630	21.770	26.940
22.870	35.150	40.160	21.050	21.230	25.210	22.850
43.520	38.890	29.230	29.800	20.120	36.510	30.080
40.730	41.930	33.980	13.580	19.060	23.660	30.990
31.890	34.090	28.800	25.730	14.190	24.410	20.020
50.380	37.820	39.070	14.870	21.240	21.930	28.930
50.980	25.680	38.410	19.670	23.890	28.110	29.830
34.280	37.350	30.210	18.130	18.780	28.780	21.660
42.780	40.530	26.570	21.400	26.860	23.960	30.370
41.340	32.690	26.770	22.030	23.930	27.170	29.720
43.560	36.680	36.860	18.950	23.110	23.550	36.100
49.720	30.330	36.010	24.350	22.370	28.130	34.720
45.730	32.240	29.040	18.010	24.560	22.240	20.530
29.760	29.710	27.480	14.530	16.350	19.100	25.060
32.670	36.390	22.000	22.370	20.420	30.560	28.410
37.530	37.770	28.690	22.590	21.820	26.440	22.920
49.360	38.410	46.430	25.480	26.080	31.030	28.490
33.080	33.010	27.060	18.640	17.430	23.670	18.640
40.610	40.090	31.350	21.530	15.180	31.140	28.400
42.020	29.650	28.880	25.020	19.930	24.350	24.780
46.000	29.610	41.700	19.770	18.740	25.700	28.440
43.280	32.510	40.700	21.420	20.500	25.450	31.230
47.110	34.280	31.710	21.180	19.280	30.720	26.040
42.990	30.910	36.040	20.690	28.040	25.710	20.940
50.370	37.740	43.690	20.590	23.670	29.870	32.860
34.440	32.050	26.320	25.490	23.480	31.220	26.540

46.390	27.270	42.920	23.860	21.510	31.970	33.330
53.920	34.610	45.290	26.940	18.790	33.030	32.290
50.230	39.730	36.910	22.870	19.170	33.130	26.860
50.190	39.560	40.740	31.140	19.160	31.630	27.750
55.980	36.070	38.660	27.430	25.160	37.000	32.120
52.020	36.140	37.090	29.030	26.310	36.830	27.820
40.100	31.540	31.060	17.330	24.950	23.360	22.830
32.230	38.360	26.330	21.800	16.690	25.770	19.650
52.780	36.830	40.440	27.030	20.810	34.970	35.220
49.360	31.460	30.330	23.010	18.120	26.350	26.920
38.280	33.460	27.810	25.720	15.890	27.930	23.700
47.850	33.960	47.150	21.480	25.480	29.570	38.410
42.740	33.310	38.510	22.470	23.290	24.790	24.140
46.130	29.770	35.430	18.580	16.200	32.780	27.210
48.160	33.100	40.210	24.310	25.200	30.980	27.150
40.210	34.180	38.400	17.850	22.220	26.120	25.700
50.130	40.900	38.710	22.640	22.530	29.510	30.610
47.050	37.320	39.590	24.310	18.950	30.570	29.100
49.330	36.960	45.380	28.850	18.910	28.310	30.040
50.410	36.810	41.390	35.990	21.610	35.150	34.770
32.720	37.770	24.870	20.090	19.660	27.580	25.050
38.840	41.300	29.560	28.970	25.040	23.120	29.110
55.010	35.950	46.120	17.470	26.180	32.400	29.990
46.380	33.050	35.920	29.240	22.470	28.880	32.340
59.640	38.380	45.610	19.810	26.050	34.350	33.300
52.700	35.430	34.030	33.910	26.870	30.910	37.700