A Systematic Review and Meta-Analysis of Sex-based Differences in Resistance Exercise Training-induced Changes in Muscle Mass, Strength, and Functional Performance in Healthy Older (≥ 60 y) Adults

Stephanie Elizabeth Hawley

Department of Kinesiology and Physical Education

McGill University

Montreal, Quebec, Canada

August 2021

A thesis submitted to McGill University in partial fulfilment of the requirements of the degree of

Master of Science

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

LIST OF ABBREVIATIONS

1-RM – One repetition maximum
ASMM – Appendicular skeletal muscle mass
AWGS – Asian Working Group for Sarcopenia
BIA – Bioimpedance Analysis
BMI – Body mass index
BP – Bench Press
CI – Confidence Interval
CIHR – Canadian Institutes of Health Research
corr – correlation coefficient
COVID-19 – Coronavirus disease 2019
CP – Chest Press
Cr – Creatine
CrM + CLA - Creatine monohydrate (CrM) + conjugated linoleic acid (CLA)
CRP – C-reactive protein
CSA – Cross sectional area
CT – Computed tomography
DXA – Dual energy x-ray absorptiometry
ES – Effect size
EWGSOP – European Working Group on Sarcopenia in Older People
EWGSOP 2 – European Working Group on Sarcopenia in Older People 2
FFM – Fat-free mass
FNIH – American Foundation for the National Institutes of Health
GH – Growth hormone
GUG – Get Up & Go
IAAT – Intra-abdominal adipose tissue
ICD-10-MC – International Classification of Diseases, Tenth Revision, Clinical Modification
IGF-1 – Insulin-like growth factor-1
IL-6 – Interleukin-6
IWGS – International Working Group on Sarcopenia
KE – Knee extension
LCn-3PUFA – long-chain n–3 polyunsaturated fatty acids (PUFAs)
LE – Leg extension
LP – Leg press
MPB – Muscle protein breakdown
MPS – Muscle protein synthesis
MRI – Magnetic resonance imaging
PHAC – Public Health Agency of Canada
PICO – Population, Intervention, Comparison, Outcome
Pla – Placebo

PRISMA – Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROSPERO – International Prospective Register of Systematic Reviews
RDA – Recommended dietary allowance
RevMan – Review Manager
SD – Standard deviation
SEM – Standard error of the mean
SMD – Standardized mean difference
SPPB – Short Physical Performance Battery
TUG – Timed Up & Go
ΔMean – Change in mean
ΔSD – Change in standard deviation

ABSTRACT

Purpose: The purpose of this thesis was to perform a systematic review and meta-analysis examining sex-based differences (i.e. differences between males and females) in resistance exercise training-induced changes in skeletal muscle mass, muscle strength, and functional performance in healthy older adults aged 60 years and older.

Design: Systematic review with meta-analysis.

Data Sources: MEDLINE and EMBASE via Ovid, CINAHL and SPORTDiscus via EBSCO, and Scopus were searched.

Eligibility Criteria: Studies included were of males and females ≥ 60 years of age who performed identical resistance training interventions and had outcome measures of skeletal muscle size, muscle strength, and/or functional performance.

Results: Data from 35 studies (1,142 participants; 518 males 624 females) were included in our systematic review and meta-analysis. Mean study quality was 17.63/28 on a modified Downs and Black checklist, considered moderate quality. Older males gained more absolute upper-body strength (ES = 0.75 [95% CI 0.54, 0.96], $p < 0.00001$; $I^2 = 0\%$, $p = 0.72$), and absolute lower-body strength (ES = 0.46 [95% CI 0.29, 0.63], $p < 0.00001$; $I^2 = 35\%$, $p = 0.02$) than older females; however, there were no sex differences in relative gains in upper-body or lower-body strength. There were no sex differences in absolute or relative gains in whole-body fat-free mass (FFM), limb muscle mass, type I, IIa, or IIx muscle fiber size, or functional performance (i.e. chair rises and walking capacity tests).

Conclusion: The results indicate the existence of some sex differences in the adaptive response to resistance exercise training in healthy older adults when the results are presented in an absolute context, but not when the results are presented in a relative context.

RÉSUMÉ

Objectif: L'objectif de cette thèse était d'effectuer une revue systématique et une méta-analyse pour examiner les différences fondées sur le sexe (par exemple, les différences entre les hommes et les femmes) dans les changements induits par l'entraînement contre résistance sur la masse musculaire squelettique, la force musculaire et la performance fonctionnelle chez les personnes âgées en bonne santé de 60 ans ou plus.

Le Devis d'Étude: Une revue systématique avec méta-analyse.

La Source des Données: MEDLINE et EMBASE à travers Ovid, CINAHL et SPORTDiscus à travers EBSCO, et Scopus ont été examinés.

Les Critères d'Éligibilité: Les hommes et les femmes âgés de 60 ans ou plus qui ont effectué l'intervention de l'entraînement contre résistance avec des mesures de résultats de la force musculaires, de la grosseur des muscles et/ou de la performance fonctionnelle.

Les Résultats: Données de 35 études (1,142 participants; 518 hommes, 624 femmes) ont été incluses pour l'analyse. La qualité moyenne des études selon la liste de contrôle de Downs et Black était 17.63/28, soit une qualité modérée. Les hommes âgés ont gagné plus de force absolue pour le haut du corps (ES = 0.75 [95% CI 0.54, 0.96], $p < 0.00001$; $I^2 = 0\%, p = 0.72$), et de la force absolue pour le bas du corps (ES = 0.46 [95% CI 0.29, 0.63], $p < 0.00001$; $I^2 = 35\%, p = 0.02$) que les femmes âgées, pourtant, il n'y avait aucune différence entre les hommes et les femmes pour la force relative pour le haut du corps ou le bas du corps. Il n'y avait aucune différence fondées sur le sexe absolues ou relatives dans les masse maigre corporelle, la masse musculaire des membres et tailles de fibres de type I, IIa, IIx, et de la mesure de la performance fonctionnelle (élévations de chaise et des tests de la marche à distance).

La Conclusion: Les résultats montrent l'existence de quelques influence des sexes pour la mesure de la force musculaire suite à un entrainement contre résistance chez les personnes âgées en bonne santé quand les résultats sont présentés dans un contexte absolues mais pas quand les résultats sont présentés dans un contextes relative.

ACKNOWLEDGEMENTS

I would sincerely like to thank my supervisor Dr. Tyler Churchward-Venne for his mentorship, support, kindness, and for his dedication to quality and perfection in research. Due to COVID-19, my thesis topic had to be changed halfway through my Master's degree. I would not be where I am today if Tyler was not always there for me, and always with my best interests at heart. I have been fortunate to have been mentored by Tyler since summer 2018. Over these past 3 years, I have had so many experiences and have learned so much, but most importantly I would like to thank Tyler for helping me mature into the student, researcher, and person I am today. Tyler has inspired me with his work ethic, achievements, and the trust and never-ending support he has given me.

I also owe a special thank you to corresponding author, Dr. Jenna Gibbs. She has been very generous in sharing her expertise. Her knowledge on meta-analyses and guidance throughout the project has been a great asset. Both Dr. Jenna Gibbs and Dr. Charlotte Usselman were members of my thesis advisory committee. They have dedicated their time and efforts in providing me with excellent feedback. I have known both Dr. Jenna Gibbs and Dr. Charlotte Usselman since the beginning of my research career (3 years ago), and they have always been friendly faces in the department for me. They never failed to show me support when I needed it, and I feel very lucky to have had the opportunity to work with such amazing, kind and accomplished mentors. I would like to thank Marcela Isuster, the Kinesiology and Physical Education Department's librarian for all her help in the early stages of the project. Her knowledge and advice were instrumental in facilitating the start of the meta-analysis and systematic review.

CONTRIBUTION OF AUTHORS

Stephanie E. Hawley (first author): conceived and designed the meta-analysis, registered the protocol, established the search strategy, conducted the search, extracted and analysed the data, interpreted the results of the included data, prepared the figures, drafted the thesis, read and approved the final thesis, and holds primary responsibility for the final content along with the principle investigator (Dr. Tyler A. Churchward-Venne).

Yi Jia Huang: Extracted and analysed the data, interpreted the results of the included data, and prepared the figures.

Dr. Jenna Gibbs: Interpreted the results of the included data, read and provided feedback on thesis drafts.

Dr. Tyler A. Churchward-Venne (principle investigator): conceived and designed the meta-analysis, oversaw the execution of the meta-analysis, interpreted the results of the included data, edited and revised the thesis, read and approved the final thesis, and holds primary responsibility for the final content.

CHAPTER 1. INTRODUCTION

Between 2017 and 2050, the global population of people 60 years of age and older is projected to increase from an estimated 962 million to over 2.1 billion (1). Advancing age is associated with profound changes in body composition. An age-related change that is increasingly being recognised to have important consequences for the older adult is the loss of muscle mass and deterioration of muscle quality. The loss of muscle mass with aging was termed 'sarcopenia' by Rosenberg (in 1989), who derived the term from the Greek 'sarx' meaning 'flesh' and 'penia' meaning 'deficiency' (2). In 2018, the European Working Group on Sarcopenia in Older People (EWGSOP2) updated the official definition of sarcopenia as a muscle disease that manifests as low levels of muscle strength, muscle mass, and physical performance (3). Sarcopenia is a complex multifactorial disease that is thought to be precipitated by several contributing factors including low levels of physical activity, decreased dietary protein and energy intake, low-grade chronic inflammation, derangements in muscle protein metabolism, motor unit loss, alterations in hormone concentrations, and impaired mitochondrial function (4). The loss of muscle mass and strength leads to a decline in functional capacity, an increased risk of falls and fractures, and an increased risk of developing chronic metabolic diseases (5). The financial burden associated with sarcopenia is vast and is expected to increase with the expanding aging demographic. For example, Janssen and colleagues found that $18.5 billion ($10.8 billion in males, $7.7 billion in females), or about 1.5% of total direct healthcare costs in the U.S. in the year 2000, were attributable to sarcopenia (6). Therefore, it is critical to identify strategies that can effectively mitigate the progression of sarcopenia in order to improve the health and well-being of the older population and reduce healthcare expenditure.

Interventions that can reduce the progression of age-related musculoskeletal decline have great potential to improve the quality of life in older adults and have a profound impact on healthcare spending. Several interventions have been investigated as potential therapeutic approaches to slow down or reverse the process of sarcopenia including hormonal interventions, nutritional supplementation, and exercise training. In a review on the optimal management of sarcopenia in older adults, Burton and Sumukadas (7) concluded that resistance exercise training (i.e. performing the concentric and eccentric phase of each muscle contraction in 2–3 secs) appeared to have the largest effect on augmenting muscle mass and strength, and was the most effective intervention at counteracting the effects of sarcopenia. While the beneficial effects of resistance exercise training on skeletal muscle mass and strength are firmly established, resistance exercise training confers benefits that extend even beyond that of skeletal muscle (8–10), such as reducing symptoms of depression (11). In 2019, the National Strength and Conditioning Association released a position statement with an overview of the current and relevant literature to provide evidence-based recommendations for resistance training for older adults (8). A potential limitation of these recommendations is that they are not sex-specific.

Until about 40 years ago, a lot of health research was only conducted on males, while females were actively excluded from participating in most clinical trials (12). However, females make up more than 50% of the population in Canada (985 males per 1000 females) and on average outlive males by ~5 years (13). There are a number of physiological differences between men and women that may contribute to the existence of sex differences in the adaptive response to resistance exercise training. It is well known that males tend to have greater skeletal muscle size and strength than females, due in part to their greater body size and height (14). In addition, there are reported differences between sexes in fatigability (15,16), inflammatory responses (17),

recovery time (18), and in overall muscle fibre size and composition (19). Despite a number of studies (20–31) comparing males and females to examine if there are sex-based differences in the adaptive response to resistance exercise training, there seems to be a discrepancy in the results (9). For example, some have noted significantly different muscle mass or strength adaptations between sexes when exposed to identical resistance training interventions (27–31), while others have revealed no differences between older males and females (21,24–26,32,33). Currently, it is unclear whether there are sex-based differences in resistance exercise training-induced changes in muscle mass, muscle strength, and functional performance in an exclusively older adult (≥ 60 years of age) population.

Therefore, the purpose of this thesis was to perform a systematic review and meta-analysis examining sex-based differences (i.e. differences between males and females) in resistance exercise training-induced changes in skeletal muscle mass, muscle strength, and functional performance in healthy older adults aged 60 years and older. It was hypothesized that older males would demonstrate greater absolute, but similar relative, gains in skeletal muscle mass, muscle strength, and functional performance compared to older females undergoing the same resistance training program.

CHAPTER 2. LITERATURE REVIEW

2.1 Aging Demographic

Between 2017 and 2050, the global population of people 60 years of age and older is projected to increase from an estimated 962 million to over 2.1 billion (1). Older adults also represent the fastest growing age group in Canada, with people aged 65 years and older reported to be at 18.0% on July 1st, 2020 (34). The average age in Canada is now 41.4 years and has increased by 4.1 years since 2000, when it was 37.3 years (35). Additionally, according to Statistics Canada, there were 11,517 centenarians reported in 2020, which is up 1,137 people (+10.4%) in one year in comparison to July 1st, 2019 (36). Within the older population females outlive males, with the average life expectancy being 80 years of age for males and 84 years of age for females in mid-2020 in Canada (37). Since females have a longer life expectancy, the vast majority of centenarians are women (81.3%) (36). With the increasing number of adults aged 65 or older, Health Canada is proactively conducting research and working to better understand the needs of older Canadians, to enact programs and services in response to the aging demographic (38).

In 2020, deaths in Canada (309,893) surpassed 300,000 for the first time in Canadian history. The Public Health Agency of Canada (PHAC) reported that 15,651 deaths (5.1% of all deaths reported) were due to coronavirus disease 2019 (COVID-19), and almost three quarters occurred among those aged 80 years and older (39). Although the COVID-19 pandemic resulted in excess mortality among seniors as well as a drop in the number of international migrants, the age and sex structure of the population over the year 2019/2020 was not significantly affected by these changes (35).

2.2 Age-Related Muscle Loss: An Overview

In 1989, Rosenberg proposed the term 'sarcopenia' (in Greek, sarx is flesh and penia is deficiency or loss) to describe the age-related loss of skeletal muscle mass (2). Aging is accompanied by a change in body composition, including a loss of skeletal muscle mass that is accompanied by a loss of strength and functional performance (40). In fact, according to Rosenberg, there is probably no decline in structure and function more dramatic than the loss of skeletal muscle over the latter decades of life (40). After the age of 60, it is estimated that muscle mass and strength are lost at a rate of ~1% and ~3% per year respectively (41). For both males and females the decrease in muscle mass is greatest in the extremities, with the rate of loss in the lowers limbs being substantially greater than the rate of loss in the upper limbs (42). Limb muscles from older men and women are 25–35% smaller and have significantly more fat and connective tissue than limb muscles from younger individuals (43). Lexell and colleagues observed a difference of up to 50% in muscle mass via cross sectional area (CSA) of the quadriceps muscle between 90-year-old and 20-year-old subjects (44). Skeletal muscles are mainly made up of type I (slow-twitch) and type II (fast-twitch) muscle fibres, and there is a decrease in both number and size of muscle fibres with age (5,43). Interestingly, the decline in skeletal muscle mass with aging is mainly attributed to a reduction in type II muscle fiber size (45). Comparisons of muscle biopsies from younger and older individuals reveal that type II fibres are smaller in the old, while the size of type I fibres is much less affected (43).

Muscle mass represents a major determinant of muscle strength (46). Goodpaster and colleagues reported an annualised rate of strength decline of 3.6% in men and 2.8% in women between 70 and 79 years of age (47). Additionally, muscle strength is closely related to functional performance in elderly. Bassey and colleagues (48) reported a significant correlation

between leg extensor strength and capacity to rise from a chair, climb the stairs, and walking

speed. Consequently, the decline in skeletal muscle mass, sarcopenia, is a major cause of the

increased prevalence of disability in the elderly (49). Sarcopenia generally increases the risk of

falls, vulnerability to injury, and is associated with an increased risk of developing chronic

metabolic diseases like type 2 diabetes, obesity, osteoporosis and cardiovascular disease (50,51).

2.2.1 Definition and Diagnosis of Sarcopenia

Rosenberg first introduced the term sarcopenia in 1989 (2) with the goal to draw more

attention towards the problem of the progressive loss of skeletal muscle mass and strength with

aging. Over the past 30 years, there has undoubtedly been more efforts in research to help

understand the epidemiology, as well as the causes and consequences of sarcopenia. However,

there are still variations in the definition and diagnosis of sarcopenia which make it difficult to

summarise the available research and decide on appropriate counteractive interventions. With

that being said, the major diagnostic guidelines concerning sarcopenia are those from the

European Working Group on Sarcopenia in Older People (EWGSOP), the International Working

Group on Sarcopenia (IWGS), the Asian Working Group for Sarcopenia (AWGS), and the

American Foundation for the National Institutes of Health (FNIH) (4,52,53). It wasn't until

2009-2010 when a practical clinical definition of age-related sarcopenia was developed by the

EWGSOP (54). In 2018, the working group (EWGSOP2) met again to update the definition of

sarcopenia as a muscle disease with an International Classification of Diseases, Tenth Revision,

Clinical Modification (ICD-10-MC) Diagnosis Code that can be used to bill for care in some

countries (3). The EWGSOP2 now define sarcopenia by low level of measures of three

parameters: muscle strength (cut-off points: grip strength <27 kg for men and <16 kg for women;

chair stand >15 s for five rises for both sexes), muscle quantity/quality (cut-off points:

appendicular skeletal muscle mass <20 kg for men and <15 kg for women), and physical

performance as an indicator of severity (cut-off points: gait speed ≤0.8 m/s) (3). As described by

the EWGSOP, a wide range of techniques can be used to measure muscle mass, muscle strength,

and functional performance (**Table 1**). Computed Tomography (CT), Dual Energy X-ray

Absorptiometry (DXA), and Magnetic Resonance Imaging (MRI) are the gold standard for the

assessment of muscle mass in research (3). Grip strength represents a reliable and simple

technique to measure muscle strength (55). On the other hand, knee extension/flexion techniques

are very suitable in scientific research, however require training and special equipment that make

it less practical for clinical use. To assess physical performance, there is the usual gait speed,

400-m walk test, the Timed-up-and-go test (TUG), and the Short Physical Performance Battery

(SPPB) which consists of gait speed, balance and sit to stand time (56).

Variable	Clinical practice	Research
Skeletal muscle mass	Cross sectional area (CSA) by Computed tomography (CT) or Magnetic Resonance Imaging (MRI)	CSA by CT or MRI,. Muscle quality by muscle biopsy, CT, MRI or Magnetic resonance Spectroscopy (MRS)
	Appendicular skeletal muscle mass (ASMM) by Dual Energy X-Ray Absorptiometry (DXA)	ASMM by DXA
	Whole-body skeletal muscle mass (SMM) or ASMM by bioimpedance Analysis (BIA)	SMM or ASMM by MRI
		Muscle quality by muscle biopsy, CT, MRI or Magnetic resonance Spectroscopy (MRS)
Skeletal muscle strength	Grip strength	Grip strength
	Chair stand test (chair rise test)	Chair stand test (5 times sit to stand)
Physical performance	Gait speed	Gait speed
	Short physical performance battery (SPPB)	SPPB
	Timed-up-and-go test (TUG)	TUG
	400-meter walk	400-m walk

Table 1. Measurements of skeletal muscle mass, muscle strength and physical performance in
research and practice (Adapted from Cruz-Jentoft et al, Age and Aging, 2019 (3)).

2.2.2 Causes of Sarcopenia

Sarcopenia is a multifactorial disease (57). The reduction of muscle mass occurs only when muscle protein content is reduced, and the protein content of a tissue is determined by the balance between the synthesis and breakdown of muscle protein (50). In healthy people at rest, muscle protein turnover occurs at a rate of ~1–2% per day (58). When the rate of muscle protein synthesis (MPS) over the course of a day matches the rate of muscle protein breakdown (MPB), muscle mass remains stable. An imbalance between MPS and MPB rates results in either a net gain (MPS > MPB = positive net protein balance) or net loss (MPS < MPB = negative net protein balance) of muscle mass (58). There is inconsistency in the literature regarding whether or not there is an age related reduction in basal resting MPS rates (59–63). However, aging is accompanied 'anabolic resistance' (64), a phenomena whereby the main anabolic signals that act to maintain muscle mass, namely nutrition (65,66) and physical activity (67), become dysregulated. Interestingly, Smith and Mittendorfer (58) demonstrated that this blunted MPS response is greater in older females than in older males. However, they also found that older females had an increased basal rate of MPS compared to older males (58). Alternatively, Horstman and colleagues (68) reported no differences in basal MPS rates between middle-aged women and men; however the response to nutrition (protein ingestion) was greater in women than in men. Therefore, there may be important sex-based differences in skeletal muscle protein metabolism that ultimately contribute to age-related muscle loss.

A few other factors that have been suggested to be involved in the etiology of sarcopenia include immunological, hormonal, neurological, nutritional, and physical activity changes. Firstly, immunological changes are characterized by a subtle increase in circulating concentrations of inflammatory cytokines. This is due to the age-related increase in production of

interleukin-6 (IL-6), which in summary, can be described as an inflammatory mediator (4,69). In acute inflammation, interleukin-6 (IL-6) promotes the expansion and activation of T cells and differentiation of B cells, and modulates the synthesis of C-reactive protein (CRP) (70,71). This inflammatory state appears to contribute to anabolic resistance and play a key role in the development of sarcopenia (4,72). Several studies indicate that high levels of IL-6 or CRP may contribute to the loss of muscle mass and strength in elderly people (73,74). Secondly, age-related hormonal changes are characterised by a decrease in concentrations of testosterone, estrogen, growth hormone (GH), and/or insulin like growth factor-1 (IGF-1) (75). With aging, there is a significant decrease in estrogen concentration in females, and testosterone concentration in males. The overall reduction of testosterone is associated with loss of muscle strength, muscle mass, a reduction in bone mineral density, and increased risk of fracture risk following falls (7). Menopause is linked to a reduced concentration of circulating estrogen in middle to older aged women. During the postmenopausal period when ovarian hormone production has decreased, there appears to be an impaired muscle performance (7). GH is also required for maintenance of muscle and bone and exerts most of its anabolic actions through IGF-1 which is synthesized in the liver for systemic release. IGF-1 may play a role in muscle function by regulating skeletal muscle satellite cell activity and stimulating the synthesis of muscle contractile proteins (7). Adults who are deficient in GH have more adipose tissue and less fat-free mass than age-matched controls (47). Third, age-related neurological changes appear to be characterised by denervation of motor units which are then reinnervated with slow motor units (44). This may cause a higher prevalence of type I fibres in comparison to type II fibres and lead to a decrease in muscle strength given the larger specific force in type II fibres (7,44,74). Furthermore, studies have shown that muscle satellite cells, which are involved in muscle

regeneration, are lower in older adults (7). Specifically, there is a decline in type II muscle fibre satellite cell content which may contribute to the accelerated loss of muscle mass and strength with aging (76).

Finally, nutrition and exercise are two key life style factors that contribute to the etiology of sarcopenia. Both exercise (particularly resistance-type exercise) and dietary protein stimulate the synthesis of new muscle proteins. However, aging is associated with a decrease in food intake due to decreased energy expenditure, early satiety, and social isolation, as well as a decrease in physical activity due to the adoption of a more sedentary lifestyle (77). Many older adults do not consume sufficient amounts of dietary protein which contributes to the age-related reduction in lean body mass and increased functional impairment (78). For example, the current recommended dietary allowance (RDA) for protein is 0.8 g/kg bodyweight/day; almost 40% of people >70 years do not meet this RDA (78). As already alluded to, aging is also associated with 'anabolic resistance' to ingested protein (72), a phenomenon characterized by a blunted capacity of ingested protein to stimulate increased MPS rates. Although the precise cause of age-related anabolic resistance is unclear, age-related reductions in physical activity are thought to be a contributing factor (72). Evidence has shown that older adults who are less physically active are more likely to have lower skeletal muscle mass and strength and are at increased risk of developing sarcopenia (7). Regardless of age group, higher percentages of older adults who reported no physical activity in the past month, or reported difficulty with one or more functional activities (difficulty walking up or down stairs, dressing and bathing, and performing errands alone), reported falls, and fall-related injuries (79).

Since the COVID-19 pandemic started at the end of 2019, social isolation has been adopted worldwide to control the severe acute transmission of the virus. Although social

isolation measures are necessary, especially for older adults who are disproportionately prone to experiencing the negative effects of the COVID-19 pandemic, these drastic measures have led to an average decline in physical activity (80). As stated earlier, low levels of physical activity are one of the main risk factors for sarcopenia (81). The combined effects of aging and an adopted sedentary lifestyle due to the COVID-19 restrictions amongst older adults will be deleterious. Therefore, it is crucial now more than ever, to identify and implement effective intervention programs to reverse the detrimental loss in muscle mass and strength, and thus functional performance in older adults (82).

2.2.3 Consequences of Sarcopenia

Muscle makes up ~ 47–60% of lean body mass in men and women, and is one of the greatest contributors to whole body energy expenditure (83). Skeletal muscle mass is essential to perform activities of daily living and regulation of overall metabolic health. Muscle impairment is associated with an increased risk of adverse outcomes including physical disability, poor quality of life, and death (84). Therefore, maintaining skeletal muscle health is critical to maintaining longevity throughout the life course, and preserving skeletal muscle mass could be a potential reversible cause of morbidity and mortality in older persons (33,85). Since adequate muscle mass and strength are fundamental in preserving functional mobility in older adults, this has been an increasingly important theme of research in recent years (49). The functional consequences of age-related sarcopenia are shown in **Figure 1** (14). Many consequences of sarcopenia are prognostic indicators of public health burden, such as the development of physical disability, nursing home admission, depression, hospitalization, and even mortality (86). Not only does sarcopenia predict a loss of independence for daily life activities, it is also associated with falls in elderly men and women (87). Muscle weakness that accompanies advanced age has

been positively related to the risk of falling and fracture in older individuals (5,88). In 2014,

Tanimoto and colleagues conducted a study with 1,110 community-dwelling Japanese subjects

aged 65 or older and found that sarcopenia was significantly associated with risk of falls in both

men (odds ratio 4.42, 95%CI: 2.08–9.39) and women (odds ratio 2.34, 95%CI: 1.39–3.94)

(89). Falls are the leading cause of injury among adults aged ≥65 years (older adults) in the U.S.

where more than 1 in 4 older adults report falling each year (79). This results in about 36 million

reported falls annually which can lead to significant functional decline and extensive medical

costs (79). Moreover, the increase in falls and fractures results in an increased tendency for

nursing home admissions and loss of independence (40).
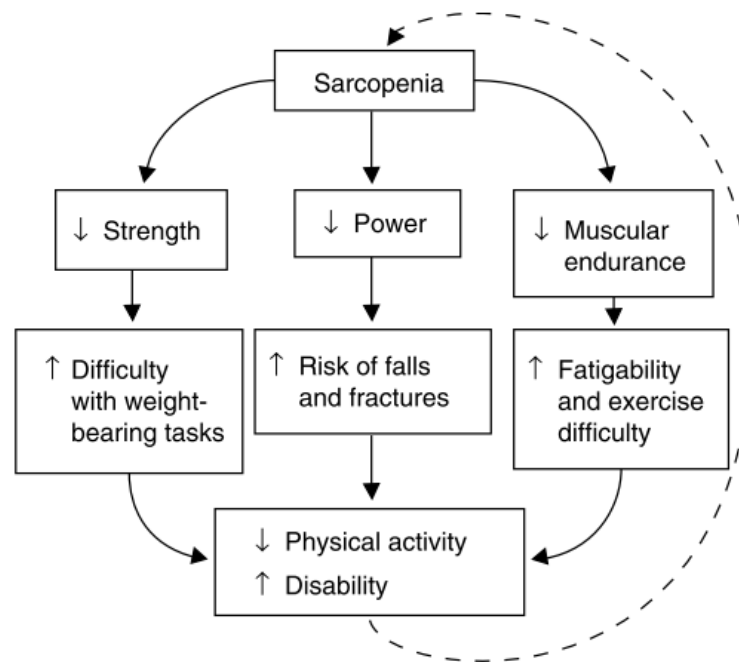
Figure 1. A model of the functional consequences of age-related sarcopenia (14).

2.2.4 Burden of Sarcopenia

A recent systematic review and meta-analysis with data from 35 articles and 58,404

individuals around the world estimated the overall prevalence of sarcopenia to be 10% both in

men and women over 60 years old (90). This number rises up to >50% in adults over 80 years old (8,91). Another recent meta-analysis from 2019 conducted by Papadopoulou and colleagues (92) with data from 41 studies and a total of 34,955 participants, concluded that the prevalence of sarcopenia in community-dwelling individuals was 11% in men and 9% in women; in nursing-home seniors it was 51% in men and 31% in women; whereas among hospitalized individuals it was found to be 23% and 24% for men and women, respectively (92). Prevalence rates are lower in community-dwelling older adults than those residing in nursing-home facilities or those hospitalized individuals.

Currently, economic data on sarcopenia is limited. Janssen and colleagues found that $18.5 billion ($10.8 billion in men, $7.7 billion in women), or about 1.5% of total direct healthcare costs in the U.S. in 2000, were attributable to sarcopenia (6). These costs are represented by hospitalization, nursing home admissions and home healthcare expenditures (6,93). These estimates suggest that, if the prevalence of moderate and severe sarcopenia were reduced by 10%, it would result in savings of $1.1 billion per year in U.S. healthcare costs (6). Thus, even a modest reduction in the prevalence of sarcopenia in older persons would bring about marked healthcare savings when compiled over a number of years (6). These costs reflect the loss of skeletal muscle mass that occurs with advancing age and could theoretically be avoided if individuals maintained a healthy skeletal muscle mass throughout the lifespan (6). As the proportion of older adults living in Canada and around the globe continues to grow, so too will the number of falls and fall-related injuries. However, many of these falls are preventable. To help keep older adults living independently and injury-free, reducing fall risk and fall-related injuries is essential (79). The financial burden associated with sarcopenia is vast and is expected to increase with the expanding aging demographic. Therefore, it is critical to identify strategies

that can effectively mitigate the progression of sarcopenia in order to prevent an epidemic of frailty, and improve the health and well-being of our older population. Interventions that can reduce the progression of age-related musculoskeletal decline have great potential to improve the quality of life in older adults and have a profound impact on healthcare spending.

2.2.5 Interventions to Counteract Sarcopenia

Many aspects of the epidemiology and pathophysiology of sarcopenia are better understood today than 10 years ago, thus researchers have been able to identify links between muscle pathology and adverse health outcomes (94). Currently, there are studies providing evidence that certain treatment strategies can help prevent or delay the adverse consequences of sarcopenia by increasing muscle mass, strength and functional capacity (7). Examples of strategies include: hormonal interventions, nutritional interventions, and exercise-based interventions (74). As the focus of this thesis is on sex-based differences in resistance exercise training-mediated changes in skeletal muscle mass, strength, and functional performance in older adults, this section will focus on resistance exercise training as a countermeasure to protect and restore skeletal muscle health in older adults. Readers interested in hormone-based therapies and/or nutritional interventions to counteract the deleterious effects of age-related musculoskeletal decline are referred to the following reviews (7,63,75,95).

2.3 Resistance Training: An Overview

One of the most effective means to counteract age-related musculoskeletal decline is a physically active lifestyle that includes resistance exercise training (7). Phillips and Winett (96) define resistance exercise training as a form of periodic exercise whereby external weights provide progressive overload to skeletal muscles in order to make them stronger and often results in hypertrophy (i.e. muscle growth). The external load lifted is classically expressed as a

percentage of the individual's one "repetition" maximum (1-RM), the maximum load that can be lifted once through a complete range of motion (96). The volume (dose) of resistance training is described by the load lifted, the number of repetitions, and the number of sets of repetitions (96). There are numerous other variables that can be manipulated within the design of resistance training programs, such as inter-set rest intervals, time under tension, number of sets/repetitions, and order of exercises (96). It is well established that traditional resistance exercise (i.e. performing the concentric and eccentric phase of each muscle contraction in 2–3 secs) is a safe and feasible mode of physical exercise that induces muscle hypertrophy and increases muscle strength in older adults (97). Since muscle strength appears to be indicative of disability (98,99), resistance training has the potential to directly improve functional capacity (100). In fact, Burton and Sumukadas (7) conducted a study to investigate the "optimal management of sarcopenia" and reported that resistance exercise training appeared to have the largest effect on augmenting muscle mass and strength, as well as attenuating the development of sarcopenia. Mechanistically, muscle accretion from resistance exercise may be caused by an increase in muscle protein synthesis (101), satellite cell activation and proliferation (102), anabolic hormone production (103), and a decrease in catabolic cytokine activity (97,104). Studies have shown that improvements in muscle strength can be achieved with as little as one 30 minute resistance exercise training session per week (105).

2.3.1 Benefits of Resistance Training in Older Adults

Numerous studies have demonstrated that resistance training is beneficial in older adults (7,106–109). According to Health Canada, weight-bearing physical activity reduces the rate of bone loss associated with osteoporosis, and also maintains flexibility, balance, and coordination (110). In addition to the fact that resistance training has the ability to induce muscle hypertrophy,

increase muscle strength, and counteract age-related declines in functional performance, current

research has shown that it confers benefits that extend beyond that of skeletal muscle (8–10).

There is an impressive array of changes in health-related biomarkers that can be derived from

regular participation in resistance training including improvements in body composition, blood

glucose regulation, insulin sensitivity, and blood pressure in individuals with mild or moderate

hypertension (111). Preliminary work suggests that resistance exercise may prevent and/or

improve depression and anxiety, increase vigour, and reduce fatigue (111).

Resistance training is even beneficial for oldest-old adults (≥ 90 years of age) and elderly

who are considered frail (112). Note that frailty and sarcopenia are distinct (94). While

sarcopenia is a disease that contributes to the development of physical frailty, the syndrome of

frailty represents a much broader concept. Frailty is a multidimensional geriatric syndrome that

is characterised by cumulative decline in multiple physiological systems over a lifetime,

resulting in negative consequences to physical, cognitive, and social dimensions (94). In a now

seminal study, Fiatarone et al. (113) examined the adaptations induced by resistance training in

100 frail elderly nursing home residents. The subjects underwent resistance training that

consisted of 3 sets of 8 repetitions at 80% of 1-RM, 3 times per week for 10 weeks (113). The

results revealed that resistance exercise training, even in older frail nursing home residents,

increases skeletal muscle size, muscle strength, gait velocity, stair-climbing ability, and overall

levels of physical activity (113,114). In a study by Serra-Rexach et al. (115), 20 very old subjects

(90–97 years of age) underwent resistance training 3 times a week for 8 weeks, with 2–3 sets of

8–10 repetitions at 30% of 1-RM in the initial phase of training, progressing to 70% of 1-RM.

The results demonstrated an increase in leg press strength (+10.6 kg; $p < 0.05$), and 1.2 fewer

falls per participant; however, they reported no significant differences in hand grip strength, 8-m

walk test, 4-step stairs test, and the TUG test (114,115). Finally, a systematic review on the effects of resistance training in physically frail older adults (70–92 years) reported only one case of shoulder pain with resistance training out of 20 studies and 2,544 subjects (114), indicating that it is a very safe intervention strategy.

Despite the known benefits of resistance training, only 8.7% of older adults over 75 years of age in the U.S. participate in muscle-strengthening activities as part of their leisure time (8). Some reported barriers to participation in resistance exercise for older adults include: safety, fear, health concerns, pain, fatigue, and lack of social support (116). In addition, participation in regular exercise training requires motivation by the individual which may be difficult for some older individuals (7). The low participation rates can be explained by the promotion of broad health benefits that are not tailored to a targeted enough population. There is a need for more specific evidence-based guidelines and individualised recommendations for resistance exercise for older adults (8). For example, if health benefits and motivation strategies were specific for older males or females, perhaps this would attract more participation.

2.3.2 Current Resistance Training Guidelines for Older Adults

In 2019, the National Strength and Conditioning Association released a position statement with an overview of the current and relevant literature to provide evidence-based recommendations for resistance training for older adults (8). The statement highlighted that resistance training is safe and beneficial for older adults. The general recommendations from this position statement (8) for resistance training amongst healthy older adults can be found in **Table 2**. In a systematic review done by Cadore and colleagues (114) on the effects of exercise interventions in frail older adults, it was concluded that resistance training programs should be performed two to three times per week, with three sets of 8–12 repetitions at an intensity that

starts at 20%–30% and progresses to 80% of 1-RM. They also found that to optimize functional

capacity, resistance training programs should include exercises in which the participants' body

weight is used for resistance and in which usual daily activities are simulated (such as the ''sit to

stand'' exercise) (114). Although these guidelines are beneficial and helpful, they do not account

for sex differences and were established based largely on data on men (12). An optimal

resistance training prescription is difficult to determine (117). Muscular adaptations mainly

depend on training intensity, frequency, and volume (117); however, they may also differ

between individuals depending on factors such genetic make-up, nutritional status, age, and/or

training status (9,107,118). Therefore resistance training programmes should be manipulated via

intensity, frequency, and volume according to individual differences.

Resistance training general recommendations for healthy older adults.†

Program variable	Recommendation†	Details
Sets	1–3 sets per exercise per muscle group	1 set for beginners and older adults with frailty progressing to multiple sets (2–3) per exercise.
Repetitions	8–12 or 10–15	Perform 6–12 reps with variation for muscular strength for healthy older adults. Perform 10–15 repetitions at a lower relative resistance for beginners.
Intensity	70–85% of 1RM	Begin at a resistance that is tolerated and progress to 70–85% of 1RM using periodization. Lighter loads are recommended for beginners, or individuals with frailty, or special considerations such as cardiovascular disease and osteoporosis. Exercises should be performed in a repetition-range intensity zone that avoids going to failure to reduce joint stress.
Exercise selection	8–10 different exercises	Include major muscle groups targeted through multijoint movements (e.g., chest press, shoulder press, triceps extension, biceps curl, pull-down, row, lower-back extension, abdominal crunch/curl-up, quadriceps extension or leg press, leg curls, and calf raise).
Modality	Free-weight or machine-based exercises	Beginners, frail older adults, or those with functional limitations benefit from machine-based resistance training (selectorized weight or pneumatic resistance equipment), training with resistance bands, and isometric training. High functioning older adults gain added benefit from free-weight resistance training (e.g., barbells, dumbbells, kettlebells, and medicine balls).
Frequency	2–3 days per week, per muscle group	Perform on 2–3 nonconsecutive days per week, per muscle group, may allow favorable adaptation, improvement, or maintenance.
Power/explosive training	40–60% of 1RM	Include power/explosive exercises where high-velocity movements are performed during the concentric phase at moderate intensities (i.e., 40–60% of 1RM) to promote muscular power, strength, size, and functional tasks.
Functional movements	Exercises to mimic tasks of daily living	Healthy, high functioning older adults benefit from the inclusion of multijoint, complex, and dynamic movements, with base of support or body position variations.

*RM = repetition maximum.
†General guidelines are provided. Resistance training programs should include variation in intensity and program variables. Strength exercises should be performed before endurance training during concurrent training sessions to optimize strength gains.

Table 2. General recommendations for resistance training amongst healthy older adults (8).

2.4 Sex Differences: An Overview

As mentioned, muscular adaptations to exercise depend on several factors, including age and sex. There is significant evidence to demonstrate that biological differences between males and females contribute to differences in their health (119). For example, the global prevalence of the number of diagnosed type 2 diabetic patients is reported to be higher in males than females (120,121). Although, for the same body mass index (BMI) females typically present with ~10% higher body fat compared to males. The 'gynoid fat distribution' with relatively more adipose tissue in the hips and thighs, confers protection against metabolic diseases, such as type 2 diabetes and atherosclerosis (122). Another notable physiological sex difference is that females generally exhibit a greater relative fatigue resistance than males (118,123). It is clear that biological sex influences the risk of developing certain diseases, the response to medical treatments, and the frequency of health care use (119). According to Countrymeters' 2020 Demographics on Canada, females make up more than 50% of the population in Canada (985 males per 1000 females) and outlive males by an average of ~5 years (13). However, females tend to have a faster onset of age-related muscle loss, and many diseases place a heavier burden on females compared to males including heart disease, cancer, rheumatoid arthritis, lupus, and osteoporosis. On the other hand, females are known to rely more on medical systems than males do, and are likely to seek treatment sooner (12).

However, until about 40 years ago, a lot of health research was only conducted on males, while females were actively excluded from participating in most clinical trials (12). Investigators believed that females were more difficult to recruit, and study because of their changes in hormone levels during the menstrual cycle, and the potential risks with pregnancies (85). Sex was not recognized as a variable in health research and was not considered to be a factor that

could affect health and illness, therefore the results from these clinical trials were being applied in medical practice to both males and females of all races (12). It was only in the late 1980s when concerns about clinical research being conducted primarily in a homogeneous white male population were first raised (12). Now, The Canadian Institutes of Health Research (CIHR) expects that all research applicants integrate sex into their research designs (119). Fortunately, the number of females participating in clinical trials has increased over the last two decades, but females are still underrepresented in general (12). Accounting for sex in health research has the potential to make health research more rigorous, more reproducible and more applicable to everyone (119).

2.5 Sex Differences in Muscle Mass, Strength, and Functional Performance

Sarcopenia is defined by low levels in three parameters: muscle mass, muscle strength, and functional performance (94). As such, it is important to understand the baseline differences or similarities in these parameters between sexes. Current research demonstrates that males and females are clearly different on many aspects of muscular health and physiology including muscle fibre composition, hormonal interactions, and mitochondrial content and function (85). It is well known that males tend to have greater skeletal muscle size and strength than females, partly because of their greater body size and height (14). For example, Janssen and colleagues conducted a study with healthy adult males ($n = 268$) and females ($n = 200$) aged 18-88 where they measured skeletal muscle mass using whole-body MRI. As can be seen in **Figure 2**, males demonstrated more absolute (kg) muscle mass in their upper and lower-body. These differences remained significant after controlling for height and body mass among participants. However, males carried a lower percentage of their total muscle mass in their lower-body than females (42).
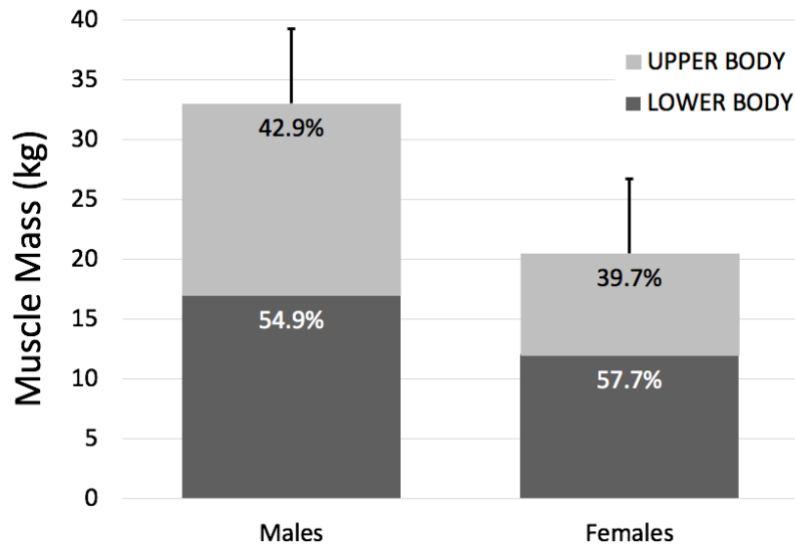
Figure 2. Skeletal muscle mass distribution in males and females (Adapted from Janssen et al, J Appl Physiol. 2000 (42)).

There is a clear reduction in total skeletal muscle mass that occurs even during healthy aging. **Figure 3** shows representative MR images depicting skeletal muscle architecture in young (3C), old-inactive (3D) and old-active (3E) males (10). It is evident that there is a reduction in muscle mass and greater abundance and infiltration of fat around the muscle tissue with age (3C vs. 3D). When comparing two older males of the same age, the protective effect of increased physical activity on skeletal muscle with aging is extremely apparent (3E vs 3D).
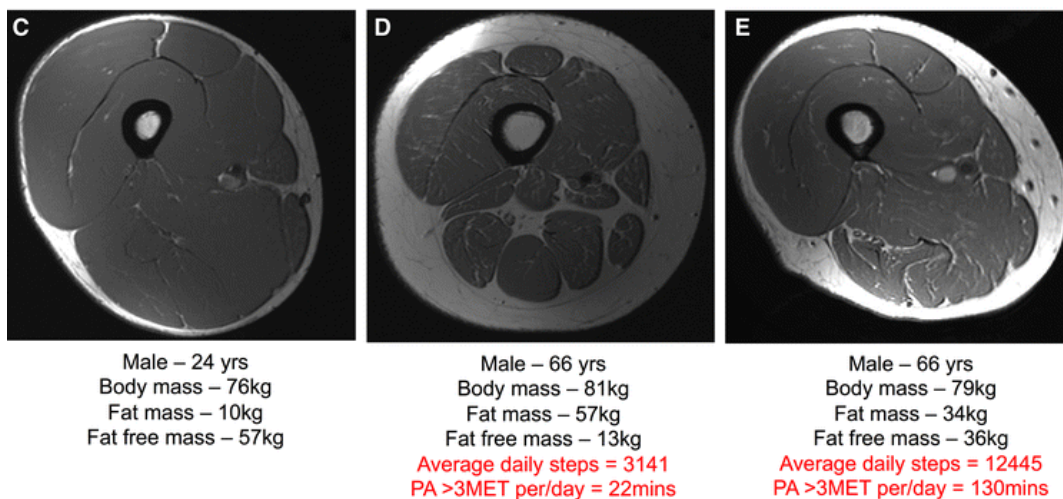
Figure 3 (C-E). Loss of skeletal muscle size and quality occurs during healthy aging (10).

34

In general, women have less muscle mass (and more body fat) than men and are therefore not able to exert the same absolute maximal force as men (124). The difference in body composition between the sexes is evident from infancy but becomes most marked after puberty (when boys experience an accelerated growth spurt) and persists into old age (42). Muscle strength plays a large role in determining overall physical health and well-being of an adult. Individuals over the age of 60 years with lower muscular strength are more likely to die of all-cause mortality than individuals with more muscular strength (125). Cheng and colleagues studied the changes in muscle strength and functional activities during aging with a total of 744 participants that were first separated by sex, then into 5 different age groups (126). They looked at muscle strength in terms of hip flexors, ankle planter flexors, and knee extensors. They found that muscle strength of knee extensors decreased in both males and females after the age of 50 years. However, this decrease appeared earlier in females than males, with the decline of muscle strength being statistically significant from the age of 70 years in females, and only from the age of 80 years in males (126). Knee extensor muscles are associated with many functional activities, and one possible explanation for earlier decline in the knee extensors may be due to the fact that females tend to suffer from more chronic health conditions.

Furthermore, amongst the 40-89 year old recruited participants in this study, it was found that functional activities deteriorated significantly after the age of 50 years in both the male and female groups. Similarly, Cheng and colleagues reported that the decrease in functional activities were earlier in female than in male individuals (126). Although results showed a decline both in functional activities and muscle strength with aging, the deterioration in functional activities appeared earlier in comparison to the deterioration of muscle strength (126). These results are concerning because females have a longer average life expectancy than males, therefore it could

lead to a rise in an already huge financial burden associated with aging related diseases, long term care facilities, and hospitalisations.

2.6 Sex Differences and Resistance Training Adaptations

Resistance training is a powerful intervention to combat sarcopenia (8,127); however, the influence of sex on resistance exercise training-induced changes in skeletal muscle mass, muscle strength, and functional performance in older adults is unclear. Older men and women both exhibit a blunted anabolic response to exercise and nutritional stimuli compared with young men and women (128). The results from studies comparing resistance exercise training-induced adaptations between older men and women have been inconsistent (9). For example, some studies have noted significantly different muscle mass or strength adaptations between sexes when exposed to identical resistance training interventions (27–31); however, other studies have revealed no difference between older men and women (21,24–26,32,33). For example, Bamman and colleagues (27) compared the effects of a 26-week resistance exercise training program (three times per week) between healthy older males and females on changes in muscle fiber size and maximal strength (1-RM). Type I, IIa, and IIx fiber size and 1-RM strength increased more in males vs. females. Alternatively, Leenders and colleagues (33) compared the effects of a 6-month resistance exercise training program (three times per week) between healthy older males and females on changes in muscle mass, muscle fiber characteristics, strength, and functional performance. Appendicular leg lean mass (3% ± 1%) and quadriceps CSA (9% ± 1%) increased similarly in both groups. Strength of the knee-extensors increased by 42% ± 3% (females) and 43% ± 3% (males). Following training, type II muscle fiber size increased and functional performance (sit-to-stand time) improved with no observed sex differences. Given the importance of skeletal muscle mass, strength, and functional performance in older adults, it is

important to clearly define whether there are sex differences in response to resistance exercise training in this population.

2.7 Knowledge Gaps and Rationale

The age-related decline in muscle mass, strength, and functional performance affects the health and general well-being of older individuals. Resistance exercise training is the ideal intervention to combat the detrimental effects of sarcopenia as it effectively increases skeletal muscle mass, strength, and functional performance (7). However, whether there are differences between healthy older (≥ 60 y) males and females in resistance exercise training-induced adaptations is unclear. Considering the uncertainty regarding the influence of sex on muscular adaptations following resistance exercise training, further research is needed to resolve this question, as it may have implications for exercise prescription in older males and females.

Therefore, the purpose of this study was to evaluate via systematic review and meta-analysis if there are differences between males and females (i.e. sex-based differences) in resistance exercise training-induced changes in skeletal muscle mass, muscle strength, and functional performance in healthy older adults ≥ 60 years of age. We hypothesized that older males would demonstrate greater absolute, but similar relative, gains in skeletal muscle mass, strength, and functional performance compared to older females undergoing the same resistance training program.

CHAPTER 3: THESIS MANUSCRIPT

3.1 Introduction

Aging is accompanied by a change in body composition, including a loss of skeletal muscle mass, and results in reduced strength and functional performance (40). The age-related decline in muscle mass is known as 'sarcopenia' and it affects the health and general well-being of elderly individuals (2). The factors driving age-related muscle loss and dysfunction are unclear but are thought to include lifestyle factors such as physical inactivity and inadequate nutrient intake, as well as more intrinsic factors such as motor unit loss, dysregulated proteostasis, inflammation, and impaired mitochondrial function (129). The loss of muscle mass and strength leads to a reduction in functional capacity, and an increased risk of both falls and fractures, and risk of developing chronic metabolic diseases (130). The financial burden associated with sarcopenia is vast and is expected to increase with the expanding aging demographic (6). Therefore, it is critical to identify strategies that can effectively mitigate the progression of sarcopenia in order to improve the health and well-being of our older population.

Resistance exercise training is arguably the most potent and effective non-pharmacological intervention to mitigate age-related musculoskeletal decline as it targets the key parameters that define sarcopenia: low muscle mass, low muscle strength, and low functional performance (3). Indeed, resistance exercise training has been well established as an effective treatment strategy to counteract the loss of muscle mass and strength in older adults (112,131–133). Even in the very old (> 90 y), substantial improvements in muscle mass, strength, and functional performance have been observed in response to resistance exercise training (112). However, whether there are differences between healthy older (≥ 60 y) males and females in resistance training-induced adaptations is unclear.

There are a number of physiological differences between men and women that may contribute to the existence of sex differences in the adaptive response to resistance exercise training. There is evidence for the existence of sex differences in fatigability (15,16), skeletal muscle protein metabolism (58) and gene transcription (134) that may alter adaptive responses to resistance exercise training between the sexes. It is also well known that when comparing muscle strength between males and females in absolute terms, females have less muscle mass (and a greater body-fat percentage) than males, and are therefore not able to exert the same absolute maximal force (124). However, current evidence comparing relative gains in resistance training adaptations between older ($\geq$ 60 y) males and females provides inconsistent observations (8). Some have noted significantly different muscle mass or strength adaptations between sexes (23–27), while others have not (19–22,30,31). In addition, females have lower absolute muscle function than males, and may suffer from a greater decline in muscle function with age due to menopause (94). However, data on sex-based differences in resistance training induced relative gains in functional performance measures are sparse, even though it is arguably the most important outcome measure related to independence and quality of life for older adults. A recent meta-analysis (135) examined sex differences in resistance training adaptations in adults aged 18–50 y and found that females gained greater relative upper-body strength, while relative muscle size gains were similar between sexes. Given the importance of skeletal muscle mass, strength, and functional performance in older adults, it is important to clearly define whether there are sex differences in response to resistance exercise training in this population.

Therefore, the purpose of this study was to evaluate via systematic review and meta-analysis if there are differences between males and females (i.e. sex-based differences) in resistance exercise training-induced changes in skeletal muscle mass, muscle strength, and

functional performance in healthy older adults ≥ 60 years of age. We hypothesized that older males would demonstrate greater absolute, but similar relative, gains in skeletal muscle mass, strength, and functional performance compared to older females undergoing the same resistance training program.

3.2 Methods and Procedures

3.2.1 Reporting Method and Protocol Registration

This systematic review and meta-analysis was performed in accordance with the guidelines provided in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (136). A 27-item PRISMA checklist addressing the Introduction, Methods, Results and Discussion sections of a systematic review report was followed to ensure all essential elements for reporting were included. The review protocol was prospectively registered as CRD42020153394 with The International Prospective Register of Systematic Reviews (PROSPERO), an open access online database of systematic review protocols on health-related topics.

3.2.2 Eligibility Criteria

We included prospective trials published in English that examined a resistance training intervention in healthy males and females ≥ 60 years of age. According to the United Nations, 60 years is the age cut-off to begin defining an older person (137). Moreover females will no longer be going through changes that occur during menopause that alter hormone levels, and may therefore moderate the effect of resistance exercise training on muscle mass, strength, and/or functional performance. Included studies must have had males and females perform the same relative exercise training program (i.e. frequency, volume, intensity). Studies were included when resistance training was delivered concurrently with nutritional supplementation and a

careful distinction was made between placebo and nutrition groups during the data extraction process. Only studies that presented relevant outcome data (i.e. a measure of changes in muscle mass/size, muscle strength and/or functional performance) for males and females separately were included.

Inclusion Criteria. Research publications were considered eligible for this systematic review if they (a) were experimental in design, (b) were published in a peer-reviewed, English-language journal, (c) were conducted in healthy human populations – with a body mass index (BMI) of < 30 kg/m^2 and > 18.5 kg/m^2, (d) made a direct comparison between sexes in at least one of the following: changes in muscle mass/size, dynamic, isometric, and/or isokinetic strength, and/or functional performance, and (e) had subjects who were ≥ 60 years of age. Participants of different sex, ethnicity and training status were included in this systematic review and meta-analysis. Studies that only presented data in graph/figure format were included by using WebPlotDigitizer (Web Plot Digitizer, V.4.4 Pacifica, California, USA: Ankit Rohatgi, 2020) to obtain the numerical data.

Exclusion Criteria. Studies were considered ineligible for this review if (a) the training protocol lasted for < 4 weeks and/or with training occurring < 2 times per week, (b) the training protocol was a concurrent exercise program that incorporated both resistance and endurance exercise, and (c) the study involved subjects with medical conditions or injuries impairing training capacity. Case studies, and qualitative studies were not included. Studies that were not written in English, conference abstracts, thesis, or posters were also excluded from this review.

3.2.3 Literature Search

Five electronic databases were searched from inception to August 2020: MEDLINE and EMBASE via Ovid, CINAHL and SPORTDiscus via EBSCO, and Scopus (**Appendix A**). The

search strategy structure for the databases was adopted using the components described in the PICO framework (population, intervention, comparison, outcome) and thus the keywords generated were divided into four main categories. The first category was "sex differences" as males and females are what was compared in the study. The second category was "resistance training" which is the intervention of interest. The third category was "muscle strength, muscle mass, and functional performance" which are the outcomes of interest. Finally, the fourth category was "older adults" as that is the population studied.

The complete search strategy for MEDLINE was as follows: ("sex differences" OR "gender differences" OR "sex characteristics" OR "gender characteristics" OR "gender factors" OR "sex factors" OR "gender comparison" OR "sex comparison" OR (male w/3 female) OR (women w/3 men)) AND ("resistance training" OR "muscle strengthening" OR "strength training" OR "weight training" OR "resistance exercise" OR "weight lifting" OR "isometric contraction" OR (weight* w/3 lift*)) AND ("muscle strength" OR "physical functional performance" OR "muscle size" OR hypertrophy OR (muscle* w/3 strength*)) AND (aged OR "older adults" OR senior OR elderly OR (older* w/3 adult*) OR "aged 60+ years")). The full search strategy for all 5 databases can be found in Appendix A. The search strategies were peer reviewed by a librarian specialising in Kinesiology and Physical Education at McGill University (M.I.).

The official search was conducted on August 3rd, 2020 and all articles found in the 5 databases listed above were downloaded and exported to EndNote (Clarivate, X9.3.3, 2013) on the same day. Duplicate articles were detected in EndNote and were deleted. Three reviewers (S.H., O.D., E.H.) independently screened articles via title and abstract using Rayyan software(138). Articles were excluded if they did not meet the inclusion criteria. The full papers

were obtained for the studies that appeared to have met the inclusion criteria or where a decision could not have been made from the title and/or abstract alone. Full texts were independently assessed for eligibility by three reviewers (S.H., O.D., E.H.). Reasons for excluding studies during the full text screening phase were recorded. Discrepancies were resolved by an initial discussion or with a forth reviewer (T.CV.), if required. Studies that were excluded after retrieval of the full text were recorded, and accompanied by a justification for exclusion. Other than the 5 databases, additional articles were identified by manual searches of the reference lists of included articles and articles on a similar topic, and were carefully examined and added as "additional data" if they met the inclusion criteria. A flowchart following the PRISMA statement was created to demonstrate the different phases of this process and display the number of articles in each phase (**Figure 4**).
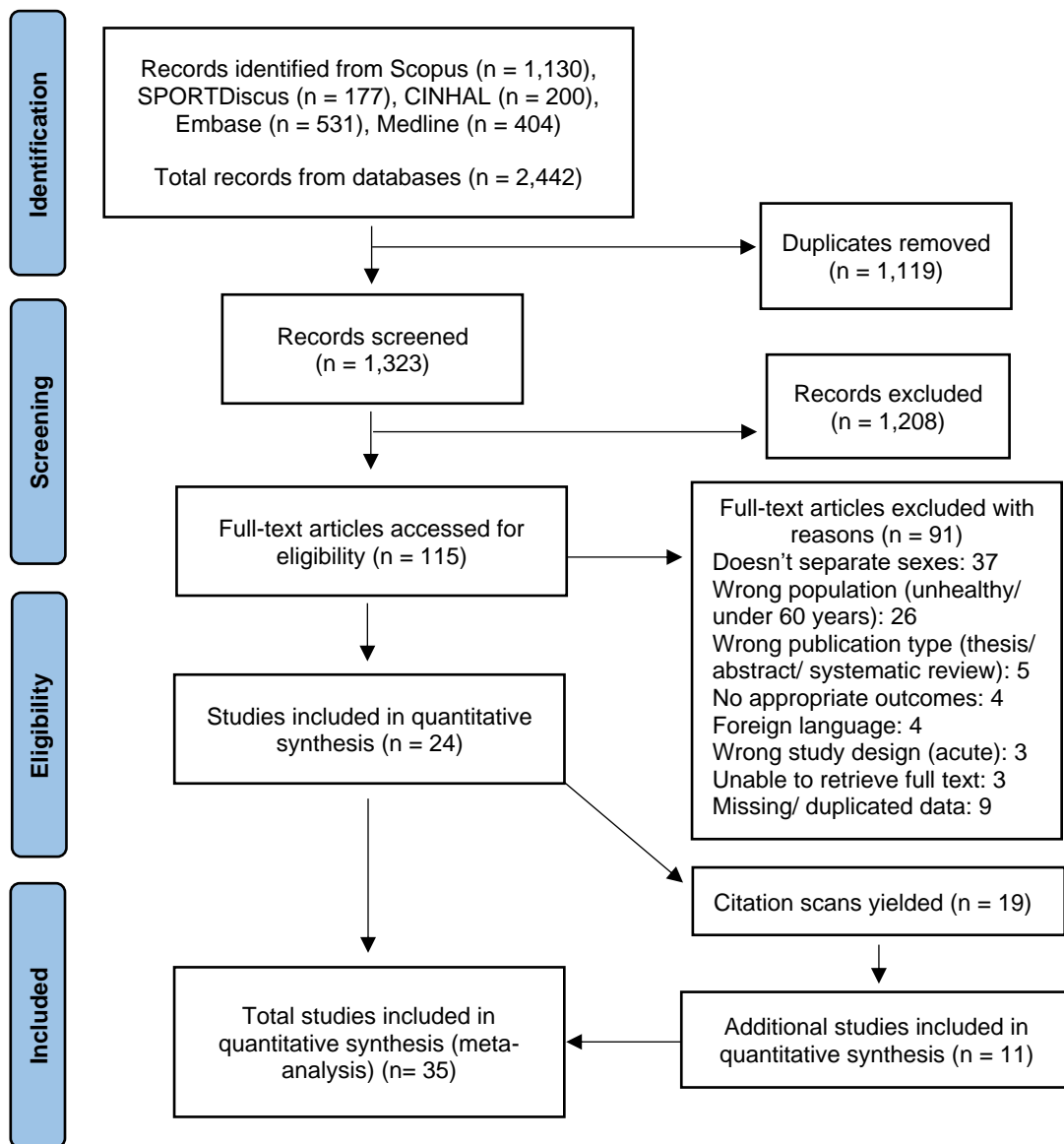
Figure 4. PRISMA flow diagram.

3.2.4 Outcomes

The outcomes for this review were the differences in resistance training adaptations between males and females for (1) muscle strength, which was categorized as (1a) upper-body strength and (1b) lower-body strength; (2) muscle mass which was categorized as (2a) whole-body fat-free mass (FFM), (2b) limb muscle mass, and (2c) type I, IIa, IIx fiber size, and (3) functional performance which was categorized as (3a) chair rises and (3b) walking capacity.

Absolute and relative (percentage) changes were determined for each of these three general outcomes. If studies used more than one method evaluating the level of change in muscle strength, the following hierarchy of outcome measures were used: 1 repetition maximum (RM); isokinetic maximal voluntary contraction (dynamometry-based); isometric maximal voluntary contraction (dynamometry-based); multiple repetition maximum (e.g., 2-15 RM) For the lower-body, the following hierarchy was used: knee/leg extension, knee/leg flexion, leg press, planter flexion, dorsi flexion. That is, if a study reported results for knee extension and planter flexion, data for the knee extension were used for the meta-analysis. For the upper-body, the hierarchy was: bench press, chest press, arm flexion, elbow flexion, shoulder press. For muscle mass, dual-energy X-ray absorptiometry (DXA) was the only assessment used to measure (a) whole-body FFM; while MRI, computerized tomography (CT), and ultrasound were used to measure (b) limb muscle mass (i.e. muscle cross sectional area (CSA), muscle volume or appendicular skeletal muscle mass (ASMM)); and muscle biopsy samples were used to measure (c) type I, IIa, and IIx muscle fiber size changes in response to resistance training. If a study reported results for muscle CSA and muscle volume, data for the muscle CSA were used for the meta-analysis. Finally, (3) functional performance was broken down into (a) chair rises - where outcome measures were: Timed Up & Go, chair rise time, sit to stand time, and bed rise time; and (b) walking capacity - where outcome measures were: 6-minute walking distance, walking endurance, and 12-minute walking distance.

3.2.5 Data Extraction

First, some general data from each of the included studies were extracted onto a custom built spreadsheet. This general data consisted of: the number of participants (male and females); the mean age of participants; the duration and frequency for the resistance training intervention,

and the desired outcome measures (**Appendix B**). Next, for all relevant outcomes, the absolute

(mean and standard deviation (SD)) and relative (percentage change and SD) changes from

baseline for males and females were extracted. In all analyses the comparator group (males vs.

females) received an identical resistance training intervention. If a study included a protein-

supplemented group, and a placebo-supplemented control group that were all part of the identical

resistance training intervention, data from both groups were retrieved. Where studies had more

than one relevant outcome measure for either muscle strength, muscle size, or functional

performance, all ΔMean and ΔSD values were independently extracted/ calculated. Two authors

(S.H., Y.H.) independently extracted the outcome data from each study into the custom built

spreadsheet. Discrepancies were resolved by an initial discussion or with a third author (T.CV.),

if required. All studies that reported the standard error of the mean (SEM) were converted to SD.

This was calculated using the following equation, where n represents the sample size:

$$SEM = \frac{SD}{\sqrt{n}}$$

Where the desired outcome data were not presented in table or text, it was either

calculated from baseline values and/or percentage change values, extracted from relevant graphs

and figures using Web Plot Digitizer (Web Plot Digitizer, V.4.4 Pacifica, California, USA: Ankit

Rohatgi, 2020), obtained from the study's corresponding author whom we contacted via email

twice in a two-week period, or we computed a correlation coefficient (corr) for each primary

outcome to calculate the change in SD (ΔSD) using the following equations according to the

Cochrane Handbook for Systematic Reviews of Interventions (139):

$$corr = \frac{(SD_{pre}{}^2 + SD_{post}{}^2 - SD_{change}{}^2)}{(2 \times SD_{pre} \times SD_{post})}$$

$$\Delta SD = \sqrt{(SD_{pre}^{2} + SD_{post}^{2} - 2 \times corr \times SD_{pre} \times SD_{post})}$$

We pooled all available data from the included studies for each outcome across males and females, identified the median correlation, and subtracted 0.1 in order to establish a conservative computed correlation for our analysis (127). For the primary analysis, we used r = 0.759 for muscle strength, r = 0.818 for muscle size, and r = 0.5 for functional performance. To investigate the influence of these decisions, we also performed sensitivity analyses with r = 0.5, and 0.75 for all analyses, and the results were consistent

3.2.6 Study Quality and Reporting

A modified version of the Downs and Black checklist was used to evaluate the included studies' quality (140). This checklist assesses the quality of original research articles in order to synthesize evidence from quantitative studies for public health purposes. Briefly, the tool consists of 28 'Yes' or 'No' questions across 5 domains, where No = 0, Unable to be determined = 0 (for certain items) and Yes = 1. The five domains comprise questions concerning study quality, external validity, study bias, confounding and selection bias, and power of the study. Studies were rated by two reviewers (S.H., Y.H.), with scores entered into our spreadsheet. Scores could range from 0 to 28 points, with higher scores reflecting higher study quality. Scores above 20 were considered good; scores of 11–20 were considered moderate; and scores below 11 were considered poor methodological quality (141).

3.2.7 Data Synthesis

The change in mean (ΔMean) and ΔSD values were extracted and calculated for each outcome measure and uploaded to RevMan (Review Manager, v5.4; The Cochrane Collaboration). A random-effects meta-analysis was employed for all main outcome measures

and all meta-analyses were performed using RevMan. The data that are presented include the standardized mean difference (SMD) which is used as a summary statistic in meta-analysis when included studies all assess the same outcome but measure it in a variety of ways, and the 95% Confidence Interval (CI). In this circumstance it is necessary to standardize the results of the studies to a uniform scale before they can be combined. The SMD expresses the size of the intervention effect in each study relative to the variability observed in that study. The particular definition of SMD used in Cochrane reviews is the effect size known in social science as Hedges' g (139). In all analyses, positive effect size values favoured males and negative values favoured females. We considered the summary effect size threshold for significance as $p < 0.05$. Meta-Analyses are illustrated using forest plots where the effect estimates for each individual study are displayed in blocks and the summary effect size is displayed as a diamond. The area of the blocks indicates the weight assigned to that study in the meta-analysis while the horizontal line depicts the confidence interval. Heterogeneity was assessed by Chi^2 and I^2, with an α value of $p < 0.05$ on RevMan. Thresholds for the interpretation of I^2 can be misleading, since the importance of inconsistency depends on several factors. A rough guide to interpretation is as follows (139):

- 0% to 40%: might not be important;

- 30% to 60%: may represent moderate heterogeneity;

- 50% to 90%: may represent substantial heterogeneity;

- 75% to 100%: considerable heterogeneity.

The importance of the observed value of I^2 depends on the magnitude and direction of effects, as well as the strength of evidence for heterogeneity (p value from the Chi^2 test or a confidence interval for I^2) (139). Finally, funnel plots were visually inspected to determine publication bias

and multiple sensitivity analyses were performed to determine if any of the results were influenced if studies were removed.

3.3 Results

3.3.1 Included Studies

We screened 1,323 records from electronic databases, assessed 115 articles for eligibility, and included a total of 24 studies (**Figure 4**). We also searched reference lists and conducted forward citation tracking on the included studies, from which we added 11 more studies. Ultimately, 35 studies were included in the review, comprising 44 comparison groups of 1,142 older adult participants (518 males; 624 females). Publications ranged from the years 1994 through to 2017. The details of included studies are outlined in **Appendix B**. The ages of included participants ranged from 60 to 92 years, and the average ages were 71.6 ± 3.4 years for males and 71.9 ± 4.1 years for females and the majority of participants were inactive with no resistance training experience. Briefly, resistance training interventions averaged 22.3 weeks in duration (range: 4 to 84 weeks in duration) and consisted of 2-3 sessions per week. The resistance training programs usually included 3-5 sets of 8-12 repetitions for upper and lower-body exercises. Typically, the participants' 1-RM for each exercise would be assessed at baseline and the load they trained at was ~70% of their individual baseline 1-RM value. For studies that were longer in duration, the participants' 1-RM values were re-evaluated and the loads were readjusted accordingly. Most included studies reported that the resistance training sessions were supervised by a qualified instructor.

3.3.2 Meta-Analyses

Muscle Strength

For upper-body strength (16 comparison outcomes; 173 males, 263 females), there was no difference in relative change between older males and females (ES = -0.20 [95% CI -0.54, 0.13], $p = 0.23$; $I^2 = 58\%$, $p = 0.002$; **Figure 5**). Older males gained more absolute upper-body strength (ES = 0.75 [95% CI 0.54, 0.96], p < 0.00001; $I^2 = 0\%$, p = 0.72; **Figure 6**). For lower-body strength (39 comparison outcomes; 477 males, 592 females), there was no difference in relative change between older males and females (ES = -0.09 [95% CI -0.27, 0.08], $p = 0.30$; $I^2 = 40\%$, $p = 0.006$; **Figure 7**). Older males gained more absolute lower-body strength (ES = 0.46 [95% CI 0.29, 0.63], $p < 0.00001$; $I^2 = 35\%$, $p = 0.02$; **Figure 8**).

Study or Subgroup	Male Mean	SD	Total	Female Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Ades 1996_1RM	42.86	23.67	6	24.24	14.83	6	4.5%	0.87 [−0.34, 2.08]
Binns 2017	42.5	93	8	0.7	38	25	6.7%	0.74 [−0.08, 1.55]
Brose 2003_Cr	26	18.54	8	31.25	30.29	6	5.3%	−0.20 [−1.27, 0.86]
Brose 2003_Pla	23	13.43	7	28.3	15.6	7	5.3%	−0.34 [−1.40, 0.72]
Bunout 2005	54.037	35.97	17	33.64	38.02	94	8.8%	0.54 [0.02, 1.06]
Galvao 2006	22.42	8.67	10	29.3	14.6	6	5.4%	−0.58 [−1.62, 0.46]
Hunter 2002	34	19	14	29	21.5	12	7.0%	0.24 [−0.53, 1.01]
Lemmer 2001	17.4	10	11	14.8	12.1	10	6.4%	0.23 [−0.63, 1.09]
Lexell 1995	54.55	12.7	6	66.7	23.36	10	5.4%	−0.57 [−1.61, 0.47]
McCartney 1995_60–70y	30.32	22	22	39	18	17	8.0%	−0.42 [−1.06, 0.22]
McCartney 1995_70–80y	24	17.06	17	38	15.16	20	7.7%	−0.85 [−1.53, −0.17]
Roth 2001	19.469	9.93	9	16	11.17	10	6.1%	0.31 [−0.59, 1.22]
Ryan 2001	18	8.94	11	18	13.73	10	6.5%	0.00 [−0.86, 0.86]
Tamopolsky 2007_CrM+CLA	40.38	24.52	10	67.92	20.2	10	5.8%	−1.17 [−2.14, −0.21]
Tamopolsky 2007_Pla	38.776	13.776	8	51.67	11.5	10	5.6%	−0.98 [−1.98, 0.02]
Tanton 2009	22.75	17.41	9	51.74	21.3	10	5.4%	−1.42 [−2.45, −0.38]
Total (95% CI)			**173**			**263**	**100.0%**	**−0.20 [−0.54, 0.13]**

Heterogeneity: Tau² = 0.26; Chi² = 35.68, df = 15 (P = 0.002); I² = 58%
Test for overall effect: Z = 1.19 (P = 0.23)

Figure 5. Forest plot of the effects of resistance training on sex differences in relative changes in upper-body strength.

Study or Subgroup	Male Mean	SD	Total	Female Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Ades 1996_1RM	8	7.81	6	4	3.262	6	3.3%	0.62 [-0.55, 1.79]
Binns 2017	373.2	818	8	3	174	25	6.6%	0.86 [0.04, 1.69]
Brose 2003_Cr	30	21.51	8	15	14.54	6	3.7%	0.74 [-0.36, 1.85]
Brose 2003_Pla	22	13.02	7	13	7.19	7	3.7%	0.80 [-0.30, 1.91]
Bunout 2005	8.7	5.79	17	3.6	4.07	94	15.5%	1.16 [0.62, 1.70]
Galvao 2006	8.7	3.36	10	6	2.99	6	4.0%	0.79 [-0.27, 1.85]
Hunter 2002	240	133.89	14	117	87.77	12	6.6%	1.04 [0.21, 1.86]
Lemmer 2001	8	4.61	11	4	3.26	10	5.4%	0.95 [0.04, 1.87]
Lexell 1995	6	1.4	6	4	1.4	10	3.4%	1.35 [0.20, 2.50]
McCartney 1995_60–70y	13.4	9.73	22	9.13	4.07	17	10.8%	0.54 [-0.11, 1.18]
McCartney 1995_70–80y	10.4	7.49	17	8.16	3.22	20	10.6%	0.39 [-0.26, 1.05]
Roth 2001	8.8	4.49	9	4.3	3.13	10	4.6%	1.12 [0.14, 2.11]
Ryan 2001	19	9.21	11	11	8.24	10	5.5%	0.88 [-0.03, 1.78]
Tamopolsky 2007_CrM+CLA	42	25.5	10	36	10.7	10	5.8%	0.29 [-0.59, 1.18]
Tamopolsky 2007_Pla	38	13.5	8	31	6.9	10	4.9%	0.65 [-0.31, 1.61]
Tanton 2009	5.56	4.23	9	6.25	2.6	10	5.5%	-0.19 [-1.09, 0.71]
Total (95% CI)			173			263	100.0%	0.75 [0.54, 0.96]

Heterogeneity: Tau² = 0.00; Chi² = 11.49, df = 15 (P = 0.72); I² = 0%
Test for overall effect: Z = 6.92 (P < 0.00001)

Figure 6. Forest plot of the effects of resistance training on sex differences in absolute changes in upper-body strength.

Study or Subgroup	Male Mean	SD	Total	Female Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Ades 1996	27.3	22.98	6	37.5	13.96	6	1.7%	-0.50 [-1.65, 0.66]
Arnarson 2013	10.92	11.9	67	13.375	12.7	94	5.7%	-0.20 [-0.51, 0.12]
Asakawa 2007	19.1	14	6	1.5	16	6	1.5%	1.08 [-0.17, 2.33]
Benka 2005 _HI	11	6.28	8	13.2	3.072	8	2.1%	-0.42 [-1.42, 0.57]
Benka 2005 _LI	4.63	5.74	8	2.53	2.301	8	2.1%	0.45 [-0.54, 1.45]
Benka 2005 _MI	9.22	7.02	8	7.92	7.586	8	2.2%	0.17 [-0.81, 1.15]
Binns 2017	42.5	93	8	0.7	38	25	2.7%	0.74 [-0.08, 1.55]
Brose 2003_Cr	36	13.13	8	59.15	22.27	6	1.6%	-1.24 [-2.42, -0.05]
Brose 2003_Pla	41	20.46	7	57.5	28.3	7	1.9%	-0.63 [-1.71, 0.46]
Bunout 2005	31.197	28.66	17	11.386	31.86	94	4.3%	0.63 [0.10, 1.15]
Capodaglio 2007	10.225	13.4	11	13.4	10.1	12	2.7%	-0.26 [-1.08, 0.56]
Da Boit 2017_LCn-3PUFA	31.3	21.83	14	30	9.04	13	3.0%	0.07 [-0.68, 0.83]
Da Boit 2017_Placebo	39.652	26.41	13	15.01	14.9	10	2.5%	1.07 [0.18, 1.96]
Fernandez 2017_2	9.52	9	7	22	16	14	2.3%	-0.85 [-1.80, 0.11]
Fernandez 2017_3	18	17	11	27	17	13	2.7%	-0.51 [-1.33, 0.31]
Fragala 2014	25.773	9.28	7	36.76	16.54	5	1.6%	-0.80 [-2.01, 0.41]
Galvao 2006	39.33	13.2	10	23.6	10.1	6	1.8%	1.22 [0.10, 2.34]
Hakkinen 1994	15.686	20.84	10	32.06	14.62	11	2.4%	-0.88 [-1.79, 0.02]
Hakkinen 2001	21.03	15.99	11	30.59	15.17	10	2.5%	-0.59 [-1.47, 0.29]
Hakkinen 2002	30.7	14.8	10	29.4	11.8	11	2.6%	0.09 [-0.76, 0.95]
Hunter 2002	35	18.8	14	46	30.1	12	2.9%	-0.43 [-1.21, 0.35]
Kobayashi 2016	22.7	26.7	17	37.9	36.1	13	3.1%	-0.48 [-1.21, 0.26]
Kosek 2006	1.4	6.2757	13	1.6	8.893	12	2.9%	-0.03 [-0.81, 0.76]
Leenders 2013	41	45.6	29	39.587	74.65	24	4.2%	0.02 [-0.52, 0.56]
Lemmer 2001	29.3	12.5	11	27.2	17.8	10	2.6%	0.13 [-0.73, 0.99]
Lexell 1995	157.9	58.7	6	158	35.4	10	2.1%	-0.00 [-1.01, 1.01]
Mackey 2007	14	17.78	13	14.4	18.02	16	3.1%	-0.02 [-0.75, 0.71]
McCartney 1995_60-70y	27.05	14	22	22	11	17	3.6%	0.39 [-0.25, 1.03]
McCartney 1995_70-80y	19	15.16	17	22	15.89	20	3.5%	-0.19 [-0.84, 0.46]
Njemini 2017_HI	31.28	10.92	8	27.01	16.08	8	2.1%	0.29 [-0.69, 1.28]
Njemini 2017_LI	20.09	11.85	7	18.18	24.38	9	2.1%	0.09 [-0.90, 1.08]
Njemini 2017_LM	24.04	15.64	8	28.84	25.66	8	2.2%	-0.21 [-1.20, 0.77]
Ochala 2007	34.4	12.88	8	40.12	22.9	8	2.1%	-0.29 [-1.28, 0.70]
Roth 2001_LP	12.037	10.8	9	27	17.44	10	2.2%	-0.97 [-1.94, -0.01]
Ryan 2001_LE	29	11.08	11	28	21.26	10	2.6%	0.06 [-0.80, 0.91]
Sharman 2001	31.2	15.3	7	34	12.4	7	2.0%	-0.19 [-1.24, 0.86]
Tamopolsky 2007_CrM+CLA	39.32	24.95	10	76.56	18.7	10	2.0%	-1.62 [-2.66, -0.58]
Tamopolsky 2007_Pla	49.057	17.547	8	34.57	22.19	10	2.2%	0.68 [-0.28, 1.64]
Tracy 1999	25.3	9.1	12	31	15.6	11	2.7%	-0.44 [-1.27, 0.39]
Total (95% CI)			477			592	100.0%	-0.09 [-0.27, 0.08]

Heterogeneity: Tau² = 0.11; Chi² = 63.14, df = 38 (P = 0.006); I² = 40%
Test for overall effect: Z = 1.05 (P = 0.30)

Std. Mean Difference IV, Random, 95% CI
-2 -1 0 1 2
Favours Female   Favours Male

Figure 7. Forest plot of the effects of resistance training on sex differences in relative changes in lower-body strength.

Study or Subgroup	Male Mean	Male SD	Male Total	Female Mean	Female SD	Female Total	Weight	Std. Mean Difference IV, Random, 95% CI
Ades 1996	12	10.11	6	9	3.351	6	1.7%	0.37 [−0.78, 1.51]
Arnarson 2013	57.8	62.8	67	53.5	50.8	94	6.3%	0.08 [−0.24, 0.39]
Asakawa 2007	6.4	26.24	6	0.4	4.3	6	1.7%	0.29 [−0.85, 1.44]
Benka 2005 _HI	10.4	5.93	8	10.1	2.35	8	2.2%	0.06 [−0.92, 1.04]
Benka 2005 _LI	4.3	5.33	8	4.9	1.73	8	2.1%	−0.14 [−1.12, 0.84]
Benka 2005 _MI	8.6	6.55	8	6	5.75	8	2.1%	0.40 [−0.59, 1.39]
Binns 2017	373.2	818	8	3	174	25	2.7%	0.86 [0.04, 1.69]
Brose 2003_Cr	43	15.63	8	42	37.48	6	1.9%	0.03 [−1.02, 1.09]
Brose 2003_Pla	44	21.89	7	42	20.67	7	1.9%	0.09 [−0.96, 1.14]
Bunout 2005	7.3	6.71	17	2.3	6.44	94	4.5%	0.77 [0.24, 1.29]
Capodaglio 2007	12.7	16.65	11	10.6	8.02	12	2.8%	0.16 [−0.66, 0.98]
Da Boit 2017_LCn−3PUFA	39.2	27.31	14	23.9	7.2	13	2.9%	0.73 [−0.05, 1.51]
Da Boit 2017_Placebo	43.3	28.84	13	11.5	11.42	10	2.3%	1.33 [0.40, 2.26]
Fernandez 2017_2	14.41	13.58	7	20.14	14.4	14	2.4%	−0.39 [−1.31, 0.53]
Fernandez 2017_3	25.48	23.51	11	24.13	15.6	13	2.8%	0.07 [−0.74, 0.87]
Fragala 2014	12.5	4.5	7	10.1	4.5	5	1.6%	0.49 [−0.68, 1.66]
Galvao 2006	26.9	9	10	10.8	4.6	6	1.4%	1.97 [0.69, 3.25]
Hakkinen 1994	484	547.77	10	667	271	11	2.6%	−0.41 [−1.28, 0.45]
Hakkinen 2001	9.8	7.45	11	9.3	4.6	10	2.6%	0.08 [−0.78, 0.93]
Hakkinen 2002	40.1	19.8	10	17.59	7.04	11	2.1%	1.48 [0.49, 2.48]
Hunter 2002	509	271.69	14	417	270.49	12	3.0%	0.33 [−0.45, 1.11]
Kobayashi 2016	15.8	18.59	17	15.9	15.14	13	3.2%	−0.01 [−0.73, 0.72]
Kosek 2006	186	70.42	13	113	77.32	12	2.7%	0.96 [0.12, 1.79]
Leenders 2013	37.7	41.95	29	24.7	47.03	24	4.4%	0.29 [−0.25, 0.83]
Lemmer 2001	46	19.57	11	25	16.4	10	2.3%	1.11 [0.18, 2.05]
Lexell 1995	30	11.15	6	19	4.2	10	1.7%	1.39 [0.24, 2.55]
Mackey 2007	80	98.86	13	62	77.66	16	3.2%	0.20 [−0.53, 0.93]
McCartney 1995_60−70y	42.3	22.23	22	23.4	11.34	17	3.5%	1.01 [0.33, 1.69]
McCartney 1995_70−80y	30.6	23.85	17	22.5	15.98	20	3.6%	0.40 [−0.26, 1.05]
Njemini 2017_HI	10.85	3.79	8	7.39	4.4	8	2.0%	0.80 [−0.23, 1.83]
Njemini 2017_LI	7.89	4.65	7	4.47	6	9	2.0%	0.59 [−0.42, 1.61]
Njemini 2017_LM	7.95	5.17	8	7.93	7.06	8	2.2%	0.00 [−0.98, 0.98]
Ochala 2007	15.3	5.73	8	13.4	7.66	8	2.1%	0.27 [−0.72, 1.25]
Roth 2001_LP	65	58.59	9	95	61.03	10	2.4%	−0.48 [−1.40, 0.44]
Ryan 2001_LE	104	39.12	11	57	43.37	10	2.3%	1.10 [0.16, 2.03]
Sharman 2001	40.7	19.97	7	19.7	7.23	7	1.6%	1.31 [0.12, 2.50]
Tamopolsky 2007_CrM+CLA	46	29.19	10	49	12	10	2.5%	−0.13 [−1.01, 0.75]
Tamopolsky 2007_Pla	52	18.6	8	28	18	10	2.0%	1.25 [0.21, 2.29]
Tracy 1999	19	6.8	12	13	6.5	11	2.6%	0.87 [0.01, 1.73]
Total (95% CI)			**477**			**592**	**100.0%**	**0.46 [0.29, 0.63]**

Heterogeneity: Tau^2 = 0.09; Chi^2 = 58.33, df = 38 (P = 0.02); I^2 = 35%
Test for overall effect: Z = 5.33 (P < 0.00001)

Figure 8. Forest plot of the effects of resistance training on sex differences in absolute changes in lower-body strength.

Muscle Mass

For whole-body FFM (20 comparison outcomes; 276 males, 390 females), there was no difference in relative change between males and females (ES = 0.03 [95% CI -0.13, 0.19], $p = 0.68$; $I^2 = 0\%$, $p = 1.00$; **Figure 9**), as well as absolute change in whole-body FFM (ES = 0.13 [95% CI -0.03, 0.30], $p = 0.10$; $I^2 = 0\%$, $p = 1.00$; **Figure 10**) between males and females. For measures of limb muscle mass (17 comparison outcomes; 274 males, 288 females), there was no difference in relative change (ES = -0.05 [95% CI -0.29, 0.19], $p = 0.67$; $I^2 = 41\%$, $p = 0.04$; **Figure 11**), as well as absolute change (ES = 0.24 [95% CI -0.06, 0.53], $p = 0.11$; $I^2 = 60\%$, $p = 0.0007$; **Figure 12**) between males and females. For type I fiber size (7 comparison outcomes; 85 males, 70 females), there was no difference in relative change (ES = 0.39 [95% CI -0.63, 1.41], $p = 0.46$; $I^2 = 86\%$, $p < 0.00001$; **Figure 13**), as well as absolute change (ES = 0.48 [95% CI -0.60, 1.56], $p = 0.38$; $I^2 = 87\%$, $p < 0.00001$; **Figure 14**) between males and females. For type IIa fiber size (7 comparison outcomes; 85 males, 70 females), there was no difference in relative change (ES = 0.66 [95% CI -0.23, 1.56], $p = 0.15$; $I^2 = 82\%$, $p < 0.00001$; **Figure 13**), as well as absolute change (ES = 0.82 [95% CI -0.12, 1.75], $p = 0.09$; $I^2 = 83\%$, $p < 0.00001$; **Figure 14**) between males and females. For type IIx fiber size (7 comparison outcomes; 85 males, 70 females), there was no difference in relative change (ES = 0.16 [95% CI -0.99, 1.31], $p = 0.79$; $I^2 = 88\%$, $p < 0.00001$; **Figure 13**), as well as absolute change (ES = 0.58 [95% CI -0.42,1.58], $p = 0.26$; $I^2 = 85\%$, $p < 0.00001$; **Figure 14**) between males and females.

Study or Subgroup	Male Mean	Male SD	Male Total	Female Mean	Female SD	Female Total	Weight	Std. Mean Difference IV, Random, 95% CI
Ades 1996	1.386	5.0814	6	-0.74	9.553	6	2.0%	0.26 [-0.88, 1.39]
Arnarson 2013	1.739	2.43	67	1.49	2.93	94	26.4%	0.09 [-0.22, 0.40]
Binns 2017	0.352	8.2	8	-3	15	25	4.1%	0.24 [-0.56, 1.04]
Brose 2003_Cr	2.5	7.81	8	5.935	7.05	6	2.2%	-0.43 [-1.50, 0.65]
Brose 2003_Pla	0	6.49	7	1.61	3.12	7	2.3%	-0.30 [-1.35, 0.76]
Bunout 2005	-0.79	6.51	17	-0.58	6.46	94	9.7%	-0.03 [-0.55, 0.48]
Fernandez 2017_2	1.67	5.4	7	0	8.5	14	3.1%	0.21 [-0.70, 1.12]
Fernandez 2017_3	0	7.8	11	2.4	8	13	4.0%	-0.29 [-1.10, 0.52]
Fragala 2014	0	14.3	7	0.94	6.53	5	2.0%	-0.07 [-1.22, 1.07]
Galvao 2006	1.3	41.14	10	2.39	6.26	6	2.5%	-0.03 [-1.04, 0.98]
Hakkinen 2002	0.93	7.07	10	-0.4	6.18	11	3.5%	0.19 [-0.67, 1.05]
Hunter 2002	4.8	6.55	14	2.6	10.1	12	4.3%	0.25 [-0.52, 1.03]
Kosek 2006	1.4	6.28	13	1.6	8.89	12	4.2%	-0.03 [-0.81, 0.76]
Leenders 2013	1.93	28.1	29	2.82	32.74	24	8.9%	-0.03 [-0.57, 0.51]
Lemmer 2001	1.77	3.5	11	2.19	4.82	10	3.5%	-0.10 [-0.95, 0.76]
Roth 2001	1.056	3.18	9	-0.2	4.91	10	3.2%	0.29 [-0.62, 1.19]
Ryan 2001	1.8	3.17	11	2.4	5.81	10	3.5%	-0.12 [-0.98, 0.73]
Tamopolsky 2007_CrM+CLA	4.647	8.86	11	3.874	6.7	10	3.5%	0.09 [-0.76, 0.95]
Tamopolsky 2007_Pla	2.509	6.039	8	0.973	7.445	10	3.0%	0.21 [-0.72, 1.15]
Tracy 1999	0.8	4.5	12	1.3	6.2	11	3.9%	-0.09 [-0.91, 0.73]
Total (95% CI)			276			390	100.0%	0.03 [-0.13, 0.19]

Heterogeneity: Tau^2 = 0.00; Chi^2 = 3.78, df = 19 (P = 1.00); I^2 = 0%
Test for overall effect: Z = 0.41 (P = 0.68)

Figure 9. Forest plot of the effects of resistance training on sex differences in relative changes in whole-body FFM.

Study or Subgroup	Male Mean	SD	Total	Female Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Ades 1996	0.8	2.932	6	-0.3	3.85	6	2.0%	0.30 [-0.84, 1.44]
Arnarson 2013	1	1.4	67	0.6	1.2	94	26.2%	0.31 [-0.01, 0.62]
Binns 2017	0.2	4.65	8	-1.1	5.5	25	4.1%	0.24 [-0.56, 1.04]
Brose 2003_Cr	1.4	4.37	8	2	2.38	6	2.3%	-0.15 [-1.21, 0.91]
Brose 2003_Pla	0	3.37	7	0.6	1.16	7	2.4%	-0.22 [-1.28, 0.83]
Bunout 2005	-0.4	3.3	17	-0.2	2.23	94	9.8%	-0.08 [-0.60, 0.43]
Fernandez 2017_2	1	3.3	7	0	3.5	14	3.1%	0.28 [-0.63, 1.19]
Fernandez 2017_3	0	4.6	11	1	3.3	13	4.0%	-0.24 [-1.05, 0.56]
Fragala 2014	0	7.49	7	0.4	2.79	5	2.0%	-0.06 [-1.21, 1.09]
Galvao 2006	0.7	2.34	10	0.9	2.36	6	2.5%	-0.08 [-1.09, 0.93]
Hakkinen 2002	0.6	4.55	10	-0.2	2.89	11	3.5%	0.20 [-0.66, 1.06]
Hunter 2002	2.8	3.85	14	1	3.91	12	4.3%	0.45 [-0.33, 1.23]
Kosek 2006	0.8	3.6	13	0.6	3.33	12	4.2%	0.06 [-0.73, 0.84]
Leenders 2013	1.2	17.45	29	1.2	13.91	24	8.9%	0.00 [-0.54, 0.54]
Lemmer 2001	1	1.98	11	0.9	1.98	10	3.6%	0.05 [-0.81, 0.91]
Roth 2001	0.6	1.81	9	-0.1	2.02	10	3.2%	0.35 [-0.56, 1.26]
Ryan 2001	1	1.8	11	1	2.4	10	3.6%	0.00 [-0.86, 0.86]
Tamopolsky 2007_CrM+CLA	2.7	5.1	11	1.6	2.8	10	3.5%	0.25 [-0.61, 1.11]
Tamopolsky 2007_Pla	1.4	3.37	8	0.4	3.1	10	3.0%	0.30 [-0.64, 1.23]
Tracy 1999	0.43	2.4	12	0.5	2.4	11	3.9%	-0.03 [-0.85, 0.79]
Total (95% CI)			**276**			**390**	**100.0%**	**0.13 [-0.03, 0.30]**

Heterogeneity: Tau² = 0.00; Chi² = 5.56, df = 19 (P = 1.00); I² = 0%
Test for overall effect: Z = 1.62 (P = 0.10)

Figure 10. Forest plot of the effects of resistance training on sex differences in absolute changes in whole-body FFM.

Study or Subgroup	Male Mean	SD	Total	Female Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Arnarson 2013	2.867	5.02	67	2.073	3.11	94	12.4%	0.20 [−0.12, 0.51]
Da Boit 2017_LCn−3PUFA	2.41	4.16	14	4.8	9.5	13	6.1%	−0.32 [−1.08, 0.44]
Da Boit 2017_Pla	3.7	9.18	13	1.89	9.73	10	5.5%	0.19 [−0.64, 1.01]
Fragala 2014	6.1	8.54	7	12.82	20.51	5	3.3%	−0.43 [−1.59, 0.74]
Hakkinen 1998	1.95	2.83	11	5.01	2.35	10	4.6%	−1.12 [−2.06, −0.19]
Kobayashi 2016	0.62	10.6	17	−1.46	21.9	13	6.5%	0.12 [−0.60, 0.85]
Leenders 2013	9.2	11	29	7.51	5.256	24	8.7%	0.19 [−0.35, 0.73]
Mackey 2007	0.8	17.37	13	8.63	23.08	16	6.3%	−0.37 [−1.11, 0.37]
McCartney 1995_60−70y	6.89	2.8	22	5.6	1.9	17	7.3%	0.52 [−0.13, 1.16]
McCartney 1995_70−80y	6	2.6	17	4	1.6	20	6.9%	0.92 [0.24, 1.61]
Melnyk 2009	8.03	9.11	11	11.9	12.8	11	5.3%	−0.34 [−1.18, 0.51]
Njemini 2017_HI	2.23	11	8	4	10.5	8	4.3%	−0.16 [−1.14, 0.83]
Njemini 2017_LI	3.41	15	7	1.39	13.7	9	4.3%	0.13 [−0.86, 1.12]
Njemini 2017_LM	0.47	14	8	3.79	11.3	8	4.3%	−0.25 [−1.23, 0.74]
Roth 2001	1.43	3.89	9	5.2	1.54	10	4.2%	−1.24 [−2.25, −0.24]
Tanton 2009	14.71	15.41	9	21.59	15.44	9	4.6%	−0.42 [−1.36, 0.51]
Tracy 1999	11.5	5.2	12	12	11	11	5.5%	−0.06 [−0.88, 0.76]
Total (95% CI)			274			288	100.0%	−0.05 [−0.29, 0.19]

Heterogeneity: Tau^2 = 0.09; Chi^2 = 27.05, df = 16 (P = 0.04); I^2 = 41%
Test for overall effect: Z = 0.43 (P = 0.67)

Figure 11. Forest plot of the effects of resistance training on sex differences in relative changes in limb muscle mass.

Study or Subgroup	Male Mean	Male SD	Male Total	Female Mean	Female SD	Female Total	Weight	Std. Mean Difference IV, Random, 95% CI
Arnarson 2013	0.8	1.4	67	0.4	0.6	94	9.5%	0.39 [0.08, 0.71]
Da Boit 2017_LCn−3PUFA	1.6	2.76	14	1.8	3.57	13	6.2%	−0.06 [−0.82, 0.69]
Da Boit 2017_Pla	2.1	5.21	13	0.7	3.61	10	5.7%	0.29 [−0.54, 1.12]
Fragala 2014	1	1.4	7	1.5	2.4	5	4.0%	−0.25 [−1.40, 0.91]
Hakkinen 1998	0.852	1.24	11	1.703	0.8	10	5.3%	−0.77 [−1.67, 0.12]
Kobayashi 2016	5	84.69	17	−9	135.2	13	6.4%	0.12 [−0.60, 0.85]
Leenders 2013	6.33	7.539	29	3.5	2.5	24	7.7%	0.48 [−0.07, 1.03]
Mackey 2007	45	965.6	13	301	804.4	16	6.4%	−0.28 [−1.02, 0.45]
McCartney 1995_60−70y	8.6	3.45	22	4.4	1.52	17	6.5%	1.48 [0.76, 2.20]
McCartney 1995_70−80y	6.6	3.05	17	2.7	1.1	20	6.1%	1.72 [0.95, 2.49]
Melnyk 2009	5.1	5.78	11	5.4	5.78	11	5.7%	−0.05 [−0.89, 0.79]
Njemini 2017_HI	4.2	20.95	8	5.1	13.4	8	4.8%	−0.05 [−1.03, 0.93]
Njemini 2017_LI	6.3	28.2	7	1.8	17.63	9	4.8%	0.19 [−0.80, 1.18]
Njemini 2017_LM	0.9	26.11	8	4.7	14.04	8	4.8%	−0.17 [−1.15, 0.81]
Roth 2001	2.1	5.7	9	5.4	5.06	10	5.2%	−0.59 [−1.51, 0.34]
Tanton 2009	2.77	2.9	9	2.28	1.63	9	5.1%	0.20 [−0.73, 1.13]
Tracy 1999	202	90.7	12	136	123.7	11	5.7%	0.59 [−0.25, 1.43]
Total (95% CI)			**274**			**288**	**100.0%**	**0.24 [−0.06, 0.53]**

Heterogeneity: Tau² = 0.21; Chi² = 40.19, df = 16 (P = 0.0007); I² = 60%
Test for overall effect: Z = 1.58 (P = 0.11)
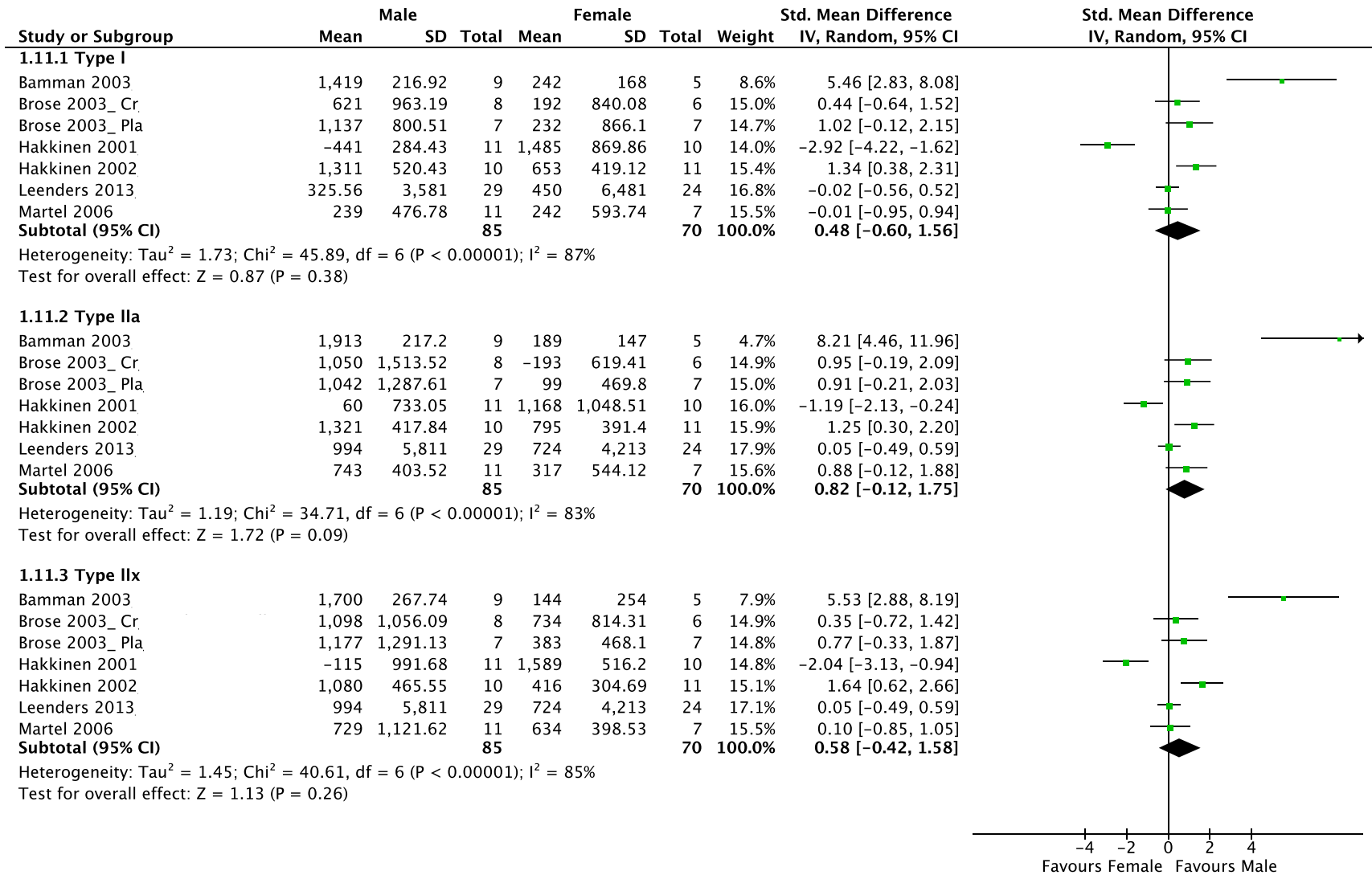

Figure 12. Forest plot of the effects of resistance training on sex differences in absolute changes in limb muscle mass

Study or Subgroup	Male Mean	Male SD	Male Total	Female Mean	Female SD	Female Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI
1.12.1 Type I									
Bamman 2003	28.95	4.43	9	6.55	4.55	5	9.2%	4.69 [2.37, 7.01]	
Brose 2003_ Cr	12.79	19.84	8	4.91	21.46	6	14.8%	0.36 [−0.71, 1.43]	
Brose 2003_ Pla	24.243	17.07	7	5.36	20.02	7	14.5%	0.95 [−0.18, 2.08]	
Hakkinen 2001	−8.52	5.5	11	34.11	19.98	10	13.8%	−2.86 [−4.14, −1.57]	
Hakkinen 2002	50.64	20.1	10	28.6	18.36	11	15.4%	1.10 [0.17, 2.03]	
Leenders 2013	5.61	61.7	29	8.82	127	24	16.8%	−0.03 [−0.57, 0.51]	
Martel 2006	6.49	12.96	11	7.07	17.35	7	15.3%	−0.04 [−0.99, 0.91]	
Subtotal (95% CI)			**85**			**70**	**100.0%**	**0.39 [−0.63, 1.41]**	

Heterogeneity: Tau² = 1.54; Chi² = 42.37, df = 6 (P < 0.00001); I² = 86%
Test for overall effect: Z = 0.75 (P = 0.46)

1.12.2 Type IIa									
Bamman 2003	41.12	4.67	9	5.7887	4.45	5	5.3%	7.19 [3.87, 10.52]	
Brose 2003_ Cr	20.77	29.94	8	−5.98	19.18	6	14.6%	0.96 [−0.18, 2.10]	
Brose 2003_ Pla	24.66	30.47	7	3.15	14.97	7	14.8%	0.84 [−0.27, 1.95]	
Hakkinen 2001	1.37	16.78	11	38.92	34.94	10	15.7%	−1.34 [−2.30, −0.37]	
Hakkinen 2002	48.44	15.32	10	33.28	16.38	11	16.0%	0.92 [0.01, 1.83]	
Leenders 2013	19.4	113	29	22.86	133	24	17.9%	−0.03 [−0.57, 0.51]	
Martel 2006	24.27	13.18	11	13.9	23.9	7	15.7%	0.55 [−0.42, 1.52]	
Subtotal (95% CI)			**85**			**70**	**100.0%**	**0.66 [−0.23, 1.56]**	

Heterogeneity: Tau² = 1.09; Chi² = 33.10, df = 6 (P < 0.0001); I² = 82%
Test for overall effect: Z = 1.45 (P = 0.15)

1.12.3 Type IIx									
Bamman 2003	42.94	6.76	9	5.07	8.94	5	10.1%	4.69 [2.37, 7.01]	
Brose 2003_ Cr	28.15	27.08	8	40.6	45.04	6	14.9%	−0.33 [−1.39, 0.74]	
Brose 2003_ Pla	40.6	44.54	7	17.02	20.81	7	14.9%	0.64 [−0.45, 1.72]	
Hakkinen 2001	−2.28	19.68	11	103.86	33.74	10	13.2%	−3.74 [−5.26, −2.22]	
Hakkinen 2002	46.23	19.93	10	18.98	14	11	15.2%	1.53 [0.53, 2.53]	
Leenders 2013	19.4	113	29	22.86	133	24	16.5%	−0.03 [−0.57, 0.51]	
Martel 2006	25.12	38.65	11	48.96	30.8	7	15.2%	−0.63 [−1.61, 0.34]	
Subtotal (95% CI)			**85**			**70**	**100.0%**	**0.16 [−0.99, 1.31]**	

Heterogeneity: Tau² = 2.02; Chi² = 51.24, df = 6 (P < 0.00001); I² = 88%
Test for overall effect: Z = 0.27 (P = 0.79)

−4 −2 0 2 4
Favours Female   Favours Male

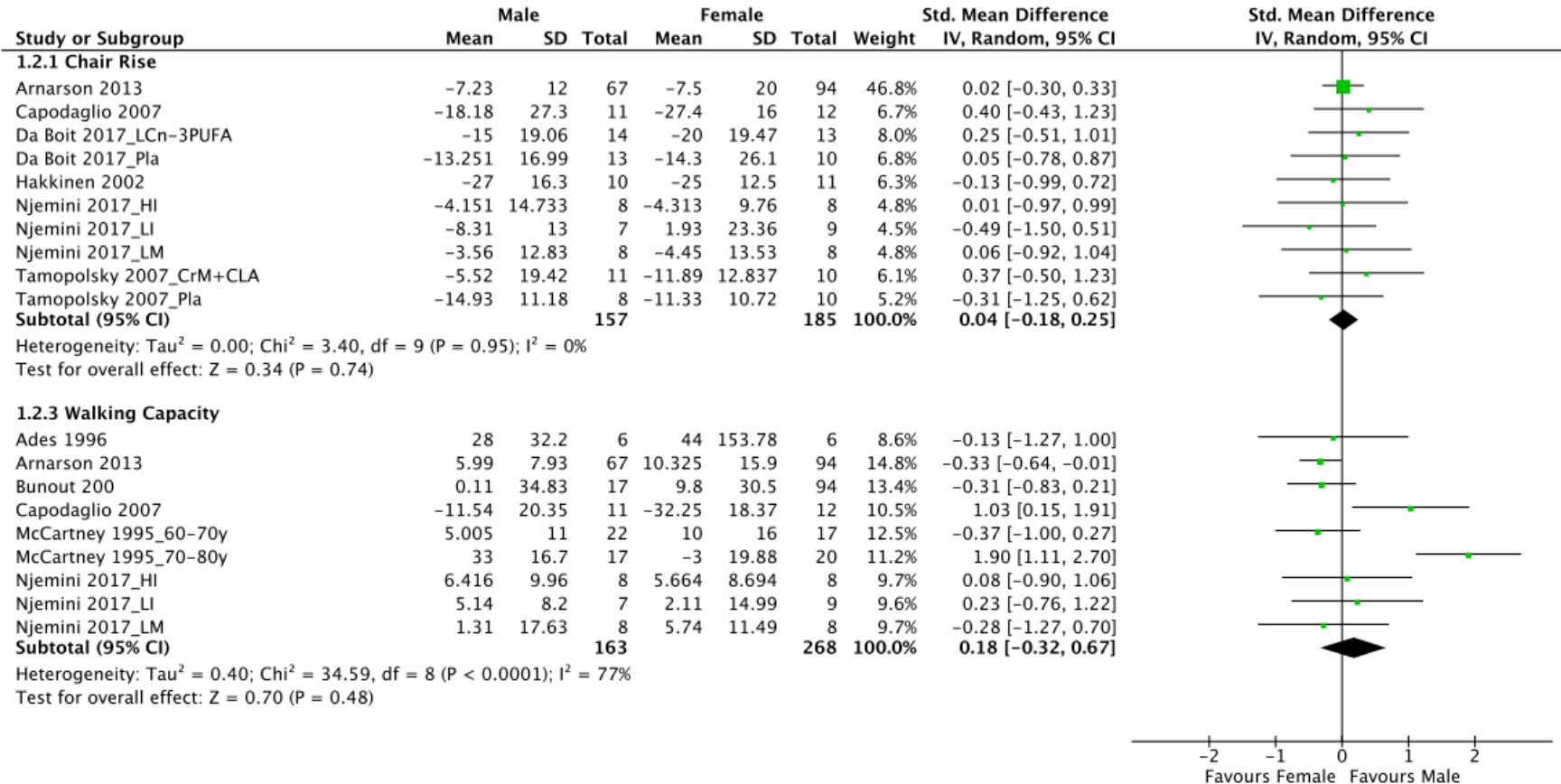**Figure 13.** Forest plot of the effects of resistance training on sex differences in relative changes in type I, IIa, IIx fiber size.

60

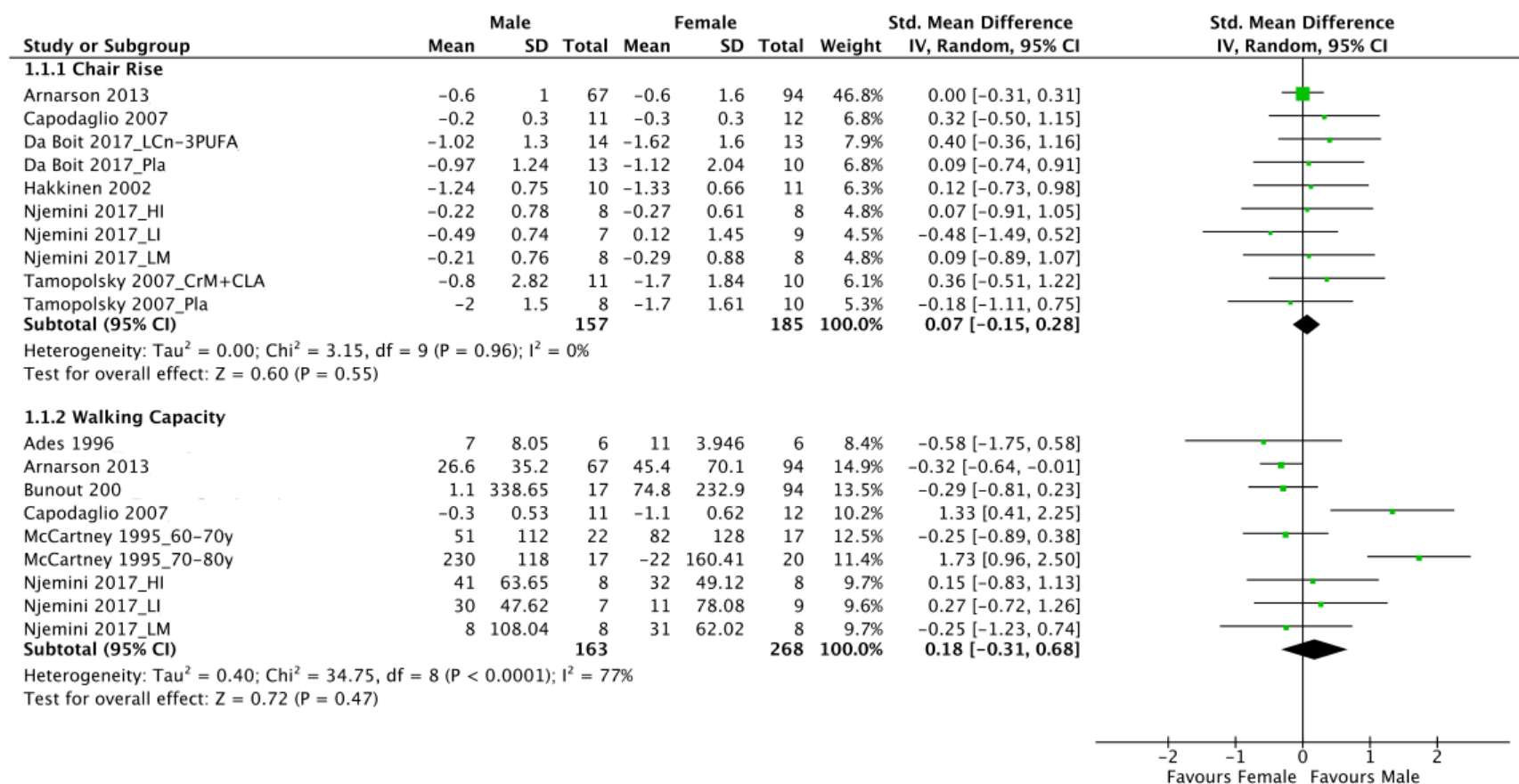| Study or Subgroup	Male Mean	Male SD	Male Total	Female Mean	Female SD	Female Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.11.1 Type I								
Bamman 2003	1,419	216.92	9	242	168	5	8.6%	5.46 [2.83, 8.08]
Brose 2003_ Cr	621	963.19	8	192	840.08	6	15.0%	0.44 [−0.64, 1.52]
Brose 2003_ Pla	1,137	800.51	7	232	866.1	7	14.7%	1.02 [−0.12, 2.15]
Hakkinen 2001	−441	284.43	11	1,485	869.86	10	14.0%	−2.92 [−4.22, −1.62]
Hakkinen 2002	1,311	520.43	10	653	419.12	11	15.4%	1.34 [0.38, 2.31]
Leenders 2013	325.56	3,581	29	450	6,481	24	16.8%	−0.02 [−0.56, 0.52]
Martel 2006	239	476.78	11	242	593.74	7	15.5%	−0.01 [−0.95, 0.94]
Subtotal (95% CI)			85			70	100.0%	0.48 [−0.60, 1.56]

Heterogeneity: Tau^2 = 1.73; Chi^2 = 45.89, df = 6 (P < 0.00001); I^2 = 87%
Test for overall effect: Z = 0.87 (P = 0.38)

Study or Subgroup	Male Mean	Male SD	Male Total	Female Mean	Female SD	Female Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.11.2 Type IIa								
Bamman 2003	1,913	217.2	9	189	147	5	4.7%	8.21 [4.46, 11.96]
Brose 2003_ Cr	1,050	1,513.52	8	−193	619.41	6	14.9%	0.95 [−0.19, 2.09]
Brose 2003_ Pla	1,042	1,287.61	7	99	469.8	7	15.0%	0.91 [−0.21, 2.03]
Hakkinen 2001	60	733.05	11	1,168	1,048.51	10	16.0%	−1.19 [−2.13, −0.24]
Hakkinen 2002	1,321	417.84	10	795	391.4	11	15.9%	1.25 [0.30, 2.20]
Leenders 2013	994	5,811	29	724	4,213	24	17.9%	0.05 [−0.49, 0.59]
Martel 2006	743	403.52	11	317	544.12	7	15.6%	0.88 [−0.12, 1.88]
Subtotal (95% CI)			85			70	100.0%	0.82 [−0.12, 1.75]

Heterogeneity: Tau^2 = 1.19; Chi^2 = 34.71, df = 6 (P < 0.00001); I^2 = 83%
Test for overall effect: Z = 1.72 (P = 0.09)

Study or Subgroup	Male Mean	Male SD	Male Total	Female Mean	Female SD	Female Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.11.3 Type IIx								
Bamman 2003	1,700	267.74	9	144	254	5	7.9%	5.53 [2.88, 8.19]
Brose 2003_ Cr	1,098	1,056.09	8	734	814.31	6	14.9%	0.35 [−0.72, 1.42]
Brose 2003_ Pla	1,177	1,291.13	7	383	468.1	7	14.8%	0.77 [−0.33, 1.87]
Hakkinen 2001	−115	991.68	11	1,589	516.2	10	14.8%	−2.04 [−3.13, −0.94]
Hakkinen 2002	1,080	465.55	10	416	304.69	11	15.1%	1.64 [0.62, 2.66]
Leenders 2013	994	5,811	29	724	4,213	24	17.1%	0.05 [−0.49, 0.59]
Martel 2006	729	1,121.62	11	634	398.53	7	15.5%	0.10 [−0.85, 1.05]
Subtotal (95% CI)			85			70	100.0%	0.58 [−0.42, 1.58]

Heterogeneity: Tau^2 = 1.45; Chi^2 = 40.61, df = 6 (P < 0.00001); I^2 = 85%
Test for overall effect: Z = 1.13 (P = 0.26)

−4 −2 0 2 4
Favours Female   Favours Male

Figure 14. Forest plot of the effects of resistance training on sex differences in absolute changes in type I, IIa and IIx fiber size.

Functional Performance

For chair rises (10 comparison outcomes; 157 males, 185 females), there was no difference in relative change (ES = 0.04 [95% CI -0.18, 0.25], $p = 0.74$; $I^2 = 0\%$, $p = 0.95$; **Figure 15**) as well as absolute change (ES = 0.07 [95% CI -0.15, 0.28], $p = 0.55$; $I^2 = 0\%$, $p = 0.96$; **Figure 16**) between males and females. For walking capacity (9 comparison outcomes; 163 males, 268 females), there was no difference in relative change (ES = 0.18 [95% CI -0.32, 0.67], $p = 0.48$; $I^2 = 77\%$, $p < 0.0001$; **Figure 15**) as well as absolute change in (ES = 0.18 [95% CI -0.31, 0.68], $p = 0.47$; $I^2 = 77\%$, $p < 0.0001$; **Figure 16**) between males and females

Study or Subgroup	Male Mean	SD	Total	Female Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.2.1 Chair Rise								
Arnarson 2013	-7.23	12	67	-7.5	20	94	46.8%	0.02 [-0.30, 0.33]
Capodaglio 2007	-18.18	27.3	11	-27.4	16	12	6.7%	0.40 [-0.43, 1.23]
Da Boit 2017_LCn-3PUFA	-15	19.06	14	-20	19.47	13	8.0%	0.25 [-0.51, 1.01]
Da Boit 2017_Pla	-13.251	16.99	13	-14.3	26.1	10	6.8%	0.05 [-0.78, 0.87]
Hakkinen 2002	-27	16.3	10	-25	12.5	11	6.3%	-0.13 [-0.99, 0.72]
Njemini 2017_HI	-4.151	14.733	8	-4.313	9.76	8	4.8%	0.01 [-0.97, 0.99]
Njemini 2017_LI	-8.31	13	7	1.93	23.36	9	4.5%	-0.49 [-1.50, 0.51]
Njemini 2017_LM	-3.56	12.83	8	-4.45	13.53	8	4.8%	0.06 [-0.92, 1.04]
Tamopolsky 2007_CrM+CLA	-5.52	19.42	11	-11.89	12.837	10	6.1%	0.37 [-0.50, 1.23]
Tamopolsky 2007_Pla	-14.93	11.18	8	-11.33	10.72	10	5.2%	-0.31 [-1.25, 0.62]
Subtotal (95% CI)			157			185	100.0%	0.04 [-0.18, 0.25]

Heterogeneity: Tau² = 0.00; Chi² = 3.40, df = 9 (P = 0.95); I² = 0%
Test for overall effect: Z = 0.34 (P = 0.74)

Study or Subgroup	Male Mean	SD	Total	Female Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.2.3 Walking Capacity								
Ades 1996	28	32.2	6	44	153.78	6	8.6%	-0.13 [-1.27, 1.00]
Arnarson 2013	5.99	7.93	67	10.325	15.9	94	14.8%	-0.33 [-0.64, -0.01]
Bunout 200	0.11	34.83	17	9.8	30.5	94	13.4%	-0.31 [-0.83, 0.21]
Capodaglio 2007	-11.54	20.35	11	-32.25	18.37	12	10.5%	1.03 [0.15, 1.91]
McCartney 1995_60-70y	5.005	11	22	10	16	17	12.5%	-0.37 [-1.00, 0.27]
McCartney 1995_70-80y	33	16.7	17	-3	19.88	20	11.2%	1.90 [1.11, 2.70]
Njemini 2017_HI	6.416	9.96	8	5.664	8.694	8	9.7%	0.08 [-0.90, 1.06]
Njemini 2017_LI	5.14	8.2	7	2.11	14.99	9	9.6%	0.23 [-0.76, 1.22]
Njemini 2017_LM	1.31	17.63	8	5.74	11.49	8	9.7%	-0.28 [-1.27, 0.70]
Subtotal (95% CI)			163			268	100.0%	0.18 [-0.32, 0.67]

Heterogeneity: Tau² = 0.40; Chi² = 34.59, df = 8 (P < 0.0001); I² = 77%
Test for overall effect: Z = 0.70 (P = 0.48)

Figure 15. Forest plot of the effects of resistance training on sex differences in relative changes in chair rises and walking capacity.

Study or Subgroup	Male Mean	SD	Total	Female Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.1.1 Chair Rise								
Arnarson 2013	-0.6	1	67	-0.6	1.6	94	46.8%	0.00 [-0.31, 0.31]
Capodaglio 2007	-0.2	0.3	11	-0.3	0.3	12	6.8%	0.32 [-0.50, 1.15]
Da Boit 2017_LCn–3PUFA	-1.02	1.3	14	-1.62	1.6	13	7.9%	0.40 [-0.36, 1.16]
Da Boit 2017_Pla	-0.97	1.24	13	-1.12	2.04	10	6.8%	0.09 [-0.74, 0.91]
Hakkinen 2002	-1.24	0.75	10	-1.33	0.66	11	6.3%	0.12 [-0.73, 0.98]
Njemini 2017_HI	-0.22	0.78	8	-0.27	0.61	8	4.8%	0.07 [-0.91, 1.05]
Njemini 2017_LI	-0.49	0.74	7	0.12	1.45	9	4.5%	-0.48 [-1.49, 0.52]
Njemini 2017_LM	-0.21	0.76	8	-0.29	0.88	8	4.8%	0.09 [-0.89, 1.07]
Tamopolsky 2007_CrM+CLA	-0.8	2.82	11	-1.7	1.84	10	6.1%	0.36 [-0.51, 1.22]
Tamopolsky 2007_Pla	-2	1.5	8	-1.7	1.61	10	5.3%	-0.18 [-1.11, 0.75]
Subtotal (95% CI)			157			185	100.0%	0.07 [-0.15, 0.28]

Heterogeneity: Tau^2 = 0.00; Chi^2 = 3.15, df = 9 (P = 0.96); I^2 = 0%
Test for overall effect: Z = 0.60 (P = 0.55)

Study or Subgroup	Male Mean	SD	Total	Female Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.1.2 Walking Capacity								
Ades 1996	7	8.05	6	11	3.946	6	8.4%	-0.58 [-1.75, 0.58]
Arnarson 2013	26.6	35.2	67	45.4	70.1	94	14.9%	-0.32 [-0.64, -0.01]
Bunout 200	1.1	338.65	17	74.8	232.9	94	13.5%	-0.29 [-0.81, 0.23]
Capodaglio 2007	-0.3	0.53	11	-1.1	0.62	12	10.2%	1.33 [0.41, 2.25]
McCartney 1995_60–70y	51	112	22	82	128	17	12.5%	-0.25 [-0.89, 0.38]
McCartney 1995_70–80y	230	118	17	-22	160.41	20	11.4%	1.73 [0.96, 2.50]
Njemini 2017_HI	41	63.65	8	32	49.12	8	9.7%	0.15 [-0.83, 1.13]
Njemini 2017_LI	30	47.62	7	11	78.08	9	9.6%	0.27 [-0.72, 1.26]
Njemini 2017_LM	8	108.04	8	31	62.02	8	9.7%	-0.25 [-1.23, 0.74]
Subtotal (95% CI)			163			268	100.0%	0.18 [-0.31, 0.68]

Heterogeneity: Tau^2 = 0.40; Chi^2 = 34.75, df = 8 (P < 0.0001); I^2 = 77%
Test for overall effect: Z = 0.72 (P = 0.47)

Std. Mean Difference IV, Random, 95% CI — scale from -2 to 2; Favours Female / Favours Male

Figure 16. Forest plot of the effects of resistance training on sex differences in absolute changes in chair rises and walking capacity.

3.3.3 Sensitivity Analysis

We completed a sensitivity analysis on all major outcomes measures where 1 study at a time was removed to determine whether a particular study had any significant impact on the overall effect size result (effects did not decrease substantially, nor did they cross the threshold for statistical significance). For absolute and relative change in lower-body strength, we decided to remove 1 outlier study (26), since there was a large enough total number of included studies remaining. Removing this study (26) did not change the overall results of absolute change in lower-body strength favouring males and relative change in lower-body strength favouring females; rather, it decreased the heterogeneity from $I^2 = 57\%$ (p = <0.00001) to $I^2 = 40\%$ (p = 0.005) for relative change in lower-body strength. Funnel plots for each analysis are presented in **Appendix C**, they were visually inspected to determine publication bias. We observed no evidence of publication asymmetry.

3.3.4 Study Quality and Reporting

The mean quality rating score was 17.63 out of a possible score of 28 (**Appendix D**), which was considered moderate-study quality. All studies clearly described main outcomes in the introduction and methods sections, the overall findings of the study, and estimates of random variability. All studies used valid and reliable outcome measures, as well as appropriate statistical tests. Three studies performed/presented their power calculation to determine the sample size required for the study.

3.4 Discussion

This systematic review and meta-analysis examined sex differences in resistance exercise training-induced changes in skeletal muscle mass, strength, and functional performance in healthy older adults ≥ 60 y of age. The results of this systematic review and meta-analysis indicate the existence of some sex differences in the adaptive response to resistance exercise training in healthy older adults. However, presentation of the results in an absolute or relative context influences the sex-dependent differences in adaptations to resistance exercise training. Specifically, the main findings were that the overall effect sizes for the relative change in skeletal muscle strength (i.e. upper-body strength, lower-body strength), skeletal muscle size (i.e. whole-body FFM, limb muscle mass, and type I, IIa, and IIx fiber size), and functional performance (i.e. chair rises and walking capacity measures) were similar between sexes in response to resistance exercise training. Alternatively, there was a significant effect in favour of males for absolute changes in upper-body (ES = 0.75 [95% CI 0.54, 0.96], $p < 0.00001$; $I^2 = 0\%$, $p = 0.72$; **Figure 6**) and lower-body (ES = 0.46 [95% CI 0.29, 0.63], $p < 0.00001$; $I^2 = 35\%$, $p = 0.02$; **Figure 8**) strength in response to resistance exercise training. However, the overall effect sizes for the absolute change in whole-body FFM, skeletal muscle size at the limb (i.e. limb muscle mass) and fiber level (i.e. type I, IIa, and IIx fiber size), as well as functional performance were similar between sexes in response to resistance exercise training.

3.4.1 Muscle Strength

It is known that when comparing males and females, females have less total body skeletal muscle (and a greater body-fat percentage) than males, and may therefore not be able to exert the same absolute maximal force (124,142,143). The results of the present meta-analysis showed that absolute changes in both upper-body strength and lower-body strength in response to

resistance exercise training were greater in older males. Interestingly, our results showed that older adult males and females displayed similar relative changes in both upper-body strength and lower-body strength after the same resistance training program. Although the overall effect sizes for relative changes in upper-body strength (ES = -0.20 [95% CI -0.54, 0.13], p = 0.23; I^2= 58%, p = 0.002; **Figure 5**) and lower body strength (ES = -0.09 [95% CI -0.27, 0.08], p = 0.30; I^2 = 40%, p = 0.006; **Figure 7)** were negative and trending towards favouring older females, the sexes were not statistically significant.

Roberts and colleagues (135) recently conducted a meta-analysis on sex differences in response to resistance exercise training in younger adults aged 18–50 years of age. They found that females had greater levels of relative strength gain in the upper-body, while relative strength gains in the lower-body were similar between males and females in response to resistance training (135). Our findings are in alignment with their results of similar relative strength gains in the lower-body between males and females. Alternatively, the sex difference in relative gains in upper-body strength favouring younger females (135) is not present when comparing older males and females (**Figure 5**). Another recent meta-analysis by Jones and colleagues (127) on sex differences following resistance exercise training in middle-aged and older adults ($\geq$ 50 years of age) found that females had greater levels of relative strength gain in the lower-body, while relative strength gains in the upper-body were similar between males and females in response to resistance training. Our findings of similar relative strength gains in the upper-body are in are in agreement with those of Jones and colleagues (127). Our findings relating to skeletal muscle strength are interesting when compared to the recent Jones et al. meta-analyses (127), as the greater relative lower-body strength gain they observed in middle-aged and older women is not apparent when examining an exclusively older ($\geq$ 60 y of age) population. Cheng and colleagues

(126) observed that the decrease in muscle strength and functional activities occurred earlier in females than in males. It may be that any beneficial effect of resistance exercise training on relative increases in strength are only present in younger and middle-aged females, neither of which were captured in the present meta-analysis. Younger females typically have lower visceral fat than males, and a gynoid fat distribution such that fat is mostly stored in the hips and thighs (30). However, menopause is followed by redistribution of adipose tissue towards a more central/android phenotype (122). It is well established that fat distributed in the trunk and especially intra-abdominal adipose tissue (IAAT) is related to the development of diabetes and heart disease, as well as mortality (30). Perhaps this change in fat distribution and increase in IAAT with age in males but especially females (30) could be the reason why the direction of the sex differences appears to differ between young and older participants in terms of relative upper-body and lower-body strength.

3.4.2 Muscle Size

In addition to increasing skeletal muscle strength, resistance exercise training results in an increase in skeletal muscle mass at the whole-body level (i.e. whole-body FFM), limb/appendicular level (i.e. based on MRI-derived muscle volume or CSA, CT-derived muscle CSA, ultrasound-derived muscle thickness, or DXA-derived appendicular FFM), and fiber (i.e. type I, IIa, and IIx fiber CSA) level (33,109). Our results indicate that the overall effect size for the absolute and relative change in whole-body FFM in response to resistance exercise training, measured using DXA, was not different between older males and females. A recent meta-analysis (127) in middle-aged to older ($\geq$ 50 years of age) adults by Jones and colleagues (127) reported no sex difference in the relative changes for muscle size in response to resistance training as well. However, they found that absolute changes in muscle size adaptations after

resistance training favoured males, contradicting our results. This could be due to the fact that they included a variety of measurement tools that had outcomes presented for regional, not whole-body, lean mass as well. Moreover, although the overall effect size for absolute change in whole-body FFM (ES = 0.13 [95% CI -0.03, 0.30], p = 0.10; I^2 = 0%, p = 1.00; **Figure 10**) was not statistically significant, it was positive and trending towards favouring older males. Nonetheless, measures of whole-body FFM derived from DXA do not directly measure skeletal muscle mass; rather it captures total body lean mass which includes tissue from organs like kidney and liver, as well as fibrotic and other lean tissue (i.e. the vasculature) (144). Although DXA is a commonly used technique, there are other imaging methods with higher accuracy (i.e. MRI and CT). Therefore, in the present systematic review and meta-analysis we separated and categorized the results for muscle mass into whole-body FFM, limb muscle mass (which are thought to better reflect skeletal muscle than whole-body FFM as these measures do not capture the visceral organs), and skeletal muscle fibre size (based on needle biopsy).

Our results for limb skeletal muscle mass indicate that there are no significant differences between older males and females in absolute and relative changes in response to resistance exercise training. Similar to whole-body FFM, it is worth noting that the even though overall effect size for absolute change in limb skeletal muscle mass (ES = 0.24 [95% CI -0.06, 0.53], p = 0.11; I^2 = 60%, p = 0.0007; **Figure 12**) was not statistically significant, it was positive and trending towards favouring older males. The recent meta-analysis in younger adults (18–50 y) by Robert and colleagues (135) also reported no significant sex differences in resistance exercise training-mediated increases in muscle size (which included MRI, fiber CSA, ultrasound, and CT scans).

Finally, we separately examined sex differences in changes in skeletal muscle fiber size (type I, IIa, IIx fiber CSA) in response to resistance exercise training in older males and females. Our results indicate no significant difference between older males and females in absolute or relative changes in muscle fiber size in response to resistance training. However, this may partially be attributed to the limited sample size, with only 7 included studies yielding a total of 85 males and 70 females. Moreover, heterogeneity for this result was considerably high, with an $I^2 > 75\%$ for both absolute and relative measures of fiber size. As can be seen in **Figure 13** and **Figure 14**, this heterogeneity is primarily the result of two studies (27,145). Sensitivity analysis indicated no change in the overall effect size by removing these studies, even though the I^2 was reduced to 39% and 42%. We therefore included these studies in the meta-analysis due to the already small number of studies reporting sex differences in skeletal muscle fiber size in response to resistance exercise training in older males and females. It is common that there is a high heterogeneity when looking at muscle fiber size, because its change in response to resistance training is often larger than any other method for assessing skeletal muscle hypertrophy (146). Furthermore, with the unit of measure for muscle fiber size being so small (μm^2), the absolute change values are much larger than other methods of assessing the outcome measures of interest, leading to a possible larger variation in results as well. Splitting up muscle fibre size into type I, IIa, and IIx, did not substantially reduce heterogeneity, nor were there differences displayed in any of their overall effect sizes.

It is important to note that increased muscle mass does not necessarily imply a causal relation with strength improvement (147,148) since the mechanisms responsible for strength development and muscle hypertrophy are different in nature (149). For example strength improvements as a result of increased neural drive are observed well before muscle hypertrophy

as a result of increased motor unit firing rate or agonist–antagonist co-activation (149), while muscle hypertrophy is thought to be stimulated by factors such as metabolic stress, mechanical tension, and muscle fiber recruitment which then activate intracellular pathways inducing muscle growth (150). Perhaps this could partially explain the lack of sex differences in our muscle mass outcomes measures.

3.4.3 Functional Performance

Physical performance refers to an objectively measured whole-body function related to locomotion (3), and is a multidimensional concept that encompasses muscle function and nervous system function, including balance (3). Activities of daily living such as rising from a chair, climbing stairs, and walking are influenced by muscle strength, especially in older people (77). In early 2018, the EWGSOP2 updated the definition of sarcopenia to: low levels of muscle strength detected reflects probable sarcopenia; a diagnosis is confirmed by the presence of low levels of muscle quantity/quality; and physical performance assessment is used to categorise the severity of sarcopenia (3). Therefore, it can be argued that functional performance is one of the most important measures to assess in older adults. Overall, in absolute terms females have lower muscle function than males, and they may suffer from a greater decline in muscle function with age due to menopause (94). There is a health-survival paradox regarding males and females: although females live longer than males, they have a greater risk of sarcopenia, and consequently, functional incapacity, with the aging process (94,151). Carvalho de Abreu and colleagues conducted a cross-sectional study with 233 community-dwelling older adults (males: n = 83; females: n = 150) to compare the functional performance of community-dwelling older adults and investigate the possible mediation aspects (151). They identified that quadriceps muscle strength is a determining factor for the sex difference regarding SPPB performance, in

contrast to gait speed, to which stature makes an important contribution. On the other hand, the association between disability and muscle mass follows a U-pattern (6), meaning that beyond a certain point, higher muscle mass becomes redundant from a functional standpoint and does not necessarily lead to better performance, perhaps due to the extra weight that needs to be displaced (152).

In the present study, we examined functional performance in terms of chair rise and walking capacity assessments. Our results indicate that the overall effect size for absolute and relative change in both of the functional performance assessments did not differ between sexes undergoing the same relative resistance exercise training program. According to Carvalho de Abreu and colleagues (151), quadriceps muscle strength is a determining factor for the sex difference regarding SPPB performance, which includes a 4-meter gait speed and five-repetition sit-to-stand test that are of interest to us as functional performance outcome measures. Our results indicate that relative increases in lower-body strength were similar between sexes in response to resistance exercise training. It is interesting though, that even in terms of absolute change, there were no significant sex differences in chair rise time and walking capacity after performing the same resistance training protocol. Functional performance measures can also be heavily influenced by several factors, including the individuals characteristics, lifestyle, and habits (151). For example, some covariates between each induvial participant could include the time they spend climbing stairs, walking for exercise, walking for other purposes, and performing moderate intensity aerobic-type exercises during their normal day (153).

3.4.4 Strengths and Limitations

Strengths of this systematic review and meta-analysis include: (a) the pre-registration of the study protocol on PROSPERO; (b) the comprehensive search strategy conducted through 5

databases using a search syntax with a broad range of relevant search terms; (c) additional

included studies yielded from citation scanning; and (d) the final list of 35 included studies with

over 1,142 participants. To our knowledge, this is also the first systematic review and meta-

analysis to investigate sex differences in responses to resistance exercise training in an

exclusively older ($\geq$ 60 years) population of healthy adults, as well as include meta-analysis on

sex differences in limb skeletal muscle mass, fiber size (type I, IIa, IIx), and functional

performance changes in response to resistance exercise training. Although the present analysis

provides important and novel data, there are limitations that we acknowledge. First, the high

heterogeneity in some of the outcome measures. Many of the included studies did not

specifically aim investigate sex differences, resulting in small sample size comparisons between

sexes. Second, many of these studies established programs that are geared to develop muscle

hypertrophy (moderate-high volume and moderate-high loading) whereas specific strength

training programmes (low volume, high load) were scarce. It would be interesting to see if

strength targeted training would reveal any more prominent differences between older males and

females, especially given the role of neurological adaptations in enhancing strength.

3.4.5 Conclusion

This systematic review and meta-analysis indicates the existence of sex differences in the

adaptive response to resistance exercise training in healthy older adults $\geq$ 60 years of age.

However, presentation of the results in either an absolute or relative context influences the sex-

dependent differences in adaptations to resistance exercise training as has been reported

previously (127,135). The main findings from this meta-analysis were that the overall effect

sizes for relative resistance exercise training-mediated changes in all outcome measures were

similar between sexes, while the overall effect sizes for absolute resistance-training induced

change in upper-body and lower-body strength favoured males. The absolute change in whole-body FFM, limb skeletal muscle mass, fiber size, and functional performance measures showed no differences between sexes. Heterogeneity for results in muscle fiber size were high which could relate to the small sample of included studies, as well as the much larger absolute change values in comparison to other methods of assessment. Finally, since our included population were healthy older adults, they may have been near their ceiling capacity to walk or time taken to rise from a chair. More research is needed on sex differences in resistance training induced changes in skeletal muscle mass and functional performance measures. Overall, healthy older males and females, as well as exercise professionals working with this demographic, can expect some sex differences in the adaptive response to resistance exercise training in absolute terms. However, in relative terms it appears that older males and females adapt similarly to resistance exercise training-induced changes in muscle mass, muscle strength, and functional performance. Although it appears that older males and females may gain the same relative benefits in terms of muscle mass, strength, and functional performance gains from performing the same resistance training programs, further research is needed to identify optimal resistance exercise training protocols for older males and females.

CHAPTER 4: OVERALL CONCLUSION AND SUMMARY

Aging is accompanied by a progressive loss of skeletal muscle mass, strength, and functional performance (40). These age-related changes are currently referred to as 'sarcopenia' (94). Sarcopenia represents a major problem for the older adult as it is associated with adverse events and diseases (154–156) and predicts disability later in life (157). Resistance exercise training is arguably the most potent non-pharmacological anabolic stimulus for skeletal muscle and has been demonstrated to effectively increase both lean body mass (158) and muscle strength (100) in older adults. However, whether there are differences between healthy older (i.e. ≥ 60 years of age) males and females in resistance exercise training-induced changes in skeletal muscle mass/size, muscle strength, and/or functional performance is unclear. It is well known that males tend to have greater skeletal muscle size and strength than females, which is partially due to their greater body size and height (14). There are also known differences between males and females in fatigability (15,16), skeletal muscle protein metabolism (128), and skeletal muscle gene transcription (134) that may alter adaptive responses to resistance exercise training between the sexes. Therefore, our purpose was to evaluate via systematic review and meta-analysis if there are sex-based differences in resistance exercise training-induced changes in skeletal muscle mass, strength, and/or functional performance in healthy older adults ≥ 60 years of age.

We searched a total of 5 databases and after the screening process ended up with a total of 35 included studies (1,142 participants; 518 males 624 females) in our systematic review and meta-analysis. The mean study quality was 17.63/28 on a modified Downs and Black checklist, considered moderate quality. The main findings from this systematic review and meta-analysis were that the overall effect sizes for the relative change in skeletal muscle strength (i.e. upper-

body strength, lower-body strength), skeletal muscle size (i.e. whole-body FFM, limb muscle mass, and type I, IIa, and IIx fiber size), and functional performance (i.e. chair rises and walking capacity measures) were similar between sexes in response to resistance exercise training. Alternatively, there was a significant effect in favour of males for absolute changes in upper-body (ES = 0.75 [95% CI 0.54, 0.96], $p < 0.00001$; $I^2 = 0\%$, $p = 0.72$; **Figure 6**) and lower-body (ES = 0.46 [95% CI 0.29, 0.63], $p < 0.00001$; $I^2 = 35\%$, $p = 0.02$; **Figure 8**) strength in response to resistance exercise training. However, the overall effect sizes for the absolute change in whole-body FFM, skeletal muscle size at the limb (i.e. limb muscle mass) and fiber level (i.e. type I, IIa, and IIx fiber size), as well as functional performance were similar between sexes in response to resistance exercise training. Therefore, there are some sex differences in the adaptive response to resistance exercise training in healthy older adults. However, presentation of the results in an absolute or relative context influences the sex-dependent differences in adaptations to resistance exercise training.

Many of the studies included in the present systematic review and meta-analysis included a relatively small sample size and/or did not specifically aim/were not powered to investigate sex differences in the adaptive response to resistance exercise training. Heterogeneity for the results of muscle fiber size (type I, IIa, IIx CSA) were particularly high ($I^2 > 75\%$) which could relate to the small number of included studies, as well as the much larger absolute change values in comparison to other methods of assessment of muscle size. Many of the included studies did not specifically aim to investigate sex differences and were therefore underpowered.

Overall, healthy older males and females, as well as exercise professionals working with this demographic, can expect some sex differences in the adaptive response to resistance exercise training in absolute terms. However, in relative terms it appears that older males and females

adapt similarly in terms of resistance exercise training-induced changes in muscle mass, strength and functional performance. Although it appears that older males and females may gain the same benefits in terms of muscle mass, strength and functional performance from performing the same resistance training programs, further research is needed to clarify the optimal exercise prescription in terms of frequency, intensity, and volume in order to best support healthy active aging in older males and females.

APPENDICES

A. Search Strategy

Database: Scopus

TITLE-ABS-KEY(("sex differences" OR "gender differences" OR "sex characteristics" OR "gender characteristics" OR "gender factors" OR "sex factors" OR "gender comparison" OR "sex comparison" OR (male w/3 female) OR (women w/3 men)) AND ("resistance training" OR "muscle strengthening" OR "strength training" OR "weight training" OR "resistance exercise" OR "weight lifting" OR "isometric contraction" OR (weight* w/3 lift*)) AND ("muscle strength" OR "physical functional performance" OR "muscle size" OR hypertrophy OR (muscle* w/3 strength*)) AND (aged OR "older adults" OR senior OR elderly OR (older* w/3 adult*) OR "aged 60+ years"))

Database: SPORTDiscus

(("sex differences" OR "gender differences" OR "sex characteristics" OR "gender characteristics" OR "gender factors" OR "sex factors" OR "gender comparison" OR "sex comparison" OR (male N2 female) OR (women N3 men)) AND ("resistance training" OR "muscle strengthening" OR "strength training" OR "weight training" OR "resistance exercise" OR "weight lifting" OR "isometric contraction" OR (weight* N3 lift*)) AND ("muscle strength" OR "muscle size" OR "physical functional performance" OR hypertrophy OR (muscle* N3 strength*)) AND (aged OR "older adults" OR senior OR elderly OR (old* N3 adult*) OR (aged: 60+ years))

Database: CINAHL

("sex differences" OR "gender differences" OR "sex characteristics" OR "gender characteristics" OR "gender factors" OR (MH "sex factors") OR "gender comparison" OR "sex comparison" OR (male N3 female) OR (men N3 women)) AND ((MH "resistance training") OR (MH "muscle strengthening") OR "strength training" OR "weight training" OR "resistance exercise" OR (MH " weight lifting") OR (MH "isometric contraction") OR (weight* N3 lift*)) AND ((MH "muscle strength") OR "muscle size" OR (MH "hypertrophy") OR (MH "physical performance") OR "physical functional

performance" OR (muscle W/3 strength*)) AND ((MH "aged") OR "older adults" OR "senior"
OR "elderly" OR (old* w/3 adult*) OR (aged: 60+ years))

Advanced search: Limiters: Age groups: Aged 60+ years

Database: EMBASE

1. Sex difference/
2. Gender differences.mp.
3. Sex characteristics.mp.
4. Gender characteristics.mp.
5. Sex factor/
6. Gender factors.mp.
7. Sex comparison.mp.
8. Gender comparison.mp.
9. (male adj3 female).mp.
10. (men adj3 women).mp.
11. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12. Resistance training/
13. Muscle strengthening.mp
14. Strength training.mp.
15. Weight training.mp.
16. Resistance exercise.mp.
17. Weight lifting/
18. Muscle isometric contraction/
19. (weight* adj3 lift*).mp.
20. 12 o 13 or 14 or 15 or 16 or 17 or 18 or 19
21. Muscle strength/
22. Muscle size.mp.
23. Hypertrophy/
24. Physical performance/
25. Functional performance.mp.
26. (muscle adj3 strength*).mp.

27. 22 or 22 or 23 or 24 or 25

28. Aged/

29. Older adults.mp.

30. Elderly.mp.

31. Senior.mp.

32. Aged 60+.mp.

33. (old* adj3 adult*).mp.

34. 27 or 28 or 29 or 30 or 31 or 32 or 32

35. 11 and 20 and 27 and 34

Database: MEDLINE

1. Sex differences.mp.

2. Gender differences.mp.

3. Exp sex characteristics/

4. Gender characteristics.mp.

5. Gender factors.mp.

6. Exp sex factors/

7. Gender comparison.mp.

8. Sex comparison.mp.

9. (male adj3 female).mp.

10. (men adj3 women).mp.

11. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10

12. Exp resistance training/

13. Muscle strengthening.mp

14. Strength training.mp.

15. Weight training.mp.

16. Resistance exercise.mp.

17. Exp weight lifting/

18. Exp isometric contraction/

19. (weight* adj3 lift*).mp.

20. 12 o 13 or 14 or 15 or 16 or 17 or 18 or 19

21. Exp muscle strength/

22. muscle size.mp.

23. Exp Hypertrophy/

24. Exp physical functional performance/

25. (muscle adj3 strength*).mp.

26. 21 or 22 or 23 or 24 or 25

27. Exp Aged/

28. Older adults.mp.

29. Elderly.mp.

30. Senior.mp.

31. Aged 60+.mp.

32. (old* adj3 adult*).mp

33. 27 or 28 or 29 or 30 or 31 or 32

34. 11 and 20 and 26 and 33

B. Summary of Included Studies

Study, Year	Participants (n)		Mean Age (y)		Duration (weeks)	Frequency (days/week)	Outcome Measures		
	Male	Female	Male	Female			Muscle Strength	Muscle Mass	Functional Performance
Ades, 1996 (108)	6	6	69.9 ± 4		12	3	1RM – LE, BP	FFM	Walking endurance
Arnarson, 2013 (159)	67	94	Range: 65 - 91		12	3	MVC – Quads	FFM; ASMM via DXA	6MWD; TUG
Asakawa, 2007 (160)	6	6	74.2 ± 4.6	74.8 ± 4.2	12	2-3	MVC – KE		
Bamman, 2003 (27)	9	5	68.7 ± 1.6	66.2 ± 1.4	26	3		Fiber Size – Type I, IIa, IIx	
Beneka, 2005_LI (161)	8	8	70.7 ± 2.3	68 ± 5.1	16	3	MVC – KE		
Beneka, 2005_MI (161)	8	8	71.7 ± 2.7	66 ± 5.5					
Beneka, 2005_HI (161)	8	8	70.8 ± 3.2	68.9 ± 6.7					
Binns, 2017 (95)	8	25	74.6 ± 4.8	77.7 ± 6.8	20	2	Total 1RM	FFM	
Brose, 2003_Pla (162)	7	7	68.3 ± 3.2	69.9 ± 5.6	20	2	1RM – CP, KE	FFM; VL Fiber Size – Type I, IIa, IIx	
Brose, 2003_Cr (162)	8	6	68.7 ± 4.8	70.8 ± 6.1	14	3			
Bunout, 2005 (163)	17	94	75 ± 5		52	2	1RM - Quads, Biceps	FFM	12 minute walking capacity
Capodaglio, 2007 (164)	11	12	76.6 ± 3	76.6 ± 4.6	52	3	MVC – KE		Chair rise-1,10; 6MWD
Da Boit, 2017_Pla (28)	13	10	69.8 ± 4	70.5 ± 3.9	18	2	MVC – KE	Muscle ACSA via MRI	Chair rise
Da Boit, 2017_LC (28)	14	13	71 ± 4	68 ± 3					
Fernández-Lezaun, 2017_2x /wk (165)	7	14	70 ± 3	69 ± 3	36	2	1RM – LP	FFM	
Fernández-Lezaun, 2017_3x /wk (165)	11	13	67.3 ± 5	74.4 ± 7.5		3			
Fragala, 2014 (166)	7	5	69.7 ± 4.3	69.6 ± 4.8	6	2	1RM – LE	FFM; VL CSA via ultrasound	

Study									
Galvão, 2006 (21)	10	6	74.6 ± 5.9	72.8 ± 5.5	20	2	1RM – upper, lower	FFM	
Hakkinen, 1994 (167)	10	11	Range: 64 - 73		12	2 - 3	MVC – LE		
Hakkinen, 1998 (26)	11	10	72 ± 3	67 ± 3	24	2	1RM – LE; MVC – LE, KF	LE CSA via ultrasound	
Hakkinen, 2001 (145)	11	10	72 ± 3	67 ± 3	26	2	1RM – KE	VL Fiber Size – Type I, IIa, IIx	
Hakkinen, 2002 (168)	10	11	65.4 ± 4.7	64.4 ± 3.5	24	2	1RM – Squat	FFM; VL Fiber Size – Type I, IIa, IIx	Chair Rise
Hunter, 2002 (30)	14	12	67.9 ± 4.4	65.9 ± 4.4	25	3	1RM – upper, lower	FFM	
Kobayashi, 2016 (169)	17	13	73 ± 5	70 ± 7	4	2	MVC – PF	Muscle Volume via ultrasound	
Kosek, 2006 (170)	13	12	64.5 ± 1.1	63.3 ± 0.9	16	3	1RM – KE	FFM; myofiber CSA – Type I, II, IIa, IIx	
Leenders, 2013 (23)	29	24	71 ± 1	70 ± 1	24	3	1RM – LE	FFM; Quads CSA via CT scan; Fiber Size – Type I, IIa, IIx	
Lemmer, 2001 (171)	11	10	69 ± 3	68 ± 3	24	3	1RM – CP, LE	FFM	
Lexell, 1995 (172)	6	10	70 - 77		11	3	1RM – EF, KE		
Mackey, 2007 (173)	13	16	76 ± 4	74 ± 3	12	3	MVC – KF	Fibre Area via MRI	
Martel, 2006 (174)	11	7	69 ± 1	68 ± 1	9	3		Fiber Size – Type I, IIa, IIx	
McCartney, 1996_60-70 (175)	15	14	60-70		84	2	1RM – BP, LP	KE CSA via CT scan	Treadmill endurance
McCartney, 1996_70-80 (175)	14	14	70-80						
Melnyk, 2009 (107)	11	11	69 ± 3	68 ± 3	9	3		Middle Quad CSA via MRI	
Njemini, 2017_HI (176)	8	8							
Njemini, 2017_LM (176)	8	8	68 ± 5.2	67.8 ± 5.3	12	3	1RM –LE	Muscle Volume via CT scan	6MWD; TUG
Njemini, 2017_LI (176)	7	9							
Ochala , 2007 (177)	8	8	75.1 ± 2.1	77.1 ± 2.2	48	2	MVC - PF		

Roth, 2001 (25)	9	10	69 ± 1	68 ± 1	26	3	1RM – LP, CP	FFM, Muscle CSA via MRI	
Ryan, 2001 (178)	10	9	70 ± 1	69 ± 1	26	3	1RM – LE, CP	FFM	
Sharman, 2001 (179)	7	7	66.4 ± 4.8	64.6 ± 3.6	24	2	1RM – Squat		
Tamopolsky, 2007_Pla (180)	8	10	74.8 ± 6.6	68.2 ± 4.4	24	2	1RM – CP, KE	FFM	Sit and stand
Tamopolsky, 2007_CrM+CRA (180)	11	10	71.8 ± 5.2	69.5 ± 3.8					
Tanton, 2009 (181)	9	9	73 ± 3.74	71.11 ± 5.88	12	2	1RM – Preacher curl	Biceps CSA via MRI	
Tracy, 1999 (31)	12	11	69 ± 1	68 ± 1	9	3	1RM – KE	FFM; Muscle Volume via MRI	

Total / Means:

Total Comparison Groups	Males	Females	Mean Male Age	Mean Female Age	Mean Duration	Mean Frequency
44	518	624	71.6 ± 3.4	71.9 ± 4.1	22.3	2.6

C. Funnel Plots
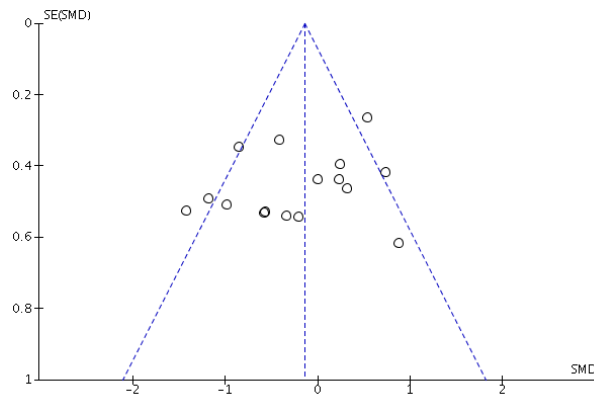
C1. Relative upper-body strength
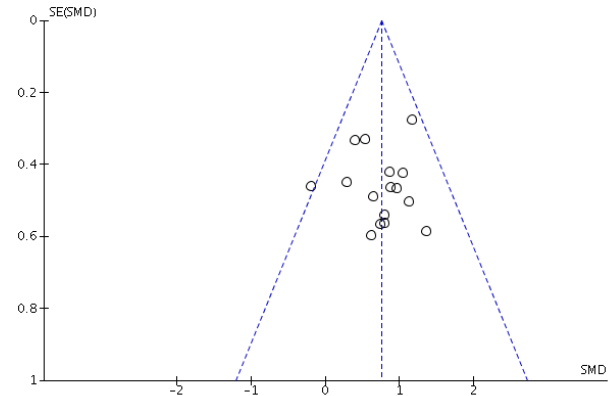
C2. Absolute upper-body strength
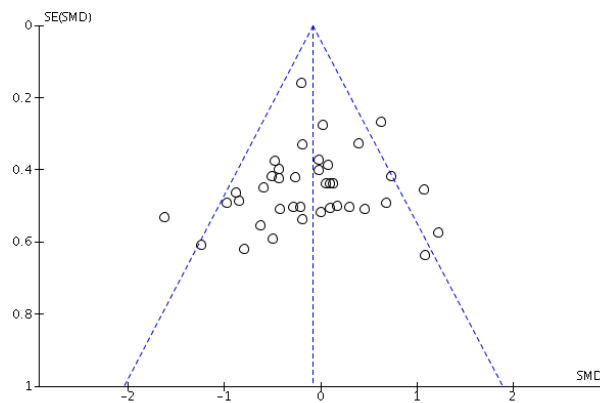
C3. Relative lower-body strength
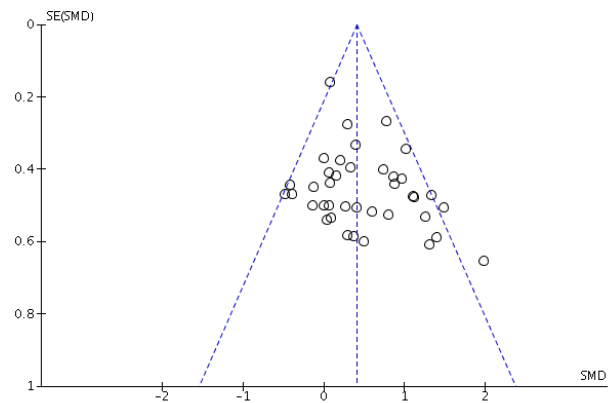
C4. Absolute lower-body strength
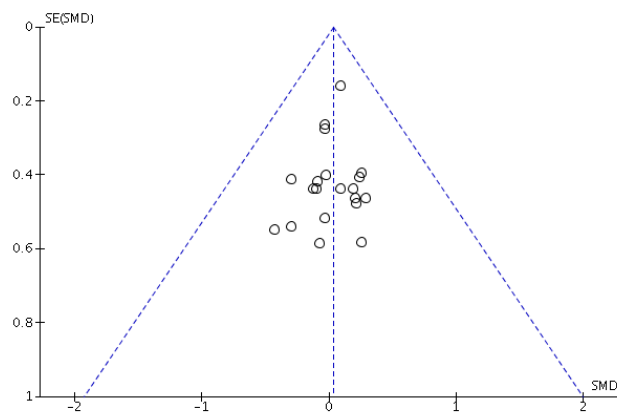
C5. Relative whole-body FFM
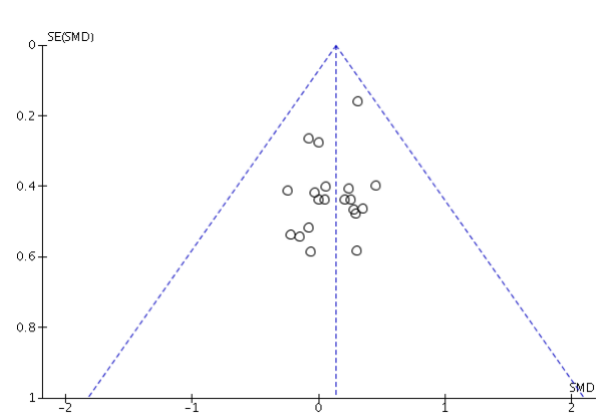
C6. Absolute whole-body FFM
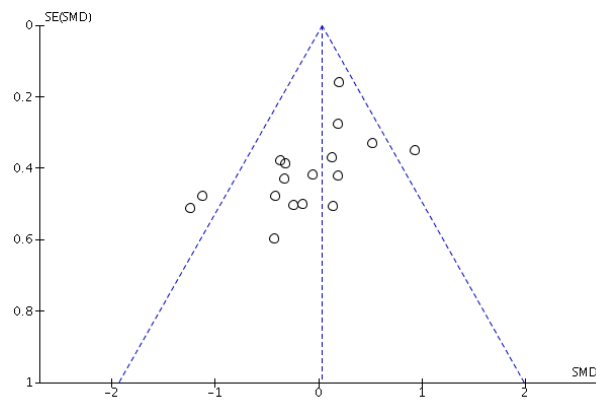
C7. Relative limb muscle mass
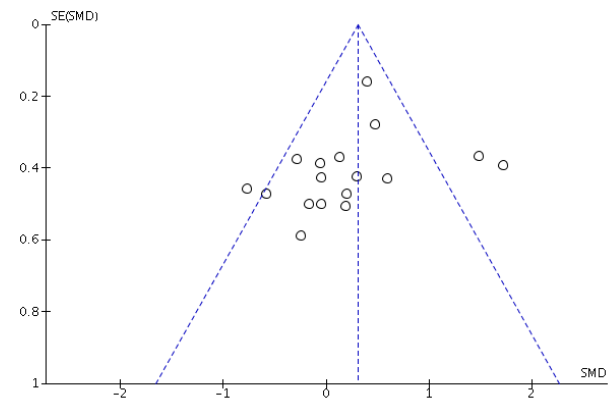
C8. Absolute limb muscle mass
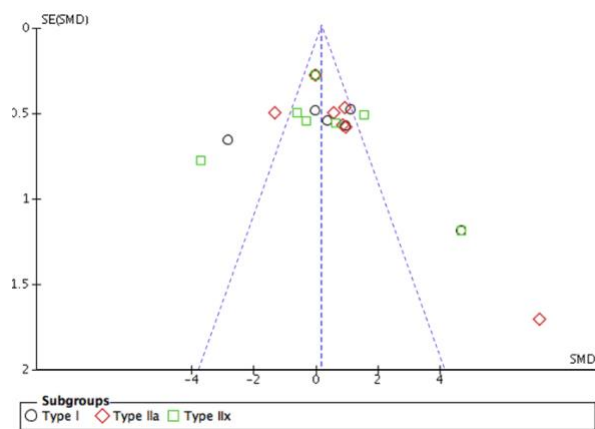
C9. Relative type I, IIa, IIx fiber size
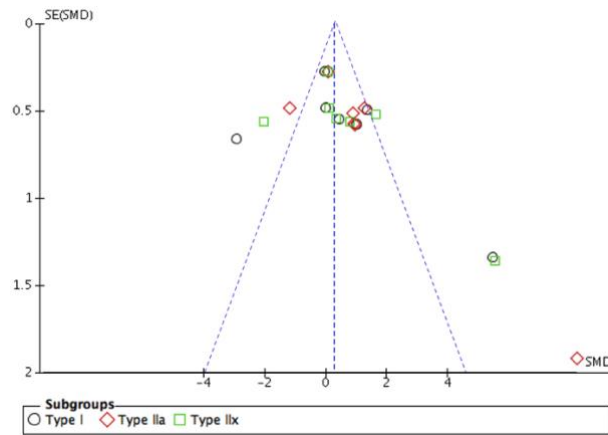
C10. Absolute type I, IIa, IIx fiber size
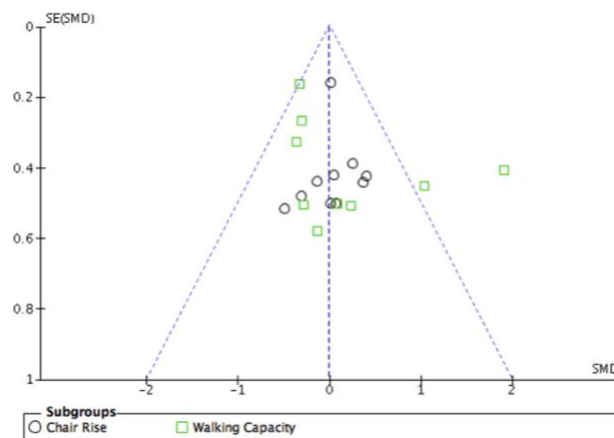
C11. Relative chair rises and walking capacity
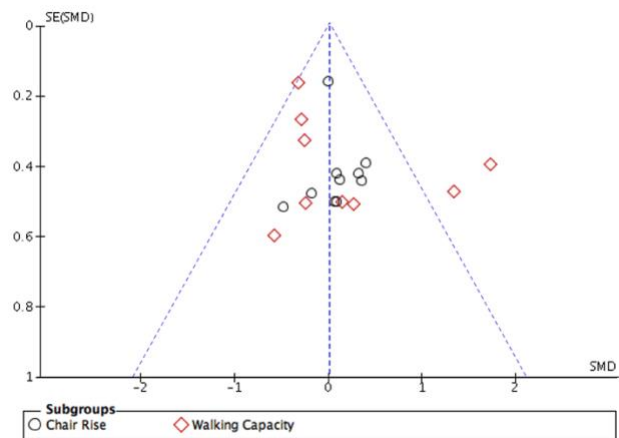
C12. Absolute chair rises and walking capacity

D. Downs and Black Checklist

Study, Year	Reporting (/11)	External Validity (/3)	Internal Validity (/7)	Confounding Internal Validity (Selection Bias) (/6)	Power (/1)	TOTAL (/28)
Ades, 1996	7	2	5	5	0	19
Arnarson, 2013	9	2	4	6	0	21
Asakawa, 2007	9	1	5	4	0	19
Bamman, 2003	8	0	4	3	0	15
Benka, 2005	8	0	4	4	0	16
Binns, 2017	8	2	4	4	0	18
Brose, 2003	9	1	7	5	0	22
Bunout, 2005	7	0	5	4	0	16
Capodaglio, 2007	9	2	4	3	0	18
Da Boit, 2017	8	1	7	5	0	21
Fernandez, 2017	8	1	5	5	0	19
Fragala, 2014	8	0	4	4	1	17
Galvao, 2006	8	0	4	4	0	16
Hakkinen, 1994	9	1	4	3	0	17
Hakkinen, 1998	8	0	4	3	0	15
Hakkinen, 2001	9	0	4	3	0	16
Hakkinen, 2002	7	1	4	4	0	16
Hunter, 2002	9	1	5	4	0	19
Kobayashi, 2016	10	1	3	4	0	18
Kosek, 2006	8	2	5	4	0	19
Leenders, 2013	7	1	3	4	0	15
Lemmer, 2001	9	0	4	3	1	17
Lexell, 1995	8	1	4	4	0	17
Mackey, 2007	10	1	4	3	0	18
Martel, 2006	9	0	4	3	0	16
McCartney, 1996	10	0	5	5	1	21
Melnyk, 2009	9	0	6	3	0	18
Njemini, 2017	9	1	4	4	0	18
Ochala, 2007	7	0	4	4	0	15
Roth, 2001	9	0	5	3	0	17
Ryan, 2001	9	0	5	4	0	18
Sharman, 2001	8	0	4	4	0	16
Tamopolsky, 2007	8	2	5	4	0	19
Tanton, 2009	7	1	6	4	0	18
Tracy, 1999	9	0	4	4	0	17
Mean Totals	8.40/11	0.71/3	4.51/7	3.91/6	0.08/1	17.63/28

REFERENCES

1.   United Nations. World Population Ageing. 2017.

2.   Rosenberg IH. Summary Comments. Am Soc Clin Nutr. 1989;50:1231–3.

3.   Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al. Sarcopenia: Revised European consensus on definition and diagnosis. Age Ageing. 2019;48(1):16–31.

4.   Papadopoulou SK. Sarcopenia: A contemporary health problem among older adult populations. Nutrients. 2020;12(5).

5.   Evans W. Symposium: Sarcopenia: Diagnosis and Mechanisms Functional and Metabolic Consequences of Sarcopenia. J Nutr. 1997;127(5):998S–1003S.

6.   Janssen I, Shepard DS, Katzmarzyk PT, Roubenoff R. The Healthcare Costs of Sarcopenia in the United States. J Am Geriatr Soc. 2004;52(1):80–5.

7.   Burton LA, Sumukadas D. Optimal management of sarcopenia. Clin Interv Aging. 2010;5:217–28.

8.   Fragala MS, Cadore EL, Dorgo S, Izquierdo M, Kraemer WJ, Peterson MD, et al. Resistance training for older adults: Position statement from the national strength and conditioning association. J Strength Cond Res. 2019;33(8):2019–52.

9.   Miller RM, Bemben DA, Bemben MG. The influence of sex, training intensity, and frequency on muscular adaptations to 40 weeks of resistance exercise in older adults. Exp Gerontol. 2021;143:111174.

10.   McLeod M, Breen L, Hamilton DL, Philp A. Live strong and prosper: the importance of skeletal muscle strength for healthy ageing. Biogerontology. 2016;17(3):497–510.

11.   Gordon BR, McDowell CP, Hallgren M, Meyer JD, Lyons M, Herring MP. Association of efficacy of resistance exercise training with depressive symptoms meta-analysis and meta-regression: Analysis of randomized clinical trials. JAMA Psychiatry. 2018;75(6):566–76.

12.   Wizemann TM. Sex-Specific Reporting of Scientific Research: A Workshop Summary. Washington, DC: The National Academic Press. 2012.

13.   Countrymeters. 2020 Demographics on Canada. 2021.

14.   Hunter GR, McCarthy JP, Bamman MM. Effects of Resistance Training on older adults. Sport Med. 2004;34(5):329–48.

15.   Hunter SK. Sex differences in fatigability of dynamic contractions. Exp Physiol. 2016;101(2):250–5.

16.   Marshall PW, Metcalf E, Hagstrom AD, Cross R, Siegler JC, Enoka RM. Changes in fatigue are the same for trained men and women after resistance exercise. Med Sci Sports Exerc. 2020;52(1):196–204.

17.   Stupka N, Lowther S, Chorneyko K, Bourgeois JM, Hogben C, Tarnopolsky MA. Gender differences in muscle inflammation after eccentric exercise. J Appl Physiol. 2000;89(6):2325–32.

18.   Flores DF, Gentil P, Brown LE, Pinto RS, Carregaro RL, Bottaro M. Dissociated time course of recovery between genders after resistance exercise. J Strength Cond Res.

2011;25(11):3039–44.

19.   Haizlip KM, Harrison BC, Leinwand LA. Sex-Based Differences in Skeletal Muscle Kinetics and Fiber-Type Composition. physiology. 2015;30:30–9.

20.   Wieser M, Haber P. The effects of systematic resistance training in the elderly. Int J Sports Med. 2007;28(1):59–65.

21.   Galvão DA, Newton RU, Taaffe DR. Does Sex Affect the Muscle Strength and Regional Lean Tissue Mass Response to Resistance Training in Older Adults? Int J Sport Heal Sci. 2006;4:36–43.

22.   Ivey FM, Tracy BL, Lemmer JT, NessAiver M, Metter EJ, Fozard JL, et al. Effects of Strength Training and Detraining on Muscle Quality: Age and Gender Comparisons. Journals Gerontol Biol Sci. 2000;55A(3):B152-157.

23.   Leenders M, Verdijk LB, Van Der Hoeven L, Van Kranenburg J, Nilwik R, Wodzig WKWH, et al. Protein supplementation during resistance-type exercise training in the elderly. Med Sci Sports Exerc. 2013;45(3):542–52.

24.   McCartney N, Hicks AL, Martin J, Webber CE. Long-term resistance training in the elderly: Effects on dynamic strength, exercise capacity, muscle, and bone. Journals Gerontol - Ser A Biol Sci Med Sci. 1995;50(2):97–104.

25.   Roth SM, Ivey FM, Martel GF, Lemmer JT, Hurlbut DE, Siegel EL, et al. Muscle Size Responses to Strength Training in Young and Older Men and Women. JAGS. 2001;49:1428–33.

26.   Hakkinen K, Kallinen M, Izquierdo M, Jokelainen K, Lassila H, Malkia E, et al. Changes in agonist-antagonist EMG, muscle CSA, and force during. J Appl Physiol. 1998;84(4):1341–9.

27.   Bamman MM, Hill VJ, Adams GR, Haddad F, Wetzstein CJ, Gower BA, et al. Gender differences in resistance-training-induced myofiber hypertrophy among older adults. Journals Gerontol - Ser A Biol Sci Med Sci. 2003;58(2):108–16.

28.   Da Boit M, Sibson R, Sivasubramaniam S, Meakin JR, Greig CA, Aspden RM, et al. Sex differences in the effect of fish-oil supplementation on the adaptive response to resistance exercise training in older people: A randomized controlled trial. Am J Clin Nutr. 2017;105(1):151–8.

29.   Hakkinen K, Kallinen M, Linnamo V. Neuromuscular adaptations during bilateral versus unilateral strength training in middle-aged and elderly men and women. Acta Physiol Scand. 1996; 158: 77-88.

30.   Hunter GR, Bryan DR, Wetzstein CJ, Zuckerman PA, Bamman MM. Resistance training and intra-abdominal adipose tissue in older men and women. Med Sci Sports Exerc. 2002;34(6):1023–8.

31.   Tracy BL, Ivey FM, Hurlbut DE, Martel GF, Lemmer JT, Siegel EL, et al. Muscle quality. II. Effects of strength training in 65- to 75-yr-old men and women. J Appl Physiol. 1999;85(1):195–201.

32.   Ivey FM, Hurley BF, Roth SM, Ferrell RE, Tracy BL, Lemmer JT, et al. Effects of age, gender, and myostatin genotype on the hypertrophic response to heavy resistance strength

training. Journals Gerontol - Ser A Biol Sci Med Sci. 2000;55A(11):M641–8.

33. Leenders M, Verdijk LB, Van Der Hoeven L, Van Kranenburg J, Nilwik R, Van Loon LJC. Elderly men and women benefit equally from prolonged resistance-type exercise training. Journals Gerontol - Ser A Biol Sci Med Sci. 2013;68(7):769–79.

34. Statistics Canada. Population estimates by age and sex, July 1st, 2020.

35. Statistics Canada. Annual Demographic Estimates: Canada, Provinces and Territories, 2020.

36. Statistics Canada. Seniors and Aging Statistics. 2021.

37. Statista. Average life expectancy in North America for those born in 2020, by gender and region. 2021.

38. Government of Canada. Healthy Living Seniors. 2021.

39. Statistics Canada. Quarterly Demographic Estimates October to December 2020. 2021;

40. Rosenberg IH. Symposium: Sarcopenia: Diagnosis and Mechanisms Sarcopenia: Origins and Clinical Relevance 1. J Nutr. 1997;127:990–1.

41. English KL, Paddon-Jones D. Protecting muscle mass and function in older adults during bed rest. Curr Opin Clin Nutr Metab Care. 2010;13(1):34–9.

42. Janssen I, Heymsfield SB, Wang ZM, Ross R. Skeletal muscle mass and distribution in 468 men and women aged 18-88 yr. J Appl Physiol. 2000;89(1):81–8.

43. Evans WJ, Lexell J. Human Aging, Muscle Mass, and Fiber Type Composition. Journals Gerontol. 1995;50A:11–6.

44. Lexell J, Taylor CC, Sjöström M. What is the cause of the ageing atrophy?. Total number, size and proportion of different fiber types studied in whole vastus lateralis muscle from 15- to 83-year-old men. J Neurol Sci. 1988;84(2–3):275–94.

45. Nilwik R, Snijders T, Leenders M, Groen BBL, van Kranenburg J, Verdijk LB, et al. The decline in skeletal muscle mass with aging is mainly attributed to a reduction in type II muscle fiber size. Exp Gerontol. 2013;48(5):492–8.

46. Frontera WR, Hughes VA, Lutz KJ, Evans WJ. A cross-sectional study of muscle strength and mass in 45- to 78-yr-old men and women. J Appl Physiol. 1991;71(2):644–50.

47. Goodpaster BH, Park SW, Harris TB, Kritchevsky SB, Nevitt M, Schwartz A V., et al. The loss of skeletal muscle strength, mass, and quality in older adults: The Health, Aging and Body Composition Study. Journals Gerontol - Ser A Biol Sci Med Sci. 2006;61(10):1059–64.

48. Bassey EJ, Fiatarone MA, O'Neill EF, Kelly M, Evans WJ, Lipsitz LA. Leg extensor power and functional performance in very old men and women. Clin Sci. 1992;82(3):321–7.

49. Papa E V., Dong X, Hassan M. Resistance training for activity limitations in older adults with skeletal muscle function deficits: A systematic review. Clin Interv Aging. 2017;12:955–61.

50. Nair KS. Aging muscle. Am J Clin Nutr. 2005;81(5):953–63.

51. Fukagawa NK, Wolfson L, Judge J, Whipple R, King M. Strength Is a Major Factor in

Balance, Gait, and the Occurrence of Falls. Journals Gerontol. 1996;50A:64–7.

52. Gao L, Jiang J, Yang M, Hao Q, Luo L, Dong B. Prevalence of Sarcopenia and Associated Factors in Chinese Community-Dwelling Elderly: Comparison Between Rural and Urban Areas. J Am Med Dir Assoc. 2015;16(11):1003.e1-1003.e6.

53. Patel HP, Syddall HE, Jameson K, Robinson S, Denison H, Roberts HC, et al. Prevalence of sarcopenia in community-dwelling older people in the UK using the European Working Group on Sarcopenia in Older People (EWGSOP) definition: Findings from the Hertfordshire Cohort Study (HCS). Age Ageing. 2013;42(3):378–84.

54. Gao Z, Lee JE, McDonough DJ, Albers C. Virtual Reality Exercise as a Coping Strategy for Health and Wellness Promotion in Older Adults during the COVID-19 Pandemic. J Clin Med. 2020;9(6):1986.

55. Lauretani F, Russo CR, Bandinelli S, Bartali B, Cavazzini C, Di Iorio A, et al. Age-associated changes in skeletal muscles and their effect on mobility: An operational diagnosis of sarcopenia. J Appl Physiol. 2003;95(5):1851–60.

56. Cesari M, Kritchevsky SB, Newman AB, Simonsick EM, Harris TB, Penninx BW, et al. Added value of physical performance measures in predicting adverse health-related events: Results from the health, aging and body composition study. J Am Geriatr Soc. 2009;57(2):251–9.

57. Laviano A, Gori C, Rianda S. Sarcopenia and nutrition. Advances in Food and Nutrition Research. Elsevier Inc. 2014. 71;101–136

58. Smith GI, Mittendorfer B. Sexual Dimorphism in Skeletal Muscle Protein Turnover. Am Physiol Soc. 2016;(120):674–682.

59. Short KR, Vittone JL, Bigelow ML, Proctor DN, Nair KS. Age and aerobic exercise training effects on whole body and muscle protein metabolism. Am J Physiol - Endocrinol Metab. 2004;286(1 49-1):92–101.

60. Welle S, Thornton C, Jozefowicz R, Statt M. Myofibrillar protein synthesis in young and old men. Am J Physiol. 1993;264(5 Pt 1):E693-8.

61. Yarasheski KE, Zachwieja JJ, Bier DM. Acute effects of resistance exercise on muscle protein synthesis rate in young and elderly men and women. Am J Physiol - Endocrinol Metab. 1993;265(2 28-2).

62. Katsanos CS, Kobayashi H, Sheffield-Moore M, Aarsland A, Wolfe RR. Aging is associated with diminished accretion of muscle proteins after the ingestion of a small bolus of essential amino acids. Am J Clin Nutr. 2005;82(5):1065–73.

63. Katsanos CS, Kobayashi H, Sheffield-Moore M, Aarsland A, Wolfe RR. A high proportion of leucine is required for optimal stimulation of the rate of muscle protein synthesis by essential amino acids in the elderly. Am J Physiol - Endocrinol Metab. 2006;291(2):381–7.

64. Cuthbertson D, Smith K, Babraj J, Leese G, Waddell T, Atherton P, et al. Anabolic signaling deficits underlie amino acid resistance of wasting, aging muscle. FASEB J. 2005;19(3):1–22.

65. Moore DR, Churchward-Venne TA, Witard O, Breen L, Burd NA, Tipton KD, et al.

Protein ingestion to stimulate myofibrillar protein synthesis requires greater relative protein intakes in healthy older versus younger men. Journals Gerontol - Ser A Biol Sci Med Sci. 2015;70(1):57–62.

66.   Wall BT, Gorissen SH, Pennings B, Koopman R, Groen BBL, Verdijk LB, et al. Aging is accompanied by a blunted muscle protein synthetic response to protein ingestion. PLoS One. 2015;10(11):1–13.

67.   Kumar V, Selby A, Rankin D, Patel R, Atherton P, Hildebrandt W, et al. Age-related differences in the dose-response relationship of muscle protein synthesis to resistance exercise in young and old men. J Physiol. 2009;587(1):211–7.

68.   Horstman AMH, Kouw IWK, Van Dijk JW, Hamer HM, Groen BBL, Van Kranenburg J, et al. The muscle protein synthetic response to whey protein ingestion is greater in middle-aged women compared with men. J Clin Endocrinol Metab. 2019;104(4):994–1004.

69.   Roubenoff R. Catabolism of aging: is it an inflammatory process? Curr Opin Clin Nutr Metab Care. 2003;6(3):295–9.

70.   Maggio M, Guralnik JM, Longo DL, Ferrucci L. Interleukin-6 in Aging and Chronic Disease: A Magnificent Pathway. J Gerontol A Biol Sci Med Sci. 2006;61(6):575–84.

71.   Gabay C, Kushner I, Epstein F. Acute-Phase Proteins and Other Systemic Responses to Inflammation. N Engl J Med. 1999;340(6):448–54.

72.   Haran PH, Rivas DA, Fielding RA. Role and potential mechanisms of anabolic resistance in sarcopenia. J Cachexia Sarcopenia Muscle. 2012;3(3):157–62.

73.   Schaap LA, Pluijm SMF, Deeg DJH, Visser M. Inflammatory Markers and Loss of Muscle Mass (Sarcopenia) and Strength. Am J Med. 2006;119(6).

74.   Leenders M. Exercise and nutrition to support healthy aging. 2016.

75.   Kamel HK, Maas D, Duthie EH. Role of hormones in the pathogenesis and management of sarcopenia. Drugs and Aging. 2002;19(11):865–77.

76.   Verdijk LB, Koopman R, Schaart G, Meijer K, Savelberg HHCM, Van Loon LJC. Satellite cell content is specifically reduced in type II skeletal muscle fibers in the elderly. Am J Physiol - Endocrinol Metab. 2007;292(1):151–7.

77.   Doherty TJ. Invited review: Aging and sarcopenia. J Appl Physiol. 2003;95(4):1717–27.

78.   Houston DK, Nicklas BJ, Ding J, Harris TB, Tylavsky FA, Newman AB, et al. Dietary protein intake is associated with lean mass change in older, community-dwelling adults: The Health, Aging, and Body Composition (Health ABC) study. Am J Clin Nutr. 2008;87(1):150–5.

79.   Moreland B, Kakara R, Henry A. Trends in Nonfatal Falls and Fall-Related Injuries Among Adults Aged ≥65 Years — United States, 2012–2018. MMWR Morb Mortal Wkly Rep. 2020;69(27):875–81.

80.   Damiot A, Pinto AJ, Turner JE, Gualano B. Immunological Implications of Physical Inactivity among Older Adults during the COVID-19 Pandemic. Gerontology. 2020;66(5):431–8.

81.   Faulkner JA, Larkin LM, Claflin DR, Brooks S V. Age-related changes in the structure and function of skeletal muscles. Clin Exp Pharmacol Physiol. 2007;34(11):1091–6.

82.   Son JS, Nimrod G, West ST, Janke MC, Liechty T, Naar JJ. Promoting Older Adults' Physical Activity and Social Well-Being during COVID-19. Leis Sci. 2021;43(1–2):287–94.

83.   Carson JA, Manolagas SC. Effects of sex steroids on bones and muscles: similarities, parallels, and putative interactions in health and disease. Bone. 2015;80:67–78.

84.   Volpato S, Bianchi L, Cherubini A, Landi F, Maggio M, Savino E, et al. Prevalence and clinical correlates of sarcopenia in community-dwelling older people: Application of the EWGSOP definition and diagnostic algorithm. Journals Gerontol - Ser A Biol Sci Med Sci. 2014;69(4):438–46.

85.   Rosa-Caldwell ME, Greene NP. Muscle metabolism and atrophy: Let's talk about sex. Biol Sex Differ. 2019;10(1):1–14.

86.   Guralnik JM, Ferrucci L, Pieper CF, Leveille SG, Markides KS, Ostir G V., et al. Lower extremity function and subsequent disability: Consistency across studies, predictive models, and value of gait speed alone compared with the short physical performance battery. Journals Gerontol - Ser A Biol Sci Med Sci. 2000;55(4):221–31.

87.   Tanimoto Y, Watanabe M, Sun W, Tanimoto K, Shishikura K, Sugiura Y, et al. Association of sarcopenia with functional decline in community-dwelling elderly subjects in Japan. Geriatr Gerontol Int. 2013;13(4):958–63.

88.   Scheibel A. Falls, motor dysfunction, and correlative neurohistologic changes in the elderly. Clin Geriatr Med. 1985;1(3):671–7.

89.   Tanimoto Y, Watanabe M, Sun W, Sugiura Y, Hayashida I, Kusabiraki T, et al. Sarcopenia and falls in community-dwelling elderly subjects in Japan: Defining sarcopenia according to criteria of the European Working Group on Sarcopenia in Older People. Arch Gerontol Geriatr. 2014;59(2):295–9.

90.   Shafiee G, Keshtkar A, Soltani A, Ahadi Z, Larijani B, Heshmat R. Prevalence of sarcopenia in the world: A systematic review and meta- analysis of general population studies. J Diabetes Metab Disord. 2017;16(1):1–10.

91.   Baum EE, Jarjoura D, Polen AE, Faur D, Rutecki G. Effectiveness of a Group Exercise Program in a Long-Term Care Facility: A Randomized Pilot Trial. J Am Med Dir Assoc. 2003;4(2):74–80.

92.   Papadopoulou SK, Tsintavis P, Potsaki G, Papandreou D. Differences in the Prevalence of Sarcopenia in Community-Dwelling, Nursing Home and Hospitalized Individuals. A Systematic Review and Meta-Analysis. J Nutr Heal Aging. 2020;24(1):83–90.

93.   Beaudart C, Rizzoli R, Bruyère O, Reginster JY, Biver E. Sarcopenia: Burden and challenges for public health. Arch Public Heal. 2014;72(1):1–8.

94.   Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al. Sarcopenia: Revised European consensus on definition and diagnosis. Vol. 48, Age and Ageing. 2019.

95.   Binns A, Gray M, Henson AC, Fort IL. Changes in lean mass and serum myostatin with habitual protein intake and high-velocity resistance training. J Nutr Heal Aging. 2017;21(10):1111–7.

96.   Phillips SM, Winett RA. Uncomplicated Resistance Training and Health-Related. Curr

Sport Med Rep. 2010;9(4):208–13.

97.   Forbes SC, Little JP, Candow DG. Exercise and nutritional interventions for improving aging muscle health. Endocrine. 2012;42(1):29–38.

98.   Janssen I, Heymsfield SB, Ross R. Is Associated with Functional Impairment and Physical Disability. 2002;889–96.

99.   Visser M, Kritchevsky SB, Goodpaster BH, Newman AB, Nevitt M, Stamm E, et al. Leg Muscle Mass and Composition in Relation to Lower Extremity Performance in Man and Women Aged 70-79: The Health, Aging and Body Composition Study. J Am Geriatr Soc. 2002;50:897–904.

100.   Peterson MD, Rhea MR, Sen A, Gordon PM. Resistance exercise for muscular strength in older adults: A meta-analysis. Ageing Res Rev. 2010;9(3):226–37.

101.   Schulte JN, Yarasheski KE. Effects of resistance training on the rate of muscle protein synthesis in frail elderly people. Int J Sport Nutr. 2001;11(SUPPL.).

102.   Verdijk LB, Gleeson BG, Jonkers RAM, Meijer K, Savelberg HHCM, Dendale P, et al. Skeletal muscle hypertrophy following resistance training is accompanied by a fiber type-specific increase in satellite cell content in elderly men. Journals Gerontol - Ser A Biol Sci Med Sci. 2009;64(3):332–9.

103.   Smilios I, Pilianidis T, Karamouzis M, Tokmakidis SP. Hormonal responses after various resistance exercise protocols. Med Sci Sports Exerc. 2003;35(4):644–54.

104.   Cornish SM, Chilibeck PD. Alpha-linolenic acid supplementation and resistance training in older adults. Appl Physiol Nutr Metab. 2009;34(1):49–59.

105.   Taaffe DR, Duret C, Wheeler S, Marcus R. Once-weekly resistance exercise improves muscle strength and neuromuscular performance in older adults. J Am Geriatr Soc. 1999;47(10):1208–14.

106.   Kemmler W, Von Stengel S. Alternative exercise technologies to fight against sarcopenia at old age: A series of studies and review. J Aging Res. 2012;2012.

107.   Melnyk JA, Rogers MA, Hurley BF. Effects of strength training and detraining on regional muscle in young and older men and women. Eur J Appl Physiol. 2009;105(6):929–38.

108.   Ades PA, Ballor DL, Ashikaga T, Utton JL, Nair KS. Weight training improves walking endurance in healthy elderly persons. Ann Intern Med. 1996;124(6):568–72.

109.   Churchward-Venne TA, Tieland M, Verdijk LB, Leenders M, Dirks ML, de Groot LCPGM, et al. There are no nonresponders to resistance-type exercise training inolder men and women. J Am Med Dir Assoc. 2015;16(5):400–11.

110.   Government of Canada. Physical Activity. 2021.

111.   The American College of Sports Medicine (ACSM). Ch.1 Benefits and Risks Associated with Physical Activity. In: Guidlelines for exercise testing. 2007. p. 1–21.

112.   Fiatarone MA, Marks EC, Ryan ND, Meredith CN, Lipsitz LA, Evans WJ. High-Intensity Strength Training in Nonagenarians: Effects on Skeletal Muscle. JAMA J Am Med Assoc. 1990;263(22):3029–34.

113. Fiatarone MA, O'Neill EF, Ryan ND, Clements KM, Solares GR, Nelson ME, et al. Exercise Training and Nutritional Supplementation for Physical Frialty in Very Elderly People. N Engl J Med. 1994;330(25):1769–75.

114. Cadore EL, Rodríguez-Mañas L, Sinclair A, Izquierdo M. Effects of different exercise interventions on risk of falls, gait ability, and balance in physically frail older adults: A systematic review. Rejuvenation Res. 2013;16(2):105–14.

115. Serra-Rexach JA, Bustamante-Ara N, Hierro Villarán M, González Gil P, Sanz Ibáñez MJ, Blanco Sanz N, et al. Short-term, light- to moderate-intensity exercise training improves leg muscle strength in the oldest old: A randomized controlled trial. J Am Geriatr Soc. 2011;59(4):594–602.

116. Burton E, Farrier K, Lewin G, Pettigrew S, Hill A-M, Airey P, et al. Older people strength training: Systematic review 1 Motivators and barriers for older people participating in resistance training: A systematic review Council on the Ageing (Western Australia). J Aging Phys Act. 2017;25(311):324.

117. Lindle RS, Metter EJ, Lynch NA, Fleg JL, Fozard JL, Tobin J, et al. Age and gender comparisons of muscle strength in 654 women and men aged 20-93 yr. J Appl Physiol. 1997;83(5):1581–7.

118. Miller AEJ, MacDougall, JD, Tarnopolsky MA, Sale, DG. Gender differences in strength and muscle fiber characteristics. Eur J Appl Physiol. 1993;(66):254–62.

119. Canadian Institutes of Health Research (CIHR). Sex, Gender and Health Research. 2021.

120. Lungsgaard A-M, Bente K. Gender differences in skeletal muscle substrate metabolism – molecular mechanisms and insulin sensitivity. Front Endocrinol (Lausanne). 2014;5(195).

121. Glenmark B, Nilsson M, Gao H, Gustafsson JÅ, Dahlman-Wright K, Westerblad H. Difference in skeletal muscle function in males vs. females: Role of estrogen receptor-β. Am J Physiol - Endocrinol Metab. 2004;287(6 50-6):1125–31.

122. Karastergiou K, Smith SR, Greenberg AS, Fried SK. Sex differences in human adipose tissues - The biology of pear shape. Biol Sex Differ. 2012;3(1):1.

123. Hicks AL, Kent-Braun J, Ditor DS. Sex differences in human skeletal muscle fatigue. Exerc Sport Sci Rev. 2001;29(3):109–12.

124. Lewis DA, Kamon E, Hodgson JL. Physiological Differences Between Genders Implications for Sports Conditioning. Sport Med. 1986;3(5):357–69.

125. Ruiz JR, Sui X, Lobelo F, Morrow JR, Jackson AW, Sjöström M, et al. Association between muscular strength and mortality in men: Prospective cohort study. Bmj. 2008;337(7661):92–5.

126. Cheng SJ, Yang YR, Cheng FY, Chen IH, Wang RY. The changes of muscle strength and functional activities during aging in male and female populations. Int J Gerontol. 2014;8(4):197–202.

127. Jones MD, Wewege MA, Hackett DA, Keogh JWL, Hagstrom AD. Sex Differences in Adaptations in Muscle Strength and Size Following Resistance Training in Older Adults: A Systematic Review and Meta-analysis. Sport Med. 2020.

128. Smith GI, Reeds DN, Hall AM, Chambers KT, Finck BN, Mittendorfer B. Sexually

dimorphic effect of aging on skeletal muscle protein synthesis. Biol Sex Differ. 2012;3:11.

129. Wiedmer P, Jung T, Castro JP, Pomatto LCD, Sun PY, Davies KJA, et al. Sarcopenia – Molecular mechanisms and open questions. Ageing Res Rev. 2021;65.

130. Forbes GB, Reina JC. Adult lean body mass declines with age: Some longitudinal observations. Metabolism. 1970;19(9):653–63.

131. Kosek DJ, Kim JS, Petrella JK, Cross JM, Bamman MM. Efficacy of 3 days/wk resistance training on myofiber hypertrophy and myogenic mechanisms in young vs. older adults. J Appl Physiol. 2006;101(2):531–44.

132. Frontera WR, Meredith CN, O'Reilly KP, Knuttgen HG, Evans WJ. Strength conditioning in older men: skeletal muscle hypertrophy and inproved function. J Appl Physiol. 1988;64(3):1038–44.

133. Verdijk LB, Jonkers RAM, Gleeson BG, Beelen M, Meijer K, Savelberg HHCM, et al. Protein supplementation before and after exercise does not further augment skeletal muscle hypertrophy after resistance training in elderly men. Am J Clin Nutr. 2009;89(2):608–16.

134. Liu D, Sartor MA, Nader GA, Gutmann L, Treutelaar MK, Pistilli EE, et al. Skeletal muscle gene expression in response to resistance exercise: Sex specific regulation. BMC Genomics. 2010;11(1).

135. Roberts BM, Nuckols G, Krieger JW. Sex Differences in Resistance Training: A Systematic Review and Meta-Analysis. J strength Cond Res. 2020;34(5):1448–60.

136. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. BMJ. 2009;339(7716):332–6.

137. United Nations. World Population Ageing Report. Dep Econ Soc Aff Popul Div New York, NY. 2015.

138. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. Syst Rev. 2016;5(1):1–10.

139. Higgins J, Thomas J, Chandler J, Cumpston M, Li T, Page M, et al. Cochrane Handbook for Systematic Reviews of Interventions version 6.2. Cochrane. 2021.

140. Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. J Epidemiol Community Health. 1998;52(6):377–84.

141. Laframboise MA, Degraauw C. The effects of aerobic physical activity on adiposity in school-aged children and youth: a systematic review of randomized controlled trials. J Can Chiropr Assoc. 2011;55(4):256–68.

142. Bishop P, Cureton K, Collins M. Sex difference in muscular strength in equally-trained men and women. Ergonomics. 1987;30(4):675–87.

143. Hosler WW, Morrow JR. Arm and leg strength compared between young women and men allowing for differences in body size and composition after. Ergonomics. 1982;25(4):309–13.

144. Cawthon PM, Orwoll ES, Peters KE, Ensrud KE, Cauley JA, Kado DM, et al. Strong relation between muscle mass determined by d3-creatine dilution, physical performance,

and incidence of falls and mobility limitations in a prospective cohort of older men. Journals Gerontol - Ser A Biol Sci Med Sci. 2019;74(6):844–52.

145. Häkkinen K, Kraemer WJ, Newton RU, Alen M. Changes in electromyographic activity, muscle fibre and force production characteristics during heavy resistance/power strength training in middle-aged and older men and women. Acta Physiol Scand. 2001;171(1):51–62.

146. Haun CT, Vann CG, Roberts BM, Vigotsky AD, Schoenfeld BJ, Roberts MD. A critical evaluation of the biological construct skeletal muscle hypertrophy: Size matters but so does the measurement. Front Physiol. 2019;10(MAR):1–23.

147. Loenneke JP, Buckner SL, Dankel SJ, Abe T. Exercise-Induced Changes in Muscle Size do not Contribute to Exercise-Induced Changes in Muscle Strength. Sport Med. 2019;49(7):987–91.

148. Ansdell P, Thomas K, Hicks KM, Hunter SK, Howatson G, Goodall S. Physiological sex differences affect the integrative response to exercise: acute and chronic implications. Exp Physiol. 2020;105:2007–21.

149. Gabriel DA, Kamen G, Frost G. Neural adaptations to resistive exercise: Mechanisms and recommendations for training practices. Sport Med. 2006;36(2):133–49.

150. Schoenfeld BJ. The mechanisms of muscle hypertrophy and their application to resistance training. Glob Fit Serv. 2010;24(10):2857–72.

151. Carvalho de Abreu DC, Freire Junior RC, Mello Porto J, Errera Magnani P, Silva Tofani P, Rodrigues Iosimuta NC. Functional performance of older adults: A comparison between men and women. Vol. 61, Women and Health. 2021. p. 372–80.

152. dos Santos L, Ribeiro AS, Schoenfeld BJ, Nascimento MA, Tomeleri CM, Souza MF, et al. The improvement in walking speed induced by resistance training is associated with increased muscular strength but not skeletal muscle mass in older women. Eur J Sport Sci. 2017;17(4):488–94.

153. Visser M, Goodpaster BH, Kritchevsky SB, Newman AB, Nevitt M, Rubin SM, et al. Muscle mass, muscle strength, and muscle fat infiltration as predictors of incident mobility limitations in well-functioning older persons. Journals Gerontol - Ser A Biol Sci Med Sci. 2005;60(3):324–33.

154. Senior HE, Henwood TR, Beller EM, Mitchell GK, Keogh JWL. Prevalence and risk factors of sarcopenia among adults living in nursing homes. Maturitas. 2015;82(4):418–23.

155. Tay L, Ding YY, Leung BP, Ismail NH, Yeo A, Yew S, et al. Sex-specific differences in risk factors for sarcopenia amongst community-dwelling older adults. Age (Omaha). 2015;37(6):1–12.

156. Du Y, Wang X, Xie H, Zheng S, Wu X, Zhu X, et al. Sex differences in the prevalence and adverse outcomes of sarcopenia and sarcopenic obesity in community dwelling elderly in East China using the AWGS criteria. BMC Endocr Disord. 2019;19(1):1–11.

157. Fielding R, Vellas B, Evans W. Sarcopenia: an undiagnosed condition in older adults.Consensus definition: prevalence, etiology, and consequences. J Am Med Dir Assoc. 2011;12(4):249–56.

158. Peterson MD, Sen A, Gordon PM. Influence of resistance exercise on lean body mass in aging adults: A meta-analysis. Med Sci Sports Exerc. 2011;43(2):249–58.

159. Arnarson A, Gudny Geirsdottir O, Ramel A, Briem K, Jonsson P V., Thorsdottir I. Effects of whey proteins and carbohydrates on the efficacy of resistance training in elderly people: Double blind, randomised controlled trial. Eur J Clin Nutr. 2013;67(8):821–6.

160. Asakawa Y, Takahashi R, Yamaguchi H. Effects of Self-Paced Resistance Training and Detraining on Knee Extension Strength in Community-Dwelling Older Adults: A Pilot Study. Physical and Occupational Therapy in Geriatics. 2009; 26(1):63-72

161. Beneka A, Malliou P, Fatouros I, Jamurtas A, Gioftsidou A, Godolias G, et al. Resistance training effects on muscular strength of elderly are related to intensity and gender. J Sci Med Sport. 2005;8(3):274–83.

162. Brose A, Parise G, Tarnopolsky MA. Creatine supplementation enhances isometric strength and body composition improvements following strength exercise training in older adults. Journals Gerontol - Ser A Biol Sci Med Sci. 2003;58(1):11–9.

163. Bunout D, Barrera G, Avendano M, Maza PD La, Gattas V, Leiva L, et al. Results of a community-based weight- bearing resistance training programme for healthy Chilean elderly subjects. Age Ageing. 2005;34(1):80–3.

164. Capodaglio P, Capodaglio Edda M, Facioli M, Saibene F. Long-term strength training for community-dwelling people over 75: Impact on muscle function, functional ability and life style. Eur J Appl Physiol. 2007;100(5):535–42.

165. Fernández-Lezaun E, Schumann M, Mäkinen T, Kyröläinen H, Walker S. Effects of resistance training frequency on cardiorespiratory fitness in older men and women during intervention and follow-up. Exp Gerontol. 2017;95:44–53.

166. Fragala MS, Jajtner AR, Beyer KS, Townsend JR, Emerson NS, Scanlon TC, et al. Biomarkers of muscle quality: N-terminal propeptide of type III procollagen and C-terminal agrin fragment responses to resistance exercise training in older adults. J Cachexia Sarcopenia Muscle. 2014;5(2):139–48.

167. Hakkinen K, Pakarinen A. Serum hormones and strength development during strength training in middle-aged and elderly males and females. Acta Physiol Scand. 1994;150:211–9.

168. Hakkinen K, Kraemer WJ, Pakarinen A, Triplett-McBride T, McBride JM, Hakkinen A, et al. Effects of Heavy Resistance/ Power Training on Maximal Strength, Muscle Morphology, and Hormonal Resonse Patterns in 65-75- year old Men and Women. Can J Appl Physiol. 2002;27(3):213–31.

169. Kobayashi Y, Ueyasu Y, Yamashita Y, Akagi R. Effects of 4 Weeks of Explosive-type Strength Training for the Plantar Flexors on the Rate of Torque Development and Postural Stability in Elderly Individuals. Int J Sports Med. 2016;37(6):470–5.

170. Kosek DJ, Kim J, Petrella JK, Cross JM, Bamman MM. Efficacy of 3 days/wk resistance training on myofiber hypertrophy and myogenic mechanisms in young vs. older adults. J Appl Physiol. 2006;101:531–44.

171. Lemmer JT, Ivey FM, Ryan AS, Martel GF, Hurlbut DE, Metter JE, et al. Effect of strength training on resting metabolic rate and physical activity: Age and gender

comparisons. Med Sci Sports Exerc. 2001;33(4):532–41.

172. Lexell J, Downham D, Larsson Y, Bruhn E, Morsing B. Heavy-resistance training in older long-term effects on arm and leg muscles Scandinavian men and women: short- and long-term effects on arm and leg muscles. Scund J Mcd Sci Sports. 1995;5:329–341.

173. Mackey AL, Esmarck B, Kadi F, Koskinen SOA, Kongsgaard M, Sylvestersen A, et al. Enhanced satellite cell proliferation with resistance training in elderly men and women. Scand J Med Sci Sport. 2007;17:34–42.

174. Martel GF, Roth SM, Ivey FM, Lemmer JT, Tracy BL, Hurlbut DE, et al. Age and sex affect human muscle fibre adaptations to heavy-resistance strength training. Exp Physiol. 2006;91(2):457–64.

175. McCartney N, Hicks AL, Martin J, Webber CE. A longitudinal trial of weight training in the elderly: Continued improvements in year 2. Journals Gerontol - Ser A Biol Sci Med Sci. 1996;51(6):425–33.

176. Njemini R, Forti LN, Mets T, Van Roie E, Coudyzer W, Beyer I, et al. Sex difference in the heat shock response to high external load resistance training in older humans. Exp Gerontol. 2017;93:46–53.

177. Ochala J, Lambertz D, Hoecke J, Pousson M. Changes in muscle and joint elasticity following long-term strength training in old age. Eur J Appl Physiol. 2007;100(5):491–8.

178. Ryan AS, Hurlbut DE, Lott ME, Ivey FM, Fleg JL, Hurley BF, et al. Insulin Action After Resistive Training in Insulin Resistant Older Men and Women. JAGS. 2001;49:247–53.

179. Sharman MJ, Newton RU, Triplett-McBride T, McGuigan MRM, McBride JM, Häkkinen A, et al. Changes in myosin heavy chain composition with heavy resistance training in 60- to 75-year-old men and women. Eur J Appl Physiol. 2001;84(1–2):127–32.

180. Tamopolsky M, Zimmer A, Paikin J, Safdar A, Aboud A, Pearce E, et al. Creatine monohydrate and conjugated linoleic acid improve strength and body composition following resistance exercise in older adults. PLoS One. 2007;2(10).

181. Tanton LC, Cappaert TA, Gordon PM, et al. Strength, Size, and Muscle Quality in the Upper Arm Following Unilateral Training in Younger and Older Males and Females. Clinical Medicine Arthritis and Musculoskeletal Disorders.2009; 2:9-18.