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# A review of studies that used B mode ultrasound to estimate age-related changes in anterior thigh skeletal muscle thickness across the adult lifespan

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ABSTRACT

*Background:* The purpose of this review was to synthesise and determine the age-related change per annum in muscle thickness of the anterior thigh across the adult lifespan.

*Methods:* Electronic databases (PubMed, SPORTDiscus and MEDLINE) were searched for primary studies that were screened for eligibility.

*Results:* Following screening against eligibility criteria, 27 studies were included in the quantitative analysis. Linear regression revealed a 0.02 cm (95 % CI: −0.01, −0.03, $p < 0.05$) decline in mean muscle thickness per annum from 18 to 80 years of age, a 0.03 cm (95 % CI: −0.01 to −0.05) decline per annum between 20 and 49 years of age and a 0.05 cm (95 % CI: −0.03, −0.07) decline per annum between 50 and 80 years of age. There was a 1.5 cm ($t(25) = 6.12$, $p < 0.05$; 95 % CI= 0.98- 1.97 cm) mean difference in muscle thickness between the youngest (18–29yrs: 5.13 cm ± 0.38) and oldest adults (70–80yrs) 3.63 cm ± 0.63). There was no difference in the rate of decline of mean muscle thickness between males (−0.05 cm/annum, 95 % CI= −0.08, −0.02) and females (−0.04 cm/annum, 95 % CI= −0.07, −0.02). There was a larger difference in anterior thigh muscle thickness between the youngest and oldest in females (4.98 cm vs. 3.34 cm, 33 %, $p < 0.05$) compared with males (5.23 cm vs. 3.98 cm, 24 %, $p < 0.05$).

*Conclusion:* Mean anterior thigh thickness was estimated to decrease at a rate of 0.02 cm per annum and this rate of decrease was greater after 50 years of age. Females were more susceptible to age-related reductions in anterior thigh muscle thickness than males.

## Introduction

Research investigating age-related changes of anterior thigh muscle mass in healthy adults <70 years (yrs) is underdeveloped. Research to date has been conducted in older adults (Frontera et al., 1985) and young vs. older adults (Maden-Wilkinson et al., 2013) because measurements in the younger adults are used to generate normative data to compare with older adults, as recommended by the European Working Group on Sarcopenia in Older People (Cruz-Jentoft et al., 2019). However, this has resulted in a paucity of data for healthy adults <70yrs of age, specifically, those aged 30–50yrs. On the other hand, research in adults over 70yrs is well established due to data gathered by The Healthy Ageing Body Composition study that measured muscle mass, strength and quality (Delmonico et al., 2009; Goodpaster et al., 2006; Newman et al., 2003). Cross sectional analysis of adults aged 70–79yrs has revealed a 9–10 % decline per decade in leg lean tissue mass, and longitudinal analysis revealed larger age-related declines in muscle strength compared to muscle mass (Delmonico et al., 2009; Goodpaster et al., 2006). Yet, due to the narrow age range of the sample population, these findings cannot be generalised across other ages.

The quantity of muscles of the thigh do not decline alike. The muscles of the anterior thigh (rectus femoris, vastus lateralis, vastus medialis, vastus intermedius) undergo larger age-related declines in mass than the muscles of the posterior thigh (Frontera et al., 1985; Janssen et al., 1985; Maden-Wilkinson et al., 2013). However, there is a lack of studies evaluating the rate of change per annum and cross-sectional differences in anterior thigh muscle mass across the adult lifespan. Thus, it is not known if anterior thigh muscle mass changes after 18–30yrs or the trajectory of anterior thigh muscle mass within the 18–30yrs age-band. Furthermore, we do not know the magnitude of change in anterior thigh

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muscle mass per annum and whether this rate of change is greater after certain time points.

Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) are the gold standard techniques to measure muscle mass (English et al., 2012). B mode ultrasonography (US) can directly image the tissue of interest and measurements of muscle thickness (MT) using B mode US have been used to estimate whole body and regional muscle mass (Sanada et al., 2006). Additionally, positive relationships have been found between measurements of knee extensor MT and muscle volume (measured by MRI) (Miyatani et al., 2002). Unlike MRI and CT, B mode US is an imaging tool which is portable, relatively inexpensive, does not have an extensive list of exclusions and the time taken to image the muscle and take measurements is relatively short (Reimers et al., 1993; Stringer & Wilson, 2018). The clinical utility of B mode US is advantageous, and research studies have evaluated measurements of anterior thigh MT across the adult lifespan in relation to muscle wasting in the lower and upper extremities (Abe et al., 2014a), site specific muscle loss in females and males (Abe et al., 2011), prevalence of site-specific thigh sarcopenia in females and males (Abe et al., 2014b) and muscle architectural differences in females (Kubo et al., 2003).

There are primary studies that measured MT at multiple sites in individuals aged 20–79yrs. For example, Abe et al. (2014a) estimated anterior thigh MT between age bands that provided evidence of age-related differences in across the adult lifespan and in males and females. However, Abe et al. did not calculate the rate of change in anterior thigh MT per annum, nor analyse potential differences in MT between age bands. Thus, there is a lack of comparative data available as we currently do not know the estimated rate of change in anterior thigh MT per annum in healthy adults aged 18–70yrs. Furthermore, it is not known whether anterior thigh MT changes alike in healthy males and females aged 18–70yrs.

To our knowledge, there has been no attempt to pool data from primary research studies to estimate age-related changes in anterior thigh MT measured using B mode US across the adult lifespan. The findings of such an analysis could provide comparative data that would be valuable for identifying individuals with low MT, and therefore low muscle quantity, which is a risk factor for sarcopenia, functional capability and strength (Abe et al., 2012a; Abe et al., 2014c; 2014d). Additionally, such data would provide further evidence on the physiological age-related changes in MT that occur across the lifespan and per age band.

The aim of this review was to determine the rate of change per annum and age-related differences in anterior thigh MT measured using B mode US across the lifespan in healthy adults.

## *Materials and methods*

This review was developed from procedures described by the Cochrane Collaboration for undertaking systematic reviews (Higgins et al., 2019). Inclusion and exclusion criteria for the screening of abstracts and full text were developed prior to conducting the search. The PICOS tool was used to develop the research question and the search strategy:

- Population-Healthy adults aged 18–80yrs.
- Intervention-Physical activity or nutritional interventions, but only baseline data will be included.
- Comparison- not applicable.
- Outcome- Rate of decline in anterior thigh MT per annum and mean MT per age band.
- Study design- Cross sectional, longitudinal (baseline data only), randomised control trials (baseline data only) and interventions (baseline data only).

### *Eligibility criteria*

Studies were included if they:

1. Used B mode US.
2. Measured the thickness of quadriceps and/or anterior thigh muscles (cm or mm) using B mode US either across the adult lifespan, between different age categories, as part of an intervention or as a comparison between groups (within a sport or between sports/exercise).
3. Measured MT to estimate muscle quality and/or MT ratios and/or cross-sectional area and/or skeletal muscle mass and/or volume.
4. Included a sample of participants aged 18yrs and over, described as healthy and independent living.
5. Cross sectional studies, longitudinal and intervention studies providing baseline data prior to an intervention i.e. pre-intervention data.
6. Only full texts of academic journal studies written in English were included.

Studies were excluded if they were reported in an abstract and/or included participants who relied on others for care or resided in a residential care home, nursing home were frail or functionally impaired.

### *Electronic searches*

One author (IJ) searched electronic databases (PubMed Central, SPORTDiscus, MEDLINE and Discover) for studies which quantified anterior thigh skeletal MT using B mode ultrasound in January 2020 and using the following search strings:

*("Skeletal muscle mass" OR "muscle mass") AND (image* technique OR MRI OR CT OR computed tomography OR ultrasound OR ultrasonography)*

*("Skeletal muscle thickness" OR "muscle thickness") AND (age OR ageing OR age-related) ("Skeletal muscle mass" OR "muscle mass") AND (age OR ageing OR age-related).*

Studies were included irrespective of language.

### *Data screening*

One reviewer (IJ) removed duplicates and screened title and abstracts of records obtained from the search followed by full text reports against the eligibility criteria.

### *Data extraction and management of relevant information*

One author (IJ) extracted information from full reports including: study characteristics (authors and year of publication), sample characteristics (sample size including the number of males and females where applicable, gender, age range (minimum and maximum) and mean age (± standard deviation)), the muscles included in the measurement anterior thigh or quadriceps MT and the mean and standard deviation of the MT value. Co-authors spot checked the results of screening and information extracted for accuracy. A table summarising the characteristics of included studies is available in supplementary file 1.

### *Data synthesis and analysis*

Numerical data for age and MT was analysed using SPPS v.25. Correlation analysis was conducted to determine the degree of the relationship between age and MT, and regression analysis was conducted to predict the amount of change in MT as a result of age. Data were plotted on a scatter graph, with the mean age range on the x axis and mean MT on the y axis to visually assess for a linear regression between age and MT. The rate of change in MT per annum was determined using the slope of the linear line.

Data for MT was grouped according to mean age(s) in a similar manner to that described by Abe et al. (2014b) as follows: 18–29yrs; 30–39yrs; 40–49yrs; 50–59yrs; 60–69yrs; 70–79yrs; 80–90yrs).

Descriptive statistics were conducted in SPSS v.25. The mean MT ± standard deviation (SD) for each age band was calculated from the single point mean MT values ± SD and the percentage difference between the youngest and oldest adults analysed using an independent *t*-test.

*Results*

The initial search returned 2326 records. After removing 27 duplicates, 2299 records were screened by title and abstract and the full text reports of 50 potentially relevant studies were obtained and screened, see Fig. 1. Nine studies were excluded because investigators did not include healthy subjects ($n = 1$), did not report or measure age of participants ($n = 1$), did not measure quadriceps MT ($n = 4$), measured muscle volume instead of thickness ($n = 1$) or did not provide the MT measurements ($n = 2$).

*Characteristics of included studies*

There were 41 studies included with a total of 7474 adults (3464 males and 4010 females). There were 29 studies that measured rectus femoris (RF) and vastus intermedius (VI) muscles (please see supplementary file 1), 7 studies measured vastus lateralis (VL) and vastus intermedius (VI) (Candow et al., 2006; Candow et al., 2008; Candow et al., 2011; Candow et al., 2014; Cornish & Chilibeck, 2009; Joy et al., 2015; Sipilä & Suominen, 1996) muscles and 5 studies measured other muscles (Cadore et al., 2012a; 2012b; Matta et al., 2017; Rech et al., 2014; Watanabe et al., 2013a). It was decided to pool data from the RF and VI because they comprised the largest data set and not to pool data from muscles used in the remaining 12 studies because of physiological heterogeneity.

The mean age of the groups was not reported in two (Fukumoto et al., 2015; Abe et al., 2014e) of the 29 studies with data for rectus femoris and vastus intermedius so these studies were not included in the analysis. Thus, data was extracted and analysed from 27 studies measuring rectus femoris and vastus intermedius variables (Abe et al., 2014f; Abe et al., 2018; Akima et al., 2017; Herrick et al., 2017; Hida & al., 2018; Kanehisa & Fukunaga, 2013; Meirelles & Gomes, 2016; Nakatani et al., 2016; Nishihara et al., 2018; Sanada et al., 2006; Abe et al., 2012a; 2012b; Abe et al., 2014a; 2014b; 2014c; 2014d; 2014g; 2014h; Abe et al., 2015a; 2015b; Takai et al., 2013; Takai et al., 2014; Taniguchi et al., 2017; Thiebaud et al., 2017; Fukumoto et al., 2012a; 2012b; Watanabe et al., 2013b), please see supplementary file 1.

*Descriptive statistics*

Descriptive statistics are provided in Table 1. There was a statistically significant difference in MT between youngest (18–29yrs: mean ± SD = 5.13 cm ± 0.38) and oldest adults (70–80yrs: 3.60 cm ± 0.66) of 1.5 cm (95 % CI = 0.94- 2.07 cm, t (21) = 5.54, $p < 0.05$).

Two studies did not report MT by gender and were excluded from the analysis (Meirelles & Gomes, 2016; Nakatani et al., 2016). In adults mean MT was larger in males (4.71 ± 0.66 cm) compared with females (4.05 cm ± 0.55 cm) with the magnitude of difference being 0.66 (t (60)

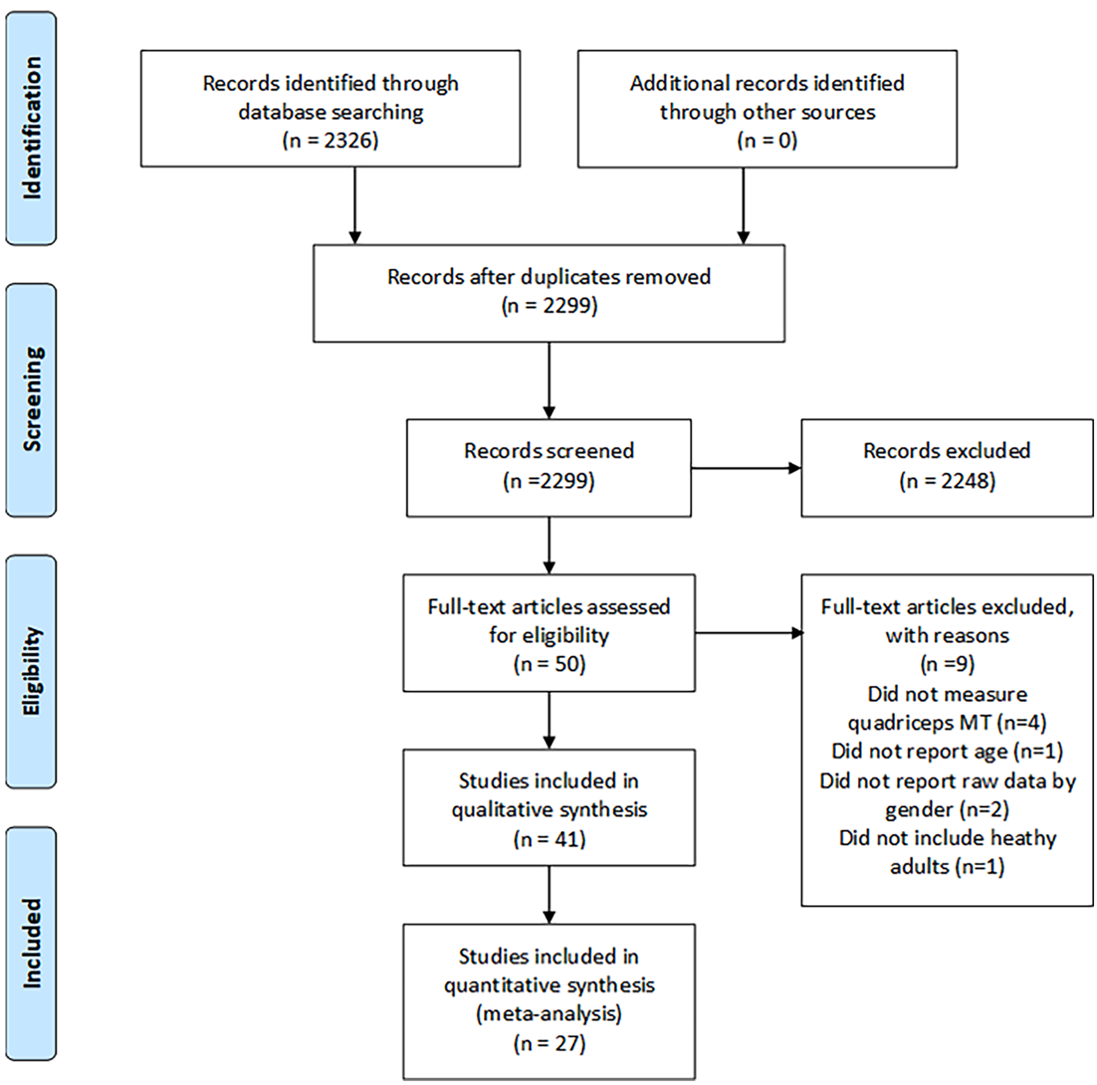


**Fig. 1.** Preferred reporting items for systematic review and meta-analysis flow diagram.

**Table 1**
Mean MT ± SD for the anterior thigh (cm) by age and gender.

| Age group (years) | 18–29yrs | 30–39yrs | 40–49yrs | 50–59yrs | 60–69ys | 70–80yrs |
|---|---|---|---|---|---|---|
| All MT | 5.13 ± 0.38 | 4.49 ± 0.54 | 4.25 ± 0.59 | 4.48 ± 0.55 | 4.24 ± 0.62 | 3.60 ± 0.66 |
| Male MT | 5.23 ± 0.38 | 5.02 ± 0.10 | 4.70 ± 0.13 | 4.82 ± 0.54 | 4.71 ± 0.58 | 3.98 ± 0.51 |
| Female MT | 4.98 ± 0.40 | 4.32 ± 0.09 | 4.30 ± 0.11 | 4.22 ± 0.37 | 3.81 ± 0.36 | 3.34 ± 0.57 |

= - 4.24, $p < 0.01$). The extent of the difference in MT between youngest and oldest females (youngest = 4.98 cm ± 0.40, oldest = 3.34 cm ± 0.57, mean (95 % CI) difference = 1.63 cm, 95 % CI= 0.85, 2.42, $p < 0.005$) was larger than that for males (youngest = 5.23 cm ± 0.38, oldest = 3.98 cm ± 0.51, mean difference = 1.25 cm, 95 % CI = 0.68, 1.82, $p < 0.05$).

*Correlations and linear regression (rate of change)*

There was a weak-moderate correlation between MT and age across the lifespan ($r^2$=0.26, $p < 0.01$). There was a decrease in anterior thigh MT per annum, estimated from the slope of the linear regression line, of 0.02 cm (95 % CI: - 0.01, −0.03, $p < 0.05$) for all adults irrespective of age. The rate of decrease in mean anterior thigh MT was 0.03 cm (95 % CI: −0.01 to −0.05) per annum between 20 and 49yrs of age and 0.05 cm (95 % CI: −0.03, - 0.07) per annum between 50 and 80yrs of age, see Fig. 2.

The data from the studies was split by gender and using the same method as previously described, the rate of change per annum was calculated. Mean MT was lower by −0.02 cm per annum (male and female 95 % CI= −0.03, −0.01) separately for both males and females aged 18–76 years. A stronger correlation between MT and age ≥50yrs was observed in the females ($r^2 = 0.33$, $p < 0.01$) compared to males ($r^2 = 0.30$, $p < 0.01$), whilst mean MT declined at a similar rate in males and females, −0.05 cm (95 % CI = −0.08, −0.02) and −0.04 cm (95 % CI = −0.07, −0.02) per annum respectively, see Fig. 3.

*Discussion*

To our knowledge this is the first attempt to analyse primary research data to determine the rate of change per annum in anterior thigh MT measured using B mode US across the adult lifespan. We estimated the rate of decrease in anterior thigh MT of 0.02 cm per annum between 18 and 80 years of age. There was a larger rate of decrease in anterior thigh MT after 50 years of age compared with adults under the age of 50 years. The difference in anterior thigh MT between youngest (18–29yrs) and oldest adults (70–80yrs) was 29 %. There was no difference in the rate of decrease in anterior thigh MT between males and females who were 50yrs or more.

The 29 % difference in MT between youngest (18–29yrs) and oldest (70–80yrs) adults measured by B mode US reported in our review is similar in magnitude to that measured using MRI (Maden-Wilkinson et al., 2013) and may be representative of age-related changes in thigh SM mass. Considering MRI is the gold standard imaging tool for quantifying SM mass, the findings from this review highlight the use of B mode US as an alternative portable and inexpensive imaging tool to quantify age-related changes in MT which can reflect changes in SM mass.

The findings from our review further evidence that there is a greater decline in MT in those ≥50 years and that B mode US is an imaging tool that can detect these changes in MT across the lifespan. The greater decline after 50yrs is similar to the findings from other research studies which have evidenced declines in thigh SM mass in those ≥50 years

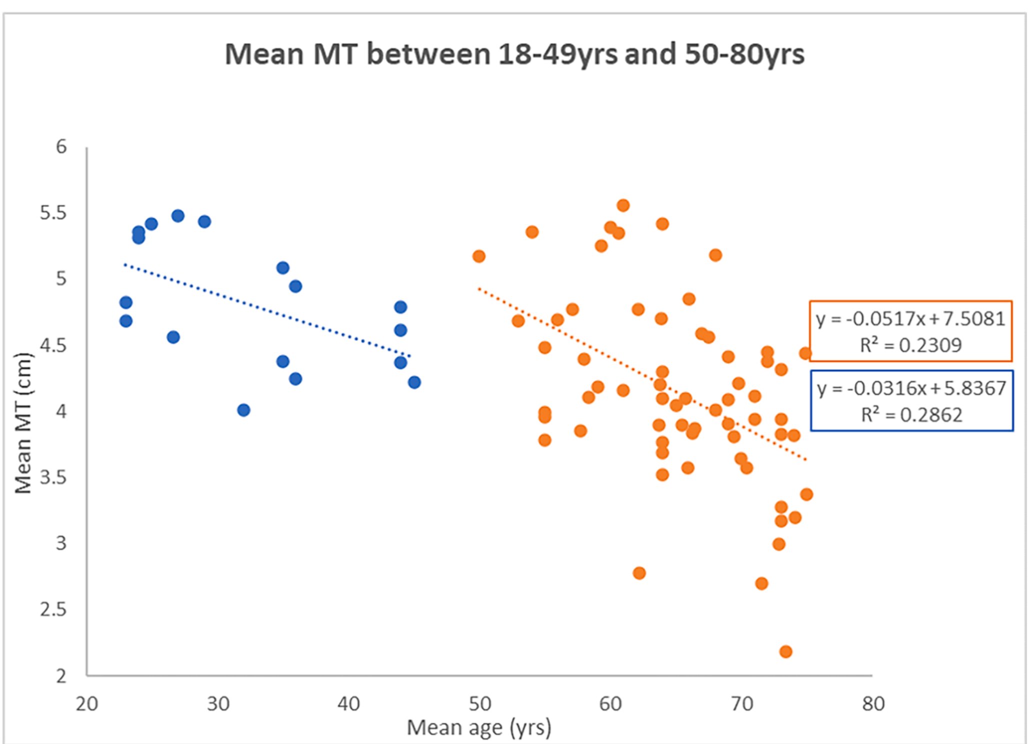


**Fig. 2.** Scatter plot of mean anterior thigh MT across the adult lifespan. Lines of regression were added to investigate the rate of decline in anterior thigh MT in adults aged 22–49yrs of age (represented by the blue line) and in adults aged ≥50yrs (represented by the red line).

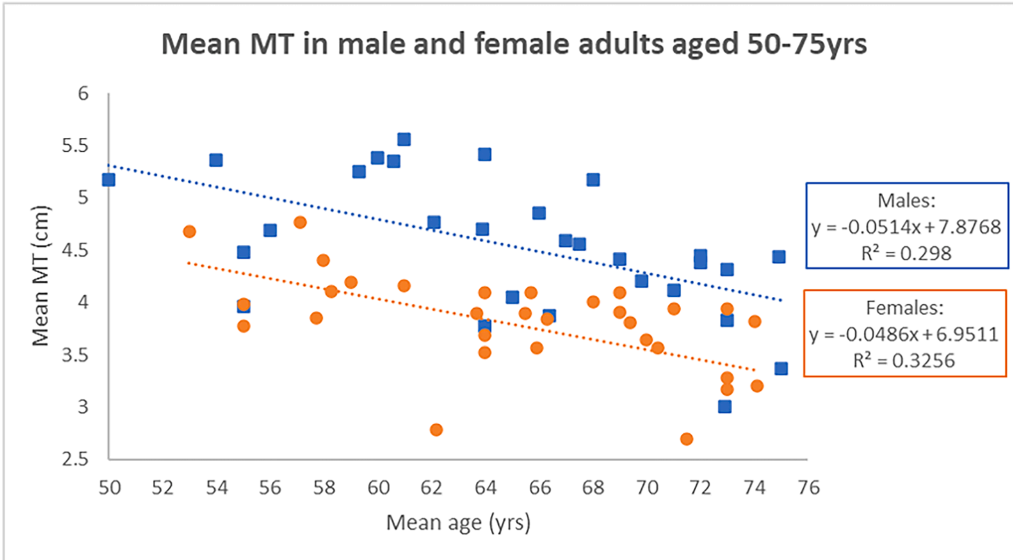


**Fig. 3.** Mean anterior thigh MT in male and female adults aged 50–75yrs. The blue squares represent the male MT data and the orange dots represent the female MT data. A line of regression was added for both males and females (blue= males and orange= females) to assess the rate of change in anterior thigh MT for both genders.

(Hughes et al., 2002; Janssen et al., 1985; Kyle et al., 2001). Collectively, the findings from this review and previous evidence support the implementation of interventions to prevent sarcopenia in adults aged 50yrs and older.

The larger rate of decrease of MT at 50 years observed in our analysis may be due to lower physical activity levels (Janssen et al., 1985). The muscles of the anterior thigh are used to perform activities of daily living such as rising from a chair and are regularly used in physical activity. When an individual is sedentary these muscles are not used as frequently. Therefore, researchers have claimed that reductions in physical activity including activities of daily living, contributes to reductions in the quantity of the anterior thigh muscles compared to muscles of the upper limbs and posterior thigh muscles (Frontera et al., 1985; Janssen et al., 1985; Kubo et al., 2003; T. Abe et al., 2014).

There is no consensus on specific interventions to preserve muscle health and prevent sarcopenia. Furthermore, most interventions target older adults (>65 years of age) despite noticeable declines in SM, MT and strength at 50yrs of age, as demonstrated by the findings of our analysis and previously studies by others (Janssen et al., 1985; Lindle et al., 1985; Lynch et al., 1985). Thus, it could be argued that interventions focussing on physical activity, nutrition and hormonal status should be introduced for individuals prior to 50yrs to slow down and/or prevent decreases in anterior thigh MT and associated functionality.

Our analysis revealed thicker anterior thigh muscle in males compared to females, this is consistent with the current knowledge that males have higher total and regional SM mass, irrespective of adult age (Abe et al., 2003; Gallagher et al., 1985). However, we found that males and females aged 50yrs and over had similar rates of decrease of MT (0.04 cm and. 0.05 cm, respectively). Physical activity levels of participants may have been a confounder in our analysis, but we could not explore the influence of physical activity in any depth because the physical activity levels of participants were not recorded in the included studies of this review. Future research should include levels of physical as a variable in data analysis when exploring age-related differences in anterior thigh MT.

When comparing differences in anterior thigh MT between the youngest and oldest adults by gender, the findings from our review revealed larger age-related differences in MT in the females compared to the males. Further analysis also revealed that age was more strongly associated with anterior thigh MT in the females compared to the males. These findings suggest that females are more sensitive to age-related changes in the thickness of the anterior thigh compared to males. In contrast, Abe et al. (Abe et al., 2011) reported stronger associations between age and anterior thigh MT relative to thigh length in males ($r= -0.53$ $p < 0.05$) than in females ($r= -0.49$, $p < 0.05$). Similarly, Janssen et al. (1985) and Maden-Wilkinson et al. (2013) reported the difference between young vs. older adults SM mass to be larger in males (25 % reported by Janssen et al. (1985) and 32 % reported by Maden-Wilkinson et al. (2013)) compared to females (22 % (Janssen et al., 1985) and 28 % (Maden-Wilkinson et al., 2013)). However, comparison of precise estimates in this field may not be appropriate due to unequal numbers of participants between genders and age bands both in the experimental studies (Janssen et al., 1985; Maden-Wilkinson et al., 2013) and this review. Therefore, there is a need for further studies which measure MT using similar proportions of healthy females and males.

*Limitations*

Variations in cut points and reporting of age bands in primary reports were managed by grouping age bands using mean age and checking whether the standard deviation overlapped age band boundaries. In fact, there was overlap of SDs between age band boundaries, reducing confidence in the accuracy of mean MT. However, we argue that this did not have a serious impact on estimates of rate of decline in mean MT because this was calculated using the mean age and single point estimates of MT reported for each study.

The number of mean MT data points in each age decade varied (18–29yrs had 8 data points, 30–39yrs=5, 40–49yrs=5, 50–59yrs=13, 60–69yrs=30 and 70–80yrs=18), as did the number of study participants with fewer participants in younger than older age bands, for example the 30–39yrs had a total of 410 participants compared to the 60–69yrs who had 2286 participants. We appreciate that variation of participants per group limits the ability to make robust comparisons per age band, however, as this was a review, we could not predict the number of studies, and subsequently the number of participants that would be included. We acknowledge this as a limitation of this review and we suggest that future studies should try to have similar numbers of data points to reduce the impact of confounding factors on the analysis, allowing for more meaningful analysis and comparisons.

The primary aim of many studies included in our review was not to determine the rate of change across the adult lifespan, and consequently, methodological heterogeneity was present across the included studies with variations in aims, levels and nature of physical activity and activities of daily living, sample population and study context. For example, some study sample populations consisted of different sports or same sports and different activity levels. Several of the included studies did not report physical activity levels, and therefore, we could not control for this as a confounding factor due to the lack of extractable data. We acknowledge the importance of physical activity levels on muscle morphology and function, however, our primary aim was to determine the magnitude of change in anterior thigh MT, Therefore, based on the evidence and studies not including physical activity data, it was decided to report the age-related decline in anterior thigh MT per annum.

Gender differences have been reported within this review, however, we have only provided crude estimates of age-related changes in anterior thigh MT rather. This was appropriate as missing data from the included studies impacted on the level of analysis that could have been included. We appreciate that we do not provide a complete picture of gender differences across age bands, and we recommend that future reviews provide a more robust analysis of gender differences which include factors such as body mass, height and physical activity levels.

A shortcoming of the analysis was that we only pooled data from studies of the rectus femoris and vastus intermedius muscles. This provided consistency but meant that studies measuring thickness of other thigh muscles were excluded. We acknowledge that this precludes gaining a complete picture of anterior thigh muscle change and we recommend that future reviewers evaluate different sites to provide a comprehensive overview. Additionally, another issue with the analysis of the review is the use of single point estimates as this makes the conclusions of about the rate of decline less reliable, however, due to the heterogeneity of the included studies, we felt that further analysis was not appropriate and instead provide a single point rate of change across the lifespan and per decade. Future reviews, with lower heterogeneity, should conduct further multi-level analysis to improve the robustness of conclusions.

The authors are aware that the conclusions made from this review are somewhat limited by not controlling for confounding factors such as physical activity data. That said, this is the first review to provide preliminary data on age-related changes in anterior MT across the lifespan and age decades. These initial findings provide comparative data that can be used both in clinical practice and future research. Despite some of these limitations being addressed in our review, we encourage investigators of future studies to document levels of physical activity and report age range and mean age of samples, and if possible, banding age categories by decades to standardise reporting and categorising of age groups.

## Conclusion

In conclusion, the rate of decrease in mean anterior thigh MT of adults (18–80yrs) was 0.02 cm per annum and 0.05 cm per annum between 50 and 80yrs of age. The 29 % difference observed within this review between the youngest and oldest group is similar to those from studies which have used MRI to quantify age related changes. We provide evidence that females are more susceptible to age-related decreases in mean anterior thigh MT (33 %) than males (24 %). These findings provide comparative data for clinical practice and future research and offer initial insights to changes in anterior thigh MT for males and females through the adult lifespan.

The evidence from primary research suggests that B mode US can detect age-related differences in anterior thigh MT and could be used by health care professionals as a diagnostic imaging tool for sarcopenia in field settings because it is portable, versatile and inexpensive compared with MRI and Dual X-ray Absorptiometry. We recommend the need for more longitudinal and cross-sectional studies on a large sample of healthy adults with similar proportions of participants in each decade to provide robust data on the age-related changes in anterior thigh MT.

## CRediT authorship contribution statement

**Isobel Jacob:** Writing – review & editing, Writing – original draft, Visualization, Validation, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Gareth Jones:** Writing – review & editing, Validation, Supervision, Methodology, Conceptualization. **Peter Francis:** Writing – review & editing, Validation, Supervision, Methodology, Conceptualization. **Mark I Johnson:** Writing – review & editing, Validation, Supervision, Methodology, Conceptualization.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Data availability

Data will be made available on request.

*Declarations*

Ethics and consent for publication: Not applicable

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no funding was received for this project

*Availability of data and materials*

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request

Peter Francis receives research funding in support of research projects from minimalist footwear company Vivobarefoot. Peter advises the live barefoot foundation on its scientific strategy and the accuracy of its outreach activities; he receives an honorarium for this work.

Mark I. Johnson reports no affiliation to private companies, founding a private company, receiving any personal grants from a private company, holding shares of a private company, and/or holding patents. Within the previous 5 years Mark I. Johnson reports that he has received book royalties from Oxford University press. Within the previous 5 years Mark I. Johnson's employer has received financial income from GlaxoSmithKline, TENSCare Ltd. and LifeCare Ltd. for expert consultancy services. Within the previous 5 years Mark I. Johnson has received research awards / grants from The Neuromodulation Society of the United Kingdom and Ireland to develop an online distance learning educational package, and GalaxoSmithKline to lead an Investigator Sponsored Study on transcutaneous electrical nerve stimulation to alleviate pain.

## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.aggp.2024.100037.

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