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## Exercise at Different Ages and Appendicular Lean Mass and Strength in Later Life: Results From the Berlin Aging Study II

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## **Exercise at different ages and appendicular lean mass and strength in later life – Results from the Berlin Aging Study II**

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Running head: Exercise at different ages and strength

## **Abstract**

**Background.** Excessive loss of muscle mass in advanced age is a major risk factor for decreased physical ability and falls. Physical activity and exercise training are typically recommended to maintain muscle mass and prevent weakness. How exercise in different stages of life relates to muscle mass, grip strength and risk for weakness in later life is not well understood.

**Methods.** Baseline data on 891 participants at least 60 years old from the Berlin Aging Study II (BASE II) were analyzed. Linear and logistic regressions of self-reported exercise in early adulthood, old age or both on appendicular lean mass (ALM), grip strength, and a risk indicator for weakness (ALM/ body mass index (BMI) cut-off) were calculated. In addition, treatment bounds are analyzed to address potential confounding using a method proposed by Oster.

**Results.** Analyses indicate that for men only, continuous exercise is significantly associated with higher muscle mass (0.24 standard deviations,  $p < 0.001$ ), grip strength (0.18 standard deviations,  $p < 0.05$ ), and lower risk for clinically relevant low muscle mass ( $OR = 0.36$ ,  $p < 0.01$ ). Exercise in early adulthood alone is not significantly associated with muscle mass or strength. No significant associations were observed for women.

**Conclusions.** The results of the current study underscore the importance of health programs to promote physical activity with a focus on young adults, a group known to be affected from environmentally associated decline of physical activity and to promote the continuation of physical exercise from early adulthood into later life in general.

Key words: appendicular lean mass, physical activity, sarcopenia, grip strength, age, BASE-II

## Introduction

Aging is associated with physiological changes in body composition, with decreasing muscle mass and increasing fat mass.(1) The resulting loss of strength is frequently accompanied by mobility disorders and increased functional dependency. In adverse circumstances, this can result in limitation of functional capacity, decreased stress resistance, frailty or sarcopenia in old subjects.(2)

Sarcopenia, the loss of muscle mass and strength,(3) is an established risk factor for decreased physical ability, falls, and increased need for care.(4, 5) The underlying mechanisms leading to sarcopenia are not yet fully understood, but inflammation, neuromuscular and hormonal changes as well as physical inactivity and inadequate nutrition are discussed as major determinants.(6, 7) To counteract the loss of muscle mass and strength, physical activity and exercise training, combined with adequate nutritional intake are essential. Although exercise and resistance training are suggested as preventive measures, it is unclear when such measures should be initiated or what they should look like in practice.(8)

The Foundation for the National Institutes of Health (FNIH) Sarcopenia Project identified cut-off points for appendicular lean mass to BMI ratio (ALM/BMI) below which older adults have a higher risk of incident mobility impairment.(9)

The aim of the current analysis was to assess associations between regular exercise in early adulthood and old age with appendicular lean mass, grip strength and low ALM/BMI (9) in a sample of community-dwelling elderly.

## **Materials and Methods:**

### *Study design*

BASE-II (Berlin Aging Study II) is a prospective epidemiological study to investigate factors associated with “healthy” or “unhealthy” aging in residents of the greater metropolitan area of Berlin, Germany. For further details, see Bertram et al. (2014). (10) For this analysis, we included all individuals who were 60 or older in 2012 and who participated in both the medical examination and the socio-economic module (970 participants). Those with missing information in the variables used in this paper are excluded. This resulted in a final sample size of 891 participants. All participants gave written informed consent and the Ethics Committee of the Charité-Universitätsmedizin Berlin approved the study (approval number EA2/029/09).

### *Appendicular lean mass, anthropometrics and hand grip strength*

Body weight was measured in light clothes to the nearest 0.1 kg and height was determined to the nearest 0.1 cm with an electronic weighing and measuring station (seca 764, seca, Hamburg, Germany). Body composition was assessed by Dual X-ray absorptiometry (DXA) using the Hologic QDR® Discovery™ device and APEX software version 3.0.1 for measurement and analysis. Appendicular lean mass (ALM) in kilograms was calculated as the sum of lean mass in arms and legs. Cut-off values for  $ALM_{BMI} < 0.789$  in men and  $< 0.512$  in women were chosen according to the lean mass thresholds for higher likelihood of incident mobility impairment as identified by the FNIH Sarcopenia Project.(9)

Hand grip strength was assessed by a Smedley Dynamometer (Scandidact, Denmark). The subjects were instructed to perform three maximal isometric contractions with each hand, the highest value out of three attempts was chosen for further analysis. The FNIH cut-off values for grip strength (11) were not used in this analysis because only 7 participants' grip strength fell below these cut-off values.

### *Exercise*

Information on exercise participation was taken from the socio-economic survey of BASE-II, which was conducted between October 2012 and January 2013. Among other topics, participants were asked whether they participated in sports or exercise (in the following simply referred to as “exercise”), which sports/exercise they practiced, when they started practicing and how often they practice. The same set of questions was then asked with regard to previous training. If a participant reported not participating in exercise currently, they were asked if they had exercised in the past. If a participant reported to exercise currently, they were asked whether they practiced another form of exercise in the past. For the purpose of this study we generated the following indicators: (i) whether the participant currently exercises, (ii) whether the participant exercised in early adulthood (before age 30), and (iii) whether the participant continuously exercised since age 30.

### *Control variables*

In addition to the indicators of exercise, we controlled for age (using a third-order polynomial), employment status, marital status, years of education and the logarithm of the per-capita-household income (“equivalence income”). When analyzing appendicular lean mass and grip strength, we also included a third-order polynomial of height and weight.

### *Statistical analysis*

We analyzed appendicular lean mass, grip strength, and risk of low ALM/BMI using linear and logistic regression models stratified by sex and robust standard errors to account for possible heteroskedasticity. Our treatment variables are binary indicators for (i) whether participants currently exercise; (ii) whether they exercised before age 30 (early adulthood); or (iii) both. This specification allowed us to disentangle the associations of exercise in early adulthood (which could imply a protective effect of exercise) from both the short-term (in old age only) and long-run associations (i.e. in both young and old age) of exercise with muscle mass and strength. We also estimated a second specification that is described in the Supplement.

Unobserved confounders affecting both exercise participation and muscle mass are a potential concern. To address this concern, we estimated treatment bounds using a method proposed by Oster (2014).<sup>(12)</sup> A detailed description of this approach is provided in the Supplement.

### **Results**

The analysis included 891 older BASE-II participants (454 women), aged between 60 and 85). Current exercise (i.e. in old age) was reported by 59.7% of the male

respondents and 73.6% of the female respondents; with 58.4% of men and 44.1% of women reporting having exercised in their early adulthood. The fractions were slightly smaller if we defined physically active to mean exercise at least every week; however, they remain similar. All in all, 181 (41.4%) of the male and 168 (37.0%) of the female participants reported having exercised both in early adulthood and at the time of the survey.

Figures 1 and 2 show mean appendicular lean mass and grip strength adjusted for age, height and weight for all four categories and both sexes (i.e. never exercised, exercised only in young adulthood, exercised in old age, exercised both in young and old age). Both figures show similar patterns. ALM and grip strength of men who have never exercised (ALM: *Mean* = -.54, *CI* = [-.89, -.19]; grip strength: *Mean* = -.93, *CI* = [-2.14, .28]), have only exercised in early adulthood (ALM: *Mean* = -.39, *CI* = [-.77, -.01]; grip strength: *Mean* = -.70, *CI* = [-2.1, .7]) or in old age only (ALM: *Mean* = -.30, *CI* = [-.68, .09]; grip strength: *Mean* = .07, *CI* = [-1.25, 1.40]) are comparable and the differences are not statistically significant (using a two-sided t-test with unequal variances and a significance level of  $p < .05$ ). In contrast, men who exercised both in early adulthood and in old age have higher muscle mass and grip strength (ALM: *Mean* = .60, *CI* = [.31, .88]; grip strength: *Mean* = .78, *CI* = [-.12, .68]). For ALM, the differences in means to all other exercise categories are statistically significant, while for grip strength only the difference in means to the reference category ("Never exercised") is statistically significant. For women, muscle mass and exercise appear similar across all four exercise categories (for ALM the means range from -.03 to .16, the confidence interval for the reference category is [-.32, .27]; for grip strength the means range from -.16 to .20, *CI* for the reference category [-.77, 1.16]). In Figure 3, the dots show the



percentage of individuals at risk of low ALM/BMI for each category. The share of men at risk of low ALM/BMI is lowest among those individuals who exercised in both early adulthood and old age (13%,  $CI = [.08, .18]$  compared to 21% for exercise in old age, 19% for exercise in early adulthood only, and 30% among those who never exercised,  $CI = [.21, .39]$ ). The share of women at risk for low ALM/BMI is similar across exercise categories (between 9-11%,  $CI$  for the reference category  $[.05, .18]$ ), with the exception of women who only exercised in early adulthood (25%,  $CI = [.09, .41]$ ). However, this is likely to be an outlier due to the group size (shown in Table 1).

We estimated the associations of exercise, muscle mass and strength conditional on confounding factors in a regression model. The estimates for appendicular skeletal muscle mass in men and women are shown in Table 2. The estimated associations of exercising in early adulthood, old age or both early adulthood and old age are provided in comparison to a reference group of those who never exercised. The results indicate that for men exercise in early adulthood alone as well as exercise in old age alone are not significantly related to muscle mass. Having exercised in both early adulthood and old age is significantly associated with higher muscle mass in men. In contrast, the estimated associations among women are not significant. The socio-economic control variables are not significantly associated with ALM.

Table 3 shows the estimated associations of exercise with risk of low ALM/BMI. The reported odds-ratios from a logistic regression are in line with the pattern of the results seen for muscle mass (Table 2). Among men, the estimates for exercise in early adulthood only or in old age alone are not statistically significant. Exercise in early adulthood and old age is positive and highly significant for men. This indicates that the risk of having an ALM/BMI ratio below clinically relevant cutoff points is less than half of

the risk for men who exercised in early adulthood and in old age compared to men who never exercised. For women, the estimates are insignificant, with the exception of an increased risk of low ALM/BMI among women who exercised only in early adulthood. As noted above, this is likely to be a statistical outlier. The associations between risk of low ALM/BMI and the socio-economic control variables are insignificant.

The estimated associations between exercise and grip strength are shown in Table 4. The results of the first specification are similar to those reported in Table 2 and 3, in particular exercise in early adulthood and old age is associated with significantly higher grip strength among men. Again, for women none of the estimates is statistically significant. However, among women we find a statistically significant positive association between income and grip strength. In all other instances the socio-economic control variables are insignificant.

Finally, we calculated treatment bounds to address potential confoundedness. The results are provided in detail in the Supplement.

## **Discussion**

In the current study, we showed that continuous exercise over a longer period of time is associated with higher appendicular lean mass and grip strength in old age. Exercise in early adulthood alone as well as exercise in old age alone were not significantly associated with higher muscle mass or strength. It is important to note that this should not be taken as evidence that exercise in old age is an ineffective measure to prevent loss of ALM as our sample is too small to obtain estimates of smaller associations.

Interestingly, these associations were only seen in men, while for women the estimates across exercise categories were insignificant. Previous research suggests that

men and women benefit equally from exercise, which suggests that the intensity of exercise might differ between men and women in the population.(13) If this is the case and when taken together with our finding that exercise participation in early adulthood is much lower among women, it indicates that health promotion programs should be aimed at women to increase exercise participation in early adulthood and encourage a higher training intensity.

Data on the benefit of exercise or resistance training in advanced age to enhance muscle mass and strength are largely unambiguous.(14-18) If a training stimulus is set sufficiently high and often, neuronal-, metabolic-, structural-morphological and anatomical changes in skeletal muscle can be observed.(19) These changes may counteract muscle atrophy and loss of muscle strength and reduce risk of falls, functional decline and dependency.(8, 20-23)

Although resistance training can preserve or increase muscle mass and strength, it is unknown how long these effects remain after termination of training and it is unclear if training in early adulthood builds a basis for effectiveness of future treatment strategies.(24) At older age, breakdown of muscle mass affects mainly the fast type II muscle fibers, whereas type I muscle fibers, which have a lower density of mitochondria, are relatively preserved.(19, 25) Glucose- and lipid metabolism contributes to synthesis of adenosine triphosphate (ATP) in the mitochondria, which is required for muscle contraction and cross-bridge formation of actin and myosin filaments. Consequently, for the preservation or increase of exercise capacity, the absolute number of mitochondria in skeletal muscle is important, but more difficult to maintain in advanced age.(26) Protein synthesis of muscle is further influenced by suitable training stimuli in combination with a correctly timed and adequate protein intake.(27-29)

It seems reasonable that for maintaining muscle mass, it is necessary to stimulate these mechanisms regularly over a long period of time.(30) This assumption is supported by our findings, as subjects who reported performing exercise in early adulthood and older age with few interruptions had higher ALM and significantly lower relative risk of low ALM/BMI.

Our findings are subject to a number of limitations. First, the data on exercise is self-reported and therefore potentially associated with the known implications of subjectivity (e.g. overstated exercise participation). Second, the data do not allow the investigation of potential heterogeneity since we do not have, e.g., data on the intensity of exercise. More intense exercise is likely more effective in increasing ALM and preventing decline.

Third, the results might be confounded, as certain conditions like obesity or disease reduce muscle mass, and might keep individuals from exercising. In this case, the result would be the effect of not having developed such a condition, instead of the effect of exercise. However, we argue that this is unlikely. BASE-II participants are on average healthier than the general population.(31) The estimated treatment bounds further indicate that our results are robust to confounding factors that are proportional to the included covariates.

Finally, the sample size might be too small to detect smaller, but non-trivial differences. For example, if the true effect of exercise in old age alone was 0.265 (with an associated increase in the  $R^2$  of 0.008), then our analysis would require approximately 3,760 men (as opposed to 437) to obtain a statistical power of 0.8. In contrast, the results reported for exercise in early adulthood and old age only require 135 men to reach the same statistical power. Consequently, we cannot exclude the

possibility that some of the insignificant estimates would exert critical values of statistical testing given a larger sample size.

Although there is no doubt that appendicular lean mass can still be increased through sport, even at older ages (32-34), assessment of early regular exercise could be a valuable and easy tool to identify subjects at increased subsequent risk for loss of appendicular lean mass and reduced strength. It is likely that these subjects could benefit from early-onset and more intensive intervention strategies. It is well known that physical activity declines significantly from adolescence through young adulthood (e.g. reviewed in Aaron et al., 2005).(35) A decline of physical activity is also shown to be associated with environments usually concern to young adults, such as long working hours (Nomaguchi and Bianchi, 2004) or parenting of young children (reviewed in Bellows-Riecken and Rhodes, 2008).(36, 37) In this context, our results underscore the importance of health promotion programs with emphasis on physical activity and suitable to the group of young adults and promoting the continuation of physical exercise from early adulthood into old age to prevent loss of muscle mass and strength in general.

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## Figures and Tables

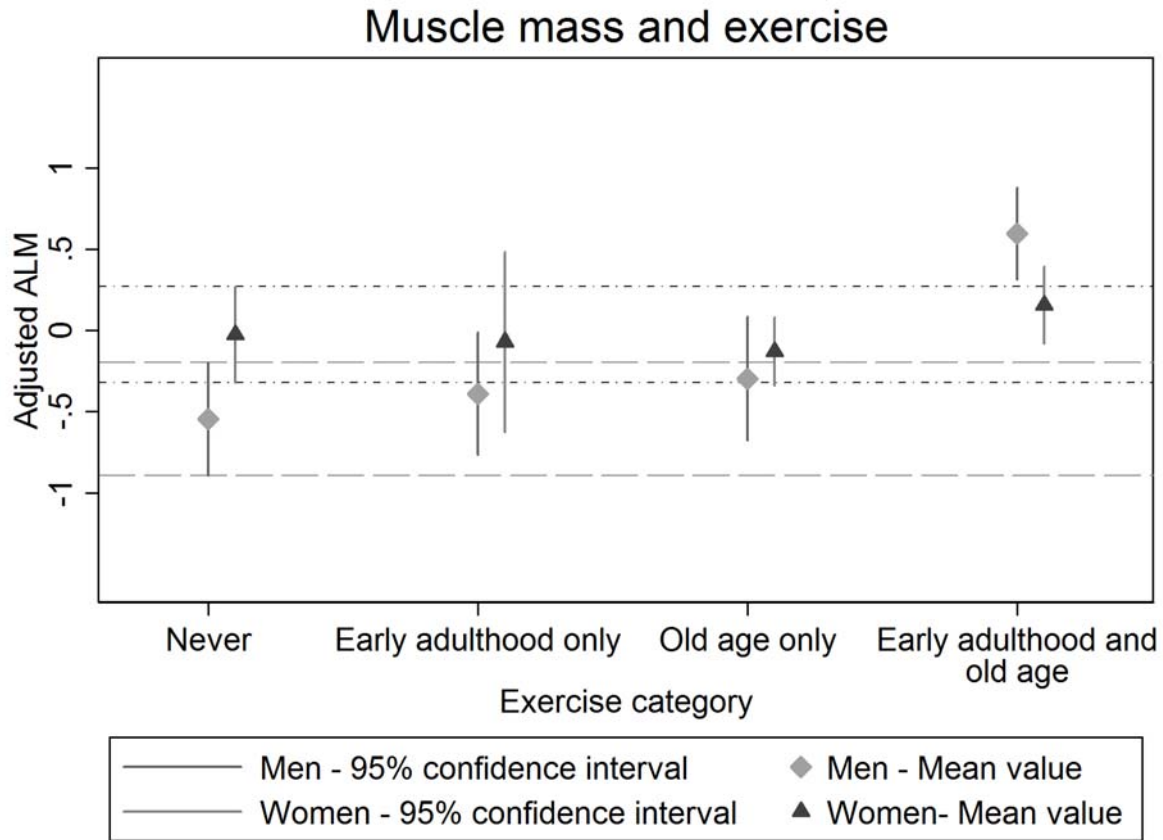


Fig. 1: Mean ALM in the four categories. Dots are averages and vertical lines provide a 95% confidence interval around the mean. The dashed and dotted horizontal lines mark the confidence intervals of the reference category for men and women, respectively. It should be noted that ALM is adjusted for cubic trends in age, height and weight.

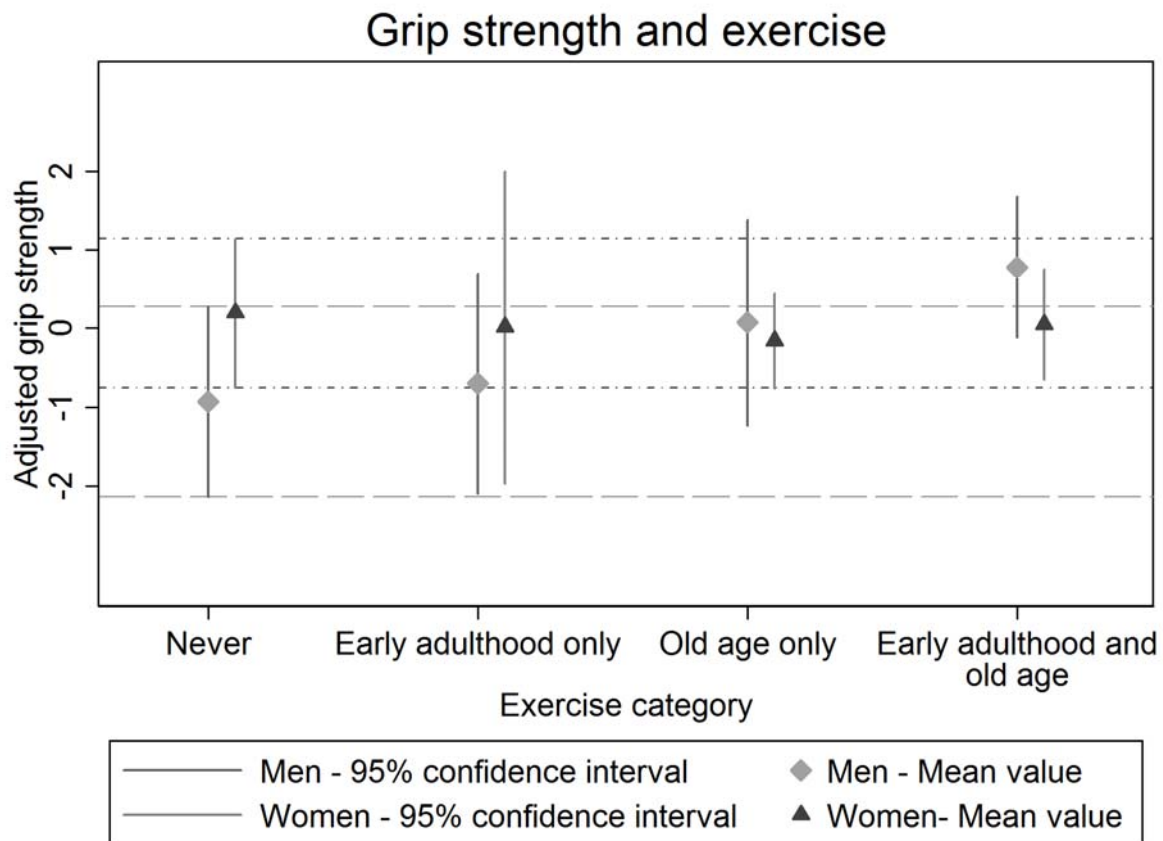


Fig. 2: Mean grip strength in the four categories. Dots are averages and vertical lines provide a 95% confidence interval around the mean. The dashed and dotted horizontal lines mark the confidence intervals of the reference category for men and women, respectively. It should be noted that grip strength is adjusted for cubic trends in age, height and weight.

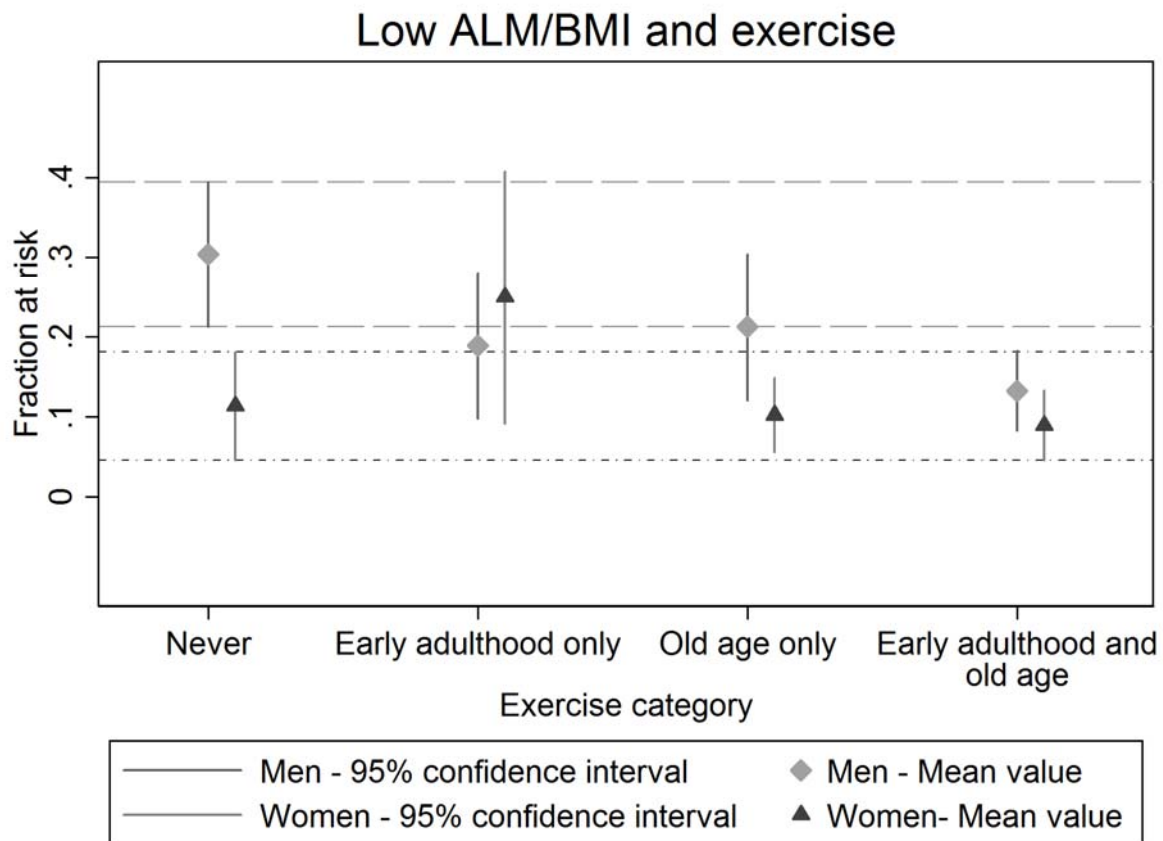


Fig. 3: Fraction at risk for ALM/BMI below clinical thresholds. Dots are averages vertical and lines provide a 95% confidence interval around the mean. The dashed and dotted horizontal lines mark the confidence intervals of the reference category for men and women, respectively.

**Table 1: Descriptive statistics of the study population**

	<i>All (n=891)</i>	<i>Men (n=437)</i>	<i>Women (n=454)</i>
Age (years)	68.6 ± 3.6	68.7 ± 3.6	68.5 ± 3.5
ASM (kg)	20.1 ± 4.7	24.0 ± 2.9	16.3 ± 2.3
Low ALM-to-BMI (%)	15.3	19.7	11.0
Grip strength <sup>1</sup> (kg)	34.5 ± 9.8	42.6 ± 6.6	26.8 ± 4.7
Years of education	13.9 ± 3.9	14.2 ± 3.9	13.6 ± 3.8
Equivalized household income (EUR)	1.779.4 ± 924.1	1897.9 ± 9821.1	1665.3 ± 850.2
Married (%)	55.7	71.4	40.5
Employed (%)	4.0	6.2	2.0
Exercise in early adulthood only (%)	11.9 (n=106)	16.9 (n=74)	7.0 (n=32)
Exercise in old age only (%)	27.6 (n=246)	18.3 (n=80)	36.6 (n=166)
Exercise in early adulthood and old age (%)	39.2 (n=349)	41.4 (n=181)	37.0 (n=168)

Notes: Net monthly household income (in Euro) is adjusted by the number of household members. Children under age 14 receive a weight of 0.3 and additional adults are weighted by 0.5. <sup>1</sup>n=889

**Table 2: Exercise and appendicular lean mass**

	Model 1 (Beta)	
	Men	Women
<i>Variables</i>		
Exercise in early adulthood	0.134	-0.053
Exercise in old age	0.265	-0.100
Exercise in early adulthood and old age	1.148 ***	0.170
Years of education	-0.005	-0.006
Log household income	-0.108	0.297
Marital status	0.245	-0.206
Employed	0.610	-0.178
Age	Cubic polynomial	
Height	Cubic polynomial	
Weight	Cubic polynomial	
R <sup>2</sup>	0.617	0.599

Notes: Estimation results come from a linear regression model. "Exercise in early adulthood" is a binary variable for individuals who claim to have exercised before age 30. "Exercise in old age" is a binary variable for individuals stating to exercise currently. The control group consists of individuals who never exercised. Significance: \*\*\* p<0.001.

**Table 3: Exercise and low ALM/BMI (below cut off points)**

	Model 1 (OR)	
	Men	Women
<i>Variables</i>		
Exercise in early adulthood	0.547	3.149 ***
Exercise in old age	0.581	0.881
Exercise in early adulthood and old age	0.364 **	0.782
Years of education	0.960	1.000
Log household income	1.091	0.860
Marital status	1.009	1.442
Employed	0.364	-
Age	Cubic polynomial	
Height	-	
Weight	-	
R <sup>2</sup>	0.047	0.038

Notes: Estimation results come from a logit regression model. “Employed” was dropped from the regressions for women, since this variable predicted the outcome perfectly. Significance: \*\* p<0.01, \*\*\* p<0.001.

**Table 4: Exercise and grip strength**

	Model 1 (Beta)	
	Men	Women
<i>Variables</i>		
Exercise in early adulthood	0.202	-0.451
Exercise in old age	1.026	-0.665
Exercise in early adulthood and old age	1.779 *	-0.514
Years of education	0.042	0.070
Log household income	-0.415	1.712 **
Marital status	0.422	-0.188
Employed	-1.422	0.756
Age	Cubic polynomial	
Height	Cubic polynomial	
Weight	Cubic polynomial	
R <sup>2</sup>	0.152	0.123

Notes: Estimation results come from a linear regression model. Significance: \* p<0.05, \*\* p<0.01.

## **Supplement**

### **A.** Alternative specification – Continuous exercise

One potential concern with the specification of our exercise categories is that the group that exercised both in early adulthood and old age could include participants that did not exercise continuously between 30 and 60 years of age. Therefore, we estimate a second specification using a binary variable for participants that continuously exercised since age 30, i.e. they either practiced their current form of exercise since age 30, or only stopped practicing after having started practicing their current form of exercise. Hence, this specification estimates the association of continuous exercise since age 30 on muscle mass and strength using all other participants as the control group (i.e. not only participants who never exercised, but also those individuals who exercised in early adulthood only, in old age only, or both in early adulthood and old age but with gaps in between). In our sample, 26.1% of the men and 25.1% of the women reported having continuously exercised since age 30.

The results are shown in Table A.1 to A.3. In line with our main specification, continuous exercise is associated with higher ALM only among men. The estimate is slightly smaller, which is likely due to the fact that in this specification the control group also consists of individuals who exercise currently. For women, the estimates are insignificant.



**Table A.1: Exercise and appendicular lean mass**

	Model 2 (Beta)	
	Men	Women
<i>Variables</i>		
Continuous exercise since age 30	0.793 ***	0.327
Years of education	-0.003	-0.003
Log household income	-0.021	0.264
Marital status	0.290	-0.210
Employed	0.596	-0.180
Age	Cubic polynomial	
Height	Cubic polynomial	
Weight	Cubic polynomial	
R <sup>2</sup>	0.601	0.600

Notes: Estimation results come from a linear regression model. "Continuous exercise since age 30" is a binary variable for individuals having exercised since age 30. The control group consists of individuals who never exercised, exercised either in early adulthood or old age only, or exercised in early adulthood and old age but with gaps in between. Significance: \*\*\* p<0.001.

Similarly, men who continuously exercised since age 30 have a significantly lower risk of low ALM/BMI, whereas for women the estimate is insignificant. Finally, the association between continuous exercise and grip strength is insignificant for both sexes. In summary, the results from this alternative specification confirm our main findings.

**Table A.2: Exercise and low ALM/BMI (below cut off points)**

	Model 2 (OR)	
	Men	Women
<i>Variables</i>		
Continuous exercise since age 30	0.332 **	0.665
Years of education	0.962	1.01
Log household income	1.019	0.881
Marital status	0.948	1.335
Employed	0.384	-
Age	Cubic polynomial	
Height	-	
Weight	-	
R <sup>2</sup>	0.019	

Notes: Estimation results come from a logit regression model. “Employed” was dropped from the regressions for women, since this variable predicted the outcome perfectly. Significance: \*\* p<0.01.

**Table A.3: Exercise and grip strength**

	Model 2 (Beta)	
	Men	Women
<i>Variables</i>		
Continuous exercise since age 30	1.252	0.575
Years of education	0.040	0.070
Log household income	-0.210	1.580 **
Marital status	0.510	-0.225
Employed	-1.526	0.679
Age	Cubic polynomial	
Height	Cubic polynomial	
Weight	Cubic polynomial	
R <sup>2</sup>	0.146	0.124

Notes: Estimation results come from a linear regression model. Significance: \*\* p<0.01.

## **B.** Treatment bounds

To assess the potential impact of unobserved confounders on the associations of exercise with appendicular lean mass and grip strength, we calculated treatment bounds using a method proposed by Oster (2014). She formalizes the heuristic of using coefficient stability (i.e. the change in the coefficient of interest when observed confounders are included) to assess the potential impact of unobserved confounders.

Intuitively, we compared the coefficient from an uncontrolled regression to the coefficient from a regression including covariates. This difference in the coefficients is weighted by the difference in the respective R<sup>2</sup>. Then, assuming that selection into the treatment (i.e. confounding) on our observed covariates is proportional to the degree of selection on

unobserved confounders, it is possible to recover the “true” treatment effect. Unfortunately, the calculation involves two additional unknowns, namely the maximum  $R^2$  (i.e. the  $R^2$  of a regression when all relevant covariates are observed) as well as the value of proportionality between the observed and unobserved covariates. However, we were able to derive bounds for the treatment effect by assuming upper bounds for both unknowns. The maximum value of  $R^2$  is bounded from above at 1. For the proportionality value we followed the recommendation of Oster and assumed a value of 1, which implies that selection on the unobserved confounders is at most as large as selection on our observed covariates. The lower bound derived by this method and the coefficient from the controlled regression form a set that is very likely to contain the true (i.e. unconfounded) treatment effect. A set that excludes zero provides further evidence for the robustness of our results. As observed confounders we included our socio-economic covariates (years of education, the logarithm of household income, marital status, employment status), cubic trends in age, height and weight, as well as indicators for whether a participant has been diagnosed with a sleep disorder, diabetes, asthma, a heart disease, cancer, stroke, migraine, hypertension, depression, dementia, arthritis, or back pain. Finally, we also include indicators for all five categories of the self-rated health status (participants were asked to rate their current health status on a five-point scale ranging from “poor” to “excellent”).

**Table B.1: Treatment bounds**

<b>A. Men</b>				
<i>Outcome</i>	<i>Treatment</i>	<i>Lower bound</i>	<i>Upper bound</i>	$\delta$
ALM	Exercise in early adulthood and old age	1.14	1.26	-7.99
ALM	Continuous exercise since age 30	0.78	0.91	-5.54
ALM/BMI below cutoff	Exercise in early adulthood and old age	-1.15	-0.15	-0.03
ALM/BMI below cutoff	Continuous exercise since age 31	-0.60	-0.13	1.76
Grip strength	Exercise in early adulthood and old age	1.62	1.84	-6.83
Grip strength	Continuous exercise since age 32	1.28	1.32	-35.73

<b>B. Women</b>				
<i>Outcome</i>	<i>Treatment</i>	<i>Lower bound</i>	<i>Upper bound</i>	$\delta$
ALM	Exercise in early adulthood and old age	-0.40	0.12	0.23
ALM	Continuous exercise since age 30	0.13	0.30	1.75
ALM/BMI below cutoff	Exercise in early adulthood and old age	-0.02	0.50	0.03
ALM/BMI below cutoff	Continuous exercise since age 31	-0.02	0.92	0.12
Grip strength	Exercise in early adulthood and old age	-9.63	-0.48	-0.05
Grip strength	Continuous exercise since age 32	-2.88	0.51	0.15

Notes: Treatment bounds for the exercise, ALM and grip strength, as proposed by Oster (2014). *Lower* and *upper bound* (columns 3 and 4) for the respective treatment effect are calculated assuming  $R^2_{\max}=1$  and  $\delta=1$ . If this identified set does exclude effects of zero, this provides evidence for the robustness of the results. *Delta* (column 5) is estimated assuming  $R^2_{\max}=1$  and shows the value of proportionality that is necessary to produce a true treatment effect of zero. Values above 2.2 provide strong evidence in favor of the estimated association. A negative value implies that the inclusion of the observed confounders moves the estimated association away from zero.

The results are shown in Table B.1. We calculated the identified set, assuming that  $R^2_{\max}=1$  and  $\delta=1$ . This set is provided in columns 3 and 4. Here, for men (Panel A) all models exclude treatment effects of zero. The estimated values for  $\delta$  are even negative in all but one model, which implies that the inclusion of observed confounders moves the estimated associations away from zero. For women (Panel B), the results indicate that a treatment effect of zero is likely in almost all cases. Exceptions are the estimated association of continuous exercise with appendicular lean mass as well as the association of exercise in early adulthood and old age and grip strength. However, in the latter case the estimated treatment bounds even imply a negative treatment effect. Since

our main results indicate that the estimated association is small and statistically not significant, this is unlikely to reflect a true negative effect of exercise on grip strength in women.

An important assumption for the validity of the results shown above is that the observed confounders are at least as important as potential unobserved confounders. We argue that this is likely to be the case. While our socio-economic covariates are unlikely to affect our estimates substantially, we also included age, height, weight as well as a comprehensive set of health indicators into the model. These characteristics should be among the most important factors that determine both strength and muscle mass as well as exercise participation.

All in all, we conclude that it is unlikely that unobserved confounders that are proportional to the observed covariates affect our results substantially. Following Oster, this implies that the robustness of our results can be compared to those from a randomized experiment.