

RESEARCH ARTICLE

Grip Strength Decline and Its Determinants in the Very Old: Longitudinal Findings from the Newcastle 85+ Study

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OPEN ACCESS

Citation: Granic A, Davies K, Jagger C, Kirkwood TBL, Syddall HE, Sayer AA (2016) Grip Strength Decline and Its Determinants in the Very Old: Longitudinal Findings from the Newcastle 85+ Study. *PLoS ONE* 11(9): e0163183. doi:10.1371/journal.pone.0163183

Editor: David J. Handelsman, University of Sydney, AUSTRALIA

Received: March 17, 2016

Accepted: September 2, 2016

Published: September 16, 2016

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Data Availability Statement: All relevant data are within the paper and its Supporting Information files. Also, additional information about the Newcastle 85+ Study are available from the Newcastle 85+ Study Core Research Team Leadership chaired by Prof Carol Jagger (carol.jagger@newcastle.ac.uk) and study's website at <http://research.ncl.ac.uk/85plus>.

Funding: This study has been funded by the National Institute for Health Research Newcastle Biomedical Research Centre in Ageing and Chronic Disease based at Newcastle Hospitals Foundation Trust and Newcastle University (AG). The Newcastle

Abstract

Background

Weak grip strength (GS) is a key component of sarcopenia and frailty and a powerful predictor of mortality, morbidity and disability. Despite increasing interest in understanding GS across the lifespan, little is known about GS decline in the very old (aged ≥ 85). We examined trajectories of GS in very old adults and identified the determinants.

Methods

GS (kg) was measured four times over 5 years in 319 men and 526 women participating in the Newcastle 85+ Study. A weak GS sub-cohort was identified as having strength of ≤ 27 kg (men), and ≤ 16 kg (women) at baseline and follow-up. Mixed models were used to establish trajectories of GS and associated factors in all participants, men and women, and in those with weak GS.

Results

Men's mean grip strength was 24.42 (SD = 6.77) kg, and women's 13.23 (4.42) kg ($p < 0.001$) at baseline, with mean absolute change of -5.27 (4.90) kg and -3.14 (3.41), respectively ($p < 0.001$) by 5-year follow-up. In the time-only mixed model, men experienced linear annual decline in GS of -1.13 (0.8) kg (β (SE), $p < 0.001$), whilst women's decline although slower, accelerated by -0.06 (0.02) kg ($p = 0.01$) over time. In the saturated model, higher baseline physical activity, height, fat-free mass, better self-rated health, and not having arthritis in hand(s) were associated with stronger GS initially in both sexes. Annual GS

85+ Study has been funded by the Medical Research Council, Biotechnology and Biological Sciences Research Council and the Dunhill Medical Trust. Parts of the work have also been funded by the British Heart Foundation, Unilever Corporate Research, Newcastle University and the North of England Commissioning Support Unit (formerly NHS North of Tyne). The research was also supported by the National Institute for Health Research Newcastle Biomedical Research Centre, based at Newcastle upon Tyne Hospitals NHS Foundation Trust and Newcastle University. The views expressed are those of the authors and not necessarily those of the National Health Service, United Kingdom. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing Interests: We have the following interest: The Newcastle 85+ Study was partly funded by Unilever Corporate Research. There are no patents, products in development or marketed products to declare. This does not alter our adherence to all the PLOS ONE policies on sharing data and materials, as detailed online in the guide for authors.

decline in men and participants with weak GS who were highly physically active was slower by 0.95 and 0.52 kg, respectively compared with inactive counterparts.

Conclusion

Grip strength decline in the very old followed linear (men) and curvilinear (women) trends. High levels of physical activity were protective of GS loss in men (but not in women) and in those with weak GS. Thus maintaining muscle strength in later life is important to reduce the morbidity and mortality in the very old.

Introduction

Grip strength (GS) is recognised as an objective measure of upper-body and general muscle strength [1] and a key component of the geriatric syndromes of sarcopenia [2] and frailty [3]. A number of studies have confirmed age- and sex-dependent decline in GS after a peak at the age of 30 [4–14], but less is known about GS trajectories in the very old (aged ≥ 85). Few studies have focused on this age group alone [15–17]—despite the very old being the most vulnerable to the adverse consequences of loss of muscle strength and function [3,18]. These include increased risk of disability [19], cognitive impairment [20], depression [21], frailty [3,22], mobility decline [23], falls [22], hospitalisation [24], institutionalisation [25] and mortality [26,27] reported in younger old. GS has therefore been proposed as a biomarker of ageing [28] although there is limited evidence about the prognostic value of GS in very old adults [27,29].

To establish population norms and explore factors influencing age-related changes in GS, a number of cross-sectional and prospective cohort studies have shown stronger hand grip in men and faster decline of GS compared with women after the age of 50 [4–18]—although only a few studies were able to follow participants into very old age [5,13,16,18]. For example, recent cross-sectional evaluations of harmonized data from eight UK cohorts (the Healthy Ageing across the Life Course) of individuals aged 50 to ≥ 90 have shown stronger GS in men and age-dependent decline, but narrowing of the sex differences in GS in very advanced age [10]—a trend also observed in other British cohort [7] and international population-based studies [5,11,13,14]. A lifespan approach applied to GS data from 12 British cohorts (ages 4 to 90) revealed a steady decline in GS from midlife onwards, and a sharp increase in weak GS prevalence in late life, defined as strength at least 2.5 standard deviations (SD) below sex-specific peak mean (or ≤ 27 kg in men, and ≤ 16 kg in women) [4]. However, the prevalence of weak versus normal GS in the very old has not been investigated separately.

Aside from age and sex, previous studies exploring factors influencing GS over time have recognized a positive association with height [1,17], BMI [8,12] (mostly in men), appendicular lean mass [30], absence of depressive symptoms [11], physical activity [31,32], self-rated health [33], and a negative association with disease burden [34], body fat [35], smoking and alcohol [14], and the risk of death [9,17], but the likely factors associated with GS trajectories in the very old are less clear [16].

We hypothesized that very old men and women, and those with weak GS may experience different GS trajectories influenced by diverse risk factors of GS decline. Utilising data from the Newcastle 85+ Study, we aimed to: (a) describe the change in GS over 5 years, and (b) identify determinants of initial level and rate of change in GS in very old men and women, and in those with weak GS at baseline and follow-up.

Methods

Study population

845 participants (319 men (37.8%) and 526 (62.2%) women) were examined from the Newcastle 85+ Study, a longitudinal cohort study of over 1,000 older adults born in 1921 (aged around 85 at baseline in 2006/2007), and residing in Newcastle and North Tyneside, UK. Study protocols, recruitment profile, representativeness of general population in England and Wales, and retention rate over 5-year follow-up have been described [36–38]. The study evaluated a range of bio-psycho-social factors related to health and functioning in very late life through multidimensional health assessment including measurement of GS and general practice records review. Participants were followed-up at 1.5 (wave 2), 3 (wave 3), and 5 years (wave 4). Complete data (from health assessment and medical records) were available for 845 participants at baseline. Of those, 821 (97.4%) attempted GS measurement, followed by 611, 460, and 307 participants at wave 2, 3 and 4, respectively (S1 Fig).

The study was approved by the Newcastle & North Tyneside Local Research Ethics Committee [36]. Signed informed consent was obtained from each participant, for those lacking capacity opinion was sought from their consultee (usually a relative).

Grip strength measurement

Isometric GS [39] was measured in kilograms (kg) using a Takei hand dynamometer (Model A5401 digital 0–100kg x 0.1kd LCD) (Takei Scientific Instruments Co., Ltd., Niigata City, Japan). The standardised measurement protocol involved a standing position with elbow extension to allow the arm to hang down by the side. Participants were instructed to squeeze the dynamometer as hard as possible to assess the maximal force for each hand. Four measurements alternating between dominant and non-dominant hand were recorded, and the mean (M, SD) of four trials was calculated as a measure of overall GS and used in analyses [40].

Potential covariates

In multivariable analyses, the following covariates identified in the literature were considered in relation to GS. Sociodemographic factors included sex, education (0–9 / 1–11 / ≥ 12 years), occupational class coded to the National Statistics Socio-economic Classification system (routine or manual / intermediate / higher managerial or administrative) [41], and marital status (single / widowed, separated, or divorced / married). Lifestyle factors included self-reported physical activity (low (score 0–1) / medium (score 2–6) / high (score 7–18)) [42], smoking (never / current smoker / former smoker), and current alcohol intake (yes / no). Anthropometry included height (cm) calculated from demi-span equations, weight (kg), BMI (<18.5 (underweight) / >18.5<25 (normal) / >25<30 (overweight) / 30 (obese); calculated as kg weight/m² height), fat mass (FM) (kg), fat-free mass (FFM) (kg) [43], and waist-hip ratio (continuous). Health-related factors were self-rated health compared to others of the same age (excellent or very good / good / fair or poor) [37], scoring <15 points on Standardized Mini-Mental State Examination (SMMSE) (yes / no) [37], and depressive symptoms (none (0–5 points) / mild or moderate (6–7 points) / severe (8–15 points)) assessed by Geriatric Depression Scale (GDS-15) [37]. Disease burden, total number of medications (continuous), and the intake of non-prescribed medication (yes / no) were established from medical records. Diseases were grouped into arthritis, hypertension, cardiac disease, respiratory disease, cerebrovascular disease, diabetes, and cancer [37]. Having difficulty related to arthritis in hand(s) (left, right, or both, in one or more joints) during GS measurement was coded as yes / no. Total medications were also categorised (0–2 / 3–4 / ≥ 5) to test for polypharmacy. A retention variable

(completed the study / dropped out) accounted for loss to follow-up (due to death and withdrawal) over 5 years [35].

All covariates used in multilevel analysis were baseline, fixed independent variables. Self-reported physical activity was evaluated with a purpose-designed questionnaire validated in a sub-cohort of the very old. Physical activity scores were derived from the frequency and intensity of physical activities per week, and correlated highly with actigraphy [42]. FM and FFM were estimated from inbuilt precision equation of the Tanita-305 body-fat bioimpedance instrument (Tanita Corp., Tokyo, Japan) [43]. Weak GS was defined as a strength of T-score equal or less than 2.5 below sex-specific peak mean at age of 32 (≤ 27 kg in men, and ≤ 16 kg in women) [4]. Description of selected variables has been published previously [36, 37], and further details from the study questionnaire can be found on the study’s website (<http://research.ncl.ac.uk/85plus/>).

Statistical analysis

Unadjusted grip strength in men and women. The differences in unadjusted GS (kg) between men and women at each wave were compared using Student’s t-test, and the difference in GS across the waves were determined using repeated-measures ANOVA with Huynh-Feldt correction (Table 1).

Trajectory of grip strength across four waves. GS data were normally distributed at each assessment (wave) and used as continuous dependent variable. We fitted liner mixed models to examine (a) the trajectory in GS over 5 years, and (b) factors associated with initial level and rate of annual change in GS in the entire cohort (i.e. those with a complete GS measure at baseline; $n = 813$), and separately by sex, and in those with weak versus normal GS at baseline and follow-up (thereafter weak and normal GS sub-cohort). The model specifications and building strategy are described in the S1 Methods. Linear mixed (multilevel) models take into account both individual trajectories of change (intra-individual variability at Level 1; random effects)

Table 1. Grip strength measurements by sex in very old adults across four waves.

Wave	All	Men	Women	p*
Baseline , n	813	313	500	
M (SD), kg	17.54 (7.70)	24.42 (6.77)	13.23 (4.42)	<0.001
Wave 2 (1.5-year follow-up), n	605	229	376	
M (SD), kg	16.94 (7.81)	23.77 (7.21)	12.78 (4.54)	
Wave 3 (3-year follow-up), n	452	167	285	
M (SD), kg	16.39 (7.28)	22.68 (7.01)	12.71 (4.30)	<0.001
Wave 4 (5-year follow-up), n	294	106	188	
M (SD), kg	14.94 (7.00)	21.05 (6.92)	11.50 (4.10)	<0.001
p†	<0.001	<0.001	<0.001	
5-year mean absolute change‡ , n	291	106	185	
M (SD), kg	-3.92 (4.14)	-5.27 (4.90)	-3.14 (3.41)	<0.001
5-year mean relative change¶ , n	291	106	185	
M (SD), %	-20.1 (23.7)	-20.0 (20.0)	-20.2 (25.6)	0.95

GS, grip strength; M, mean; SD, standard deviation.

*Student t-test.

†Repeated-measures ANOVA with Huynh-Feldt correction.

‡Calculated as: $GS_{wave4} - GS_{baseline}$.

¶Calculated as: $(GS_{wave4} - GS_{baseline}) / GS_{baseline} * 100\%$.

doi:10.1371/journal.pone.0163183.t001

and population averages (inter-individual variability at Level 2; fixed effect) by using all available measurement and including participants with incomplete data [44]. The Level 1 sub-model evaluated how GS changed over time for each participant. The Level 2 sub-model examined the effect of covariates on GS change.

Time was scaled in years (continuous) to account for both linear (i.e. constant rate of change over 5 years) and quadratic (i.e. acceleration or deceleration in rate of change) GS trajectory. All predictors were fixed (baseline), and continuous variables (height and FFM) were centred to sex-specific mean to aid the interpretability of intercepts and slopes. Negative β estimates (coefficients) indicated weaker GS and positive described stronger GS compared to the specified referent group. β coefficients for predictors (covariates) represented their effect on the GS intercept. The coefficient for Time represented average annual linear change, and Time*Time captured additional quadratic (curvilinear) change in GS. A significant coefficient of time interactions with a covariate indicated whether time slopes varied by the covariate (Tables 2 and 3). All models included a random intercept and slope (i.e. taking into account each participant's GS at baseline and the linear slope).

Sensitivity analysis. The prevalence of weak GS (%) was calculated for each wave in the entire cohort, and separately by sex, and compared using χ^2 test at each wave, and Cochran's Q-test to assess differences in prevalence across waves (S1 Table). We used the cut-offs of ≤ 27 kg (men) and ≤ 16 kg (women) at each GS assessment (wave) to create a time-dependent variable and identify the weak (1607 GS observations) and normal GS sub-cohort (557 GS observations) in linear mixed models.

Sociodemographic, lifestyle, anthropometry and health-related characteristics of participants with weak versus normal GS at baseline were summarised by descriptive statistics, and compared using χ^2 test for categorical, Student's t-test for continuous normally distributed and Mann-Whitney U-test for non-normally distributed and ordinal variables (S2 Table). We used similar statistics to compare the characteristics of 813 participants who had a complete GS measure at baseline with those who did not ($n = 32$).

To account for survivor bias, mixed models were repeated in participant who completed the 5-year follow-up (thereafter 'survivor sub-cohort') (S3 Table).

All analyses were performed using IBM SPSS (V2.1; IBM Corporation, Armonk, NY, USA), and all statistics were reported at two-tailed $\alpha = 0.05$.

Results

Unadjusted grip strength in men and women

Table 1 summarises unadjusted (raw) mean GS values in the entire cohort and by sex across four waves (over 5 years). At baseline, 313 men (38.5%) and 500 women (61.5%) had a complete grip GS (average of 2 measurement per each hand). As expected, men had higher mean GS initially (M (SD) = 24.42 (6.77) kg) compared with women (13.23 (4.42) kg) and thereafter (p for all < 0.001), and experienced greater mean absolute change (-5.27 (4.90) kg versus -3.14 (3.41) kg ($p < 0.001$) in women). However the mean relative change was similar in both sexes.

Trajectory of grip strength across four waves

Entire cohort. The unconditional time-only model (Model 1, Table 2), showed both linear and quadratic effects of decline in GS in the entire cohort or an overall loss of -0.56 kg per year with accelerated loss of -0.05 kg annually over the 5-year follow-up (both $p < 0.001$). In the saturated model (Model 2, Table 2), we found a significant association between GS initially and sex, physical activity, height, FFM, self-rated health, presence of arthritis in hand(s), and

Table 2. Grip strength trajectory estimates[†] in the entire cohort, men and women over 5 years.

Fixed effects [‡]	Entire cohort				Men				Women			
	n = 813				n = 313				n = 500			
	Model 1 [¶]		Model 2 [#]		Model 1		Model 2		Model 1		Model 2	
	β (SE)	p	β (SE)	p	β (SE)	p	β (SE)	p	β (SE)	p	β (SE)	p
GS intercept	17.44 (0.27)	<0.001	7.13 (0.97)	<0.001	24.47 (0.39)	<0.001	14.54 (2.05)	<0.001	13.14 (0.20)	<0.001	13.78 (2.47)	<0.001
Sex												
men			10.81 (0.37)	<0.001								
women (ref)			0									
Physical activity												
high			4.06 (0.53)	<0.001			5.00 (1.02)	<0.001			2.74 (0.54)	<0.001
medium			2.69 (0.49)	<0.001			3.57 (1.02)	0.001			1.58 (0.48)	0.001
low (ref)			0									
Height			0.23 (0.04)	<0.001			0.23 (0.08)	0.004			0.16 (0.04)	<0.001
FFM			0.11 (0.03)	<0.001			0.17 (0.06)	0.008			0.08 (0.03)	0.004
Waist-hip ratio											-5.77 (2.66)	0.03
Self-rated health												
excellent/ very good			1.49 (0.48)	0.002			2.15 (1.01)	0.04			1.02 (0.46)	0.003
good			0.95 (0.47)	0.05			1.08 (1.0)	0.28			0.90 (0.46)	0.05
fair/			0				0				0	
poor (ref)												
Disease count			-0.24 (0.14)	0.09							-0.34 (0.14)	0.02
Arthritis in hand(s)												
no			3.58 (0.69)	<0.001			6.18 (1.90)	0.001			2.93 (0.63)	<0.001
yes (ref)			0				0				0	
Retention												
completed the study			0.91 (0.36)	0.01							0.83 (0.35)	0.02
dropped out (ref)			0									
GS decline												
Time	-0.56 (0.1)	<0.001	-0.45 (0.11)	<0.001	-1.13 (0.8)	<0.001	-2.00 (0.27)	<0.001	-0.31 (0.11)	0.006	-0.43 (0.12)	<0.001
Time*Time	-0.05 (0.02)	<0.001	-0.04 (0.02)	0.04					-0.06 (0.02)	0.01	-0.05 (0.02)	0.05
GS rate of decline (slope)												
Time*sex												
Time*men			-0.52 (0.09)	<0.001								
Time*women (ref)			0									
Time*physical activity												
Time*high							0.95 (0.29)	0.001				
Time*medium							0.82 (0.31)	0.009				
Time*low (ref)							0					

FFM, fat-free mass; GS, grip strength; ref, reference; SE, standard error.

[†]Estimated β coefficients (SE) using GS longitudinal data.

[‡]Fixed effects assessed population average change in GS. Fixed effect covariates estimated initial level and trajectory differences in GS as a function of included covariate. Random effects included both intercepts and slopes (linear change). Time in years (continuous) since the baseline interview tested linear change. Time*Time (continuous) represented curvilinear change.

[¶]Model 1 includes a linear and quadratic trend of time (except in men).

[#]Model 2 is adjusted for sociodemographic, lifestyle, anthropometry, health-related factors, retention variable, and time interaction terms. Only significant predictors and interactions at first entry were retained in the model.

doi:10.1371/journal.pone.0163183.t002

retention, and a significant interaction between linear time and sex, indicating a steeper rate of GS decline in men (β (SE) = -0.52 (0.09), $p < 0.001$).

Men and women. In the time-only model (Model 1, [Table 2](#)), men's GS trajectory showed a higher intercept (24.47 (0.39) kg, $p < 0.001$) and linear decline (-1.13 (0.8) kg, $p < 0.001$), whilst women started with lower intercept (13.14 (0.20), $p < 0.001$) but experienced accelerated loss of -0.06 (0.02) kg ($p = 0.01$) per each follow-up year above the loss seen in the first year. In men, significant determinants of GS initially were: physical activity (high: 5.00 (1.02), $p < 0.001$; medium: 3.57 (1.02), $p = 0.001$), height (0.23 (0.08), $p = 0.004$), FFM (0.17 (0.06), $p = 0.008$), self-rated health (excellent or very good: 2.15 (1.01), $p = 0.04$), and arthritis in hand(s) (6.18 (1.90), $p = 0.001$) (Model 2, [Table 2](#)). In women, additional significant covariates of GS included greater disease burden and waist-hip ratio which predicted a weaker GS, and retention (completing the study) which was associated with a stronger GS at baseline. Of all significant covariates, the rate of GS decline was only affected by high (0.95 (0.29), $p = 0.001$) and medium physical activity (0.82 (0.31), $p = 0.009$) in men, but not in women.

Estimated 5-year trajectories in GS based on β coefficients from the saturated model (Model 2) in the entire cohort and by sex are presented in [S2 Fig](#) (panel A).

Weak and normal GS sub-cohorts. To account for weak baseline GS affecting the trajectory in GS in very old adults and the possibility of the floor effect in women over follow-up, we examined the association (fixed effects) between GS and important covariates (initially and over time) in participants belonging to the weak and normal GS sub-cohort ([Table 3](#); [S2 Fig](#), panel B). The time-only model (Model 1) revealed a linear (-0.37 (0.12), $p = 0.002$) and quadratic (-0.05 (0.02), $p = 0.03$) (acceleration) decline in GS over 5 years in those with overall weak GS (as in the entire cohort), but linear loss of GS in the normal GS sub-cohort (-0.48 (0.06), $p < 0.001$). In both groups, sex (men), higher physical activity (medium and high), and height were significantly associated with a stronger GS initially. Additional determinants of GS in the weak GS sub-cohort included BMI (and not FFM; data not shown), self-rated health, arthritis in hand(s), and retention. In both sub-cohorts, men experienced steeper slopes of GS decline compared with women, but only those in the weak GS sub-cohort benefited from physical activity, and had slower rate of GS decline (medium: 0.52 (0.17) kg, $p = 0.003$); high: 0.56 (0.17), $p = 0.001$ compared with low physical activity).

Sensitivity analyses. Participants with a complete GS measure ($n = 813$) were more likely to be men ($p = 0.02$), to be more educated ($p = 0.01$) and physically active ($p < 0.001$), and less likely to be cognitively impaired ($p < 0.001$), but did not differ on any other health and anthropometry measures (details not shown).

Baseline prevalence of weak GS was higher in women (74.2% vs 63.6% in men, $p < 0.001$), and increased over time for both sexes ($p < 0.001$), but levelled off by wave 4 ([S1 Table](#)). Compared with participants with normal GS at baseline ($n = 243$), those with weak GS ($n = 570$) were more likely to be women ($p = 0.001$), to have low physical activity ($p < 0.001$), to be shorter ($p < 0.001$), have lower weight and be classified as underweight, to have lower FM and FFM (all $p < 0.001$), to be cognitively impaired (SMMSE < 15 points) ($p = 0.002$), to have greater disease burden ($p = 0.005$), arthritis in hand(s) ($p < 0.001$), history of falls ($p = 0.03$), to take more medication ($p < 0.001$), and not to complete the study ($p < 0.001$) ([S2 Table](#)).

The models fitted to survivor sub-cohort ($n = 343$) showed similar GS trajectory and determinants of initial level and rate of change in GS ([S3 Table](#)).

Discussion

To our knowledge, this is the first prospective cohort study to (a) quantify sex-specific decline in GS, and (b) describe determinants thereof in very old adults (aged ≥ 85) living in Britain.

Table 3. Grip strength trajectory estimates[†] in the weak and normal grip strength sub-cohorts over 5 Years.

Fixed effects [‡]	Weak GS sub-cohort				Normal GS sub-cohort			
	Model 1 ^{††}		Model 2 [#]		Model 1		Model 2	
	β (SE)	p	β (SE)	p	β (SE)	p	β (SE)	p
GS intercept	15.13 (0.24)	<0.001	8.41 (0.85)	<0.001	24.32 (0.42)	<0.001	15.68 (0.83)	<0.001
Sex								
men			9.28 (0.30)	<0.001			12.93 (0.42)	<0.001
women (ref)			0				0	
Marital status								
single							0.77 (0.69)	0.26
widowed/separated/divorced							0.98 (0.40)	0.02
married (ref)							0	
Occupational class								
routine/manual			-0.57 (0.29)	0.052				
intermediate			-0.16 (0.41)	0.70				
managerial/administrative (ref)			0					
Physical activity								
high			2.53 (0.42)	<0.001			2.09 (0.73)	0.004
medium			1.40 (0.38)	<0.001			1.56 (0.72)	0.03
low (ref)			0				0	
Height			0.08 (0.03)	0.005			0.16 (0.04)	<0.001
BMI								
underweight			-1.82 (0.65)	0.005				
normal			-0.91 (0.47)	0.052				
overweight			-0.95 (0.49)	0.053				
obese (ref)			0					
Self-rated health								
excellent/very good			0.88 (0.36)	0.02				
good			0.67 (0.35)	0.06				
fair/poor (ref)			0					
GDS								
severe							-2.22 (0.73)	0.003
mild/moderate							-0.61 (0.72)	0.4
no depression							0	
Arthritis in hand(s)								
no							3.07 (0.51)	<0.001
yes (ref)							0	
Retention								
completed the study			0.64 (0.29)	0.03				
dropped out (ref)			0					
GS decline								
Time	-0.37 (0.12)	0.002	-0.64 (0.18)	0.001	-0.48 (0.06)	<0.001	-0.27 (0.08)	0.001
Time*Time	-0.05 (0.02)	0.03	-0.07 (0.02)	0.005				
GS rate of decline (slope)								
Time*sex								
Time*men			-0.40 (0.11)	<0.001			-0.34 (0.12)	0.004
Time*women (ref)			0				0	
Time*physical activity								

(Continued)

Table 3. (Continued)

Fixed effects [‡]	Weak GS sub-cohort				Normal GS sub-cohort			
	Model 1 [†]		Model 2 [#]		Model 1		Model 2	
	β (SE)	p	β (SE)	p	β (SE)	p	β (SE)	p
Time*high			0.52 (0.17)	0.003				
Time*medium			0.56 (0.17)	0.001				
Time*low (ref)			0					

FFM, fat-free mass; GS, grip strength; ref, reference; SE, standard error.

[†]Estimated β coefficients (SE) using GS longitudinal data.

[‡]Fixed effects assessed population average change in GS. Fixed effect covariates estimated initial level and trajectory differences in GS as a function of included covariate. Random effects included both intercepts and slopes (linear change). Time in years (continuous) since the baseline interview tested linear change. Time*Time (continuous) represented curvilinear change. Cut-offs of ≤27 kg (men) and ≤16 kg (women) were used to identify participants with weak versus normal GS at each assessment (1607 weak and 557 normal GS observations).

^{††}Model 1 includes a linear and quadratic trend of time (except in normal GS sub-cohort).

[#]Model 2 is adjusted for sociodemographic, lifestyle, anthropometry, health-related factors, retention variable, and time interaction terms. Only significant predictors and interactions at first entry were retained in the model.

doi:10.1371/journal.pone.0163183.t003

Decline of GS in the entire cohort followed a nonlinear trajectory (i.e. accelerated over 5 years), and was more pronounced in men. Men had about 11 kg stronger initial GS than women and declined linearly (-2 kg/year), whilst women’s initial rate of loss was -0.43 kg but accelerated by -0.05 kg through the follow-up. For both, higher physical activity, height, FFM, and better self-rated health were associated with a stronger grip initially. Disease burden predicted weaker GS only in women, whilst the presence arthritis in hand(s) was associated with worst GS in both sexes. Men, but not women who were physically active experienced slower rate of GS decline. Similarly, the rate of decline was steeper among men in the weak and normal GS sub-cohorts, but more physically active participants in the weak GS group experienced slower decline.

Consistent with previous research which included very old adults, the present study showed that GS declines with advancing age in both sexes, and that men experienced steeper slope of decline [7,9–11,14,18], although they started with stronger GS compared with women—confirming also that those who have greater GS initially tend to lose more and faster over time [10,14]. Women experienced accelerated (nonlinear) GS decline, which was also observed among 2,200 Danish nonagenarians followed up for 8 years [13], although previous analysis of several Danish cohorts (aged ≥70) suggested a horizontal plateau in the oldest women (aged ≥95) when withdrawal and mortality was accounted for [18]. GS in women participating in the Mini-Finland Health examination declined linearly 4 N (0.41 kg/year) over 10-year follow-up after the age of 80, and additionally by 5.2 N (0.53 kg/year) when mortality (right censoring) was taken into consideration [9]. Due to change in the rate of decline in women’s GS, the annual rate of loss in our cohort is difficult to summarize, but fully adjusted estimates indicate less steep GS decline in women compared with men. In the Leiden 85+ Study, men’s absolute loss in GS was 1.5 kg/years and women’s 0.9 kg/year over 4 years, although relative loss between sexes was similar (-19% in men and -16% in women) [29]—a trend that we confirmed in our cohort (i.e. -20% over 5 years). In addition, while women were more likely to have weak baseline GS, the prevalence of weak grip was similar between men and women 5 years later.

Observed sex differences in GS loss may be partially explained by body composition [43], multimorbidity [37,45], and survival [46]. Sex differences in muscle quality (loss of lean mass and increase in fat mas) [43] with advancing age may be one of the factors contributing to sex differences in GS decline. In our cohort, disease burden was a significant predictor of weaker

GS initially in women, but not in men. Also, having difficulty with GS assessment because of arthritis in hand(s) but not polypharmacy predicted worse baseline GS in both sexes. Despite weaker GS over time, which predicted accelerated decline in disability and global cognition in the very old in the Leiden 85+ Study [16], women's less steep GS decline adds to the previously observed male-female health-survival paradox [45,46]. In the present cohort, we have previously shown that women lived longer with more disability than men, which was attributed to the sex differences in the type of diseases and their impact on disablement process [45]. Women's longer life expectancy (spent in less good health and with more disabilities) and the greater survival of healthier men [46] (survivor effect) in very old age may partly explain the sex differences in GS.

Although multilevel models use all available data, selection bias due to mortality and withdrawal is still a possibility. We included the variable 'retention' (i.e. completed the study over 5 years or not) as an inter-individual covariate to account for selective mortality/withdrawal. This method was used in the recent study of older Japanese (aged ≥ 65) investigating bio-psycho-social factors of GS trajectory [35], and in other prospective studies of change in health in older adults [47]. We also explored GS trajectory in survivors and confirmed the results.

The main finding from the present study points to the role of physical activity in the rate of decline in GS in men and in participants with overall weak GS. Compared with those reporting low levels of physical activity, men and participants with overall weak GS who had both high and medium levels of physical activity at baseline experienced slower loss of GS (0.95 and 0.82 kg/year in men, and 0.52 and 0.56 kg/year in the weak GS sub-cohort, respectively) after adjusting for important covariates. To our knowledge, this is the first prospective study to report the importance of physical activity for GS maintenance in very late life, including in those who had low GS over 5 years. Others have shown similar and opposite sex-specific influence of physical activity on GS in general and older adults population. For example, higher leisure time physical activity (LTPA) assessed longitudinally across midlife was associated with stronger GS at age 60–64 in both men and women [31]. In Danish Health2006 study (aged 19–72), higher LTPA was also significantly related to stronger GS in both sexes [48], whilst women (aged ≥ 64) in the Toledo Study of Healthy Aging benefited more from higher physical activity than men, but adults aged ≥ 85 benefited less compared with younger counterparts [49]. The finding from the present study suggests the importance of maintaining higher level of physical activity for muscle strength well into late adulthood.

Our study has several limitations: (a) the findings regarding predictors of the initial level and decline in GS came from observational data and may not be causal; (b) dichotomisation of certain predictors (e.g. current alcohol intake), and the fact that all predictors were baseline (fixed) covariates may have affected the results; (c) participants with a complete GS measure at baseline were more likely to be men, well-educated and more physically active compared with those not included in analyses; (d) as with any cohort of very old adults, mortality was high [38] and may have resulted in biased sample of very fit survivors, especially men; (e) although we adjusted for mortality and withdrawal and included important confounders, the results may be influenced by selective mortality and by uncontrolled confounding (e.g. biological factors, individual diseases, nutritional status); and (f) our sample was derived from a single urban area in North-East England, with predominantly white ethnicity and had a slight under-representativeness of women compared with census data from 2001. The study has several strengths: (a) the prospective design; (b) multilevel analysis of stratified sub-cohorts (by sex and presence of sex-specific weak GS at baseline and follow-ups); (c) inclusion of important confounders reported in the literature; and (d) a broad representativeness of the general population in England and Wales.

Conclusions

We have found different GS trajectories in very old men and women, and recognized factors influencing GS decline in advancing age. Men and participants with overall weak GS who were physically active experienced slower rate of decline even after adjusting for important confounders. This study provided additional evidence supporting benefits of physical activity into very late life, which should be explored in other cohorts of the very old.

Supporting Information

S1 Fig. Flow chart of participants in the Newcastle 85+ Study by grip strength (GS). At baseline, 845 participants had a complete data (health assessment and medical records review). Of those, 821 participants attempted grip strength measurement (2 per each hand) and had complete multidimensional health assessment and general practice medical records review. At 5-year follow-up (wave 4), 307 remained in the study. The loss to follow-up was mainly due to mortality.

(TIF)

S2 Fig. Estimated 5-year trajectories of grip strength (GS) in the entire cohort, men and women, and in the participant with weak and normal GS at baseline and follow-up in the Newcastle 85+ Study. The fully-adjusted β estimates indicated a linear decline in grip strength in men (dashed line) and curvilinear (acceleration) decline in the entire cohort (full line) and women (dotted line) over 5 years (A). On average, men lost 2 kg/year (A) and the participants in the normal grip strength sub-cohort lost -0.3 kg/year in GS (B). Women and those in the weak grip strength sub-cohort experienced accelerated rate of decline of -0.05 and -0.07 kg per each follow-up year above the average loss of -0.43 and -0.64 kg experienced in the first year, respectively.

(TIF)

S1 Methods. Model building strategy.

(DOCX)

S1 Table. Sex-specific prevalence of weak grip strength in the Newcastle 85+ Study.

(DOCX)

S2 Table. Characteristics of participants with weak and normal grip strength at baseline in the Newcastle 85+ Study.

(DOCX)

S3 Table. Grip strength trajectory estimates in the survivor sub-cohort (n = 343) over 5 year.

(DOCX)

Acknowledgments

We acknowledge the operational support of the North of England Commissioning Support Unit and the local general practitioners and their staff. We thank the research, management and administrative team for their outstanding work, and our colleagues for their expert advice. Special thanks are due to the study participants and, when appropriate, their families and carers.

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