

The association of grip strength with depressive symptoms and cortisol in hair: a cross-sectional study of older adults

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Abstract

Background: Low handgrip strength has been shown to be associated with higher levels of depressive symptoms. One area of mental health that is understudied in relation to grip strength is chronic stress, which can exist independently to depression, or as a comorbidity or precursor to this condition. The present study examined cross-sectional associations between grip strength, an established marker of physical function, and (i) depressive symptoms and (ii) chronic stress utilising hair cortisol concentrations, while accounting for multiple pertinent confounding variables.

Method: Data were used from wave 6 (2012/13) of the English Longitudinal Study of Ageing, a panel study of older (≥ 50 y) community-dwelling men and women. Grip strength was measured in kg using a handheld dynamometer. Depressive symptoms were assessed using the 8-item Center for Epidemiologic Studies Depression scale. Hair cortisol concentrations (pg/mg) were determined from samples of scalp hair and log-transformed for analysis to correct skewness. Associations of grip strength with depressive symptoms and hair cortisol concentration were tested using linear regression models adjusted for age, sex, ethnicity, wealth, smoking status, physical activity, body mass index, limiting long-standing illness, arthritis, diabetes, and hair treatment.

Results: The sample comprised 3,741 participants (mean age 68.4 years, 66.4% female). After adjustment for age and sex, grip strength was significantly and negatively associated with both depressive symptoms ($B=-0.038$, $SE=0.004$, $p<0.001$) and hair cortisol ($B=-0.003$, $SE=0.001$, $p=0.029$). However, in the fully-adjusted models, both associations were attenuated and only the association with depressive symptoms remained statistically significant ($B=-0.015$, $SE=0.004$, $p<0.001$; hair cortisol $B=-0.002$, $SE=0.001$, $p=0.088$).

Conclusion: In a large sample of older adults in England, grip strength was negatively associated with depressive symptoms. Results were inconclusive regarding the association between grip strength and chronic stress. Further research examining the longitudinal relationships between muscular strength and specific aspects of mental health, while also exploring the neurobiological mechanisms underlying these associations, is warranted before recommendations for policy and practice can be made.

Key words: grip strength; physical function; older adults; depression; depressive symptoms; stress; hair cortisol.

Introduction

The health benefits of aerobic physical activity are well established (1,2) although less is known about muscle strength. Handgrip strength is a valid measure of physical function/ performance (muscle strength) that has been widely used in observational cohort studies and clinical settings (3–5). A growing body of literature has shown that low grip strength is associated with non-communicable disease (6,7), mortality risk (8), as well as impaired cognitive functioning (9,10).

Handgrip strength has also been shown to be associated with depression (9,11,12). Two cross-sectional studies have identified an inverse association between handgrip strength and depression (13,14). Another study using a large population-based adult sample found that lower handgrip strength, standardised for age and sex, was both cross-sectionally and longitudinally associated with depressive symptoms (15). Other recent studies have found similar results (11,16). One area of mental health that is understudied in relation to grip strength is chronic stress, which can exist independently to depression, or as a comorbidity or precursor to this condition.

Chronic stress is associated with a plethora of physical health conditions (17,18), with the stress biomarker cortisol likely playing a pivotal role (19). Literature suggests that excessively accumulating life stress, not only diminishes health, but simultaneously reduces physical activity uptake (20). Indeed, both a reduction in physical health and low levels of physical activity have been shown to be associated with lower grip strength (7,21). Importantly, cortisol may be independently associated with grip strength as it stimulates degradation and inhibits synthesis of muscle proteins (22), and thus is feasibly associated with grip strength. A relationship between grip strength and stress is likely bidirectional; that is, stress may lead to lower grip strength via the mechanisms explained above and low grip strength (an indicator of frailty) may lead to higher chronic stress via, for example, reduced quality of life or increasing difficulty in completing daily tasks.

Previous research has already indicated that an inverse association exists between muscular strength and stress markers. For instance, one study among 26 middle-aged and 21 older healthy men found that serum cortisol levels were negatively related to muscle strength of the knee extensor (23). One other study has shown a relationship between higher cortisol and poorer physical performance (24). In analyses using data from the Longitudinal Aging Study Amsterdam it was found that high salivary cortisol was associated with a higher risk of loss of grip strength in older persons (22). However, this study failed to control for one important confounding variable, physical activity. Indeed, physical activity has been shown to be associated with grip strength (25,26) and cortisol levels (27,28).

Another limitation of the extant literature is the focus of the measurement of cortisol in saliva, serum, or urine. These capture real-time cortisol levels and are subject to substantial fluctuation throughout the day. By contrast, hair cortisol analysis captures accumulated cortisol exposure over longer periods and thus provides a better measure of chronic stress exposure (19). Because of its ability to provide a long-term measure of systemic cortisol exposure, it is possible that hair and salivary measures of cortisol do not entirely correlate, as has been shown in previous studies (29). The relationship between grip strength and chronic stress (measured using hair cortisol) is therefore not known.

The present study aimed to investigate the associations between grip strength and different aspects of mental health, by (i) replicating the previously indicated relationships between grip strength and depression, then (ii) examining whether grip strength is related to objective markers of chronic stress (utilising hair cortisol concentrations), while accounting for multiple pertinent confounding variables such as physical activity.

Method

Study population

The sample was drawn from men and women taking part in Wave 6 (2012/13) of the English Longitudinal Study of Ageing, a panel study of over-50s living in England (30). This wave of data collection is the only one to date to include hair sampling for analysis of cortisol levels. Ethics approval was granted by the London Multi-Centre Research Ethics Committee. All participants provided full informed consent.

Measures

Handgrip strength (kg) of the dominant hand was assessed using a hand held dynamometer, with the average of three measures used in the analyses, and analysed as a continuous variable.

Depressive symptoms were measured using the 8-item Center for Epidemiologic Studies Depression scale (CES-D), which asks about symptoms over the last month (e.g. "Over the last month have you felt sad?") with a binary response format (yes/no) (31). Positively worded items were reverse-coded and the items scores were summed for a total score ranging from 0 (no symptoms) to 8 (highest number of symptoms).

The hair cortisol assessment procedure has been described in detail elsewhere (32). Briefly, a scalp-proximal hair sample at least 2cm long and weighing at least 10mg was taken from the posterior

vertex of all eligible consenting participants, cut as close to the scalp as possible. The wash procedure and steroid extraction were undertaken using high performance liquid chromatography–mass spectrometry, as described by Gao et al. (33). Assuming an average hair growth of approximately 1cm per month (34), the scalp-nearest hair segment of 2cm represents average cortisol accumulated over an approximate time span of two months prior to sampling.

Potential confounders included age, sex, ethnicity (white, non-white), household non-pension wealth (a proxy for socioeconomic status shown to be particularly sensitive in this population (35); in quintiles across all individuals taking part in Wave 6 of ELSA), smoking status (current, never/former), level of physical activity (inactive, moderate at least once a week, vigorous at least once a week (36)), body mass index (BMI; in kg/m² based on objective measurements of height and weight), self-reported presence of a limiting long-standing illness (defined as any chronic illness, disability or infirmity that limits activities in any way), doctor-diagnosed arthritis and diabetes, and hair treatment (chemical treatment or dye).

Statistical analyses

Analyses were performed using IBM SPSS Statistics v.24. A log transformation was applied to hair cortisol data to correct the high degree of skewness. For descriptive purposes, Table 1 provides the mean and standard deviation (SD) hair cortisol concentration in original units (pg/mg). We used descriptive statistics to summarise the sample characteristics and linear regression models to analyse the associations between grip strength and (i) depressive symptoms and (ii) hair cortisol concentration. For each outcome, we constructed three regression models. The first was partially adjusted for age and sex (as these two variables are used for international benchmarks of grip strength). The second was adjusted for age, sex, and health behaviours (smoking, physical activity, BMI). The third was fully adjusted for multiple putative factors which could theoretically confound the relationships between grip strength and depressive symptoms and cortisol concentrations, including age, sex, smoking status, physical activity, BMI, ethnicity, wealth, limiting long-standing illness, arthritis, diabetes, and hair treatment. Results are presented as unstandardised betas (*B*) with standard errors (SE) and 95% confidence intervals (CI). *B* values represent the change in depressive symptoms or cortisol concentration (log pg/mg) associated with a 1kg increase in grip strength. Because CES-D scores were not normally distributed, we repeated models using log-transformed values as a sensitivity check.

Results

Of the 7,731 participants who took part in the Wave 6 nurse visit (in which hair samples and measures of physical performance were taken), measurements of grip strength was available for 7,502 participants. Due to financial constraints, hair analysis was only performed for a random subset of participants who provided hair samples ($n=4,726$). We excluded 577 participants who did not have detectable hair cortisol values and a further 408 with missing data on covariates, leaving a final sample for analysis of 3,741 participants.

There were 1,257 men and 2,484 women in the analysed sample, ranging in age from 54 to 89 years. Sample characteristics are summarised in Table 1. Participants were on average 68.4 years and the vast majority (97.9%) were white. The upper quintiles of wealth were overrepresented relative to the whole ELSA sample. One in ten was a current smoker, two in ten were inactive, and three in ten reported a limiting long-standing illness. The mean BMI was in the overweight range at 28.29 kg/m² (range 15.1 to 59.4 kg/m²). Relative to the total sample of ELSA participants who participated in the Wave 6 nurse visit, the analysed sample was more likely to be female, white, and wealthy. They had a higher mean BMI, but were more likely to be physically active and less likely to report a limiting long-standing illness, arthritis, or diabetes. Their mean grip strength was lower, they reported fewer depressive symptoms, but did not differ significantly on hair cortisol.

Mean grip strength was 28.22 (SD 10.47) kg; 38.39 (SD 9.25) kg for men and 23.08 (6.55) kg for women. The mean number of depressive symptoms reported was 1.23 (SD 1.79) and mean hair cortisol concentration was 26.21 (SD 68.83) pg/mg. After adjustment for age and sex, there was a significant negative association between grip strength and depressive symptoms (Table 2, Model 1). This association was attenuated but remained significant after additional adjustment for smoking status, physical activity, BMI, ethnicity, wealth, limiting long-standing illness, arthritis, diabetes, and hair treatment (Table 2, Models 2 and 3). The same results were observed when depressive symptoms were analysed with a log transformation applied (Model 1: $B=-0.005$, $SE=0.001$, $p<0.001$; Model 2: $B=-0.004$, $SE=0.001$, $p<0.001$; Model 3: $B=-0.002$, $SE=0.001$, $p=0.004$). There was also a significant negative association between grip strength and hair cortisol concentration in the age and sex-adjusted model (Table 3, Model 1). This remained significant after additional adjustment for smoking status, physical activity, and BMI (Table 3, Model 2) but was non-significant in the fully adjusted model (Table 3, Model 3).

Discussion

In this large sample of older adults in England, a significant inverse association between grip strength and depressive symptoms was observed, even when accounting for potentially confounding factors, thus replicating the recent emergent findings on the relationship between muscular strength and depression (11,13–16). To the best of our knowledge, for the first time we found a similar inverse association between grip strength and an objective marker of chronic stress (measured using hair cortisol) when controlling for age and sex. However, this relationship was attenuated and became non-significant after adjusting for additional sociodemographic, behavioural, and health-related factors.

Although the present findings confirm those of previous research showing grip strength to be associated with depressive symptoms (11,13–16), the causal mechanisms underlying this relationship have yet to be determined. One possibility is that depression may cause a decline in systemic physical functioning (37) through its association with adverse health behaviours. For instance, depressive symptoms – such as changes in appetite, sleep disturbances and reductions in physical activity – have the potential to change body composition and metabolism, thereby accelerating a decline in physical functioning over time (38). However, this cannot fully account for the relationships previously observed, as grip strength also seems protective for developing depression over time (15). In older adults, decreased muscle function is closely related to frailty, which has been shown to be highly comorbid with depression in cross-sectional and longitudinal studies (39). Moreover, in older age decreased muscle mass/strength and sarcopenia has been related to increased peripheral inflammation (40,41) and increased oxidative stress (42), both of which are closely related to the underpinning mechanisms of depression (43,44). Another important mechanism could be the fact that decreased functional performance results in reduced ability to undertake one's activities of daily living, increased fear of falling, and ultimately increased social isolation, which increases the risk of depression (45). Taken together it is likely that the relationship between depression and grip strength is bidirectional. Clearly, further research is warranted to disentangle mechanisms.

Whereas the above findings replicate previous research, our examination of the relationship between muscular strength and stress differs from previous research. While previous studies have reported a significant inverse relationship between grip strength and serum or salivary cortisol (22–24), we found no evidence of a significant association between grip strength and hair cortisol after adjustment for relevant confounders. This difference may be due to the types of cortisol measures used, as two previous studies comparing hair and salivary cortisol measurements in the same

individuals have not observed a significant correlation between the two measures (29,46). Specifically, these alternative measures of cortisol are thought to represent different types of stress, with saliva/serum cortisol representing acute stress and hair cortisol indicating chronic stress exposure. However, the discrepant findings between ours and previous studies might also be partially explained by inclusion of different covariates in the models. Indeed, the study by Peeters and colleagues did not control for physical activity, where the present study did (22). Further supporting this rationale, we found significant associations in our partially adjusted models.

Clear strengths of this study are the large sample, objective markers of chronic stress, and the inclusion of a wide range of potential confounders in the statistical modelling. However, findings from the present study must be interpreted in light of its limitations. The cross-sectional design means we are not able to draw any inferences on the direction of causation, i.e. whether low grip strength causes depressive symptoms/stress, whether depressive symptoms/stress cause a decline in grip strength, or whether low grip strength and depressive symptoms/stress are caused by a third factor. It is however likely that the relationship is bidirectional. Moreover, while we adjusted for a range of potential confounders in an effort to rule out the latter possibility, there may be residual confounding by unmeasured variables. Studies using a longitudinal design are required to shed light on this issue. In addition, while the sample was drawn from a representative sample of older adults living in England, there was a substantial amount of missing data due to participants being ineligible or not providing consent for hair sampling or measurement of grip strength, non-response to questionnaire items on depressive symptoms or covariates, and financial limitations on the processing and analysis of collected hair samples. Comparison of descriptive characteristics indicated the analysed sample differed from the total ELSA sample on a number of variables. As such, results may not be generalisable to the wider population of older adults in England. Finally, we did not test non-linear associations between grip strength and depressive symptoms or hair cortisol, or moderation of associations by sociodemographic or health-related factors (e.g. age, sex, presence of chronic disease). Future research exploring these issues could provide a useful addition to the literature.

Perspectives

Our findings confirm the association between grip strength and depressive symptoms, while also suggesting this relationship exists separately to chronic stress. Further research examining the longitudinal relationships between muscular strength and specific aspects of mental health, while also exploring the neurobiological mechanisms underlying these associations, is warranted.

References

1. Wienbergen H, Hambrecht R. [Physical exercise training for cardiovascular diseases]. *Herz*. 2012 Aug;37(5):486–92.
2. Zschucke E, Gaudlitz K, Ströhle A. Exercise and Physical Activity in Mental Disorders: Clinical and Experimental Evidence. *J Prev Med Pub Health*. 2013 Jan;46(Suppl 1):S12–21.
3. Giampaoli S, Ferrucci L, Cecchi F, Lo Noce C, Poce A, Dima F, et al. Hand-grip strength predicts incident disability in non-disabled older men. *Age Ageing*. 1999 May;28(3):283–8.
4. Rantanen T, Guralnik JM, Foley D, Masaki K, Leveille S, Curb JD, et al. Midlife hand grip strength as a predictor of old age disability. *JAMA J Am Med Assoc*. 1999 Feb 10;281(6):558–60.
5. Rantanen T, Avlund K, Suominen H, Schroll M, Frändin K, Pertti E. Muscle strength as a predictor of onset of ADL dependence in people aged 75 years. *Aging Clin Exp Res*. 2002 Jun;14(3 Suppl):10–5.
6. Pavasini R, Serenelli M, Celis-Morales CA, Gray SR, Izawa KP, Watanabe S, et al. Grip strength predicts cardiac adverse events in patients with cardiac disorders: an individual patient pooled meta-analysis. *Heart*. 2018 Nov 19;heartjnl-2018-313816.
7. Celis-Morales CA, Welsh P, Lyall DM, Steell L, Petermann F, Anderson J, et al. Associations of grip strength with cardiovascular, respiratory, and cancer outcomes and all cause mortality: prospective cohort study of half a million UK Biobank participants. *BMJ*. 2018 May 8;361:k1651.
8. Wu Y, Wang W, Liu T, Zhang D. Association of Grip Strength With Risk of All-Cause Mortality, Cardiovascular Diseases, and Cancer in Community-Dwelling Populations: A Meta-analysis of Prospective Cohort Studies. *J Am Med Dir Assoc*. 2017 Jun 1;18(6):551.e17-551.e35.
9. Firth J, Firth JA, Stubbs B, Vancampfort D, Schuch FB, Hallgren M, et al. Association Between Muscular Strength and Cognition in People With Major Depression or Bipolar Disorder and Healthy Controls. *JAMA Psychiatry*. 2018 Jul 1;75(7):740–6.
10. Firth J, Stubbs B, Vancampfort D, Firth JA, Large M, Rosenbaum S, et al. Grip Strength Is Associated With Cognitive Performance in Schizophrenia and the General Population: A UK Biobank Study of 476559 Participants. *Schizophr Bull*. 2018 06;44(4):728–36.
11. Smith L, White S, Stubbs B, Hu L, Veronese N, Vancampfort D, et al. Depressive symptoms, handgrip strength, and weight status in US older adults. *J Affect Disord*. 2018 Oct 1;238:305–10.
12. Rijk JM, Roos PR, Deckx L, Akker M van den, Buntinx F. Prognostic value of handgrip strength in people aged 60 years and older: A systematic review and meta-analysis. *Geriatr Gerontol Int*. 2016;16(1):5–20.
13. Gale CR, Sayer AA, Cooper C, Dennison EM, Starr JM, Whalley LJ, et al. Factors associated with symptoms of anxiety and depression in five cohorts of community-based older people: the HALCYon (Healthy Ageing across the Life Course) Programme. *Psychol Med*. 2011 Oct;41(10):2057–73.

14. van Milligen BA, Lamers F, de Hoop GT, Smit JH, Penninx BWJH. Objective physical functioning in patients with depressive and/or anxiety disorders. *J Affect Disord*. 2011 Jun;131(1–3):193–9.
15. Fukumori N, Yamamoto Y, Takegami M, Yamazaki S, Onishi Y, Sekiguchi M, et al. Association between hand-grip strength and depressive symptoms: Locomotive Syndrome and Health Outcomes in Aizu Cohort Study (LOHAS). *Age Ageing*. 2015 Jul 1;44(4):592–8.
16. Veronese N, Stubbs B, Trevisan C, Bolzetta F, De Rui M, Solmi M, et al. Poor Physical Performance Predicts Future Onset of Depression in Elderly People: Progetto Veneto Anziani Longitudinal Study. *Phys Ther*. 2017 Jun 1;97(6):659–68.
17. Schoenthaler AM, Rosenthal DM. Stress and Hypertension. In: Berbari AE, Mancina G, editors. *Disorders of Blood Pressure Regulation: Phenotypes, Mechanisms, Therapeutic Options* [Internet]. Cham: Springer International Publishing; 2018 [cited 2019 Feb 27]. p. 289–305. (Updates in Hypertension and Cardiovascular Protection). Available from: https://doi.org/10.1007/978-3-319-59918-2_19
18. Kivimäki M, Steptoe A. Effects of stress on the development and progression of cardiovascular disease. *Nat Rev Cardiol*. 2018 Apr;15(4):215–29.
19. Russell E, Koren G, Rieder M, Van Uum S. Hair cortisol as a biological marker of chronic stress: Current status, future directions and unanswered questions. *Psychoneuroendocrinology*. 2012 May 1;37(5):589–601.
20. Cowley J, Kiely J, Collins D. Is there a link between self-perceived stress and physical activity levels in Scottish adolescents? *Int J Adolesc Med Health*. 2017 Jul 18;31(1).
21. Haider S, Luger E, Kapan A, Titze S, Lackinger C, Schindler KE, et al. Associations between daily physical activity, handgrip strength, muscle mass, physical performance and quality of life in prefrail and frail community-dwelling older adults. *Qual Life Res*. 2016;25(12):3129–38.
22. Peeters GMEE, Schoor NMV, Rossum EFCV, Visser M, Lips P. The relationship between cortisol, muscle mass and muscle strength in older persons and the role of genetic variations in the glucocorticoid receptor. *Clin Endocrinol (Oxf)*. 2008 Oct 1;69(4):673–82.
23. Izquierdo M, Häkkinen K, Antón A, Garrues M, Ibañez J, Ruesta M, et al. Maximal strength and power, endurance performance, and serum hormones in middle-aged and elderly men. *Med Sci Sports Exerc*. 2001 Sep;33(9):1577–87.
24. Peeters GMEE, van Schoor NM, Visser M, Knol DL, Eekhoff EMW, de Ronde W, et al. Relationship between cortisol and physical performance in older persons. *Clin Endocrinol (Oxf)*. 2007 Sep;67(3):398–406.
25. Kuh D, Basseij EJ, Butterworth S, Hardy R, Wadsworth MEJ. Grip Strength, Postural Control, and Functional Leg Power in a Representative Cohort of British Men and Women: Associations With Physical Activity, Health Status, and Socioeconomic Conditions. *J Gerontol Ser A*. 2005 Feb 1;60(2):224–31.
26. Rantanen T, Era P, Kauppinen M, Heikkinen E. Maximal Isometric Muscle Strength and Socioeconomic Status, Health, and Physical Activity in 75-Year-Old Persons. *J Aging Phys Act*. 1994 Jul 1;2(3):206–20.

27. Heaney JLJ, Carroll D, Phillips AC. Physical Activity, Life Events Stress, Cortisol, and DHEA: Preliminary Findings That Physical Activity May Buffer Against the Negative Effects of Stress. *J Aging Phys Act.* 2014 Oct 1;22(4):465–73.
28. Rimmele U, Seiler R, Marti B, Wirtz PH, Ehlert U, Heinrichs M. The level of physical activity affects adrenal and cardiovascular reactivity to psychosocial stress. *Psychoneuroendocrinology.* 2009 Feb 1;34(2):190–8.
29. Sauvé B, Koren G, Walsh G, Tokmakejian S, Van Uum SHM. Measurement of cortisol in human hair as a biomarker of systemic exposure. *Clin Investig Med Med Clin Exp.* 2007;30(5):E183-191.
30. Steptoe A, Breeze E, Banks J, Nazroo J. Cohort profile: the English Longitudinal Study of Ageing. *Int J Epidemiol.* 2013 Dec;42(6):1640–8.
31. Steffick DE. Documentation of affective functioning measures in the Health and Retirement Study. HRS Documentation Report DR-005; 2000.
32. Jackson SE, Kirschbaum C, Steptoe A. Hair cortisol and adiposity in a population-based sample of 2,527 men and women aged 54 to 87 years. *Obesity.* 2017;25(3):539–44.
33. Gao W, Stalder T, Foley P, Rauh M, Deng H, Kirschbaum C. Quantitative analysis of steroid hormones in human hair using a column-switching LC-APCI-MS/MS assay. *J Chromatogr B Analyt Technol Biomed Life Sci.* 2013 Jun 1;928:1–8.
34. Kintz P, Villain M, Cirimele V. Hair Analysis for Drug Detection: *Ther Drug Monit.* 2006 Jun;28(3):442–6.
35. Banks J, Karlsen S, Oldfield Z. Socio-economic position. 2003 [cited 2014 Mar 4]; Available from: <http://discovery.ucl.ac.uk/15366/1/15366.pdf>
36. Hamer M, Lavoie KL, Bacon SL. Taking up physical activity in later life and healthy ageing: the English longitudinal study of ageing. *Br J Sports Med.* 2014 Feb 1;48(3):239–43.
37. Penninx BW, Leveille S, Ferrucci L, van Eijk JT, Guralnik JM. Exploring the effect of depression on physical disability: longitudinal evidence from the established populations for epidemiologic studies of the elderly. *Am J Public Health.* 1999 Sep;89(9):1346–52.
38. Lenze EJ, Rogers JC, Martire LM, Mulsant BH, Rollman BL, Dew MA, et al. The association of late-life depression and anxiety with physical disability: a review of the literature and prospectus for future research. *Am J Geriatr Psychiatry Off J Am Assoc Geriatr Psychiatry.* 2001;9(2):113–35.
39. Soysal P, Veronese N, Thompson T, Kahl KG, Fernandes BS, Prina AM, et al. Relationship between depression and frailty in older adults: A systematic review and meta-analysis. *Ageing Res Rev.* 2017 Jul;36:78–87.
40. Soysal P, Stubbs B, Lucato P, Luchini C, Solmi M, Peluso R, et al. Inflammation and frailty in the elderly: A systematic review and meta-analysis. *Ageing Res Rev.* 2016;31:1–8.
41. Schaap LA, Pluijm SMF, Deeg DJH, Harris TB, Kritchevsky SB, Newman AB, et al. Higher Inflammatory Marker Levels in Older Persons: Associations With 5-Year Change in Muscle Mass and Muscle Strength. *J Gerontol Ser A.* 2009 Nov 1;64A(11):1183–9.

42. Bano G, Trevisan C, Carraro S, Solmi M, Luchini C, Stubbs B, et al. Inflammation and sarcopenia: A systematic review and meta-analysis. *Maturitas*. 2017 Feb;96:10–5.
43. Köhler CA, Freitas TH, Maes M, de Andrade NQ, Liu CS, Fernandes BS, et al. Peripheral cytokine and chemokine alterations in depression: a meta-analysis of 82 studies. *Acta Psychiatr Scand*. 2017 May;135(5):373–87.
44. Liu T, Zhong S, Liao X, Chen J, He T, Lai S, et al. A Meta-Analysis of Oxidative Stress Markers in Depression. *PloS One*. 2015;10(10):e0138904.
45. Choi H, Irwin MR, Cho HJ. Impact of social isolation on behavioral health in elderly: Systematic review. *World J Psychiatry*. 2015 Dec 22;5(4):432–8.
46. Steudte S, Stalder T, Dettenborn L, Klumbies E, Foley P, Beesdo-Baum K, et al. Decreased hair cortisol concentrations in generalised anxiety disorder. *Psychiatry Res*. 2011 Apr 30;186(2–3):310–4.

Table 1 Sample characteristics

	ELSA Wave 6 nurse visit sample (n=7731)	Analysed sample (n=3741)	<i>p</i> (analysed vs. excluded)
Age (years), mean (SD)	68.53 (8.19)	68.40 (7.98)	0.161
Sex			
Men	44.7	33.6	<0.001
Women	55.3	66.4	-
Ethnicity			
White	97.1	97.9	<0.001
Non-white	2.9	2.1	-
Wealth quintile			
1 (poorest)	15.6	14.0	<0.001
2	18.3	17.9	-
3	21.4	21.3	-
4	22.4	22.6	-
5 (richest)	22.3	24.3	-
Smoking status			
Non-smoker	89.3	89.8	0.110
Smoker	10.7	10.2	-
Physical activity			
Inactive	24.4	20.7	<0.001
Moderate at least once a week	46.6	48.7	-
Vigorous at least once a week	29.0	30.6	-
Body mass index, mean (SD)	26.98 (7.95)	28.29 (5.33)	<0.001
Limiting long-standing illness			
No	64.0	67.5	<0.001
Yes	36.0	32.5	-
Arthritis			
No	57.2	58.6	0.010
Yes	42.8	41.4	-
Diabetes			
No	87.9	89.1	0.001
Yes	12.1	10.9	-
Grip strength (kg), mean (SD)	29.90 (11.36)	28.22 (10.47)	<0.001
Depressive symptoms (range 0-8), mean (SD)	1.32 (1.87)	1.23 (1.79)	<0.001
Hair treatment			
No	97.2	97.1	0.368
Yes	2.8	2.9	-
Hair cortisol concentration (pg/mg), mean (SD)	26.30 (69.26)	26.21 (68.83)	0.838

Values are percentages unless otherwise stated. Means and percentages for the total Wave 6 nurse visit sample are provided for participants with available data.

SD = standard deviation.

Table 2 Associations between grip strength and depressive symptoms

	Model 1				Model 2				Model 3			
	<i>B</i>	SE	95% CI	<i>p</i>	<i>B</i>	SE	95% CI	<i>p</i>	<i>B</i>	SE	95% CI	<i>p</i>
Grip strength	-0.038	0.004	-0.047; -0.030	<0.001	-0.030	0.004	-0.038; -0.022	<0.001	-0.015	0.004	-0.023; -0.007	<0.001
Age	-0.013	0.004	-0.020; -0.005	0.001	-0.016	0.004	-0.024; -0.009	<0.001	-0.018	0.004	-0.026; -0.011	<0.001
Female sex	-0.040	0.088	-0.213; 0.133	0.651	-0.012	0.086	-0.180; 0.156	0.889	0.123	0.084	-0.043; 0.288	0.146
Current smoker	-	-	-	-	0.607	0.094	0.422; 0.791	<0.001	0.438	0.093	0.255; 0.620	<0.001
Physical activity	-	-	-	-	-0.467	0.043	-0.551; -0.382	<0.001	-0.286	0.043	-0.371; -0.201	<0.001
Body mass index	-	-	-	-	-0.025	0.005	0.015; 0.036	<0.001	0.005	0.005	-0.005; 0.016	0.317
Non-white ethnicity	-	-	-	-	-	-	-	-	0.341	0.189	-0.030; 0.711	0.072
Wealth	-	-	-	-	-	-	-	-	-0.153	0.021	-0.195; -0.111	<0.001
Limiting long-standing illness	-	-	-	-	-	-	-	-	0.715	0.064	0.589; 0.840	<0.001
Arthritis	-	-	-	-	-	-	-	-	0.199	0.059	0.082; 0.315	0.001
Diabetes	-	-	-	-	-	-	-	-	0.268	0.090	0.092; 0.444	0.003
Hair treatment	-	-	-	-	-	-	-	-	0.421	0.162	0.103; 0.739	0.009

SE = standard error; CI = confidence interval.

Model 1 was adjusted for age and sex.

Model 2 was adjusted for age, sex, smoking status, physical activity, and body mass index.

Model 3 was adjusted for age, sex, smoking status, physical activity, body mass index, ethnicity, wealth, limiting long-standing illness, arthritis, diabetes, and hair treatment.

Table 3 Associations between grip strength and hair cortisol

	Model 1				Model 2				Model 3			
	<i>B</i>	SE	95% CI	<i>p</i>	<i>B</i>	SE	95% CI	<i>p</i>	<i>B</i>	SE	95% CI	<i>p</i>
Grip strength	-0.003	0.001	-0.006; 0.000	0.029	-0.003	0.001	-0.006; 0.000	0.036	-0.002	0.001	-0.005; 0.000	0.088
Age	0.001	0.001	-0.001; 0.004	0.402	0.002	0.001	-0.001; 0.004	0.248	0.001	0.001	-0.001; 0.004	0.263
Female sex	-0.103	0.029	-0.159; -0.047	<0.001	-0.109	0.029	-0.165; -0.053	<0.001	-0.104	0.029	-0.160; -0.047	<0.001
Current smoker	-	-	-	-	0.064	0.031	0.003; 0.125	0.041	0.058	0.032	-0.005; 0.121	0.069
Physical activity	-	-	-	-	-0.010	0.014	-0.038; 0.018	0.492	-0.004	0.015	-0.033; 0.026	0.806
Body mass index	-	-	-	-	0.010	0.002	0.006; 0.013	<0.001	0.009	0.002	0.005; 0.013	<0.001
Non-white ethnicity	-	-	-	-	-	-	-	-	0.025	0.065	-0.102; 0.153	0.695
Wealth	-	-	-	-	-	-	-	-	-0.006	0.007	-0.020; 0.008	0.420
Limiting long-standing illness	-	-	-	-	-	-	-	-	0.020	0.022	-0.023; 0.063	0.370
Arthritis	-	-	-	-	-	-	-	-	0.002	0.020	-0.038; 0.042	0.921
Diabetes	-	-	-	-	-	-	-	-	0.023	0.031	-0.038; 0.083	0.461
Hair treatment	-	-	-	-	-	-	-	-	0.016	0.056	-0.094; 0.125	0.779

SE = standard error; CI = confidence interval.

Model 1 was adjusted for age and sex.

Model 2 was adjusted for age, sex, smoking status, physical activity, and body mass index.

Model 3 was adjusted for age, sex, smoking status, physical activity, body mass index, ethnicity, wealth, limiting long-standing illness, arthritis, diabetes, and hair treatment.