

The association between adverse childhood experiences and muscle strength in older age

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Words: 3'384

Tables: 1

Figures: 1

Supplemental materials: 6

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Paper accepted for publication in Gerontology (October 2018)



Abstract

Background: Muscle weakness – a biomarker of health – may have its origins in early life and be related to factors such as adverse childhood experiences (ACE), which refers to a set of early-life traumatic and stressful psychosocial events out of the child's control. To date, evidence of an association between ACE and muscle strength in older age is lacking.

Objective: Here, we assessed the associations between ACE during the first 15 years of life and the risk of low muscle strength (LMS) later in life. We also examined whether adult-life socioeconomic circumstances (i.e., educational attainment, main occupational position, and satisfaction with household financial situation) and unhealthy behaviours (i.e., physical inactivity, unhealthy eating, smoking, and high level of alcohol consumption) explained this association.

Methods: We used data from the Survey of Health Ageing and Retirement in Europe, a 12-year cohort study with 6 repeated measurements between 2004 and 2015. Muscle strength was measured using a handheld dynamometer. Confounder-adjusted logistic mixed-effect models were used to examine the associations between ACE (child in care, parental death, parental mental illness, parental drinking, period of hunger, property taken away) and the risk of LMS in older age.

Results: 24,179 participants (96,372 observations; 13,477 women) aged 50-96 living in 14 countries were included. LMS increased with age for both genders. For women, there was a gradual increase of the risks of LMS with the number of experienced ACE (ORs =1.22 for one ACE, 1.74 for two or more ACE, compared to no ACE). However, there was no significant association among men. This association was only slightly attenuated when adjusting for socioeconomic circumstances and unhealthy behaviours in adulthood.

Conclusions: ACE are associated with later-life muscle weakness among women. These associations were not compensated by the adoption of healthy behaviours or an improvement in socioeconomic circumstances in adulthood. These results suggest that tackling these early-life risk factors in women could promote long-term grip strength, a biomarker of ageing.

Keywords: childhood misfortune, grip strength, health, ageing, gender

Introduction

Muscle weakness, as measured by grip strength, is a biomarker of ageing [1] and has been shown to predict a range of adverse health outcomes including future disability [2,3], morbidity [2,4], and mortality [5-7]. Because of its high prognostic value, a better understanding of the factors influencing the decline of muscle strength as adults grow older is important.

Muscle weakness may have its origins in early life and therefore be associated with risk factors such as childhood socioeconomic circumstances [8-10] and adverse childhood experiences (ACE), which is defined as a set of early-life traumatic and stressful psychosocial events out of the child's control (e.g., parental separation, mental illness, or death) [10-12]. These early-life events may influence muscle strength through socioeconomic, behavioural, and biological mechanisms [13]. For example, individuals from disadvantaged childhood socioeconomic backgrounds and who experienced ACE are more likely to engage in unhealthy and risky behaviours (e.g., smoking, alcohol consumption) [14,15] and develop physiological wear-and-tear in response to chronic stress [16,17]. This stress hypothesis is based on previous studies showing that the physiological stress response and immune systems are developed and calibrated by early life experiences [18]. For example, children suffering from chronic stress build up higher levels of the stress hormone cortisol, making the body's response to threats more pronounced [19]. As such, early-life chronic stress has been found to be linked to a host of diseases [20] through mechanisms including the dysregulation of the immune system [21].

Although some studies have found that ACE are associated with poorer objective physical capability [11], very few studies have assessed whether these associations are independent of childhood socioeconomic circumstances [10,11]. Yet, socioeconomic disadvantage and adverse experiences in childhood co-occur [22-24]. As such, adjusting for socioeconomic circumstances during childhood is required to examine the independent association of ACE with muscle strength. Furthermore, to the best of our knowledge, no study has assessed the associations between ACE and muscle strength or any other objective measure of physical function in adults aged 65+. Accordingly, evidence for an independent association of ACE with objectively measured muscle strength in older age has not been investigated yet.

The objective of this study was to assess the association between ACE and risk of low muscle strength (LMS) at older age, independently of childhood socioeconomic circumstances. We also examined whether this association is explained by socioeconomic circumstances and

health-related behaviours in adulthood. We hypothesized, in line with the stress hypothesis, that individuals who experienced ACE would show a higher risk of LMS at older age (H1) and show a higher rate of increased risk of LMS with ageing (H2). We further expected that the associations between ACE and LMS would be partly explained by adult-life socioeconomic circumstances and unhealthy lifestyle behaviours (H3).

Methods

Study population and design

Data were retrieved from the Survey of Health Ageing and Retirement in Europe (SHARE), a longitudinal (12-years; 2004-2015; 6 waves of data collected every 2 years), European, and retrospective database of individuals aged 50 or older [25]. Muscle strength was assessed at each of the 6 waves. Retrospective life-course data including ACE were collected in the third wave. We included data for participants aged 50 to 96 years, who participated in the third wave and had at least one observation of muscle strength. Participants with no information on their childhood life history, adult-life socioeconomic circumstances or healthy behaviours were excluded. Supplementary Table S1 shows the flow diagram of participant inclusion. Supplemental materials 1 and 2 show more details on the design and all measures described below.

Measures

ACE

ACE were identified as a set of traumatic events (emotional, physical, or linked to household dysfunction) occurring during childhood and being out of a child's control [14]. We carefully screened SHARE for variables that matched this definition. The following binary indicators reflecting specific ACE (from 0 to 15 years) were included: child in care (living in a children's home or with a foster family), parental death (father, mother or both), parental mental illness, parental drinking abuse, period of hunger, and property taken away. Consistent with previous studies [26], by combining these 6 indicators, we computed a three-level categorical variable of participants with no ACE (i.e., participants who only answered "no"), one ACE (i.e., participants who answered "yes" at one indicator only), and with two or more ACE (i.e., participants who answered "yes" at least twice). When information was missing for some indicators, the score was calculated using the non-missing data.

Outcome

Grip strength was measured twice in both hands, alternating between the hands, using a handheld dynamometer (Smedley, S Dynamometer, TTM, Tokyo, 100 kg). Participants were instructed to stand (preferably) or sit, with the elbow at a 90° angle, the wrist in neutral position, and to keep the upper arm tight against the trunk. Interviewers applied standardized instructions to ensure that the grip strength was performed with maximum effort. The mean of the maximum values obtained for each hand was used as an indicator of muscle strength [5,8]. When values for one hand were missing or were equal to 0, the measurement at this time point was excluded from the analysis. Then, consistent with previous literature, the cut-off for LMS was computed based on gender and body mass index quartiles [27,28] following the Fried criterion (i.e., grip strength in the lowest 20% adjusted for gender and body mass index). For men with body mass index (BMI) lower or equal to 24, between 24 and 26, between 26 to 28, and higher than 28 kg/m², the cut-offs for LMS were ≤ 26, 29, 30, and 32 kg, respectively. For women with BMI lower or equal to 23, between 23 and 26, between 26 and 28, and higher than 28 kg/m², the cut-offs for LMS were 17, 17.3, 18, and 21 kg, respectively.

Explanatory variables

Adult-life socioeconomic circumstances. The following variables were included: highest educational attainment, main occupational position during adult life, and satisfaction with household financial situation.

Unhealthy behaviours. The following self-reported behaviours were included: physical inactivity, unhealthy eating, smoking, and alcohol consumption.

Covariates

We considered childhood socioeconomic circumstances [29], birth cohorts, countries, attrition, childhood health problems (long or multiple hospitalisations, childhood illness, and childhood serious health condition), and height as covariates.

Statistical analysis

To account for the nested structure of the data (multiple observations within a single individual), logistic mixed-effect models were used [30]. Analyses were stratified by gender because previous studies have shown potential differences between women and men disease development over the life course [26]. Model 0 tested the association between ACE and the risk of LMS, adjusting for height only. Height was controlled for because it has been shown to be

strongly correlated with grip strength [3,5] and to be socioeconomically patterned (low socioeconomic position is associated with shorted height) [31,32]. As such, adjusting for height is deemed necessary to ensure that the association observed between ACE and muscle strength did not simply result from differences in height. Model 1 tested the association between ACE and the risk of LMS, adjusting for childhood socioeconomic circumstances, birth cohort, attrition, childhood health problems, and height. Age was centred at the midpoint of the age range (73 years) and divided by ten so that the coefficient yielded effects of increase in risk of LMS over a 10-year period (model 1). Additionally, an interaction term between ACE and age was added to test whether ACE moderated the effect of age on the risk of LMS (model 1b). Highest educational attainment (model 2), main occupational position during adult life (model 3), satisfaction with household financial situation (model 4), and unhealthy behaviours (model 5) were added as potential explanatory variables. Interaction terms between these variables and age were also tested (models 2b, 3b, 4b, and 5b).

We performed the following 6 sensitivity analyses: 1) assessing ACE exposure until 18 years, 2) assessing ACE exposure until 20 years, 3) controlling for the following chronic conditions: self-reported heart attack, high blood pressure, stroke, diabetes, chronic lung disease, Parkinson's disease, or cancer, 4) excluding participants who dropped out for reasons other than death, 5) excluding participants who died during the survey, and 6) modeling grip strength as a continuous variable. The rationale and main results of these sensitivity analyses are presented in the supplemental materials. Statistical analyses were performed using the R language and the lme4 and lmerTest packages [33-35].

Results

Descriptive results

Table 1 shows the characteristics of the analytical sample stratified by gender. The sample included 24,179 participants (96,372 observations; 13,477 women [55.7%]) living in 14 European countries. LMS was less frequent in men than women (-3.14%, $p < 0.001$). Men reported slightly more ACE than women, but this difference was not significant. Women had a lower level of educational attainment, lower main occupational position during adult life, a lower satisfaction with household financial situation, and reported less unhealthy-related behaviours than men ($ps < 0.001$).

Minimally adjusted model (Model 0)

For women, results of the model adjusted for height only, showed a gradual increase of the odds of LMS with the number of experienced ACE (ORs=1.41, $p=0.003$ for having reported one ACE and 1.98, $p=0.003$ for two or more ACE).

For men, results showed that the odds of LMS were greater for men who had reported one ACE (OR=1.33 $p=0.036$). The association with having reported two or more ACE was, however, only marginal (OR=1.56, $p=0.099$) (Table 2).

Association of ACE with LMS (Model 1)

For women, the odds of LMS increased 4.77-fold every ten years ($p<0.001$). The odds of LMS were greater for women who grew up in disadvantaged childhood socioeconomic circumstances (e.g., advantaged childhood socioeconomic circumstances were associated with a decreased risk of LMS compared with most disadvantaged childhood socioeconomic circumstances; OR=0.64, $p=0.006$). Compared to women with no ACE, the odds of LMS were greater for women who had reported one ACE (OR=1.22, $p=0.033$). For women who had reported two or more ACE, the odds of LMS were even higher (OR=1.74, $p=0.002$) (Table 2 and Figure 1). Interactions between ACE and age were not significant (See Supplemental materials Table S2).

For men, the odds of LMS increased 10.59-fold every 10 years ($p<0.001$). The odds of LMS were greater for men who grew up in disadvantaged childhood socioeconomic circumstances compared to men who grew up in most disadvantaged childhood socioeconomic circumstances (OR=0.72, $p=0.010$). The odds of LMS were not significantly associated with ACE (ORs=1.17, $p=0.165$ for having reported one ACE and 1.30, $p=0.230$ for two or more ACE; Table 3 and Figure 1). Interactions between ACE and age were not significant. (See supplemental materials Table S2).

Associations of adult-life socioeconomic circumstances and unhealthy-related behaviours with LMS (models 2-5)

For women, the association between ACE and the odds of LMS was only slightly attenuated with the addition of adult-life socioeconomic circumstances and unhealthy behaviours. The associations remained significant for women who had reported two or more ACE (OR=1.55, $p=0.011$) but not for women who had reported one ACE (OR=1.16, $p=0.107$). The odds of LMS were greater for women with lower educational attainment (OR=1.97, $p<0.001$; model 2), a disadvantaged main occupational position in adulthood (OR=1.98, $p<0.001$; model 3), a lower

satisfaction with household financial situation (ORs=1.46, 2.51, 5.45, p s<0.001; model 4), and a higher number of unhealthy-related behaviours (OR=4.65, p <0.001; model 5). The interactions between these explanatory variables and age were not significant.

For men, the associations between ACE and the odds of LMS remained non-significant. The odds of LMS were greater for men with a disadvantaged main occupational position in adulthood (OR=1.83, p <0.001; model 3), a lower satisfaction with household financial situation (ORs=1.85 and 3.22, p s<0.001; model 4), and a higher number of unhealthy-related behaviours (OR=3.08, p <0.001; model 5), but not with educational attainment (OR=1.16, p =0.206; model 2). The interactions between these explanatory variables and age were not significant.

Sensitivity analyses

Results of the 6 sensitivity analyses were consistent with those of the main analyses, except for the association between having reported one ACE and LMS in women which became marginal in some models (Supplementary Table S3).

Discussion

Main findings

This study aimed to assess the associations between ACE during the first 15 years of life and the risk of LMS later in life, and whether adult-life socioeconomic circumstances and unhealthy behaviours partly explained these associations. Based on previous literature and theoretical models, we hypothesized that individuals who experienced ACE would show a higher risk of LMS at older age (H1) and would show a higher rate of increased risk of LMS with ageing (H2). Additionally, we expected that the associations between ACE and risk of LMS would be only partially explained by adult-life socioeconomic circumstances and unhealthy behaviours (H3). In this large European study, consistent with H1, we found that ACE were associated with an increased risk of LMS in women, independently of socioeconomic circumstances during childhood. However, there was no strong evidence of associations among men. Our H2 was not confirmed, however, since we did not observe an association between ACE and the increased risk of LMS with ageing in both men and women. Finally, consistent with H3, adjustment for adult-life socioeconomic circumstances (i.e., education, main occupational position, and satisfaction with household financial situation) and unhealthy behaviours (i.e., physical inactivity, unhealthy eating, smoking, and alcohol consumption) did not explain the association between ACE and risk of LMS among women.

Comparison with previous studies

Our study showed that ACE was associated with a higher risk of LMS in older women, independently of socioeconomic circumstances during childhood. To our knowledge, this study was the first one to find evidence for this unique association between ACE and muscle weakness in older age. Indeed, although a few previous studies have found ACE and objective measures of physical capability to be associated, these associations did not remain significant after adjusting for childhood socioeconomic circumstances [10,11]. Three factors could explain this discrepancy. Our study used a single indicator to assess physical capability, whereas the two previous studies used a composite score involving grip strength, chair rise time, one-leg standing balance with eyes closed, and walking speed. Scores derived from a single test (grip strength) are likely more stable than scores derived from multiple tests. Additionally, grip strength may be more strongly associated with ACE than other physical indicators. Finally, the samples of the previous studies were smaller ($n = 2,221$ and $5,362$), younger (middle life and 60-64), and involved only British adults.

In our study, ACE were associated with an increased risk of LMS in women only. These results may be explained by gender differences in the puberty period, which occurs later in men and involves different physiological processes [36]. For muscle tissue, puberty induces change of cell metabolism and typology, associated to an increased muscle growth. These muscle maturation occurs at the end of adolescence for women whereas boys achieve it in young adulthood [37,38]. Muscle tissue maturation occurs earlier for women with a fibre diameter peaking during adolescence, whereas boys achieve this peak in young adulthood [38,39]. This result suggests that events occurring before this developmental period may have a small influence on muscle growth, whereas events occurring during this period may be particularly influential and have a permanent effect on muscle function for the rest of the life. In addition, gender differences may be linked to the fact that women are more susceptible to cumulative disadvantage over the life course compared to men [40]. For instance, women generally reach a lower level of education, earn less, and are more likely to sacrifice their professional careers to take care of their child [41].

In line with previous studies, adjustment for adult-life socioeconomic circumstances and health-related behaviours did not explain the association between ACE and physical function [42]. A

potential explanation of this result is linked to the chronic stress hypothesis [43,44]. Stress response and immune systems are shaped and calibrated by early life experiences [18]. Chronic stress in childhood can lead to a cumulative wear-and-tear effect on the physiological systems that governs individuals' response to their environment, permanently altering the equilibrium and reactivity of these systems leading to long-lasting consequences on health. Difficult life events, such as parental drinking abuse or separation from caregivers are associated with higher levels of stress that can permanently disrupt the ability to be healthy in older age.

Disadvantaged socioeconomic circumstances and unhealthy-related behaviours during adulthood were associated with an increased risk of LMS for both genders. These associations between adulthood socioeconomic circumstances and physical performance are consistent with previous studies [45] and with the stress hypothesis, as disadvantaged adulthood socioeconomic circumstances strongly correlates with chronic stress [43,44]. In addition, the results for unhealthy behaviours were expected as physical inactivity, unhealthy eating, smoking, and alcohol consumption have an adverse impact on the musculoskeletal system. These findings confirm that adopting healthy lifestyle behaviours, such as physical activity, may improve physical function even at older ages [46]. They also reinforce the importance of adopting a life course approach to better understand (un)healthy ageing [47].

Strengths and weaknesses

To the best of our knowledge, this study was the first to assess the association between ACE and an objective measure of muscle strength in older age. Our longitudinal study used a large sample of men and women aged 50-96 from 14 European countries. We examined the risk of LMS in relation to ACE after taking into account childhood socioeconomic circumstances, thereby reducing the effect of confounders related to early-life conditions. In 2050, one in four Europeans should be aged 65 and older [48]. These findings revealing a unique association between adversities in early-life and a biomarker of health in older age are important in this context of an ageing population.

However, there are some limitations that should be noted. First, ACE information was retrospectively self-reported during adult life, leading to potential recall bias. Previous studies showed that retrospective recall measures of exposure to adverse life events in childhood showed satisfactory validity [49] and that retrospective measures of adversity during childhood underestimated the association with objectively assessed health outcomes [50]. Therefore, the

associations observed between ACE and our objective measure emerged despite this bias associated with the retrospective nature of the design, not because of it. In contrast, this bias requires cautious interpretation of the non-significant associations, especially among men. Second, because of the longitudinal design (i.e., 6 waves of measurement over 12 years) and the old age of the participants, a selection bias due to attrition cannot be excluded. To minimize this bias, we performed statistical analyses adjusted for attrition (i.e., for participants who died or dropped out during the follow-up) and conducted sensitivity analyses without participants who died or dropped out during the follow-up, which yielded similar results. Third, the adverse events available in SHARE to construct the ACE score were not exactly the same as those used in the previous literature [14]. Thus, comparison of our results with previous studies should be done cautiously. Fourth, although grip strength has been shown to predict a range of adverse health outcomes [2-7] and is considered as a biomarker of ageing [1], using other indicators of physical performance (e.g., chair stand, walking speed, balance) should draw a broader picture of the individual's physical capability. Finally, although main occupational position during adult life is associated with the physical job demands (i.e., higher skill levels require less physical or manual tasks than lower skill levels), the objective level of exercise during daily work was not controlled for in this study. Assessing the association between objective daily work physical demands and grip strength will be important in future research.

Conclusion and policy implications

Our results reveal that ACE are associated with an increased risk of LMS in older women, independently of childhood socioeconomic circumstances. This risk is not offset by the adoption of healthy behaviours or an improvement in socioeconomic circumstances in adulthood. These findings reveal that in women, childhood events out of their control are linked to long-term grip strength, a biomarker of healthy ageing, thereby suggesting that a tougher start in life has a direct and long-lasting effect on women's health. They reinforce the importance of considering the public health implications of ACE and the necessity to develop both primary prevention programs aimed at reducing them [12] and secondary prevention interventions to mitigate their negative impact over the lifecourse. However, as this is the first study to assess the association between ACE and an objective measure of muscle strength in older age, further research is needed to confirm our findings.

Contributors

B.C, S.C. designed the analyses. B.C. analysed the data. B.C., S.C., M.P.B. drafted the manuscript. All authors critically appraised and approved the final version of the manuscript.

Funding

This work was supported by the Swiss National Centre of Competence in Research “LIVES – Overcoming vulnerability: Life course perspectives”, which is financed by the Swiss National Science Foundation (SNSF; 51NF40-160590). B.C. is supported by an Ambizione grant (N°: PZ00P1_180040) from the of the SNSF. M.P.B. is supported by the Research Foundation – Flanders (FWO) (1504015N; 1501018N). The authors are grateful to the SNSF for financial assistance. RC was funded by the UK Medical Research Council (Programme Code: MC_UU_12019/4).

Competing interests

The authors declare no conflict of interests

Ethical approval

This study was part of the SHARE study, approved by the relevant research ethics committees in the participating countries, and all participants provided written informed consent.

Data sharing

This SHARE dataset is available at <http://www.share-project.org/data-access.html>

Transparency

The lead author affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

Acknowledgements

This paper uses data from SHARE Waves 1, 2, 3 (SHARELIFE), 4, 5 and 6 (DOIs:

[10.6103/SHARE.w1.600](https://doi.org/10.6103/SHARE.w1.600), [10.6103/SHARE.w2.600](https://doi.org/10.6103/SHARE.w2.600), [10.6103/SHARE.w3.600](https://doi.org/10.6103/SHARE.w3.600),

[10.6103/SHARE.w4.600](https://doi.org/10.6103/SHARE.w4.600), [10.6103/SHARE.w5.600](https://doi.org/10.6103/SHARE.w5.600), [10.6103/SHARE.w6.600](https://doi.org/10.6103/SHARE.w6.600)),

The SHARE data collection was primarily funded by the European Commission through FP5 (QLK6-CT-2001-00360), FP6 (SHARE-I3: RII-CT-2006-062193, COMPARE: CIT5-CT-

2005-028857, SHARELIFE: CIT4-CT-2006-028812) and FP7 (SHARE-PREP: no.211909, SHARE-LEAP: no.227822, SHARE M4: no.261982). Additional funding from the German Ministry of Education and Research, the Max Planck Society for the Advancement of Science, the U.S. National Institute on Aging (U01_AG09740-13S2, P01_AG005842, P01_AG08291, P30_AG12815, R21_AG025169, Y1-AG-4553-01, IAG_BSR06-11, OGHA_04-064, HHSN271201300071C) and from various national funding sources is gratefully acknowledged (see www.share-project.org).

The authors are thankful to Angèle Gayet-Ageron for providing useful comments on the manuscript.

Table captions

Table 1. Participants' characteristics by gender at baseline

Table 2. Predictors of low muscle strength in older age in women

Table 3. Predictors of low muscle strength in older age in men

Figure captions

Figure 1. ACE and predicted probability of a LMS in older age

References

- 1 Syddall H, Cooper C, Martin F, Briggs R, Aihie Sayer A: Is grip strength a useful single marker of frailty? *Age Ageing* 2003;32:650-656.
- 2 Cooper R, Kuh D, Cooper C, Gale CR, Lawlor DA, Matthews F, Hardy R: Objective measures of physical capability and subsequent health: a systematic review. *Age Ageing* 2011;40:14-23.
- 3 Rantanen T, Guralnik JM, Foley D, Masaki K, Leveille S, Curb JD, White L: Midlife hand grip strength as a predictor of old age disability. *JAMA* 1999;281:558-560.
- 4 Sayer AA, Dennison EM, Syddall HE, Gilbody HJ, Phillips DI, Cooper C: Type 2 diabetes, muscle strength, and impaired physical function. *Diabetes Care* 2005;28:2541-2542.
- 5 Leong DP, Teo KK, Rangarajan S, Lopez-Jaramillo P, Avezum Jr A, Orlandini A, Seron P, Ahmed SH, Rosengren A, Kelishadi R: Prognostic value of grip strength: findings from the Prospective Urban Rural Epidemiology (PURE) study. *Lancet* 2015;386:266-273.
- 6 Newman AB, Kupelian V, Visser M, Simonsick EM, Goodpaster BH, Kritchevsky SB, Tylavsky FA, Rubin SM, Harris TB: Strength, but not muscle mass, is associated with mortality in the health, aging and body composition study cohort. *J Gerontol A Biol Sci Med Sci* 2006;61:72-77.
- 7 Cooper R, Kuh D, Hardy R: Objectively measured physical capability levels and mortality: systematic review and meta-analysis. *BMJ* 2010;341:c4467.
- 8 Cheval B, Boisgontier MP, Orsholits D, Sieber S, Guessous I, Gabriel R, Stringhini S, Blane D, van der Linden BW, Kliegel M, Burton-Jeangros C, Courvoisier DC, Cullati S: Association of early- and adult-life socioeconomic circumstances with muscle strength in older age. *Age Ageing* 2018
- 9 Birnie K, Cooper R, Martin RM, Kuh D, Sayer AA, Alvarado BE, Bayer A, Christensen K, Cho S-i, Cooper C: Childhood socioeconomic position and objectively measured physical capability levels in adulthood: a systematic review and meta-analysis. *PloS One* 2011;6:e15564.
- 10 Caleyachetty R, Hardy R, Cooper R, Richards M, Howe LD, Anderson E, Kuh D, Stafford M: Modeling Exposure to Multiple Childhood Social Risk Factors and Physical Capability and Common Affective Symptoms in Later Life. *J Aging Health* 2018;30:386-407.
- 11 Anderson EL, Heron J, Ben-Shlomo Y, Kuh D, Cooper R, Lawlor DA, Fraser A, Howe LD: Adversity in childhood and measures of aging in midlife: Findings from a cohort of british women. *Psychol Aging* 2017;32:521-530.
- 12 Anda RF, Butchart A, Felitti VJ, Brown DW: Building a framework for global surveillance of the public health implications of adverse childhood experiences. *Am J Prev Med* 2010;39:93-98.
- 13 Phillips DA, Shonkoff JP: From neurons to neighborhoods: The science of early childhood development. National Academies Press, 2000.
- 14 Felitti VJ, Anda RF, Nordenberg D, Williamson DF, Spitz AM, Edwards V, Koss MP, Marks JS: Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults: The Adverse Childhood Experiences (ACE) Study. *Am J Prev Med* 1998;14:245-258.
- 15 Danese A, Tan M: Childhood maltreatment and obesity: systematic review and meta-analysis. *Mol Psychiatry* 2014;19:544-554.
- 16 Hertzman C, Boyce T: How experience gets under the skin to create gradients in developmental health. *Annu Rev Public Health* 2010;31:329-347.
- 17 Hertzman C: The Biological Embedding of Early Experience and Its Effects on Health in Adulthood. *Ann N Y Acad Sci* 1999;896:85-95.

- 18 Johnson SB, Riley AW, Granger DA, Riis J: The science of early life toxic stress for pediatric practice and advocacy. *Pediatrics* 2013;131:319-327.
- 19 Wolf JM, Nicholls E, Chen E: Chronic stress, salivary cortisol, and α -amylase in children with asthma and healthy children. *Biol Psychol* 2008;78:20-28.
- 20 Johnson SB, Riley AW, Granger DA, Riis J: The science of early life toxic stress for pediatric practice and advocacy. *Pediatrics* 2013:peds. 2012-0469.
- 21 Fagundes CP, Glaser R, Kiecolt-Glaser JK: Stressful early life experiences and immune dysregulation across the lifespan. *Brain Behav Immun* 2013;27:8-12.
- 22 Evans GW, English K: The environment of poverty: Multiple stressor exposure, psychophysiological stress, and socioemotional adjustment. *Child Dev* 2002;73:1238-1248.
- 23 Kim P, Evans GW, Chen E, Miller G, Seeman T: How socioeconomic disadvantages get under the skin and into the brain to influence health development across the lifespan; *Handbook of Life Course Health Development*, Springer, 2018, pp 463-497.
- 24 Evans GW: The environment of childhood poverty. *Am Psychol* 2004;59:77-92.
- 25 Börsch-Supan A, Brandt M, Schröder M: SHARELIFE—One century of life histories in Europe. *Adv Life Course Res* 2013;18:1-4.
- 26 Solís CB, Kelly-Irving M, Fantin R, Darnaudéry M, Torrisani J, Lang T, Delpierre C: Adverse childhood experiences and physiological wear-and-tear in midlife: Findings from the 1958 British birth cohort. *PNAS* 2015;112:E738-E746.
- 27 Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, Seeman T, Tracy R, Kop WJ, Burke G: Frailty in older adults evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001;56:M146-M157.
- 28 Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, Martin FC, Michel J-P, Rolland Y, Schneider SM: Sarcopenia: European consensus on definition and diagnosis Report of the European Working Group on Sarcopenia in Older People. *Age Ageing* 2010;39:412-423.
- 29 Wahrendorf M, Blane D: Does labour market disadvantage help to explain why childhood circumstances are related to quality of life at older ages? Results from SHARE. *Aging Ment Health* 2015;19:584-594.
- 30 Boisgontier MP, Cheval B: The anova to mixed model transition. *Neurosci Biobehav Rev* 2016;68:1004-1005.
- 31 Pillas D, Marmot M, Naicker K, Goldblatt P, Morrison J, Pikhart H: Social inequalities in early childhood health and development: a European-wide systematic review. *Pediatr Res* 2014;76:418-424.
- 32 Ruiz M, Goldblatt P, Morrison J, Kukla L, Švancara J, Riitta-Järvelin M, Taanila A, Saurel-Cubizolles M-J, Lioret S, Bakoula C: Mother's education and the risk of preterm and small for gestational age birth: a DRIVERS meta-analysis of 12 European cohorts. *J Epidemiol Community Health* 2015:205387.
- 33 Bates D, Mächler M, Bolker B, Walker S: Fitting Linear Mixed-Effects Models Using lme4. 2015 2015;67:48.
- 34 R Core Team: R: A language and environment for statistical computing.; in *Computing RfFS* (ed). Vienna, Austria, 2017,
- 35 Kuznetsova A, Brockhoff, P.B., Christensen, R.H.B.: ImerTest: Tests in Linear Mixed Effects Models. R package version 2.0-33., 2016,
- 36 Tanner JM: Growth and maturation during adolescence. *Nutr Rev* 1981;39:43-55.
- 37 Falgairette G, Bedu M, Fellmann N, Van-Praagh E, Coudert J: Bio-energetic profile in 144 boys aged from 6 to 15 years with special reference to sexual maturation. *Eur J Appl Physiol Occup Physiol* 1991;62:151-156.
- 38 Oertel G: Morphometric analysis of normal skeletal muscles in infancy, childhood and adolescence: an autopsy study. *J Neurol Sci* 1988;88:303-313.

- 39 Armstrong N, Welsman J, Chia M: Short term power output in relation to growth and maturation. *British Journal of Sports Medicine* 2001;35:118-124.
- 40 O'Rand AM: The precious and the precocious: Understanding cumulative disadvantage and cumulative advantage over the life course. *Gerontologist* 1996;36:230-238.
- 41 Costa DL: From mill town to board room: The rise of women's paid labor. *J Econ Perspect* 2000;14:101-122.
- 42 Rose SMS-F, Xie D, Stineman M: Adverse childhood experiences and disability in US adults. *PM&R* 2014;6:670-680.
- 43 Baum A, Garofalo J, Yali A: Socioeconomic status and chronic stress: does stress account for SES effects on health? *Ann N Y Acad Sci* 1999;896:131-144.
- 44 Juster R-P, McEwen BS, Lupien SJ: Allostatic load biomarkers of chronic stress and impact on health and cognition. *Neurosci Biobehav Rev* 2010;35:2-16.
- 45 Kuh D, Bassey EJ, Butterworth S, Hardy R, Wadsworth ME: 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 A Biol Sci Med Sci* 2005;60:224-231.
- 46 Pahor M, Guralnik JM, Ambrosius WT, Blair S, Bonds DE, Church TS, Espeland MA, Fielding RA, Gill TM, Groessl EJ: Effect of structured physical activity on prevention of major mobility disability in older adults: the LIFE study randomized clinical trial. *JAMA* 2014;311:2387-2396.
- 47 Kuh D, Cooper R, Hardy R, Richards M, Ben-Shlomo Y: *A life course approach to healthy ageing*. Oxford, UK, Oxford University Press, 2013.
- 48 Mladovsky P, Allin S, Masseria C: *Health in the European Union: trends and analysis*. WHO Regional Office Europe, 2009.
- 49 Hardt J, Rutter M: Validity of adult retrospective reports of adverse childhood experiences: review of the evidence. *J Child Psychol Psychiatry* 2004;45:260-273.
- 50 Reuben A, Moffitt TE, Caspi A, Belsky DW, Harrington H, Schroeder F, Hogan S, Ramrakha S, Poulton R, Danese A: Lest we forget: comparing retrospective and prospective assessments of adverse childhood experiences in the prediction of adult health. *J Child Psychol Psychiatry* 2016;57:1103-1112.

Table 1.

| | Women (n= 13,477) | | Men (n= 10,702) | | <i>p</i> |
|---|-------------------|--------|-----------------|--------|----------|
| Outcome | | | | | |
| Muscle weakness | | | | | |
| Yes | 1643 | 12.19% | 968 | 9.05% | |
| No | 11834 | 87.81% | 9734 | 90.96% | <0.001 |
| Covariates | | | | | |
| Age (years), SD | 62.3 | 9.3 | 62.8 | 8.9 | <0.001 |
| Countries | | | | | |
| Belgium | 1374 | 10.20% | 1138 | 10.63% | |
| Austria | 485 | 3.60% | 334 | 3.12% | |
| Denmark | 1060 | 7.87% | 891 | 8.33% | |
| France | 1181 | 8.76% | 894 | 8.35% | |
| Germany | 890 | 6.60% | 778 | 7.27% | |
| Greece | 1490 | 11.06% | 1172 | 10.95% | |
| Italy | 1247 | 9.25% | 1040 | 9.72% | |
| Netherlands | 1033 | 7.67% | 867 | 8.10% | |
| Spain | 977 | 7.25% | 738 | 6.90% | |
| Sweden | 921 | 6.83% | 733 | 6.85% | |
| Switzerland | 654 | 4.85% | 498 | 4.65% | |
| Czech Republic | 919 | 6.82% | 664 | 6.20% | |
| Ireland | 342 | 2.54% | 265 | 2.48% | |
| Poland | 904 | 6.71% | 690 | 6.45% | 0.0891 |
| Birth cohort | | | | | |
| After 1945 | 6155 | 45.67% | 4489 | 41.95% | |
| between 1939 and 1945 | 3024 | 22.44% | 2617 | 24.45% | |
| between 1929 and 1938 | 2992 | 22.20% | 2631 | 24.58% | <0.001 |
| between 1919 and 1928 | 1306 | 9.69% | 965 | 9.02% | |
| Attrition | | | | | |
| No drop out | 9685 | 71.86% | 7276 | 67.99% | |
| Drop out | 2851 | 21.16% | 2312 | 21.60% | |
| Death | 941 | 6.98% | 1114 | 10.41% | <0.001 |
| Childhood socioeconomic circumstances | | | | | |
| Most Disadvantaged | 2430 | 18.03% | 2030 | 18.97% | |
| Disadvantaged | 3409 | 25.30% | 2660 | 24.86% | |
| Middle | 4415 | 32.76% | 3380 | 31.58% | |
| Advantaged | 2466 | 18.30% | 2009 | 18.77% | |
| Most advantaged | 757 | 5.62% | 623 | 5.82% | 0.1345 |
| Childhood health problems | | | | | |
| No | 10129 | 75.16% | 7921 | 74.01% | |
| Yes | 3348 | 24.84% | 2781 | 25.99% | 0.0439 |
| ACE | | | | | |
| None | 10674 | 79.20% | 8389 | 78.39% | |
| One | 2305 | 17.10% | 1904 | 17.79% | |
| Two or more | 498 | 3.70% | 409 | 3.82% | 0.3046 |
| Adult socioeconomic circumstances | | | | | |
| Level of education | | | | | |
| High education | 2332 | 17.30% | 2530 | 23.64% | |
| Low education | 11145 | 82.70% | 8172 | 76.36% | <0.001 |
| Main occupation class | | | | | |
| High skill | 2226 | 16.52% | 3351 | 31.31% | |
| Low skill | 11251 | 83.48% | 7351 | 68.69% | <0.001 |
| Satisfaction with household income | | | | | |
| Easily | 4763 | 35.34% | 4239 | 39.61% | |
| Fairly easily | 4132 | 30.66% | 3324 | 31.06% | |
| With some difficulty | 3043 | 22.58% | 2170 | 20.28% | |
| With great difficulty | 1539 | 11.42% | 969 | 9.05% | <0.001 |
| Unhealthy-related behaviours index, SD | 0.25 | 0.27 | 0.3 | 0.27 | <0.001 |

ACE = adverse childhood experiences; SD = standard deviations; *p*-values are reported for formal tests of gender difference

Table 2.

| | Model 0 | | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|------------------------------|--------------------|----------|--------------------|----------|--------------------|----------|--------------------|----------|--------------------|----------|--------------------|----------|
| Women | <i>OR</i> (95% CI) | <i>P</i> | <i>OR</i> (95% CI) | <i>P</i> | <i>OR</i> (95% CI) | <i>P</i> | <i>OR</i> (95% CI) | <i>P</i> | <i>OR</i> (95% CI) | <i>P</i> | <i>OR</i> (95% CI) | <i>P</i> |
| Age (ten years) | | | 4.77 (4.27-5.33) | <0.001 | 4.72 (4.22-5.27) | <0.001 | 4.79 (4.28-5.35) | <0.001 | 4.81 (4.30-5.37) | <0.001 | 4.74 (4.25-5.29) | <0.001 |
| ACEs | | | | | | | | | | | | |
| None | | | (ref) | | (ref) | | (ref) | | (ref) | | (ref) | |
| One | 1.41 (1.12-1.76) | 0.003 | 1.22 (1.02-1.47) | 0.033 | 1.21 (1.01-1.46) | 0.038 | 1.25 (1.04-1.50) | 0.016 | 1.17 (0.98-1.40) | 0.082 | 1.16 (0.97-1.38) | 0.107 |
| Two or more | 1.98 (1.26-3.11) | 0.003 | 1.74 (1.22-2.48) | 0.002 | 1.73 (1.22-2.47) | 0.002 | 1.81 (1.27-2.58) | 0.001 | 1.68 (1.19-2.37) | 0.003 | 1.55 (1.10-2.17) | 0.011 |
| Childhood SEC | | | | | | | | | | | | |
| Most Disadvantaged | | | (ref) | | (ref) | | (ref) | | (ref) | | (ref) | |
| Disadvantaged | | | 0.66 (0.50-0.86) | 0.002 | 0.67 (0.51-0.87) | 0.003 | 0.69 (0.53-0.90) | 0.006 | 0.72 (0.55-0.93) | 0.012 | 0.72 (0.55-0.93) | 0.012 |
| Middle | | | 0.65 (0.49-0.86) | 0.002 | 0.68 (0.51-0.90) | 0.006 | 0.74 (0.56-0.98) | 0.035 | 0.81 (0.61-1.07) | 0.131 | 0.81 (0.61-1.06) | 0.123 |
| Advantaged | | | 0.64 (0.46-0.88) | 0.006 | 0.70 (0.50-0.97) | 0.032 | 0.82 (0.59-1.15) | 0.25 | 0.87 (0.62-1.20) | 0.392 | 0.89 (0.65-1.24) | 0.497 |
| Most advantaged | | | 0.82 (0.52-1.28) | 0.382 | 0.94 (0.59-1.49) | 0.785 | 1.14 (0.71-1.82) | 0.589 | 1.24 (0.78-1.96) | 0.37 | 1.23 (0.78-1.95) | 0.376 |
| Level of education | | | | | | | | | | | | |
| High education | | | | | (ref) | | (ref) | | (ref) | | (ref) | |
| Low education | | | | | 1.97 (1.57-2.47) | <0.001 | 1.51 (1.17-1.93) | 0.001 | 1.30 (1.02-1.67) | 0.035 | 1.26 (0.99-1.61) | 0.063 |
| Main occupation class | | | | | | | | | | | | |
| High | | | | | | | (ref) | | (ref) | | (ref) | |
| Low | | | | | | | 1.98 (1.55-2.53) | <0.001 | 1.75 (1.37-2.23) | <0.001 | 1.70 (1.34-2.16) | <0.001 |
| Income | | | | | | | | | | | | |
| Easily | | | | | | | | | (ref) | | (ref) | |
| Fairly easily | | | | | | | | | 1.46 (1.22-1.76) | <0.001 | 1.41 (1.18-1.69) | <0.001 |
| With some difficulty | | | | | | | | | 2.51 (2.04-3.09) | <0.001 | 2.23 (1.82-2.74) | <0.001 |
| With great difficulty | | | | | | | | | 5.45 (4.23-7.02) | <0.001 | 4.56 (3.55-5.85) | <0.001 |
| Health behaviours | | | | | | | | | | | 4.65 (3.58-6.05) | <0.001 |

ACE = adverse childhood experiences. All models are adjusted for country of residence, birth cohort, attrition, height, and childhood health problems. Interactions terms between ACE and age (model 1b), level of education and age (model 2b), main occupation class and age (model 3 b), satisfaction with household income and age (model 4b), and health behaviours and age (models 5 b) were also tested. Only the interaction between age and health behaviours was significant. Model 0 was only adjusted for height. Health behaviours included physical inactivity, unhealthy eating, smoking, and alcohol consumption (higher score indicating higher number of unhealthy behaviours).

Table 3.

| | Model 0 | | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|------------------------------|------------------|-------|--------------------|----------|--------------------|----------|--------------------|----------|--------------------|----------|--------------------|----------|
| Men | | | <i>OR</i> (95% CI) | <i>P</i> | <i>OR</i> (95% CI) | <i>P</i> | <i>OR</i> (95% CI) | <i>P</i> | <i>OR</i> (95% CI) | <i>P</i> | <i>OR</i> (95% CI) | <i>P</i> |
| Age (ten years) | | | 10.59 (9.10-12.32) | <0.001 | 10.59 (9.10-12.33) | <0.001 | 10.57 (9.08-12.30) | <0.001 | 10.61 (9.12-12.34) | <0.001 | 10.64 (9.15-12.37) | <0.001 |
| ACEs | | | (ref) | | (ref) | | (ref) | | (ref) | | (ref) | |
| None | (ref) | | (ref) | | (ref) | | (ref) | | (ref) | | (ref) | |
| One | 1.33 (1.02-1.75) | 0.036 | 1.17 (0.94-1.47) | 0.165 | 1.17 (0.94-1.47) | 0.164 | 1.16 (0.93-1.45) | 0.187 | 1.12 (0.90-1.40) | 0.316 | 1.05 (0.84-1.31) | 0.652 |
| Two or more | 1.56 (0.92-2.65) | 0.099 | 1.30 (0.85-1.99) | 0.23 | 1.31 (0.85-2.00) | 0.219 | 1.31 (0.85-2.00) | 0.219 | 1.24 (0.82-1.89) | 0.315 | 1.18 (0.78-1.79) | 0.437 |
| Childhood SEC | | | (ref) | | (ref) | | (ref) | | (ref) | | (ref) | |
| Most Disadvantaged | | | (ref) | | (ref) | | (ref) | | (ref) | | (ref) | |
| Disadvantaged | | | 0.72 (0.55-0.92) | 0.01 | 0.71 (0.55-0.92) | 0.009 | 0.74 (0.58-0.96) | 0.023 | 0.77 (0.60-0.99) | 0.045 | 0.79 (0.62-1.01) | 0.064 |
| Middle | | | 0.78 (0.60-1.02) | 0.065 | 0.79 (0.60-1.03) | 0.079 | 0.87 (0.66-1.14) | 0.309 | 0.95 (0.73-1.24) | 0.69 | 0.97 (0.75-1.27) | 0.836 |
| Advantaged | | | 0.81 (0.59-1.10) | 0.178 | 0.83 (0.61-1.15) | 0.265 | 1.00 (0.72-1.38) | 0.997 | 1.06 (0.77-1.46) | 0.734 | 1.05 (0.76-1.44) | 0.77 |
| Most advantaged | | | 1.05 (0.68-1.63) | 0.821 | 1.11 (0.71-1.75) | 0.647 | 1.41 (0.90-2.23) | 0.137 | 1.50 (0.96-2.36) | 0.076 | 1.51 (0.97-2.37) | 0.07 |
| Level of education | | | | | (ref) | | (ref) | | (ref) | | (ref) | |
| High education | | | | | (ref) | | (ref) | | (ref) | | (ref) | |
| Low education | | | | | 1.16 (0.92-1.47) | 0.206 | 0.93 (0.72-1.19) | 0.57 | 0.84 (0.66-1.08) | 0.181 | 0.83 (0.65-1.07) | 0.147 |
| Main occupation class | | | | | | | (ref) | | (ref) | | (ref) | |
| High | | | | | | | (ref) | | (ref) | | (ref) | |
| Low | | | | | | | 1.83 (1.46-2.29) | <0.001 | 1.72 (1.37-2.15) | <0.001 | 1.67 (1.34-2.10) | <0.001 |
| Income | | | | | | | | | (ref) | | (ref) | |
| Easily | | | | | | | | | (ref) | | (ref) | |
| Fairly easily | | | | | | | | | 1.21 (0.97-1.51) | 0.087 | 1.17 (0.94-1.46) | 0.152 |
| With some difficulty | | | | | | | | | 1.85 (1.42-2.40) | <0.001 | 1.72 (1.33-2.23) | <0.001 |
| With great difficulty | | | | | | | | | 3.22 (2.30-4.52) | <0.001 | 2.81 (2.01-3.93) | <0.001 |
| Health behaviours | | | | | | | | | | | 3.08 (2.22-4.29) | <0.001 |

ACE = adverse childhood experiences. All models are adjusted for country of residence, birth cohort, attrition, height, and childhood health problems. Interactions terms between ACE and age (model 1b), level of education and age (model 2b), main occupation class and age (model 3 b), satisfaction with household income and age (model 4b), and health behaviours and age (models 5 b) were also tested. All the interactions were non-significant. Model 0 was only adjusted for height. Health behaviours included physical inactivity, unhealthy eating, smoking, and alcohol consumption (higher score indicating higher number of unhealthy behaviours).

Figure 1.

