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## Sex Differences in the Level and Rate of Change of Physical Function and Grip Strength in the Danish 1905-Cohort Study

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### Abstract

**Objectives**—The study was conducted to examine sex differences in the initial level and rate of change in physical function and grip strength.

**Method**—The baseline survey included 2,262 Danes born in 1905 and alive in 1998 and followed-up in 2000, 2003, and 2005. Hence, the authors fully used the power of having a cohort with multiple assessments in late life and virtually complete follow-up of lifespan (through December 2008). Latent growth curve modeling was used.

**Results**—Men had higher initial levels and rates of decline in strength score and grip strength. Lifespan was positively correlated with intercepts and slopes.

**Discussion**—The Danish data suggested that the longest-living individuals have higher initial levels of strength score and grip strength and smaller rate of change. The data further suggested that the initial level of strength score and grip strength was more predictive of mortality than the rate of change was, and the predictive effects were similar in men and women.

### Keywords

sex; activities of daily living; grip strength; oldest old; mortality; growth-curve analysis; Denmark

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Empirical evidence accumulated over recent decades revealed an apparent contradiction between health and survival of men and women (Case & Paxson, 2005; Nathanson, 1975; Waldron, 1985). Women enjoy a longer life than men in almost all countries of the world (Barford, Dorling, Smith, & Shaw, 2006), but women tend to report poorer self-rated health (Bambra et al., 2008; Olsen & Dahl, 2007), have higher disability levels at all ages (Arber & Cooper, 1999; Leveille, Penninx, Melzer, Izmirlian, & Guralnik, 2000), and perform more poorly on physical tests than men (Frederiksen et al., 2006; Jeune et al., 2006).

It has been suggested that handgrip strength is better than chronological age in predicting the frailty of people (Syddall, Cooper, Martin, Briggs, & Sayer, 2003). Several studies have found that grip strength is predictive of disability among middle-aged men (Rantanen et al., 1999), as well as older persons (Giampaoli et al., 1999). Others have demonstrated that grip strength

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#### Declaration of Conflicting Interests

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predicts all-cause, cardiovascular (CVD), and cancer mortality among men, but it ceased to predict mortality among elderly women in multivariate analyses (Fujita et al., 1995; Gale, Martyn, Cooper, & Sayer, 2007).

Previous research proposed that many physiological functions begin to decline around 30 years (Sehl & Yates, 2001) and that the course of the decline accelerates with increasing age (Bassey, 1998; Forrest, Zmuda, & Cauley, 2005; Forrest, Zmuda, & Cauley, 2007; Rantanen et al., 1998). The median loss for the bone-mineral density in lumbar spine from age 30 to 70 years has been estimated to be 0.3% per year, and the mean annual decline in muscle strength was 0.7% in men and 0.6% in women (Sehl & Yates, 2001). It has been indicated that the decline is steeper in individuals with greater levels of muscle strength at baseline (Forrest et al., 2005, 2007) and among men (Proctor et al., 2006).

Previous studies suggest that the rate of change in physical and cognitive functioning is associated with longevity (Deeg, Hofman, & van Zonneveld, 1990). However, little information is available on rate of change among the oldest-old population due to logistical challenges (high mortality and nonresponse). Available data suggest that although the level of functioning is predictive of survival, the rate of decline is also important. Data from the Baltimore Longitudinal Study of Aging suggest that the rates of change in muscle power and isometric strength predict mortality independently from the power and strength levels (Metter, Talbot, Schrager, & Conwit, 2004). However, little is known about sex differences in the rate of change in physical function and grip strength in the oldest population. Most previous studies were restricted to small or specific samples, such as one ethnic or sex group, were limited in the number of measurement occasions, and did not specifically focus on sex differences in the decline or on the sex-specific effect of rate of change on survival. It is also unclear to what extent the male–female health–survival paradox is due to sex differences in level and/or rate of change in physical functioning.

The present study focuses on determining whether there are sex differences in the initial level and rate of change in reported physical function and grip strength, whether it is the level or rate of change that is more predictive of mortality, and, finally, whether sex moderates the associations of the level and rate of change with lifespan. To address these research questions we used previously collected longitudinal data on the entire national Danish cohort born in 1905 and followed from ages 92 to 93 to 100 years with follow-up of survival status through December 2008. Hereby, we are using the full power of having a cohort with multiple assessments in late life and virtually complete follow-up of lifespan.

## Method

### Study Population

The study uses the data collected in the Danish 1905-Cohort Study described in detail elsewhere (Christensen, Bathum, & Christiansen, 2008; Nybo, Gaist, Jeune, Bathum et al., 2001). In brief, the individuals eligible to participate in the survey were identified in the Danish Civil Registration System (Pedersen, Gøtzsche, Møller, & Mortensen, 2006) and included all Danes born in 1905 and alive on August 1, 1998 (Figure 1). A total of 3,600 persons were approached irrespective of their residency, physical health, and cognitive status. If a person refused or was unable to participate in the face-to-face interview, a proxy respondent, usually a close relative, was sought. A total of 2,262 people (62.8% of the 3,600 persons eligible to participate in the baseline survey) participated in the intake survey in 1998. The consecutive waves in 2000, 2003, and 2005 were follow-up assessments of survivors from previous waves, with participation rates among survivors between 69% and 78%. In addition, for the 2005 survey all nonrespondents from previous waves were contacted, and 90 persons agreed to participate.

Participants and nonparticipants were compared using the extensive registration of the Danish population. No differences were found in housing and marital status, but men and persons living in rural areas were more likely to participate than women and urban dwellers. An analysis of hospitalization patterns from 1973 to 1998 indicated that participants were not healthier than nonparticipants. Nevertheless, in the 6-month period immediately following the start of the survey, nonparticipants had higher mortality, suggesting that terminal illness was one of the reasons for nonparticipation (Nybo, Gaist, Jeune, Bathum et al., 2001; Nybo, Gaist, Jeune, McGue et al., 2001; Nybo et al., 2003).

The questionnaire included items asking respondents about their sociodemographic characteristics, family and lifecycle characteristics, health, and lifestyle behavior. Physical and cognitive functions and depression symptomatology were also assessed, and the participants were asked to give a biological sample, either blood or a cheek swab. Interviewers from the Danish National Institute of Social Research were not medically or para-medically trained but do, however, have substantial experience in interviewing the elderly (Christensen, Holm, McGue, Corder, & Vaupel, 1999). Data in each wave were collected within approximately three months.

### Reported Physical Function

The assessment of physical function was based on self-reports of the activities the participant was able to do on the day of the interview. The Avlund instrument was previously validated in Denmark and was shown to discriminate between levels of functional ability among community-dwelling elderly persons (Avlund, Davidsen, & Schultz-Larsen, 1995; Schultz-Larsen, Avlund, & Kreiner, 1992). The Avlund instrument was extended to include assessment of the need for medical equipment or aids in relation to functional abilities, on the basis of results showing that equipment and aids can improve functional abilities among the elderly (Manton, Corder, & Stallard, 1993). All of the items from the Katz index of Activities of Daily Living (Katz, Ford, Moskowitz, Jackson, & Jaffe, 1963) were included, as well as questions about the ability to see and hear and the ability to engage in more demanding activities (Christensen et al., 2000). A 11-item self-reported measure of physical function was administered at each wave and ranged broadly, from relatively simple physical tasks to more demanding activities: walk around in the house, walk up and down stairs one floor, walk up and down stairs to the second floor, get outdoors, walk 400 m without resting, do light and hard exercise, walk in nice and bad weather for 30 minutes to 1 hour, run 100 meters, and carry 5 kg. Each item was answered on a scale ranging from 1 to 4 points (1 = *can do without fatigue*, 2 = *can do with fatigue or minor difficulties*, 3 = *can do with aid or major difficulties*, 4 = *cannot do*). The scale score also ranges from 1 to 4, being an average of the 11 items, and it was reversed to make higher scores correspond to higher levels of physical function. Consistent with our previous publications, this scale is called the strength score. If an item was missing or skipped, the mean for that item was substituted. If more than one item was skipped, the scale was coded as missing. This scale has been shown to provide a sensitive quantitative measure of physical ability, to be moderately heritable, and to have high internal consistency (.93) for both in-person and proxy interviews (Christensen, Frederiksen, Vaupel, & McGue, 2003; Christensen, Gaist, Vaupel, & McGue, 2002; Christensen et al., 2000). If a person refused or was unable to participate in the face-to-face interview, a proxy respondent was asked to rate the physical function of the person. Among 2,295 subjects (1,709 women and 586 men) with at least 1 measurement occasion of physical function, 462 (20.1%) were proxy respondents. In total, there were 1,084 individuals (832 women and 252 men) with at least 2 measurements of physical function, 441 persons (356 women and 85 men) with at least 3 measurements, and 155 people (124 women and 31 men) had valid measurement of physical function at all 4 waves.

## Grip Strength

Grip strength in kilograms was measured using a Smedley dynamometer (TTM; Tokyo, Japan) for three trials with the stronger hand and with brief pauses between each performance (Frederiksen et al., 2006; Nybo et al., 2003). The best performance of these three was used for the analysis. To measure maximal strength, the width of the handle was adjusted to fit the hand size; the second phalanx should rest against the inner stirrup; the elbow had to be in a 90-degree position and the upper arm to be tight against the trunk (Oxford, 2000). Participants who made fewer than 3 attempts or had a difference of 20 kg or more between two measures were excluded. By definition, proxy respondents had no measurement of grip strength. In total, there were 1,617 participants (450 men and 1,167 women) with at least 1 measurement of grip strength, 689 (182 men and 507 women) with at least 2 measurements, 240 (61 men and 179 women) had their grip strength assessed at least 3 occasions, and 64 (15 men and 46 women) at all 4 waves.

## Lifespan

Survival status was available through the end of December 2008. The mean observed lifespan among individuals was 95.9 years ( $SE = 0.09$ ) for men and 96.6 years ( $SE = 0.06$ ) for women. Half of the male population died between May 1998 and October 2000, whereas 50% of women died between February 1998 and July 2001. The lifespan of 53 individuals (9 men and 44 women) who were still alive at the end of December 2008 was estimated by adding remaining life expectancy to their last known age using male and female life tables for Denmark from the Human Mortality Database (HMD; 2009).

## Statistical Analysis

Latent growth-curve models (LGM) were used to investigate sex differences in age-related changes in strength score and grip strength by the method of maximum likelihood using the Mx software (Neale, Boker, Xie, & Maes, 2003). The LGM for change in strength score is presented in Figure 2.

The availability of multiple measurements of strength score and grip strength permits estimation of rate of change rather than the amount of change, which is commonly examined in the analysis of the traditional difference score. LGM is a special case of multilevel or mixed model analysis in which the first, or within-subject level, is modeled as follows:

$$y_{it} = \pi_{0i} + \pi_{1i}(a_{it}) + \pi_{2i}(a_{it}^2) + e_{it}$$

where  $y_{it}$  is the observed score for the  $i^{\text{th}}$  person at time  $t$ ,  $a_{it}$  is the age of the person at time  $t$ ,  $\pi_{0i}$  is the intercept or level random effect for the  $i^{\text{th}}$  individual,  $\pi_{1i}$  is the slope score for the  $i^{\text{th}}$  individual,  $\pi_{2i}$  is the nonlinear change score for the  $i^{\text{th}}$  individual, and  $e_{it}$  is the residual term. The second-, or between-subject, level models random effects in  $\pi_{0i}$ ,  $\pi_{1i}$ , and  $\pi_{2i}$ .

$$\begin{aligned}\pi_{0i} &= \beta_{00} + \sum \beta_{0j} x_{ij} + \mu_{0i} \\ \pi_{1i} &= \beta_{10} + \sum \beta_{1j} x_{ij} + \mu_{1i} \\ \pi_{2i} &= \beta_{20} + \sum \beta_{2j} x_{ij} + \mu_{2i}\end{aligned}$$

where  $\beta_{00}$ ,  $\beta_{10}$ , and  $\beta_{20}$  are, respectively, the fixed (i.e., group level) intercept, slope and quadratic effects;  $\mu_{0i}$ ,  $\mu_{1i}$ , and  $\mu_{2i}$  are residual terms;  $x_{ij}$  are observations on covariates; and  $\beta_{0j}$ ,  $\beta_{1j}$ , and  $\beta_{2j}$  are the effects of these covariates on individual differences in intercepts and slopes.

As the reliable estimation of random effects on the quadratic component of change requires large number of observations on each individual (Bryk & Raudenbush, 1992), we estimated the fixed quadratic effect only. In addition, the analysis focused on how sex differences in the intercept and slope are associated with lifespan and how these associations differ in men and women. The mean intercepts and slopes of strength score and grip strength were estimated freely in sex-specific groups. To reveal sex differences in the initial level and rate of change, the intercept and slope were consecutively constrained to be equal in men and women. The log likelihood ratio test was used to evaluate the model fit. A  $p$  value of .05 is considered to indicate statistical significance, and the estimates are presented with 95% confidence intervals (CI), unless otherwise stated.

In line with previous research, we expected to find sex differences in both the initial level and rate of change with men having an initial advantage over women and also a more rapid age-related decline. Sex differences in the correlations between intercept and slope and lifespan were evaluated by testing the equality between two correlation coefficients. A sex difference in the correlations between slope and lifespan would indicate that the rate-of-change in strength score and grip strength is differentially predictive of mortality in men and women. Consistent with the “terminal decline” hypothesis (Wilson, Beck, Bienias, & Bennett, 2007), we also expected the rate of change to be a stronger predictor of survival than the initial level among the oldest old.

## Results

### Change in Strength Score

In total, there were 2,295 (586 men [25.5%] and 1,709 women [74.5%]) elderly with at least one reported measure of physical function. In Table 1, Model 1 assumes linear change in strength score, whereas Model 2 additionally includes the fixed quadratic effect. As the fixed quadratic effect of change in strength score was very small and failed to reach statistical significance in both samples, the reduced linear model was considered.

Initially, men aged 93 years had a higher strength score compared with women, 2.07 (2.01, 2.14) versus 1.74 (1.71, 1.77), respectively. However, the linear rate of change in strength score among women of  $-0.12$  units ( $-0.14$ ,  $-0.11$ ) per year was lower than the rate of change among men,  $-0.20$  ( $-0.23$ ,  $-0.17$ ).

As compared to the fully saturated model ( $-2 \text{ LnL} = 17,631$  with 6,244  $df$ ), models in which the intercepts ( $-2 \text{ LnL} = 17,705$  with 6,245  $df$ , difference  $\chi^2 = 74$  with 1  $df$ ,  $p < .00001$ ) and the slopes ( $-2 \text{ LnL} = 17,648$  with 6,245  $df$ , difference  $\chi^2 = 17$  with 1  $df$ ,  $p < .00001$ ) were constrained to be equal in men and women had significantly worse fit. This indicates that the mean initial level of strength score was significantly higher in men than in women and that the strength declined at a significantly greater rate in men than in women.

The significant variance component for the intercept suggests some remaining explainable residual variation in the initial status of strength score in both sexes. All correlation coefficients were in the expected direction (Table 2). Negative correlation coefficients between intercept and slope in both men,  $-0.50$  ( $-0.69$ ,  $-0.23$ ), and women,  $-0.53$  ( $-0.63$ ,  $-0.41$ ) indicates that elderly individuals with higher initial levels of strength score decline in their functioning at a faster pace (as smaller negative values correspond to larger absolute decline). Lifespan and intercept were positively correlated, both in men and women. Likewise, there were also positive correlations between lifespan and slope in both sex-specific samples, though it was not significant in men. These findings suggest that the persons with higher initial levels and slower rates of decline in physical function had longer lives.

The test of equality revealed that the correlation coefficient between lifespan and intercept was greater than that between lifespan and slope in both men and women. In addition, there was no statistically significant sex difference in the correlation coefficients of lifespan with intercept and slope. These suggest that the initial level of strength score is more important for mortality prediction than the rate of decline and that the predictive effect of the initial level is similar in men and women.

### Change in Grip Strength

In total, there were 1,617 (450 men and 1,167 women) individuals with at least 1 occasion of grip strength measurement. The mean initial level of grip strength was higher in men than in women, 22.6 kg (22.0, 23.3) and 13.4 kg (13.2, 13.7), respectively. Men declined in grip strength by  $-1.17$  kg ( $-1.49, -0.87$ ) per year, whereas the decline was  $-0.29$  kg ( $-0.49, -0.08$ ) in women at the baseline, but it increased with age due to the quadratic effect in women. The fixed quadratic effect of change in grip strength was statistically significant in the women only (Table 3), so that in the final model the quadratic effect in men was fixed to zero.

The negative fixed quadratic effect of  $-.05$  ( $-0.09, -0.01$ ) indicates that in women the rate of decline increases with advanced age. Because the pace at which women decline in grip strength changes with age, the overall annual drop is difficult to summarize by a single number. The left panel in Figure 3 illustrates observed (cross-sectional means) and right panel predicted (based on the final models) trajectories of strength score and grip strength in the Danish 1905-Cohort study from 1998 to 2005. Both the observed and predicted trajectories point toward more rapid decline in strength score and grip strength in men than in women.

According to the log-likelihood ratio test, the saturated model ( $-2 \text{ LnL} = 22,851$  with 4,200 *df*) fit the data better than the models with either the intercepts ( $-2 \text{ LnL} = 23,310$  with 4,201 *df*, difference  $\chi^2 = 449$  with 1 *df*,  $p < .00001$ ) or the slopes ( $-2 \text{ LnL} = 22,873$  with 4,201 *df*, difference  $\chi^2 = 22$  with 1 *df*,  $p < .00001$ ) constrained to be equal in the two groups. This indicates that the initial level and rate of change in grip strength are significantly higher in men than in women.

Variance components of intercepts and slopes were significant in both groups, suggesting that potentially explainable residual variations in the initial level and rate of change still remain. The correlation between the intercept and slope in men,  $-.10$  ( $-0.75, 0.94$ ), and women,  $-.28$  ( $-0.50, 0.05$ ), were negative, but they failed to reach a statistically significant level (Table 2). It may imply that among nonagenarian Danes grip strength declines at a similar pace regardless of its initial level.

Lifespan was significantly and positively correlated with intercept in men,  $.29$  ( $0.19, 0.38$ ), and women,  $.31$  ( $0.24, 0.38$ ), indicating that within both sexes individuals with higher grip strength have longer lifespan (Table 2). The correlation coefficient between lifespan and slope failed to reach statistically significant level in both men,  $.33$  ( $-0.03, 1.00$ ), and women,  $.23$  ( $-0.03, 0.59$ ). These findings suggest that among Danish nonagenarians the initial levels of grip strength are more predictive of survival than the rate of change. However, insignificant correlation coefficients between slope and lifespan may also be due to small number of individuals with at least 3 measurements of grip strength necessary to reliably estimate linear slope. The test of equality revealed no statistically significant sex difference in the correlation coefficients of lifespan with either intercept or slope.

### Discussion

Consistent with previous research, the present study revealed that in the Danish 1905-cohort men had a higher strength score and grip strength, compared with women (Beckett et al.,



1996; Frederiksen et al., 2006; Fujita et al., 1995; Gale et al., 2007; Taylor & Lynch, 2004). Although nonagenarian men had the initial advantage, they also experienced steeper declines in strength score and grip strength, compared with the women. The data analysis showed that the strength score declined linearly in both sexes, whereas the decline in grip strength was nonlinear in women. It appeared that among women the decline in grip strength accelerates with increasing age. The nonsignificant quadratic effect among men was possibly due to the small number of male participants ( $n = 15$ ), with valid measurements at all four surveys necessary to estimate a nonlinear quadratic effect. The present study suggests that, in absolute terms, elderly men showed a more rapid decline in the reported physical function and grip strength than did women.

Our results are in agreement with a longitudinal study among Swedish twins that revealed significantly greater change for grip strength in men compared with women (Proctor et al., 2006). Hughes et al. found that although men had higher isokinetic strength in all muscle groups, the absolute 10-year decline in strength of each muscle group was greater in men than in women (Hughes et al., 2001). Forrest et al. showed that over a 10-year follow-up period women declined in grip strength by 2.4% per year, whereas men declined by 2.8% annually (Forrest et al., 2005, 2007). Other studies also reported steeper rates of decline in handgrip strength in men than in women (Proctor et al., 2006; Vianna, Oliveira, & Araujo, 2007). Several studies, however, found that longitudinal changes in handgrip strength were similar in men and women (Basse, 1998) or even greater in women than in men (Rantanen, Era, & Heikkinen, 1997; Rantanen & Heikkinen, 1998). A greater rate of change in physical function was found among women 65 years and older than among men of the same age (Beckett et al., 1996; Liang et al., 2008; Taylor & Lynch, 2004).

Age-related decline in concentrations of testosterone and estrogen (Lamberts, van den Beld, & van der Lely, 1997) have been suggested to underlie decline in muscle strength among elderly persons. However, the evidence for causal relationship between decline in muscle strength and decrease in free testosterone levels, as well as the risks and benefits of testosterone replacement therapy are still controversial (Bassil, Alkaade, & Morley, 2009). Some studies indicated that total and bioavailable testosterone and estrogen levels were unrelated to the maximum handgrip strength, to the 3-year decline in performance of chair stand and walk tests, or to the 3-year decline in muscle strength among men and women aged 55 years and older (Schaap et al., 2008; van Geel, Geusens, Winkens, Sels, & Dinant, 2009). Other researchers, however, found that total and bioavailable testosterone were positively related with muscle strength in elderly men (van den Beld, de Jong, Grobbee, Pols, & Lamberts, 2000) and that, beyond certain concentration, no additional benefits of increased testosterone level on the performance of functional tasks was indicated (O'Donnell, Trivison, Harris, Tenover, & McKinlay, 2006).

Our analysis of change in strength score revealed significant negative correlation between intercept and slope, suggesting that the oldest-old individuals with higher initial levels of strength score have higher rate of decline. However, we could not detect a similar pattern in the analysis of change in grip strength, which may suggest that a decline in grip strength among oldest-old Danes occurs at a similar pace, regardless of the initial level of muscular strength.

Consistent with previous research in mixed and sex-specific samples, our study suggests that the decline in physical performance increases with advancing age (Basse, 1998; Forrest et al., 2005, 2007; Rantanen et al., 1998). Onder et al. reported that women aged 65 to 79 years showed a decline in grip strength by 0.50 kg per year, with those aged 80 years or older showing an annual decline of 0.60 kg (Onder et al., 2002). The 59-year longitudinal Terman study pointed out that the decline in self-rated health accelerated after age 50 for both men and women, though the mean rate of change in men was significantly higher than that found in women (McCullough & Laurenceau, 2004).

The analysis of change in strength score revealed a consistently greater correlation between lifespan and intercept than the correlation between lifespan and slope. In the analysis of change in grip strength, the correlation between lifespan and slope failed to reach statistically significant level. In both cases, no sex differences were indicated in correlation of lifespan with intercepts and slopes. These findings suggest that the initial level of strength score and grip strength are more predictive of mortality than the rate of change, but the predictive effects of the initial levels are similar in men and women. A larger correlation coefficient between slope and lifespan compared with that between intercept and lifespan in the sample of men is likely a result of the sample being small. Only 60 men and 179 women had  $\geq 3$  measurements of grip strength that are necessary to reliably fit the linear growth model. It is also possible that the initial selection of individuals, sufficiently strong at the baseline to have several follow-up measurements, may account for the more rapid drop in grip strength.

At present, knowledge about decline–mortality association based on measures of physical health is limited. Information is especially sparse for oldest-old individuals due to high mortality and loss to follow-up. Metter et al. found that changes in muscle power and muscle strength predicted mortality risk, independent of the strength and power levels (Metter et al., 2004). A study among Medicare recipients revealed that the individuals with rapid age-related decline in physical abilities had a substantially higher risk of death, compared to those with slower rates of decline or preserved functions; however, the decline–mortality association was stronger in individuals aged  $\leq 75$  years (Schupf et al., 2005).

The literature regarding “terminal decline” based on cognitive health is also contradictory (Bosworth & Siegler, 2002). Several studies demonstrated that cognitive change predicts subsequent survival (Bosworth, Schaie, & Willis, 1999; Deeg et al., 1990), whereas others have found that the level but not the decline is predictive of mortality (Ghisletta, 2008; Laukka, MacDonald, & Backman, 2006). The Nun Study has indicated that the linguistic abilities from early life were significantly inversely related with Alzheimer’s disease lesions in the brain neocortex that underscore the importance of the initial level (Snowdon, Greiner, & Markesbery, 2000). To add complexity, another study found decline–mortality association for some specific cognitive tasks and age groups only (Lavery, Dodge, Snitz, & Ganguli, 2009; Kliegel et al., 2004). It has been proposed that the effect of cognitive (Lavery et al., 2009; Kliegel, Moor, & Rott, 2004) or functional decline (Schupf et al., 2005) on mortality levels off at very old age. A diminishing decline–mortality association at very advanced age may partially explain the fact that the rate of change in our study failed to be more predictive of mortality than the initial levels of strength score and grip strength.

Some issues in our study deserve consideration. First, our analysis highlights the difficulties of estimating the rate of change in the oldest-old individuals, due to high mortality and loss to follow-up. Despite an initially large sample, with almost complete follow-up of lifespan, we still had limited power to estimate more precisely the rate of change in those health measures for which proxy interviews cannot be used. A possible decline–mortality association based on grip strength requires further investigation with a larger number of male participants.

Second, because censoring cannot be easily accommodated in growth-curve analysis, lifespan of individuals still alive at the end of December 2008 was estimated by adding the remaining life expectancy to their last known age, using the life tables for Denmark. It may restrict the variance of the lifespan variable, and, consequently, correlations of lifespan with intercept and slope may be biased towards zero. However, this bias is likely to be small and insignificant because only 53 individuals were affected.

Third, the analysis was based exclusively on the observed data, without accounting for selective loss to follow-up due to nonresponse or mortality. Recent studies in Denmark showed that



correcting disability score for missing data because of nonparticipation using inverse probability weights (Dufouil, Brayne, & Clayton, 2004) gave results very similar to the unadjusted score (Christensen, McGue, Petersen, Jeune, & Vaupel, 2008). Even though the curves of the age-related decline in grip strength were shifted downwards when selective dropout due to nonparticipation was taken into consideration (Frederiksen et al., 2006), this refinement, probably, would not affect male–female differences in the initial levels and rates of change in strength score and grip strength or the sex difference in the correlations of lifespan with intercepts and slopes.

The present study had a single geographic focus, Denmark, and may not be representative of other population settings. A cross-country comparison study of grip strength among nonagenarians and centenarians in three different European regions found a significant North–South gradient in handgrip strength, with substantially lower values in Southern countries, which may be due to genetic variation, differences in early life conditions, and sociocultural differences (Jeune et al., 2006).

Finally, grip-strength measurements were performed by different lay interviewers, which could have introduced a measurement bias attributable to interviewers. However, a previous study in Denmark reported that differences attributable to interviewer effects accounted for only 1% to 2% of the population variation in grip strength (Frederiksen et al., 2006).

In conclusion, this study revealed that despite their initial advantage, nonagenarian Danish men have more rapid age-related decline in physical function and grip strength than women do. Our findings suggest that the initial levels are more important in predicting mortality than the rate of change and that the predictive effect is similar in women and men. Although this study indicated steeper decline in physical function and grip strength in men than in women, there was no indication for sex-specific effect of the initial level or rate of change on survival. Therefore, this study contributed little to the explanations for the male–female health–survival paradox.

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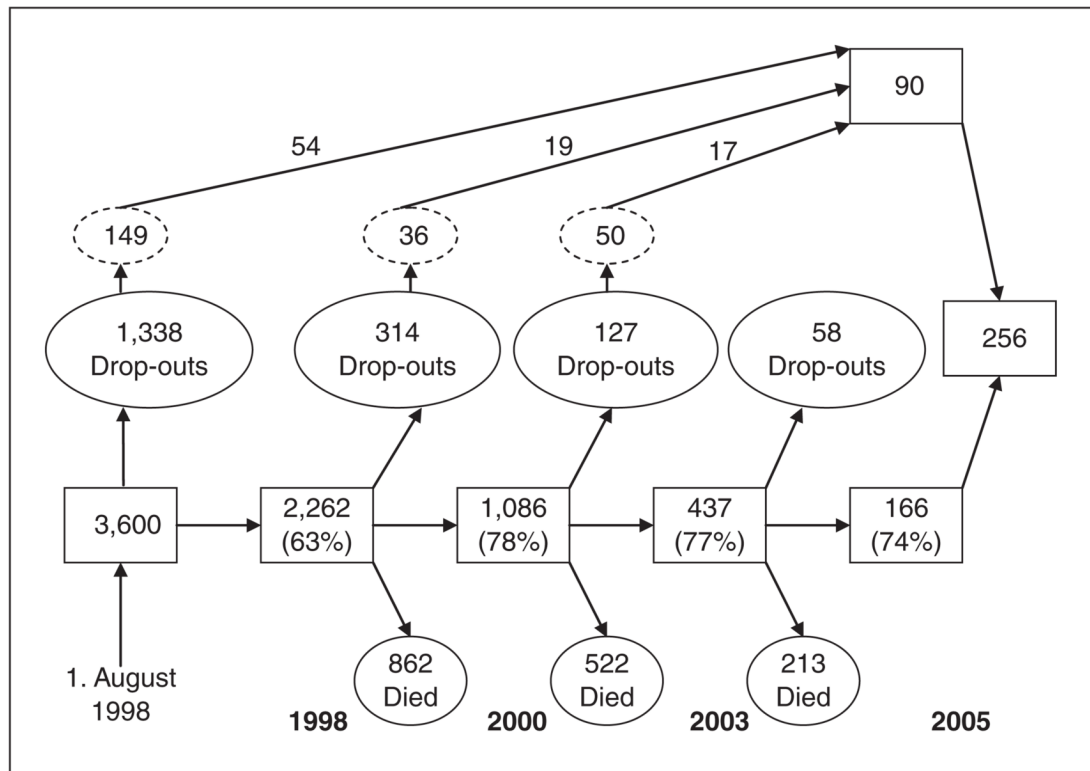
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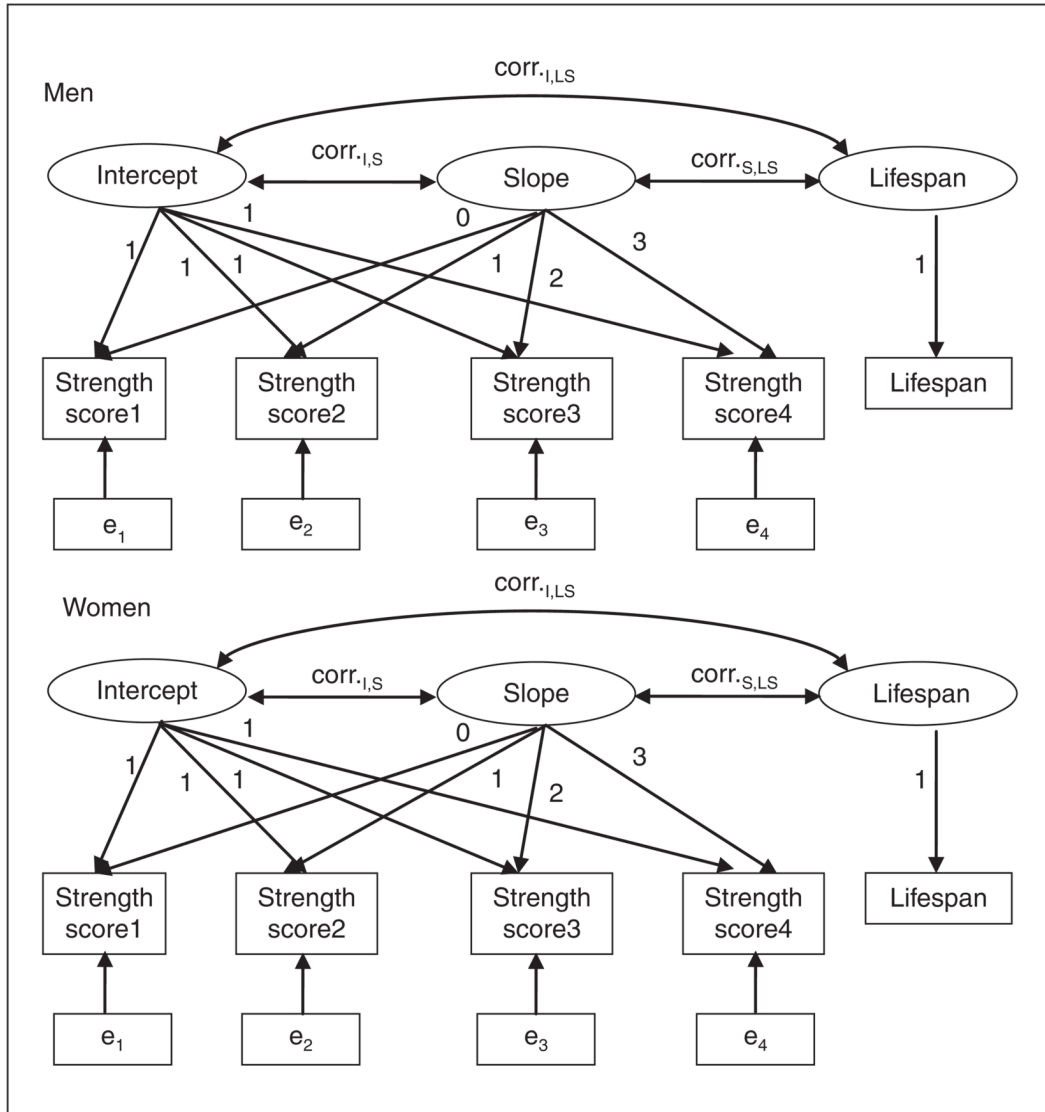
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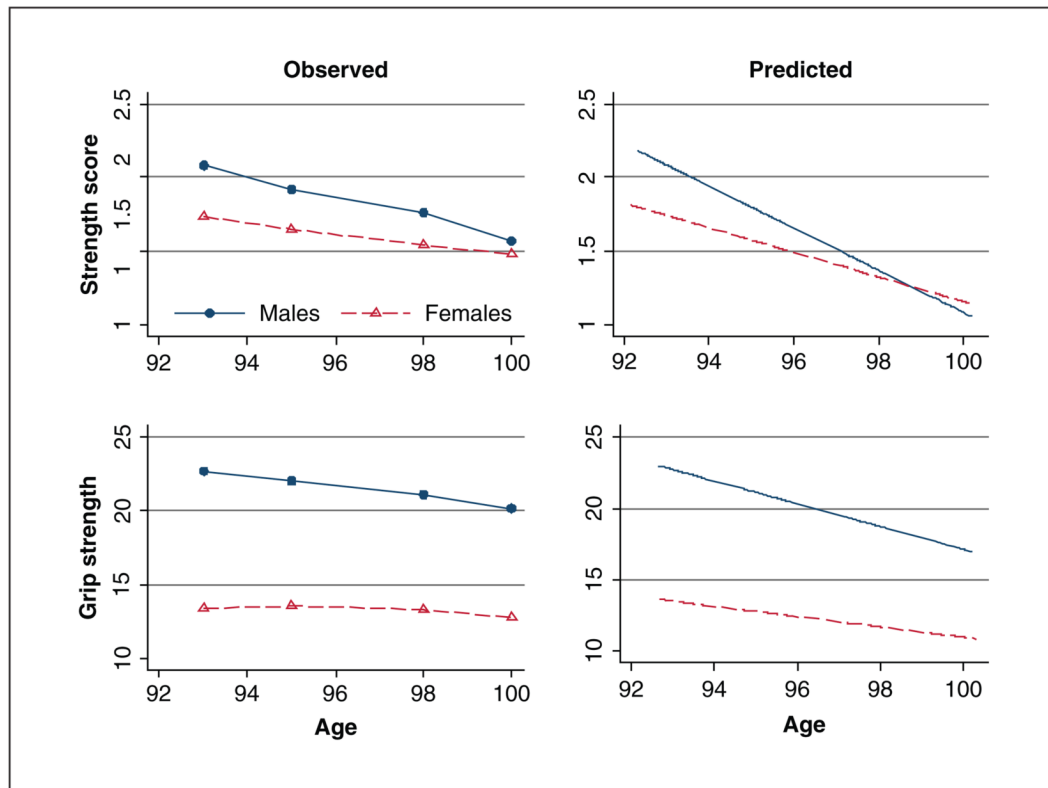
**Figure 1.**  
 Flow-chart of the Danish 1905-Cohort Study  
 Note: The square boxes give the number of participants and participation rates. The dashed circles give the initial number of dropouts who were recontacted for participation in 2005.  
 Source: Christensen, Bathum, and Christiansen (2008).





**Figure 2.** Graphical presentation of latent growth-curve model for change in strength score in the 1905-Cohort Study

Note: corr. = correlation coefficient; I = intercept; S = slope; LS = lifespan.



**Figure 3.**

Observed and predicted trajectories of change in strength score and grip strength in the Danish 1905-Cohort Study (1998–2005)

a. Predicted trajectories of change in strength score are based on the linear model. Predicted trajectories of change in grip strength are based on the linear model for men and quadratic model for women.

**Table 1**

Change in Strength Score Between 1998 and 2005 in the Danish 1905-Cohort Study

	<b>Model 1 (linear)</b>		<b>Model 2 (quadratic)</b>	
	<b>Men (n = 586)</b>	<b>Women (n = 1,709)</b>	<b>Men (n = 586)</b>	<b>Women (n = 1709)</b>
Fixed effects				
Intercept	2.07 (2.01, 2.14)	1.74 (1.71, 1.77)	2.08 (2.01, 2.15)	1.74 (1.71, 1.78)
Slope	-0.20 (-0.23, -0.17)	-0.12 (-0.14, -0.11)	-0.23 (-0.27, -0.18)	-0.13 (-0.15, -0.11)
Lifespan	96.0 (95.8, 96.2)	96.8 (96.7, 96.9)	96.0 (95.8, 96.2)	96.8 (96.7, 96.9)
Quadratic effect			0.008 (-0.002, 0.017)	0.001 (-0.002, 0.004)
Variance components				
Variance (I)	0.48 (0.39, 0.58)	0.34 (0.31, 0.38)	0.49 (0.40, 0.58)	0.34 (0.31, 0.38)
Variance (S)	0.006 (0.002, 0.011)	0.004 (0.002, 0.005)	0.006 (0.002, 0.006)	0.004 (0.003, 0.004)
Covariance (I, S)	-0.03 (-0.05, -0.01)	-0.02 (-0.03, -0.01)	-0.03 (-0.05, -0.01)	-0.02 (-0.03, -0.01)
Covariance (I, LS)	0.80 (0.63, 0.99)	0.77 (0.68, 0.88)	0.82 (0.65, 1.01)	0.78 (0.68, 0.88)
Covariance (S, LS)	0.03 (-0.02, 0.07)	0.03 (0.003, 0.05)	0.003 (-0.05, 0.06)	0.024 (-0.002, 0.052)
2 LnL	17,631	—	17,628	—
AIC	5,143	—	5,144	—
df	6,244	—	6,242	—

Note: Total number of participants studied,  $n = 2,295$ . I = intercept; S = slope; LS = lifespan; LnL - loglikelihood; AIC - Akaike's Information Criterion.

**Table 2**

Correlations Among Intercepts, Slopes, and Lifespan for Strength Score and Grip Strength in the Danish 1905-Cohort Study

	Men		Women	
	Intercept	Slope	Intercept	Slope
Strength score	<i>n</i> = 586	—	<i>n</i> = 1,709	—
Intercept	1	—	1	—
Slope	-0.50 (-0.69, -0.23)	1	-0.53 (-0.63, -0.41)	1
Lifespan	0.46 <sup>b</sup> (0.37, 0.53)	0.13 (-0.09, 0.37)	0.47 <sup>b</sup> (0.42, 0.51)	0.15 (0.02, 0.29)
Grip strength <sup>a</sup>	<i>n</i> = 450	—	<i>n</i> = 1,167	—
Intercept	1	—	1	—
Slope	-0.10 (-0.75, 0.94)	1	-0.28 (-0.50, 0.05)	1
Lifespan	0.29 (0.19, 0.38)	0.33 (-0.03, 1.00)	0.31 (0.24, 0.38)	0.23 (-0.03, 0.59)

<sup>a</sup>Correlations for grip strength are from the linear model in men and the quadratic model – in women.

<sup>b</sup>Correlation between intercept and lifespan is significantly different from the correlation between slope and lifespan in sex-specific samples.

Table 3

Change in Grip Strength Between 1998 and 2005 in the Danish 1905-Cohort Study

	Model 1 (linear)		Model 2 (quadratic)	
	Men n = 450	Women n = 1,167	Men n = 450	Women n = 1,167
Fixed effects				
Intercept	22.6 (22.0, 23.3)	13.5 (13.2, 13.8)	22.7 (22.1, 23.3)	13.4 (13.2, 13.7)
Slope	-1.17 (-1.49, -0.87)	-0.48 (-0.60, -0.36)	-1.39 (-1.80, -0.98)	-0.29 (-0.49, -0.08)
Lifespan	96.4 (96.2, 96.7)	97.4 (97.2, 97.6)	96.4 (96.2, 96.7)	97.4 (97.2, 97.6)
Quadratic effect	—	—	0.07 (-0.02, 0.15)	-0.05 (-0.09, -0.01)
Variance components				
Variance (I)	32.8 (26.6, 39.9)	13.8 (11.8, 15.9)	32.9 (26.7, 39.9)	13.5 (11.5, 15.7)
Variance (S)	0.22 (0.001, 0.61)	0.13 (0.02, 0.25)	0.15 (0.00, 0.52)	0.14 (0.07, 0.26)
Covariance (I, S)	-0.28 (-1.88, 1.06)	-0.50 (-0.97, -0.06)	-0.29 (-1.83, 1.00)	-0.39 (-0.86, 0.05)
Covariance (I, LS)	4.25 (2.70, 5.94)	3.44 (2.66, 4.25)	4.48 (2.90, 6.21)	3.28 (2.50, 4.09)
Covariance (S, LS)	0.39 (-0.04, 0.84)	0.07 (-0.17, 0.31)	0.14 (-0.38, 0.68)	0.25 (-0.03, 0.53)
2 LnL	22,857	—	22,849	—
AIC	14,454	—	14,451	—
df	4,201	—	4,199	—

Note: I = intercept; S = slope; LS = lifespan. Total number of participants studied, n = 1,617; LnL=loglikelihood; AIC-Akaike's Information Criterion.