SECTION ON LONGITUDINAL STUDIES

Longitudinal changes in physical functional performance among the oldest old: insight from a study of Swedish twins

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ABSTRACT. ***Aims and Methods:*** *The primary purpose was to characterize mean and individual-level patterns of change in physical functional performance over eight years (2 year intervals) in a community dwelling sample of Swedish twins (579 men and women aged 79-96 years at baseline).* ***Results:*** *Mixed linear models revealed linear rates of decline for handgrip strength (grip) and time to complete five chair stands, and accelerating decline for peak expiratory flow rate (PEFR) for both sexes. Significant random effects were found for intercept and time for grip and PEFR tests, indicating differences between participants initially and over time. Individual differences in chair-stand performance were significant for initial status only. Age at baseline was predictive of initial status in grip, PEFR and chair performance (women only), but not rate of change. Measures of body size at baseline were predictive of individual variation in initial grip (height), PEFR (weight in men, height in women), and chair performance (height), but had less consistent associations with changes in test performance over time. In the deceased sub-sample (85% of participants), having been further from death was related to less steep declines in grip, but not PEFR or chair performance. Twins from the same pair were related in initial status (twin level variance ~30-70%), but they were not generally related in rate of change.* ***Conclusions:*** *These results indicate that changes in physical functional performance in an elderly, community-dwelling population vary across individuals in a test- and sex-dependent manner. Constitutional variables (age, sex, body size) are predictive of baseline performance, but explain little variance in change over time. Initial status and rate of change in grip strength had the strongest association with proximity from death, indicating that while PEFR and repeated chair stand time are useful tests to assess function, grip strength appears to be a particularly useful biomarker in the oldest-old.*

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INTRODUCTION

The maintenance of a physically independent lifestyle in old age depends, to a significant extent, on adequate levels of functional ability (1, 2). Most measures of function in physical ability (e.g., strength, endurance, balance, agility) indicate that adults' performance peaks between the second and fourth decades of life and then declines progressively with advancing age (3). Adults in very late life (>80 yrs), and particularly those who are sedentary, tend to demonstrate significantly reduced performance in basic physical functions and are therefore at a higher risk of developing disability. These individuals may be functioning close to their maximum capacity during normal daily activities (lifting, carrying objects, climbing stairs), and even an acute illness or minor physical setback can result in further decrements in physical function and the subsequent loss of independence in performance of daily activities (2). Because performance of basic physical function plays such a significant role in determining outcomes for the oldest-old, it is important to understand pat-

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terns of change in physical functional performance over time in this age group.

There are several tests of physical performance that are commonly used in studies of older adults. Peak isometric handgrip strength (i.e., grip strength) has been the most widely used objective measure of upper body strength in large-scale, longitudinal studies due to its simplicity, low cost, and its relevance to many activities of daily living (food preparation, opening cans, carrying objects; [4]). Grip strength is also positively associated with total body muscle mass and strength measured in other muscle groups (arms, leg, and trunk; [2, 5, 6] and therefore is often used as a global index of muscular aging. In addition to measuring limitations in upper body function, tests of lower body function have also been widely used as measures of physical performance. Lower extremity strength is closely associated with mobility in older women (7, 8) and men (7, 9). Lower body function has important implications for independence and disability in older adults. Past studies have shown that repeated chair stand performance, a common method of assessing lower body function in older adults, is significantly correlated with criterion measures of lower extremity strength (2).

Peak expiratory flow (PEF) and other indicators of lung function are also parameters of interest in the functional assessment of older adults. Within normal limits, lung function is not generally considered a limiting factor to the performance of daily activities, including strenuous exercise (3, 10, 11). Individuals who are exposed to tobacco smoke and/or who have a condition(s) that causes lung damage (chronic bronchitis, emphysema, or possibly asthma), however, exhibit accelerated declines in lung function that can eventually limit their daily physical activities (12). Deviations from normative, age-related decline in expiratory lung function within a given individual could reflect a change in his or her overall health status (i.e., accumulated effects of exposure to oxidative stress or discontinuation of a negative health habit such as smoking), and these changes could impact his or her ability to function independently in everyday activities.

Poor levels of grip strength, lower body strength, and expiratory lung function have each been linked to negative outcomes in later life. Recent longitudinal studies of middle-aged and older populations have determined that these abilities are highly predictive of subsequent functional decline and mortality. Rantanen et al. reported that men in the lowest tertile for grip strength at middle age were twice as likely as men in the highest tertile to experience functional limitations later in old age (71-96 years; [13]). A series of studies has demonstrated that poor performance on tests of lower extremity strength and power is predictive of future falls, mobility related impairment, and placement in dependent care facilities for women (14-16). In both of these examples, the research participants were functionally independent and reported little or no disability at baseline. These findings suggest that objective tests of muscle strength may serve as valid pre-clinical markers of disability. Finally, in addition to the outcomes of functional decline, falls, and institutionalization, compromised muscle strength (upper and lower body) and reduced lung function have also been cited as long-term predictors of mortality (17-21). The association between muscle function and survival has been observed in multiple populations of middle-aged and older adults.

To date, most longitudinal investigations of physical performance and aging have focused on describing the patterns and predictors of "group", or "mean-level", change over time. Longitudinal data on peak grip strength, for example, are characteristically described via three group-level patterns of change: stability, decline, or the less common category of improvement over time (13, 22, 23). Changes in function have also been described using mean-level data on discrete age categories (i.e., accelerated decline beginning in late midlife; (24). These approaches are useful for describing and predicting average changes over time within and between groups of older adults, but tend to over-generalize and over-simplify individual differences in the aging process. A longitudinal analysis of any outcome at the mean level is unfortunately more likely to describe patterns of the group better than the pattern for any individual within that group. Because mean-level analyses have the potential to mask underlying patterns of intra-individual variability and change, models that include both mean-level and individual-level parameters are more valid in describing actual change patterns over time (25).

Although it is acknowledged that large inter-subject variation in muscle function is likely to increase with age, and that group trajectories differ between various tests of muscle function (24), there are few, if any, longitudinal studies of the oldest old (>80 yr) that have directly examined inter-individual differences in rates of change in muscle and lung function.

The purpose of the present investigation was to examine the patterns and predictors of individual rates of change over time for grip strength, expiratory lung function, and repeated chair stand performance in the oldest-old. In addition to analyses of average levels of change in a population-based sample of the oldest-old, we also specifically tested for the presence of inter-individual variation in initial level (variation in level at the first study occasion) as well as inter-individual variation in the rate of change over time.

The models for these analyses were evaluated as a function of age, sex, height and weight, and models examined the effect of proximity to death as a predictor of decline in these three functional tests. For the current analyses, we hypothesized that although there would be mean-level patterns of decline in performance over the eight-year course of the study, there would also be significant levels of inter-individual variability in change over time. Thus, we expected that models including individual-level parameters would be better at describing patterns of change over time in performance of muscular and lung function in the oldest-old. We also expected that much of the individual variation in change over time would be explained by factors such as age, height, weight, and distance to death.

METHODS

Participants

Participants included 579 community dwelling men (n=191) and women (n=388) drawn from the longitudinal population-based twin study, Origins of Variance in the Old-Old (OCTO-Twin; [26]). Only participants with baseline data on the three examined variables were included in subsequent analyses. Participants were assessed at five different occasions at 2-year intervals. Age at the first occasion ranged from 79 to 96 years (M=83.2, SD=2.8) and years of formal schooling ranged from 0 to 23 (M=7.1, SD=2.3). The gender ratio, education, socio-economic status, marital status, and housing of the OCTO-Twin sample correspond to population statistics for this age segment of the Swedish population (27). Dates of death were obtained from the Swedish death registry for approximately 85% of participants, with the remaining 15% still living at the time of analysis. The deceased subsample of men (n=173) and women (n=320) was similar to the total sample in age at the first occasion (79-93 years, M=83.4, SD=2.9) and in years of formal schooling (0-23 years, M=7.1, SD=2.3).

The OCTO-Twin study protocols were approved by the Swedish Data Inspection Authority and the Ethical Review Board at the Karolinska Institute, Stockholm. Permission to conduct secondary data analyses was granted by Penn State's Office for Research Protections.

Measures

The OCTO-Twin Study includes a broad spectrum of bio-behavioral measures of health and functional capacity, personality, well-being, and interpersonal functioning. The three outcome measures used in the current study were grip strength, pulmonary expiratory function, and time to complete five chair stands. Grip strength was measured by having participants squeeze a Martin vigorimeter (Elmed Inc., Addison, IL, USA; medium size bulb) three times for each hand, with the final score being the maximum force (in pounds per square inch) exerted in the 6 trials. Peak expiratory flow rate is an index of expiratory lung function (28) and was measured by asking participants to place a spirometer in their mouth and blow out as forcefully as possible on three separate trials. The results from the trial with the highest expelled flow rate (measured in liters per second) were used as the measure of maximum pulmonary expiratory function. Time to complete five chair stands is an index of lower body strength and was measured by asking participants to sit in a chair, cross their arms at their chest, and stand up from the chair five times as quickly as possible without using their arms for assistance. The nurse administering the interview used a stopwatch to measure the amount of time it took (in seconds) for the participant to complete this task.

Procedures

The participants were assessed in their place of residence by licensed nurses (RNs) who were trained to conduct assessments of cognitive, motor, and physical function of elderly residents. Test-retest reliability of the grip, chair stand and expiratory tests was not formally quantified. However, consistency of testing procedures across waves was ensured by 1) using standardized testing procedures and participant instructions, 2) scheduling regular meetings and inter-tester comparisons among the five nurses performing these functional assessments and 3) the involvement of two nurses across the entire duration of the study (i.e. these two nurses were involved in testing at all 5 waves).

A complete testing session for each wave of OCTO-twin typically lasted eight-hours, which included an average of 3.5 - 4.0 hours of actual cognitive, motor and physical functional testing. The "pace" of these tests were individually adjusted and multiple rest periods were allowed throughout the day (including a nap if needed) to minimize participant fatigue.

Scheduling was arranged to minimize geographical, age, or gender order effects, and different nurses assessed the members in a pair within one month of the sibling's test date. The nurses were deliberately kept blind to zygosity of the twins to avoid expectation biases.

RESULTS

Analytic method

Univariate mixed linear models (29) were estimated using SAS PROC MIXED software in order to examine the overall pattern and individual differences in change across the five occasions for the three functional outcomes. Time was centered such that the intercept reflected initial status (baseline, or wave 1). The fit of models differing in both fixed and random effects was evaluated with maximum likelihood deviances and Information Criteria (AIC, BIC). The significance of fixed effects was evaluated with Wald's tests in which degrees of freedom were estimated using the Satterthwaite method. Fixed effects representing average initial level (intercept) and average rate of change and deceleration of change across time (linear and quadratic slopes) were estimated, as well as person-specific deviations of the intercepts and slopes, or random effects. The magnitude of the random effects was expressed using 95% confidence intervals (CI), calculated as ± 2 SD of

Table 1 - *Descriptive statistics and intraclass correlations (ICC) by outcome variable and sex.*

	Grip Strength		Expiratory Flow Rate		Chair Stand Time	
	Women	Men	Women	Men	Women	Men
Proportions of variance:						
Level 1 (time)	0.48	0.50	0.44	0.34	0.41	0.55
Level 2 (twin)	0.33	0.46	0.33	0.27	0.21	0.37
Level 3 (pair)	0.19	0.05	0.23	0.39	0.38	0.08
ICC Time (twin)[a]	0.52	0.50	0.56	0.66	0.59	0.45
ICC Twin (pair)[b]	0.36	0.09	0.41	0.60	0.64	0.18
Estimated Means (SE):						
Year 0	8.03 (0.14)	11.34 (0.21)	277.20 (5.05)	390.34 (10.25)	16.83 (0.33)	15.36 (0.37)
Year 2	7.25 (0.14)	10.07 (0.22)	289.99 (5.47)	392.32 (10.65)	17.50 (0.36)	16.79 (0.42)
Year 4	6.23 (0.15)	9.07 (0.24)	273.09 (6.00)	369.57 (11.59)	17.54 (0.40)	16.24 (0.51)
Year 6	5.64 (0.16)	8.22 (0.27)	245.55 (6.29)	340.70 (12.55)	17.51 (0.43)	16.42 (0.60)
Year 8	5.08 (0.17)	7.47 (0.30)	224.62 (7.12)	298.36 (14.25)	18.25 (0.50)	17.57 (0.74)

[a]Proportion of total variance at the twin and pair levels. [b]Proportion of person-level variance at the pair level.

the random variance around each fixed effect (i.e., average) estimate.

Table 1 displays, by sex, the estimated means and standard errors for each outcome, which show the expected decline over time. It is important to note that these means are freely estimated in a saturated model using full information maximum likelihood, which adjusts the estimates in the presence of missing data based on prior observations for individual and other covariates. Thus, these values would not precisely correspond to the observed means, which would likely be too high given non-random attrition (e.g., observations that are missing due to health problems would likely lower mean estimates of function). Full information maximum likelihood model estimates are unbiased and efficient given the assumption of missing at random, or that the probability of missingness is not related to what the outcome would have been once covariates are included in the model (30). Although it is not possible to formally test whether this assumption is met, we believe it is likely given the covariates included in the models below (e.g., age, height, weight, years to death, and prior observations for each individual).

In order to account properly for the correlation between individuals from the same twin pair, a three-level model was specified as time within twin pair for each outcome separately for each sex. Proportions of variance at each level and the intraclass correlations are provided in Table 1. As shown, between 33% and 55% of the outcome variance occurred within-twin (intraclass correlations of time within twin and pair ranged from 0.45 to 0.67), and between 21% and 39% of the outcome variance occurred within-pair (intraclass correlations of twin within pair ranged from 0.22 to 0.64). Random intercepts were specified at the pair level in each model, but adding a random slope at the pair level did not significantly improve fit in any model, suggesting that although twins from the same pair were related in initial status, they were not generally related in rate of change. Separate random effects and residual variances across zygosity type were examined in order to account for differences in the correlations within twin pairs of different zygosity types, but the models were not substantially improved, as indicated by the information criteria. Thus each model included a random intercept at level 3 (the pair level), and both random intercepts and slopes at level 2 (the twin level), and did not differ by zygosity.

The unconditional models (i.e., with predictors of time only) are described first for each outcome and sex. The extent to which variance in the random effects (i.e., individual intercepts and slopes) could be predicted by covariates of initial height, initial weight, initial age, and years to death from first occasion was then examined. Main effects (i.e., effects on the intercept) and interactions with time (i.e., effects on the slope) of initial height in centimeters (men: M=171.1 cm, SD=6.5; women M=157.1 cm, SD=5.9) and initial weight in kilograms (men: M=73.0 kg, SD=10.9; women M=60.0 kg, SD=10.5) were included in the conditional models as control variables. The extent to which initial age could predict initial status and rate of change was then examined, thus allowing for separate between- and within-person effects of age, respectively. Finally, the extent to which years to death from first occasion (available for 85% of the sample; M=6.2, SD=3.3) could further predict initial status and rate of change was examined. Interactions of age with height, with weight, with years to death, and of years to death with height and with weight were included in all models, but were significant only where noted in the results text below. The effect of change in weight over time (i.e., time-varying weight) was non-significant, and is thus not reported here.

Initial height and weight were each centered at the grand mean within sex, age was centered at 85 years, and years to death from the first occasion was centered at 6 years. Thus the intercept in the age-conditional models represented the expected initial status for an 85-year-old, of average height and weight within sex, with the additional reference in the death-conditional models of a person who died 6 years after the first occasion. Separate models were estimated for men and women within each outcome because of the large sex differences at the first occasion (i.e., baseline effects). Provided in the text separately by sex are the fixed effects (with 95% CI for the random effects) from the unconditional growth models and standardized coefficients (based on the first occasion within sex) for the effects of the covariates within the age- and death-conditional models. Psuedo R^2 values were calculated as described in Singer and Willett (29).

Provided next are the predicted absolute and relative decline for persons who were examined for the first time, i.e. baseline ages at either age 80 or 90 and tests of sex differences in initial status, in linear and quadratic rates of change, and in the effects of age and years to death on initial status and linear rates of change. Finally, conditional model unstandardized parameters and predicted trajectories at example levels of initial age and years to death for grip strength, expiratory function, and chair stand time are given in Tables 2, 3, and 4, and Figures 1, 2, and 3, respectively. Alpha was set at 0.05.

Grip strength

Women. The unconditional growth model of grip strength for women included random intercepts at the pair and twin levels, and random linear and fixed quadratic effects of time at the twin level. The expected value at the first occasion was 8.06 pounds per square inch (95% CI for pair = 5.80 to 10.31, for twin = 4.63 to 11.48), the instantaneous rate of decline at the first occasion was -0.47 pounds per square inch per year (95% CI=-0.85 to -0.09), and the expected deceleration of decline was 0.01 pounds per square inch per year. The fixed quadratic effect of time was no longer significant in the full and deceased samples in the conditional models.

As seen in the bottom of Table 2 and Figure 1, in the full sample, initial grip strength was greater for taller women (0.04 SD/cm) and for younger women (-0.06 SD/year), although there was an under-additive interaction between initial height and age (0.01 SD/cm/year).

Table 2 - *Grip strength conditional model parameters by sex for age and years to death (Ytd).*

	Women						Men					
	Age			Ytd			Age			Ytd		
Fixed effects	**Est**	**SE**	***p***	**Est**	**SE**	***p***	**Est**	**SE**	***p***	**Est**	**SE**	***p***
Intercept	7.83	0.14	0.00	7.71	0.15	0.00	10.87	0.26	0.00	11.03	0.26	0.00
Linear	-0.47	0.05	0.00	-0.47	0.06	0.00	-0.70	0.10	0.00	-0.72	0.10	0.00
Quadratic	0.01	0.01	0.12	-0.01	0.01	0.14	0.02	0.01	0.17	-0.01	0.01	0.60
Initial height	0.10	0.02	0.00	0.11	0.02	0.00	0.07	0.04	0.08	0.13	0.04	0.00
Initial weight	0.03	0.01	0.07	0.01	0.02	0.36	0.02	0.03	0.43	0.02	0.03	0.42
Height by linear	0.00	0.00	0.95	0.00	0.00	0.74	0.00	0.01	0.50	0.00	0.01	0.93
Weight by linear	0.00	0.00	0.24	0.00	0.00	0.50	0.00	0.00	0.67	0.00	0.00	0.45
Initial age	-0.15	0.04	0.00	-0.12	0.05	0.01	-0.22	0.07	0.00	-0.16	0.08	0.04
Age by linear	0.00	0.01	0.85	0.01	0.01	0.56	-0.02	0.02	0.17	-0.01	0.02	0.49
Height by age	0.01	0.01	0.04	0.02	0.01	0.01	-0.01	0.01	0.38	0.01	0.01	0.56
Weight by age	0.00	0.00	0.42	-0.01	0.00	0.13	0.01	0.01	0.43	0.00	0.01	0.79
Years to death				0.04	0.04	0.34				0.12	0.09	0.18
Years to death by linear				0.04	0.01	0.00				0.07	0.02	0.00
Height by years to death				0.00	0.01	0.79				0.04	0.01	0.00
Weight by years to death				-0.01	0.00	0.09				-0.01	0.01	0.06
Age by years to death				-0.01	0.01	0.51				0.00	0.02	0.89

Height, weight, and age did not predict linear rate of change. Twin-level variance in initial status and linear rate of change comprised 51% and <1%, respectively, of the variance in grip strength; the covariates accounted for 7% and 1% of these variances. In the deceased subsample, being further from death was related to a less steep linear rate of change (0.02 SD/year), but not to initial status. Twin-level variance in initial status and linear rate of change comprised 59% and <1%, respectively, of the variance in grip strength; the covariates with years to death accounted for 6% and 8% of these variances.

Men. The unconditional growth model of grip strength for men included random intercepts at the pair and twin levels, and random linear and random quadratic effects of time at the twin level. The expected value at the first occasion was 11.33 pounds per square inch (95% CI for pair = 9.98 to 12.68, for twin = 6.57 to 16.09), the instantaneous rate of decline at the first occasion was -0.65 pounds per square inch per year (95% CI= -2.15 to 0.84), and the expected deceleration of decline was 0.02 pounds per square inch per year (95% CI= -0.13 to 0.16). Although the fixed quadratic effect of time was not significant, random quadratic variation remained significant in the full and deceased samples in the conditional models.

As seen in the top of Table 2 and Figure 1, in the full sample, initial grip strength was greater for taller men (0.02 SD/cm; although this effect was only marginally significant with p=0.08) and for younger men (-0.07 SD/year). Neither height nor age predicted linear rate of change. Weight did not predict initial status or linear rate of change. Twin-level variance in initial status, linear rate of change, and quadratic rate of change comprised 68%, 7%, and <1%, respectively, of the variance in grip strength; the covariates accounted for 8%, 0%, and 0% of these variances. In the deceased subsample, being further from death was related to greater initial status in taller men (main effect of years to death =0.04 SD/year, interaction with height =0.01 SD/year/cm), and years to death was related to a less steep linear rate of change in all men (0.02 SD/year). Twin-level variance in initial status, linear rate of change, and quadratic rate of change comprised 67%, 7%, and <1% of the variance in grip strength; the covariates with years to death accounted for 18%, 4%, and 0% of these variances.

Sex differences. Men had significantly higher initial grip strength (full sample z=10.35, p<0.001, deceased subsample z=10.97, p<0.001), and had a significantly greater linear rate of change (full sample z=2.13, p<0.05, deceased subsample z=2.06, p<0.05). There were no sex differences in the quadratic rate of change or in the effects of age or years to death. Absolute 8-year decline in grip strength for an 80- or 90-year-old woman was predicted as 3.12 or 3.23 pounds per square inch, respectively, or 4.5% or 5.7% loss of strength per year. Absolute 8-year decline in grip strength for an 80- or 90-year-old man was predicted as 3.73 or 5.45 pounds per square inch, respectively, or approximately 3.9% or 7.0% loss of strength per year.

Expiratory lung function

Women. The unconditional growth model of expiratory function for women included random intercepts at the pair and twin levels, and random linear and fixed quadratic effects of time at the twin level. The expected value at the first occasion was 4.65 liters per second (95% CI for pair = 3.32 to 5.99, for twin = 2.76 to 6.55), the instantaneous rate of change at the first occasion was 0.09 liters per second per year (95% CI= -0.12 to 0.29), and the expected acceleration of decline was -0.03 liters per second per year. The fixed quadrat-

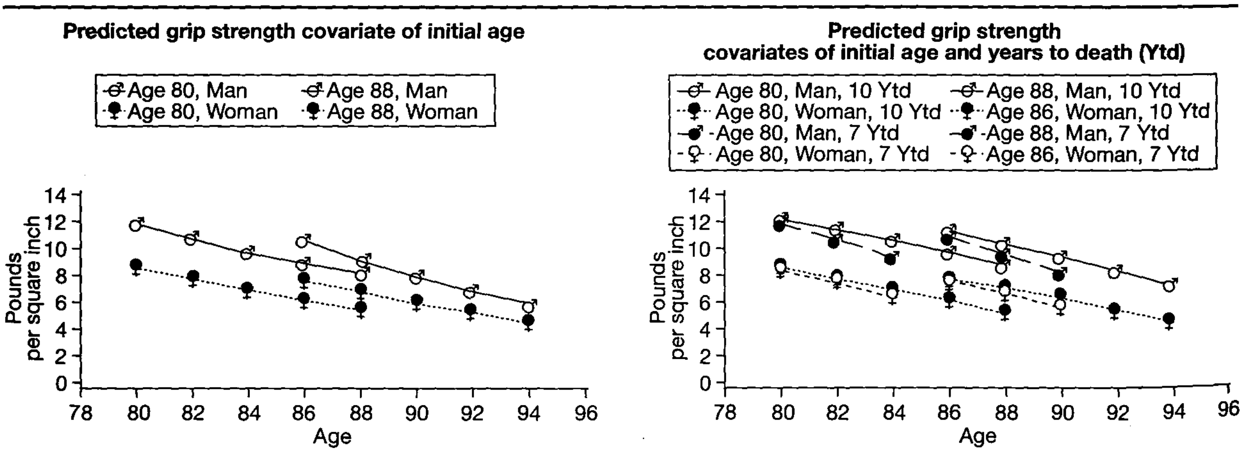

Fig. 1 - *Left: predicted grip strength conditional on age. Right: predicted grip strength conditional on age and years to death. Estimates for men and women were generated in separate models. Height and weight were controlled at the sample means.*

Table 3 - *Expiratory function conditional model parameters by sex for age and years to death (Ytd).*

	Women						Men					
	Age			Ytd			Age			Ytd		
Fixed effects	**Est**	**SE**	***p***	**Est**	**SE**	***p***	**Est**	**SE**	***p***	**Est**	**SE**	***p***
Intercept	270.65	5.93	0.00	266.26	6.42	0.00	369.54	13.32	0.00	376.89	13.43	0.00
Linear	6.16	2.12	0.00	6.13	2.74	0.03	2.76	3.98	0.49	-0.89	4.22	0.83
Quadratic	-1.52	0.27	0.00	-1.92	0.38	0.00	-1.81	0.46	0.00	-2.23	0.61	0.00
Initial height	2.50	1.00	0.01	3.40	1.08	0.00	1.42	2.56	0.58	2.22	2.63	0.40
Initial weight	0.57	0.59	0.34	-0.12	0.65	0.86	2.74	1.23	0.03	2.67	1.23	0.03
Height by linear	-0.26	0.15	0.08	-0.17	0.20	0.41	0.29	0.25	0.25	0.42	0.25	0.10
Weight by linear	0.09	0.09	0.30	0.04	0.12	0.75	-0.15	0.16	0.37	-0.13	0.15	0.41
Initial age	-4.41	1.81	0.02	-4.54	2.02	0.03	-9.91	3.83	0.01	-7.43	3.88	0.06
Age by linear	0.57	0.31	0.07	0.46	0.43	0.28	-0.09	0.79	0.91	-0.36	0.76	0.64
Height by age	-0.22	0.29	0.45	0.01	0.31	0.97	0.58	0.76	0.44	1.09	0.83	0.19
Weight by age	0.10	0.17	0.56	-0.12	0.18	0.52	0.35	0.34	0.30	0.17	0.34	0.61
Years to death				2.32	1.87	0.21				6.32	4.00	0.12
Years to death by linear				0.36	0.52	0.49				1.00	0.75	0.18
Height by years to death				-0.61	0.28	0.03				0.88	0.53	0.09
Weight by years to death				0.06	0.15	0.69				-0.40	0.30	0.19
Age by years to death				0.74	0.58	0.20				-0.38	1.14	0.74

ic effect of time remained significant in the full and deceased samples in the conditional models.

As seen in the bottom of Table 3 and Figure 2, in the full sample, initial expiratory function was greater for taller women (0.03 SD/cm) and for younger women (-0.05 SD/year). Weight did not predict initial status. Age, weight, and height did not predict linear rate of change. Twin-level variance in initial status and linear rate of change comprised 47% and <1% of the variance in expiratory function; the covariates accounted for 12% and 11% of these variances. In the deceased subsample, being further from death was related to greater initial status in shorter women (main effect of years to death =0.03 SD/year, interaction with height =-0.01 SD/year/cm), but years to death was not related to linear rate of change. Twin-level variance in initial status and linear rate of change comprised 48% and <1%, respectively, of the variance in expiratory function; the covariates with years to death accounted for 11% and 0% of these variances.

Men. The unconditional growth model of expiratory function for men included random intercepts at the pair and twin levels, and random linear and fixed quadratic effects of time at the twin level. The expected value at the first occasion was 6.51 liters per second (95% CI for pair = 4.06 to 8.96, for twin = 4.02 to 9.00), the instantaneous rate of change at the first occasion was 0.05 liters per second per year (95% CI=-0.22 to 0.32), and the expected acceleration of decline was -0.03 liters per second per year. The fixed quadratic effect of time remained significant in the full and deceased samples in the conditional models.

As seen in the top of Table 3 and Figure 2, in the full sample, initial expiratory function was greater for heavier men (0.02 SD/kg) and younger men (-0.08 SD/year). Weight and age did not predict linear rate of change. Height did not predict initial status or linear rate of change. Twin-level variance in initial status and linear rate of change comprised 40% and <1%, respectively, of the variance in expiratory function; the covariates accounted for 5% and 2% of these variances. In the deceased subsample, being further from death was not related to initial status or linear rate of change. Twin-level variance in initial status and linear rate of change comprised 44% and <1% of the variance in expiratory function; the covariates with years to death accounted for 11% of the variance in initial status. Psuedo R^2 for linear rate of change was not calculated because its variance was estimated as 0 in the death-conditional model.

Sex differences. Men had significantly higher initial expiratory function (full sample z=6.78, p<0.001, deceased subsample z=7.43, p<0.001). There were no sex differences in the linear or quadratic rates of change or in the effects of age or years to death. Because the rate of decline accelerated over time, declines were calculated separately for years 1 to 4 and 5 to 8. Absolute decline in expiratory function for an 80- or 90-year-old woman was predicted during the first 4 years as 0.19 or -0.20 liters per second, respectively, or approximately 1.0% or

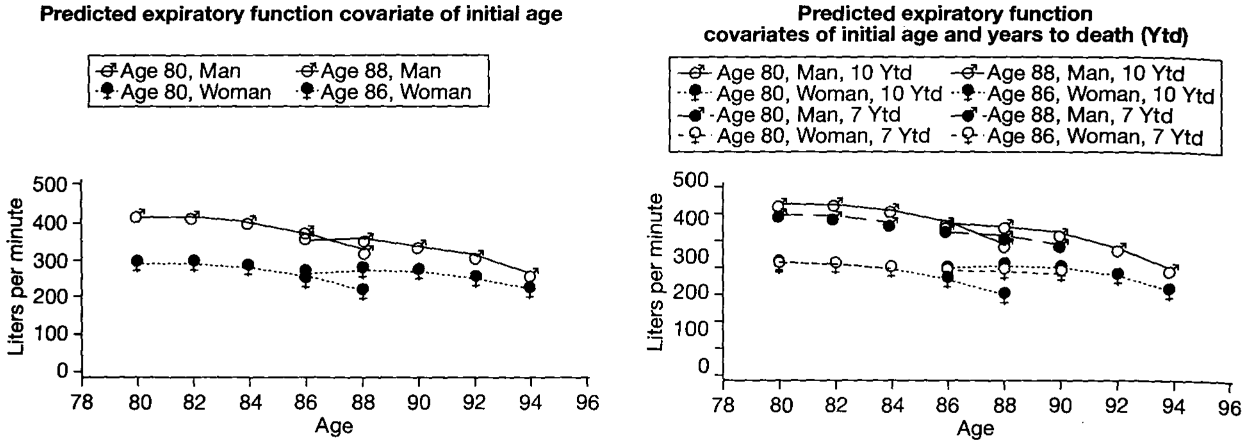

Fig. 2 - *Left: predicted expiratory function conditional on age. Right: predicted grip strength conditional on age and years to death. Estimates for men and women were generated in separate models. Height and weight were controlled at the sample means.*

-1.2% per year, and during the second 4 years as 1.00 or 0.62, or 5.3% or 3.6% per year. The unlikely overall increase in expiratory function for a 90-year-old woman during the first 4 years may be the result of selection processes, or even the effect of practice. Absolute decline in expiratory function for an 80- or 90-year-old man was predicted during the first 4 years as 0.27 or 0.33 liters per second, or approximately 1.0% or 1.5% per year, and during the second 4 years as 1.23 or 1.29, or 4.6% or 6.5% per year.

Chair stand time

Women. The unconditional growth model of time to complete five chair stands for women included random intercepts at the pair and twin levels, and random linear effects of time at the twin level. Although the fixed quadratic effect of time was not significant, it was left in the model for comparability across outcomes and sexes. The expected value at the first occasion was 16.91 seconds (95% CI for pair = 10.85 to 22.78, for twin = 11.05 to 22.78), the expected instanta-

Table 4 - *Chair stand time conditional model parameters by sex for age and years to death (Ytd).*

	Women						Men					
	Age			Ytd			Age			Ytd		
Fixed effects	Est	SE	p	Est	SE	p	Est	SE	p	Est	SE	p
Intercept	17.38	0.40	0.00	17.79	0.44	0.00	15.84	0.51	0.00	15.80	0.54	0.00
Linear	0.14	0.15	0.33	0.10	0.20	0.60	0.39	0.24	0.10	0.74	0.30	0.01
Quadratic	-0.01	0.02	0.62	0.00	0.03	1.00	-0.02	0.03	0.38	-0.09	0.05	0.06
Initial height	-0.04	0.06	0.56	-0.06	0.07	0.40	-0.03	0.11	0.76	-0.09	0.11	0.45
Initial weight	0.01	0.04	0.84	0.04	0.04	0.34	-0.02	0.05	0.77	0.00	0.05	0.98
Height by linear	-0.03	0.01	0.02	-0.03	0.01	0.06	0.03	0.01	0.01	0.04	0.02	0.05
Weight by linear	0.01	0.01	0.38	0.00	0.01	0.66	-0.01	0.01	0.30	-0.01	0.01	0.39
Initial age	0.30	0.12	0.01	0.29	0.14	0.04	0.15	0.15	0.30	0.09	0.15	0.57
Age by linear	-0.01	0.02	0.61	0.00	0.03	1.00	-0.03	0.04	0.54	-0.03	0.06	0.61
Height by age	0.02	0.02	0.40	0.00	0.02	0.95	0.00	0.03	0.91	-0.02	0.03	0.56
Weight by age	-0.02	0.01	0.07	-0.01	0.01	0.60	0.00	0.01	0.95	0.00	0.01	0.87
Years to death				-0.41	0.11	0.00				-0.18	0.16	0.28
Years to death by linear				0.03	0.03	0.43				0.00	0.06	0.99
Height by years to death				0.00	0.02	0.94				-0.02	0.02	0.45
Weight by years to death				0.00	0.01	0.74				0.00	0.01	0.76
Age by years to death				-0.08	0.03	0.01				0.03	0.04	0.47

neous rate of increase at the first occasion was 0.19 seconds per year (95% CI=-0.45 to 0.83), and the expected deceleration of increase was -0.01 seconds per year.

As seen in the bottom of Table 4 and Figure 3, in the full sample, initial chair stand time was significantly shorter for younger women (0.06 SD/year). Height did not predict initial status, but shorter women had a steeper linear rate of change (-0.01 SD/cm). Weight did not predict initial status, and neither weight nor age predicted linear rate of change. Twin-level variance in initial status and linear rate of change comprised 32% and <1% of the variance in chair stand time; the covariates accounted for 10% and 4% of these variances. In the deceased subsample, being further from death was associated with requiring less time to complete the five chair stands at baseline (-0.08 SD/year), especially for older women (interaction with age =-0.02 SD/year/year), but years to death was not related to linear rate of change. Twin-level variance in initial status and linear rate of change comprised 26% and <1% of the variance in chair stand time; the covariates with years to death accounted for 21% and 23% of these variances.

Men. The unconditional model of time to complete five chair stands for men included random intercepts at the pair and twin levels, and random linear effects of time at the twin level. Although the fixed quadratic and random linear effects of time were not significant, they were left in the model for comparability across outcomes and sexes. The expected value at the first occasion was 15.52 seconds (95% CI for pair = 12.93 to 18.11, for twin = 10.57 to 20.46), the expected instantaneous rate of increase at the first occasion was 0.40 seconds per year (95% CI=0.22 to 0.59), and the expected deceleration in the rate of increase was -0.02 seconds per year.

As seen in the top of Table 4 and Figure 3, in the full sample, initial chair stand time was not related to any of the covariates, but linear rate of change was steeper for taller men (0.01 SD/cm). Neither weight nor age predicted linear rate of change. Twin-level variance in initial status and linear rate of change comprised 36% and <1% of the variance in chair stand time; the covariates accounted for 7% of the variances in initial status. Psuedo R^2 for linear rate of change was not calculated because its variance was estimated as 0 in the conditional models. In the deceased subsample, years from death was not significantly related to initial status or linear rate of change. Twin-level variance in initial status and linear rate of change comprised 38% and <1% of the variance in chair stand time; the covariates with years to death accounted for 3% of the variances in initial status. The Psuedo R^2 value for linear rate of change again could not be calculated.

Sex differences. Men had significantly lower initial chair stand times (full sample z=2.37, $p<0.05$, deceased subsample z=2.88, $p<0.05$). There were no sex differences in the linear or quadratic rates of change or in the effects of age or years to death. Absolute 8-year increase in chair stand time for an 80- or 90-year-old woman was predicted as 1.02 or 0.12 seconds, or 0.8% or 0.1% per year. Absolute 8-year increase in chair stand time for an 80- or 90-year-old man was predicted as 2.60 or 0.45 seconds, or approximately 2.2% or 0.3% per year.

DISCUSSION

Mean patterns of change in physical function of the oldest old

Results from the growth curve modeling indicated primarily linear rates of decline in grip strength over the eight-year period of study. The average declines in grip

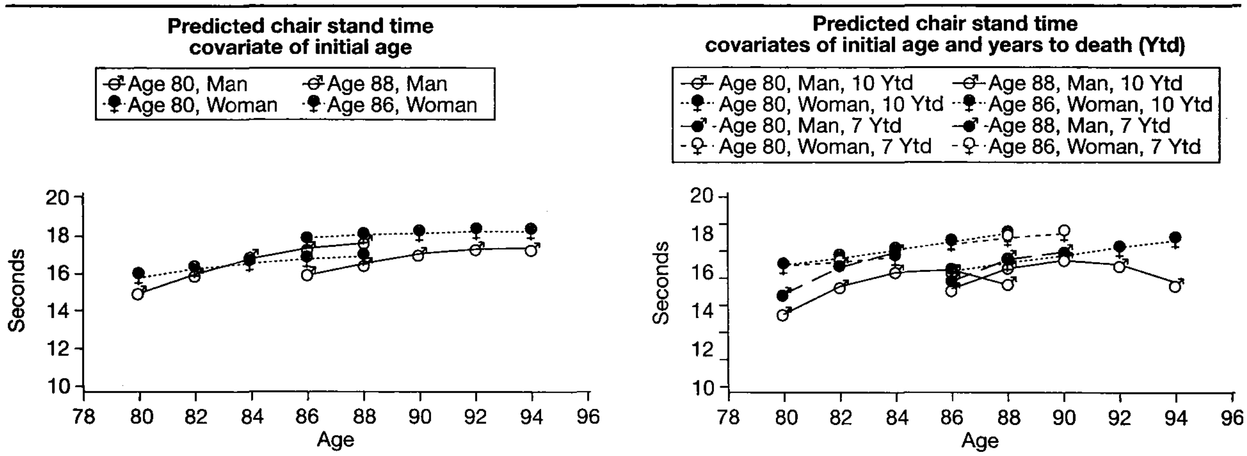

Fig. 3 - *Left: predicted time to complete five chair stands conditional on age. Right: predicted grip strength conditional on age and years to death. Estimates for men and women were generated in separate models. Height and weight were controlled at the sample means.*

strength for women (e.g., -5.7% per year at age 90 yr) and men (e.g., -7.0 % per year at age 90) appear larger than those reported in previous longitudinal studies of community dwelling participants over age 70 at baseline, which ranged from 2.6 to 4.8% per year for women (22, 23, 31, 32) and 1.2 to 3.0% per year for men (22, 23, 31-33). The more rapid declines in grip strength observed in the present investigation could reflect the advanced age of these subjects (i.e., 79 to 96 at baseline) and the longer follow-up period. Prior longitudinal studies included very few subjects over age 85 and with one exception (e.g., [33] the duration of follow-up did not exceed five years). The instrument used to measure grip strength also differed between the present study (vigorimeter) and previous studies (adjustable handgrip dynamometer). However, grip strength measured using the vigorimeter (which records pressure applied to a rubberized bulb) correlates well with grip strength measured with a conventional (static force) hand-grip dynamometer in older participants (34). An additional consideration is the manner in which the rate of change in grip strength was computed. The present study used a latent growth curve analysis which provides a true slope estimate by accounting for non-random attrition (i.e., missing data due to health problems) and adjustment for highly influential data outliers. Prior longitudinal studies of grip strength based their slope estimates exclusively on observed data, which would, to the extent that dropouts (or deaths) occurred, tend to underestimate the mean rate of decline in strength. As such, the present estimates of the average decline in grip strength probably provide a more accurate description of the natural loss of muscle strength in late life for both sexes.

Although declines in peak expiratory flow were expected, the accelerated rate of loss over time (curvilinear pattern) was not. Published longitudinal data for this particular expiratory variable are not available, but longitudinal rates of decline in other expiratory functions (i.e., FEV1.0 and FVC) are reportedly linear (35). Moreover, clinical prediction equations for each of these variables, including peak expiratory flow, are based on a linear rate of change with age (28). The advanced age of these subjects, the longer period of follow-up and the larger number of time points (n=5) from which to model change over time in comparison to previous studies (2 or 3 time points) may have increased the statistical power to detect a quadratic trend in the present study. Smoking status is unlikely to have contributed in a substantial way to the accelerated decline in expiratory function in the present sample due to the very small proportion of the sample currently smoking (13% for men, 5% for women). Due to the advanced age of this sample, long-term smokers are more likely to have died prior to becoming eligible for this study. A practical implication of the accelerated loss of expiratory function may be that published prediction equations, which have been primarily based on cross-sectional lung function data collected in younger age cohorts, have overestimated predicted normal values in the oldest old.

The average rates of change in chair-stand performance over time (<2.2% per year) were significant, but generally smaller than those observed for grip strength or peak expiratory flow. Noteworthy, there were considerably fewer participants at any wave with chair stand data compared to the other functional outcomes, which reflects the fact that analysis of the chair-stand test was restricted to participants who could actually complete five chair stands. Thus, the smaller relative decline in chair-stand performance compared to grip strength and expiratory function is likely to reflect a larger drop-off in the number of subjects who were unable to complete five chair stands, presumably those with the poorest functional ability. Such an effect ("selective dropout") is likely to truncate the sample in the low performing end of the distribution. It is noteworthy that a higher percentage of the women in the present study were able to complete five chair stands (77% at baseline; mean age 83 years) than a large sample of American women (55% of >85 yr olds; [8]). However, the average performance of the women able to complete this test across both studies was similar (16.9 *vs* 16.3 seconds, respectively).

Inter-subject variation and change in physical function in the oldest old

For grip strength, significant random effects were observed for both intercept and time in the full sample, indicating that there were significant individual differences in initial strength and in change over time. Grip strength was lower in subjects who were initially older in age and shorter. This was observed in both sexes and probably reflects the influence of limb muscle size, which is age- and height- dependent (36). Age and body size (height or weight) were not predictive of changes in grip strength. The men, in particular, varied greatly in the rate of grip strength change. This variation can be seen in the 95% confidence interval for the men, which crossed zero (-2.15 to 0.84), indicating that some older men maintained or even increased their strength over time. This variability in the rate of change in grip strength has been documented previously (13, 33). There were also significant individual differences in grip strength change in women, but most of the women lost strength (i.e., 95% C.I.=-0.85 to -0.09). To the best of our knowledge, inter-subject variation in grip strength over time has not previously been quantified in this manner in older women.

Age-associated reductions in peak expiratory flow are thought to result from normal reductions in elastic recoil of the chest wall and expiratory muscle strength with advancing age (11, 28, 37). Indeed, peak expiratory flow rate at baseline (initial level) was lower in the oldest subjects. Interestingly, the influence of body size on baseline expiratory flow was sex dependent, i.e., peak flow was higher in taller women and in heavier men. The influence of height on lung function is well established (lung size is scaled to height) and provides the basis for height- (and sex-) based lung function prediction equations (12). The higher expiratory flow rates produced by heavier men in this study are more difficult to explain. Previous studies suggest a negative influence of excess weight (i.e., fat) in the abdominal region on expiratory lung function in men (38, 39), whereas a recent study indicates a dominant, positive influence of fat-free weight (i.e., muscle) on expiratory lung function in older (55-86 yrs) adults (12). The OCTO-twin data set does not contain detailed information about body composition or fat distribution, so the nature of the weight dependency of peak expiratory flow rate in these men cannot be fully explored. Nevertheless, these results do suggest that body dimensions (i.e., height and weight) can have an effect on expiratory lung function in elderly men and women.

In contrast to grip strength and expiratory flow rate, chair-stand performance did not exhibit significant inter-subject variation in change over time, either in women or men. This test did appear better at discriminating baseline differences in performance among women (i.e., age effect), which could reflect greater difficulty of this test among older women and its association with mobility problems in this particular group (7, 8). However, as in men, the variation in change in chair stand time across individuals was not statistically significant in these women. This is somewhat surprising because the chair-stand test requires lower extremity strength, balance, coordination, and joint range of motion, and is therefore more complex (i.e., should be subject to more sources of variation) than the grip strength and expiratory function tests, the latter of which are peak, single effort tasks requiring primarily muscle strength. However, the apparent inability of the chair stand test to detect individual-level differences at baseline or over time could reflect the large dropout of subjects associated with the specific procedure we used to assess chair stand performance, rather than a limitation of lower body functional testing *per se*. That is, the assessment of the time to complete five chair stands significantly reduced the sample size at each wave by excluding all subjects who were unable to complete this number of stands, perhaps leaving a more homogeneous groups of subjects at each wave with respect to chair stand ability.

To improve the discriminating ability of the chair stand test, particularly among non-disabled community-dwelling older populations, some researchers have assessed chair stand performance as the number of successful stands in a fixed period of time (i.e., 30 seconds; [2]). When conducted in this manner, each participant has a score. In such cases, chair stand performance, either alone (8, 40) or as part of a composite functional performance score (9, 15, 40), is predictive of subsequent disability in older women and men. Therefore, it is possible that greater variability in individual rates of change may have been detected in the present study if we had assessed chair stand number rather than chair stand time.

It is interesting to note that chair stand "finishers" in the present study generally scored significantly higher on the grip strength test at each wave of testing than those who could not complete five chair stands (i.e., "non-finishers"; data not shown). This is further evidence of the utility of grip strength as a global measure of physical function in elderly subjects.

Sex differences in physical function among the oldest old

Women had lower initial performance scores than men for each of the three functional tests evaluated, consistent with previous reports (7, 9, 12, 19, 22, 23, 28. 32, 41, 42), mostly from "younger" age groups. At baseline, women's grip strength, expiratory flow, and chair stand performance averaged 29, 28, and 9% lower than in men. Sex differences in these physical function tests do not appear to be simply a function of the women's smaller body size, because significant baseline sex differences persisted when height-normalized scores were compared for each of the three tests (all p's<0.001, data not shown).

In addition to differences in baseline levels of functioning, men and women also had differential rates of decline for one variable: grip strength. Other than the smaller between-subject variation in grip strength change over time in women *vs* men (discussed in preceding section), grip strength declined at a slower absolute rate in women. The cause of this sex difference is not immediately apparent, but could involve diversity in daily domestic activities between women and men; for example, women may have more daily use and activity in tasks requiring manual strength, such as food preparation and they may maintain this performance over time. Bassey and Harries (22) found that grip strength deterioration over time in older women and men was associated with reported lower overall usage of the hands, i.e., disuse. Alternatively, differential rates of decline in grip strength between men and women could simply reflect a baseline effect (i.e., men had significantly more strength to lose).

The overall patterns of change for grip strength, peak expiratory flow and chair stand performance were similar in women and men. However, at least for grip strength and chair stand performance, variation between subjects in rate of change over time appeared to be sex-dependent (i.e., larger in men for grip strength and larger in women for chair stand performance as indicated by comparing the 95% confidence intervals). Failure to take such inter-subject variation into account could lead to incorrect conclusions regarding sex differences in functional declines occurring late in life. This further highlights the importance of assessing both the mean levels of performance and the dynamic changes in function over time.

Is proximity to death predictive of functional decline in the oldest old?

Several previous studies have reported an association between baseline muscle strength (13) or expiratory lung function (18, 21) and subsequent mortality in older adults. That is, participants who were deceased at follow-up had significantly lower mean performance levels on these tasks at baseline than similarly aged subjects who survived. These findings have led to the conclusion that baseline muscle function and lung function are predictors of mortality in middle-aged and older populations. In the present study, we addressed the questions of whether proximity to death is associated with baseline levels and/or rates of change in these functional outcomes. Results suggest that the influence of time to death on baseline functioning is sex-dependent. That is, men closer to death had a greater rate of decline in grip strength as compared to women, while women closer to death had poorer initial levels of expiratory function. Why elderly women with poorer grip strength would be less prone to physical deterioration and death than elderly men with poor strength cannot be determined from these results. Previous longitudinal studies in older men have not specifically explored time to death as a predictor of muscle function, and studies in non-disabled older women are lacking (20).

In the deceased sub-sample (85% of the participants at final wave), time to death was predictive of the rate of grip strength change over time in both sexes, i.e., grip strength in participants who were closer to dying declined at a faster rate. The fact that this effect was observed in both women and men (i.e., with widely varying initial strength levels) is suggestive of a more dynamic link between muscle strength loss and terminal decline than has been revealed through previous studies that examined baseline or mean changes in strength as a function of mortality risk (19, 20, 43, 44).

Although changes in peak expiratory flow and chair stand performance over time were not associated with time to death in either sex, the proximity of subsequent death had a significant interaction with height on baseline levels of peak expiratory flow in women, and also predicted baseline levels of chair stand performance in women (with an additional significant interaction with age on baseline levels of chair stand performance). Collectively, the results of the proximity to death analysis indicate that the relationship between changes in physical functional performance and "impending death" is not consistent across functional tests or between men and women.

Study limitations

The primary limitation of the present study was the manner in which repeated chair stand performance was quantified and the subsequent elimination of chair stand data for any participant who could not complete five stands. Another potential weakness of this test was the fact that chair height was not strictly maintained across the five waves of testing. However, the height of the chairs used probably varied minimally (i.e., a "normal" kitchen chair within each participant's residence). Additionally, the impact of chair height discrepancies over time on chair stand performance would be expected to be small in relation to changes in body weight over time. As indicated above in the results section, the effect of change in body weight over time was not significant for any of the three functional tests.

Participants with severe physical impairments were excluded from the present study to ensure that reliable results could be obtained for these "effort dependent" functional tests. Therefore, the present findings should be generalized only to the moderately to highly functioning oldest old, with demographic characteristics typical of the oldest-old age segment in Sweden.

Finally, it should be noted that cognitive impairment can influence the ability of older persons to understand and execute tests of physical function, particularly effort dependent tasks such as the ones examined in this paper. Although extensive cognitive data are available for the participants of OCTO-twin (26), it is beyond the scope of the present study to determine the impact of cognition on these physical function tests. It is certainly possible that cognitive status could have influenced grip, PEFR or chair stand performance given the advanced age of these participants. However, a systematic influence of cognitive impairment on functional performance in this OCTO-twin analysis remains unlikely because most participants were 1) community dwelling residents at baseline (i.e., only 7 participants lived in an institutional/nursing home setting) and 2) all participants received individualized instructions and encouragement from nurses trained in geriatrics and functional assessment. Nevertheless, further research should be conducted to determine if these physical functional outcomes are in any way influenced by changes in cognitive status among the oldest old.

CONCLUSIONS

The results of this longitudinal study indicate that changes in physical functional performance over time in a population-based sample of the oldest-old vary across individuals in a test- and sex-dependent manner. Constitutional variables (age, sex, body size) are predictive of baseline functional performance, but explain little variance in change over time in this population. Of the three functional tests reported here, initial status and rate of change in grip strength performance had the strongest association with proximity to death, indicating that while repeated chair stand time and peak expiratory flow may be useful tests to assess function, grip strength is a particularly useful biomarker for predicting meaningful outcomes in the oldest-old. Also, these findings support the emerging view that an accurate portrayal of functional change over time among older adults should include estimates of both mean-level and individual-level variation over time.

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REFERENCES

1. Gill TM, Williams CS, Richardson ED, Tinetti ME. Impairments in physical performance and cognitive status as predisposing factors for functional dependence among nondisabled older persons. J Gerontol A Biol Sci Med Sci 1996; 51: M283-8.
2. Rikli RE, Jones CJ. Development and validation of a functional fitness test for community-residing older adults. J Aging Phys Activity 1999; 7: 129-61.
3. Spirduso WW, Francis KL, MacRae PG. Physical dimensions of aging. Champaign, IL: Human Kinetics, 2005.
4. Innes E. Handgrip strength testing: A review of the literature. Australian Occupational Therapy Journal 1999; 46: 120-40.
5. Frederiksen H, Gaist D, Petersen HC, et al. Hand grip strength: a phenotype suitable for identifying genetic variants affecting mid- and late-life physical functioning. Genet Epidemiol 2002, 23: 110-22.
6. Rantanen T, Pertti E, Kauppinen M, Keikkinen E. Maximal isometric muscle strength and socioeconomic status, health, and physical activity in 75-year-old persons. J Aging Phys Activity 1994; 2: 206-20.
7. Guralnik JM, Ferrucci L, Pieper CF, et al. Lower extremity function and subsequent disability: consistency across studies, predictive models, and value of gait speed alone compared with the short physical performance battery. J Gerontol A Biol Sci Med Sci 2000; 55: M221-31.
8. Guralnik JM, Fried LP, Simonsick EM, Kasper JD, Lafferty ME. The Women's Health and Aging Study: Health and Social Characteristics of Older Women with Disability. Bethesda, MD: National Institute on Aging, 1995; NIH Pub. No. 95-4009.
9. Guralnik JM, Ferrucci L, Simonsick EM, Salive ME, and Wallace RB. Lower-extremity function in persons over the age of 70 years as a predictor of subsequent disability. N Engl J Med 1995; 332: 556-61.
10. Cheng YJ, Macera CA, Addy CL, Sy FS, Wieland D, Blair SN. Effects of physical activity on exercise tests and respiratory function. Br J Sports Med 2003; 37: 521-8.
11. Johnson BD, Dempsey JA. Demand vs. capacity in the aging pulmonary system. Exerc Sport Sci Rev 1991; 19: 171-210.
12. Amara CE, Koval JJ, Paterson DH, Cunningham DA. Lung function in older humans: the contribution of body composition, physical activity and smoking. Ann Hum Biol 2001; 28: 522-36.
13. Rantanen T, Masaki K, Foley D, Izmirlian G, White L, Guralnik JM. Grip strength changes over 27 yr in Japanese-American men. J Appl Physiol 1998; 85: 2047-53.
14. Onder G, Penninx BW, Lapuerta P, et al. Change in physical performance over time in older women: the Women's Health and Aging Study. J Gerontol A Biol Sci Med Sci 2002, 57: M289-93.
15. Ostir GV, Volpato S, Fried LP, Chaves P, Guralnik JM. Reliability and sensitivity to change assessed for a summary measure of lower body function: results from the Women's Health and Aging Study. J Clin Epidemiol 2002; 55: 916-21.
16. Posner JD, McCully KK, Landsberg LA, et al. Physical determinants of independence in mature women. Arch Phys Med Rehabil 1995; 76: 373-80.
17. Laukkanen P, Heikkinen E, Kauppinen M. Muscle strength and mobility as predictors of survival in 75-84-year-old people. Age Ageing 1995; 24: 468-73.
18. Mannino DM, Buist AS, Petty TL, Enright PL, Redd SC. Lung function and mortality in the United States: data from the First National Health and Nutrition Examination Survey follow up study. Thorax 2003; 58: 388-93.
19. Metter EJ, Talbot LA, Schrager M, Conwit RA. Arm-cranking muscle power and arm isometric muscle strength are independent predictors of all-cause mortality in men. J Appl Physiol 2004; 96: 814-21.
20. Rantanen T, Volpato S, Ferrucci L, Heikkinen E, Fried LP, Guralnik JM. Handgrip strength and cause-specific and total mortality in older disabled women: exploring the mechanism. J Am Geriatr Soc 2003; 51: 636-41.
21. Schunemann HJ, Dorn J, Grant BJ, Winkelstein W Jr., Trevisan M. Pulmonary function is a long-term predictor of mortality in the general population: 29-year follow-up of the Buffalo Health Study. Chest 2000, 118: 656-64.
22. Bassey EJ, Harries UJ. Normal values for handgrip strength in 920 men and women aged over 65 years, and longitudinal changes over 4 years in 620 survivors. Clin Sci (Lond) 1993; 84: 331-7.
23. Rantanen T, Era P, Heikkinen E. Physical activity and the changes in maximal isometric strength in men and women from the age of 75 to 80 years. J Am Geriatr Soc 1997; 45: 1439-45.
24. Finkel D, Pedersen NL, Reynolds CA, Berg S, de Faire U, Svartengren M. Genetic and environmental influences on decline in biobehavioral markers of aging. Behav Genet 2003; 33: 107-23.
25. Johansson B, Hofer SM, Allaire JC, et al. Change in cognitive capabilities in the oldest old: the effects of proximity to death in genetically related individuals over a 6-year period. Psychol Aging 2004; 19: 145-56.
26. McClearn GE, Johansson B, Berg S, et al. Substantial genetic influence on cognitive abilities in twins 80 or more years old. Science 1997; 276: 1560-3.
27. Simmons SF, Johansson B, Zarit SH, Ljungquist B, Plomin R, McClearn GE. Selection bias in samples of older twins? A comparison between octogenarian twins and singletons in Sweden. J Aging Health 1997; 9: 553-67.
28. Knudson RJ, Lebowitz MD, Holberg CJ, Burrows B. Changes in the normal maximal expiratory flow-volume curve with growth and aging. Am Rev Respir Dis 1983; 127: 725-34.
29. Singer JDW, Willett JB. Applied longitudinal data analysis: Modeling change and event occurrence. New York: Oxford University Press, 2003.
30. Schafer JL. Analysis of Incomplete Multivariate Data. New York: Chapman and Hall, 1997.

31. Christensen H, Korten AE, Mackinnon AJ, Jorm AF, Henderson AS, Rodgers B. Are changes in sensory disability, reaction time, and grip strength associated with changes in memory and crystallized Intelligence? A longitudinal analysis in an elderly community sample. Gerontology 2000, 46: 276-292.
32. Clement FJ. Longitudinal and cross-sectional assessments of age changes in physical strength as related to sex, social class, and mental ability. J Gerontol 1974; 29: 423-9.
33. Kallman DA, Plato CC, Tobin JD. The role of muscle loss in the age-related decline of grip strength: cross-sectional and longitudinal perspectives. J Gerontol 1990; 45: M82-8.
34. Desrosiers J, Hebert R, Bravo G, Dutil E. Comparison of the Jamar dynamometer and the Martin vigorimeter for grip strength measurements in a healthy elderly population. Scand J Rehabil Med 1995; 27: 137-43.
35. Griffith KA, Sherrill DL, Siegel EM, Manolio TA, Bonekat HW, Enright PL. Predictors of loss of lung function in the elderly: the Cardiovascular Health Study. Am J Respir Crit Care Med 2001; 163: 61-8.
36. Proctor DN, O'Brien PC, Atkinson EJ, Nair KS. Comparison of techniques to estimate total body skeletal muscle mass in people of different age groups. Am J Physiol 1999; 277: E489-95.
37. Knudson RJ, Burrows B, Lebowitz MD. The maximal expiratory flow-volume curve: its use in the detection of ventilatory abnormalities in a population study. Am Rev Respir Dis 1976; 114: 871-9.
38. Harik-Khan RI, Wise RA, Fleg JL. The effect of gender on the relationship between body fat distribution and lung function. J Clin Epidemiol 2001; 54: 399-406.
39. Schoenberg JB, Beck GJ, Bouhuys A. Growth and decay of pulmonary function in healthy blacks and whites. Respir Physiol 1978; 33: 367-93.
40. Bean JF, Kiely DK, Herman S, et al. The relationship between leg power and physical performance in mobility-limited older people. J Am Geriatr Soc 2002; 50: 461-7.
41. Ferrucci L, Penninx BW, Leveille SG, et al. Characteristics of nondisabled older persons who perform poorly in objective tests of lower extremity function. J Am Geriatr Soc 2000; 48: 1102-10.
42. Guralnik JM, Simonsick EM, Ferrucci L, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. J Gerontol 1994; 49: M85-94.
43. Era P, Rantanen T. Changes in physical capacity and sensory/psychomotor functions from 75 to 80 years of age and from 80 to 85 years of age—a longitudinal study. Scand J Soc Med Suppl 1997; 53: 25-43.
44. Metter EJ, Talbot LA, Schrager M, Conwit R. Skeletal muscle strength as a predictor of all-cause mortality in healthy men. J Gerontol A Biol Sci Med Sci 2002; 57: B359-65.