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Predictors of Extraordinary Survival in the Iowa Established Populations for Epidemiologic Study of the Elderly: Cohort follow-up to 'Extinction'

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Abstract

OBJECTIVES—To identify predictors of extraordinary survival (ES).

DESIGN—Longitudinal study of a cohort of elderly people followed up until almost all have died

SETTING—Two counties in Iowa, USA, a part of the Epidemiological Study of the Elderly.

PARTICIPANTS—2890 community-dwelling citizens, 65–85 years at baseline, surviving at least three years.

MEASUREMENTS—Data relating to age, sex, birth order, parental longevity, marital status, education, family income, social support, self-reported health, chronic diseases, blood pressure, body mass index, physical ability, exercises, life attitude and mental health were obtained. Extraordinary survivors were defined as those belonging to approximately top 10% longest survivors for their sex group.

RESULTS—253 ES were far more likely to have never smoked. In basic models (age/sex/smoking adjusted) for earlier-life factors, parent's longevity, being earlier in the birth order (in women only) and BMI at age 50 were associated with ES.

In similar models for predictors at age 65–85 years (later-life or baseline), ES was associated with excellent self-reported health, fewest chronic diseases, better physical mobility, memory and positive attitude towards life, but not with depression, anxiety or sleep. In multi-variable models, attitude towards life was not an independent predictor. On a cumulative score of independent predictors, women in the top third of longevity attributes were 9.26 (CI 4.38–19.57, $p < 0.0001$) times as likely to reach ES compared to bottom third.

CONCLUSION—Extraordinary survivors had fewer 'classical' risk factors and were in better health than their contemporaneous controls. Earlier-life, possibly genetic factors appear less predictive in men.

Keywords

Extraordinary survivor; oldest old; predictors; heritable

INTRODUCTION

Survival into advanced old age is still a relatively rare phenomenon with less than 1% of Americans currently expected to survive to age 95¹. Explaining why some people live much longer than others may be key to improving mid and later life health, and has long intrigued both scientists and the public.

Research on longevity and extraordinary survivors (ES) has suggested that lifespan is influenced by a combination of heritable factors, non-heritable environmental factors and stochastic events². Mechanisms involved are hypothesized to include free radical mediated damage, diet and calorie intake, physical activity, fecundity, familial clustering, and age related chronic inflammatory processes³⁻⁶.

Much of the leading research on longevity focuses on centenarians or nonagenarians, mainly comparing long lived individuals to younger controls, because contemporary controls of ES have long deceased². However, the comparability of these groups has been questioned, as the younger cohorts have generally experienced very different material circumstances, social patterns and medical care from those born several decades before them. In addition, information collected from these long-lived individuals after they have reached their ES status may be subject to recall bias.

The National Institute on Aging's Established Populations for Epidemiological Study of the Elderly (EPESE), Iowa⁷ site interviewed a large population representative sample of community living elderly people aged 65 years and over starting in 1981. This cohort was longitudinally followed up for approximately 26 years until virtually every member of this cohort had died i.e. almost to the 'extinction' of the cohort. These data provide a rare opportunity to explore exceptional longevity in a large population based prospective cohort. In our analysis, we aimed to identify the characteristics in this cohort that predict extraordinary survival, in both men and women.

METHODS

Sampling and data collection

In Iowa EPESE, all eligible participants (community dwelling citizens aged more than 65 years) residing in two counties in the state (Iowa and Washington) were enumerated using a list from the area's Agency on Aging, a local government agency and the lower tier of the countrywide Aging Services Network. It is responsible for collecting comprehensive records of all senior citizens aged 60 or above, living in the community in the local area. This was supplemented by additional listings from local informants, thus ensuring a population representative sample of elderly community-dwelling Iowans. The majority inhabitants of these counties were farm-dwelling, with few employed in local light industrial, service and tourism related jobs. A total of 4,601 study subjects were enumerated. Baseline interviews could be conducted for 3,674 persons between November 1981 and January 1983 (84% underwent full household interview, 3.3% appeared for abbreviated interview, 6.8% answered through proxy interviews and 5.6% were interviewed over the telephone). Non-respondent's basic demographic characteristics were similar to those of study participants⁷.

The Iowa-EPESE was designed as a prospective study with an initial baseline survey and continuous surveillance that included monitoring of all deaths, institutional admissions and changes in functional abilities. Baseline data were collected through an interview and simple measurements of blood pressure of the interviewees. The baseline data collection did not involve collection of any blood or tissue samples. The initial baseline interview was

followed by re-contacts⁷. In the current analysis, data collected at baseline from Iowa EPESE is analyzed to identify predictors for ES in men and women.

Ascertainment of death

The survival status of each participant was examined through the surveillance system and death was ascertained through obtaining death certificates and scrutiny through National Death Index. The first death in the cohort occurred on 17th February 1982 and the last recorded death we identified took place on 18th September 2008. For 190 individuals (6% of all the respondents) no death certificates were available at the time when the last death records were collected (September 2008). For one participant the date of birth was missing.

Extraordinary survival

Extraordinary survivors (ES) were defined as men who reached 94 years plus and women 97 years plus. These full year of age cut-offs were chosen to include approximately the top 10% of the longest surviving individuals in each sex group (9.11% in case of males and 8.44% in case of females). This cut-point was chosen to provide sufficient statistical power for the analysis.

Predictors: domains and scales

The domains of potential predictors for modeling ES were selected from the baseline dataset based on the existing literature on ageing. The descriptions of the domains and the variables follow.

The participant's birth order amongst siblings was coded as a continuous variable. Parental age at death (whether parents of study participants lived to 85 years or older - the commonly used cut-off point for defining "oldest of the old") was classified into 'neither', 'one' or 'both' and scored 0, 1 and 2. Ever having been pregnant was dichotomized.

Social predictors included whether the participants ever married and whether they were living with their spouses (both coded as binary variables). We coded a composite score for social support received from children, relatives and friends. This was divided into three ordered categories, the lowest category: marked by absence of any support and the highest category representing maximum support from social networks. Family income and education status of participants were included in the analysis as ordered categorical variables. Participants were shown a card containing many income categories from which they had to choose one closest to their own family income. Single individuals reported their personal income whereas married individuals reported gross family income.

Self-reported health was entered in models in three categories ranging from excellent to very poor. Average of the two systolic blood pressure (categorized into <119, 120–139, 140–159, 160) and diastolic blood pressure (categorized into <80, 80–89, 90–99, 100) measurements obtained at baseline were entered as ordered categories based on accepted definition of hypertension. Body Mass Index (BMI) at ages 50 and at study baseline was divided into the standard four ordered categories (<20, 20–25, 25–30 'overweight' and >30 'obese').

The physical functioning assessment included a score for seven independent Activities of Daily Living (ADL) adapted from the index developed by⁸. The second variable used in this domain was a composite score calculated from seven activities related to gross mobility and physical abilities in lines with Rosow-Breslau Functional Health Scale (1966) and Nagi's work on disability (1976) viz. heavy chores, climbing stairs, walking ½ mile, pull/push heavy objects, stooping, raising arms and writing. The ADL variable was dichotomized (one

group with no difficulty and the other with at least some difficulty – because there was only a small proportion with any ADL difficulty at all) and the variable related to score of gross mobility and physical ability was divided into three ordered categories (No difficulty, difficulties in 2/7 activities and difficulties in > 2/7 activities). The third variable used in this domain was a composite score of exercises (both moderate and heavy exercises) undertaken which was then divided into tertiles.

Cognition and mental health was measured using the modified Short Portable Mental Status Questionnaire (SPMSQ)⁹ score computed from nine questions (“What is the name of this place?” was not asked) and then dichotomized as with full score or less than full score. Self-assessed memory and numbers of words recalled were included in the models as tertiles. Presence of depressive symptoms was computed from an abbreviated version of Centre for Epidemiological Study – Depression scale. Anxiety and panic variables were dichotomized (whether present or absent). An attitude towards life score was computed from ten questions covering respondent’s feelings about the present in comparison to the past and their outlook on the future. This variable was divided into tertiles, ranging from positive to negative attitude towards life. The composite sleep score was collated from five questions regarding sleep difficulty (difficulties falling asleep, waking in the night, waking too early in the morning, feeling rested and need to take nap during the day) and divided into tertiles.

Statistical analysis

Initially the variables were individually included in basic adjusted logistic regression models to test for association with ES (after adjusting for age, sex and smoking status). Basic adjusted models were used on pooled data (males and females together where the variable sex was adjusted); and then used on data stratified by sex. Interaction terms with sex were also included in the models for statistically significant associations ($p < 0.05$). Observations with missing values for each variable (except for missing dates of death or birth) were coded as a “missing” category and included in the models. Missing values were excluded from the models only when continuous variables were used. Age of participants at baseline was treated as a primary confounder in the analysis and was controlled in all the models. Sex was also adjusted for during analysis of pooled data. Smoking status was recoded into never smoked, ex-smoker and current smoker.

As all of the predictors were selected on the basis of previous evidence, we did not correct for multiple testing.

Variables which showed significant association in the basic adjusted models ($p < 0.05$) were used to construct two parsimonious multi-variable models. The first multi-variable model consisted of predictors from the earlier lives of participants (subsequently referred to as earlier-life predictors). The second multi-variable model included predictors reflecting the characteristics of the participants at baseline (subsequently referred to as baseline predictors). Stata, version 10.1 (StataCorp, College Station, Texas) was used to analyze the data.

A single accumulated survival advantage score was created from the ten significant predictors (both earlier-life and baseline). Each variable was divided into tertiles/three natural groups, scored 0, 1 and 2 and summed to reflect higher chances of achieving ES, yielding a score range of 0 to 20.

Race stratified analysis could not be conducted as almost all the enumerated elderly population in those two counties were of white European ancestry.

Inclusion criteria and missing values

Out of the 3674 interviewees, 191 respondents whose ages at death could not be obtained (discussed above) were excluded from this analysis because at the time of collection of last death certificate i.e. September 2008, it was unknown whether some of them were still alive then or had dropped out of the study prior to that date. Of these 191 excluded observations with missing death records, 81% were women and their other demographic characteristics were comparable with the included participants.

Participants aged more than 85 years during the baseline interview or who lived less than 3 years from the baseline interview were excluded from analysis (784 participants excluded based on these two criteria). The first criterion was used to exclude the “oldest olds” (i.e. aged 85 years or more) who were already close to or within the ES group. The second criterion was used to exclude groups with terminal illnesses during baseline data collection. Consequently 2890 study participants were included in the analysis.

RESULTS

A total of 1092 men and 1698 women were included in the analysis (Table 1). Of these, 253 were extraordinary survivors (ES): 99 men (surviving to 94 plus) and 154 women (surviving to 97 plus). The mean age at baseline of the sample (Table 1) was 72 years for men and 74 for women, with a mean survival of 11 and 14 years from baseline, respectively. A history of smoking was more common in men (60% had smoked) compared to women (14%). At study baseline in both men and women, 19% rated their health as excellent, with 27% rating it as poor or very poor. Disability was uncommon, with only 6% of men and 10% of women reporting at least one activity of daily living difficulty. Approximately 30% of the sample had social support from children, friends or relatives.

Never having smoked made achieving extraordinary survival much more likely in men (for never-smokers vs current OR= 8.87, 95% CI=2.12 – 37.08, $p=0.003$) in age and sex adjusted models (Table 2). In basic adjusted models testing one risk factor at a time (adjusted for age, sex and smoking status), nine variables (at $p<0.05$) were associated with ES (Table 2).

Earlier-life predictors

Age at death of parents was strongly associated with ES for women (Table 2). Female participants whose parents (one or both) had lived to 85 years or beyond were more likely to become ES themselves compared to those women whose parents (both) died before reaching the age of 85. Parental age remained associated with extreme longevity of women when included in the model as continuous variables. This determinant did not show an association with extreme longevity of men: the sex interaction term for this variable was significant ($p=0.05$).

Being later in their family birth order emerged as a ‘negative’ predictor of ES only for women (OR= 0.87, 95% CI 0.79–0.96, p value= 0.02): the later in their sibling birth order, the lower their chances of ES. This association was not evident in men or for the pooled data and a significant sex interaction term ($p= 0.016$) suggests that this factor is specific to women.

High reported Body Mass Index (BMI) at age 50 was negatively associated with ES (men and women together): those with BMI>30 (obesity) were less likely to achieve ES status (OR=0.50 95%CI 0.28 – 0.91, $p=0.02$) compared to the ‘normal’ BMI group (20 to 25). In gender specific analyses estimates were in the same direction but did not reach significance in men: the gender interaction term was non-significant. There was no association of ES with BMI at baseline.

Associations with educational attainment were not significant. Marital status of participants did not influence ES.

Baseline predictors

Living with spouses did not influence ES. Similarly, social support networks comprising of children, friends and relatives were not associated with ES.

High measured systolic blood pressure (≥ 160) in women was negatively associated with ES (OR=0.37, 95% CI 0.18 – 0.75, $p < 0.01$) with a significant interaction term for sex ($p = 0.04$) showing this effect to be specific for females.

Overall self-rated health status was strongly associated with ES. Participants with good to excellent self-rated general health were more likely to survive to the exceptional range than participants with a poor to very poor general health (OR=3.25, 95% CI= 2.09 – 5.06, $p < 0.000$). This association was significant for both men and women.

The ADL scores and exercise scores were not associated with ES whereas the score of gross mobility & physical ability for elderly people emerged as a predictor for extreme longevity ($p < 0.01$). Participants with no difficulty in this scoring system were more likely to achieving ES, compared to their contemporaries who reported some difficulty. The effects of this score were more pronounced in men.

Two cognitive measures (modified SPMSQ and self-assessed memory scores) were not associated with ES. However, memory assessment as scored by numbers of words recalled was positively associated ($p < 0.01$) with ES but this association was only statistically significant in females. Other criteria considered for mental health in the study (viz. depression, anxiety and panic scores) were not associated with ES. The third of participants with the most positive attitudes toward life were more likely to achieve ES compared to the least positive third (OR= 1.54, 95% CI= 1.07–2.21, $p = 0.02$). Linear trends with ES were also observed across the categories of attitude among the participants.

Multi-variable models—We next examined which of the above statistically significant factors were predictive, while adjusting for the other significant variables. We analyzed earlier-life (pre-existing) and baseline predictors (later life) separately. The earlier-life factor model (Table 3) included measures of birth order among siblings, parental age at death and BMI at 50 years. All three factors remained associated with ES, with estimates little changed from the basic adjusted models. BMI at age 50 lost its significant association for women but remained associated in the pooled data ($p = 0.04$).

The multi-variable model (Table 4) of significant baseline predictors measuring status of participants at study baseline (i.e. at ages 65 to 85) included smoking, life attitude, self-reported health, chronic medical conditions, systolic BP, numbers of words recalled and gross mobility & physical ability. Among the set of variables, the independent association of positive life attitude was attenuated in the fully adjusted multi-variable model. The other variables retained their independent association (for blood pressure in women only).

Accumulated survival advantage score—Modeling an accumulated survival advantage score (computed from the ten significant predictors - see Methods) showed (Fig. 1) the upper tertile group with the highest scores were far more likely to achieve ES. The magnitude of this effect was very large in women (OR=9.26, 95% CI 4.38 – 19.57, $p < 0.0001$) and less dramatic in men (OR=3.69, 95% CI 1.83 – 7.43, $p < 0.0001$).

DISCUSSION

Previous studies of nonagenarian and centenarian groups have provided many important insights, but have been limited to comparing ES with younger controls. In the Iowa-EPESE cohort with baseline data and death certification on almost all the original respondents, we have tested the significance of a range of earlier and later life factors for achieving ES. We defined ES as being amongst the longest lived 10% of the 65 to 85 year old sample when first interviewed. Some of our findings are familiar, such as the evidence that extraordinary survivors have better self rated health, lower rates of disease and less mobility limitation in earlier old age. However, several of our findings appear novel, including the male - female differences in possibly genetic factors, the powerful role of established health risks such as smoking and obesity, and the evidence that positive attitude and psychological measures may not be strong independent predictors when measured earlier in old age.

An important earlier-life finding of this study was the positive association between parental lifespan and the longevity for female offspring only. Although the New England Centenarian Study¹⁰ and others¹¹⁻¹³ have reported associations between parental lifespan and longevity of offspring, we found this effect to be restricted to women participants in the Iowa EPESE. Evidence for a stronger association of parental age with female longevity has been reported from the genealogy study¹⁴. The effect of parental age on ES is suggested to be partly a genetic effect^{15, 16} contributing to the approximately 25%¹⁷ of the variability in human lifespan that is heritable. It may be that the poorer health behaviors (e.g. much higher smoking rates) in men overshadow the effect of these heritable determinants. It appears therefore that determinants for extreme human longevity may be different for males and females, as suggested by Franceschi et al¹⁸.

Another novel result of our analysis is that women born early in their sibling sequence are likely to live longer. Plausible mechanisms may relate to possible poorer social circumstances in larger families in earlier part of the twentieth century. Alternatively, the mechanism may possibly be genetic, with offspring late in their birth orders being more likely to be born with harmful mutations. Greater parental age at conception is known to increase the risk of transferring harmful mutations to the next generation. However, there are reports to the contrary^{19, 20}, showing lack of association between parental age at birth and longevity of offspring. In addition, it is difficult to see why the environmental or genetic mechanisms would be sex specific. This finding, especially the apparent specificity to women, clearly needs further exploration. This finding, especially the apparent specificity to women, clearly needs further exploration.

Obesity is widely acknowledged as a major determinant of morbidity and mortality. In our analysis, the respondents who reported Body Mass Index >30 at age 50 were less likely to achieve ES. Low BMI (<20) measured later in life has been linked to excess morbidity and mortality^{21, 22}, but in our analyses BMI at baseline (ages 65 to 85 years) shows no association with ES. This is consistent with previous studies which showed BMI in the middle aged to have significant predictive power for survival, but that BMI with advancing age is less predictive^{23, 24}.

As previously shown²⁵⁻²⁷ self-reported general health earlier in old age continues to be one of the strongest predictors of ES, suggesting that extreme survival is associated with delayed onset of disease until later in life. Not surprisingly, we found that having fewer common chronic medical conditions strongly predicts ES. Both these variables (self-reported health and chronic medical conditions) were strongly associated with ES in elderly Iowa men and women and also maintained their independent significant association with ES in the multi-variable models. As both self-reported health and chronic medical diseases are inevitably

incomplete measures of 'true physical health status', both contribute independently to longevity prediction.

Positive attitude towards life was associated with extreme longevity in Iowa EPESE, in simple age, sex and smoking adjusted models. This was similar to previous findings^{28, 29} suggesting that life satisfaction and positive attitude towards life predict human longevity. However, in our analysis this predictor lost significance in models adjusted for other ES predictors. Analysis of this suggested that loss of significance was attributable to adjustment for the markers of self reported health, physical disease and mobility. This suggests that association of positive attitude to life with ES may be mediated through the better physical health of ES individuals. We note also that measures of anxiety and depression were not predictive of ES. It may be that life attitude is influenced by physical health rather than being an independent predictor, and popular prescription to adopt a positive attitude to improve health and prolong life may therefore be unfounded.

In contrary to conventional wisdom and evidence from several studies^{30–32} the prominent markers of social support in old age (from children, relatives and friends) was not a significant predictor of extreme longevity in this study. This may be due to the limitations of the measure, which asked about the presence of support in this predominantly rural community where social were likely to be spread out further than would be expected in other communities. Alternatively there may have been mechanisms of community support that were not recorded in the measurement scale used in the baseline interview. Marital status of respondents was not associated with ES as expected, given the little variability in this domain in this cohort (only 4% women and 6% men never married). Other common socio-economic predictors, including years of education and family income level, showed no association with extreme longevity in the Iowa EPESE as in some other studies³³. This can be due to measurement issues in this farming community, where wealth may be less accurately monetized into income categories than in communities drawing occupational pensions.

In this study, the modified Short Portable Mental Status Questionnaire score and self-rated memory failed to show association with longevity. In contrast, the test of memory scored through numbers of words recalled emerged as a strong predictor of ES, especially in women. The conventional ADL score also failed to predict ES in the Iowa community, although this might be because this sample had a low prevalence of difficulties. Interestingly, a score grading gross mobility in old age and physical ability to perform heavy chores came out as a substantial predictor in both the sexes.

Using the accumulated survival advantage score computed from all the ten significant predictors we showed that women belonging to the tertile subgroup with the highest accumulated score were over nine times more likely to achieve ES, with the similar effect in men being a more modest three times (Fig.1). This observation summarizes our findings that the earlier-life and baseline predictors of extreme longevity have a larger effect sizes in women than men. As discussed, this may reflect the poorer lifestyle health habits among men, which may be attenuating the influence of other determinants.

Overall our results in the Iowa EPESE are consistent with James Fries' hypothesis of "compression of morbidity"³⁴ among ES, and suggesting that many heritable and non-heritable lifestyle related factors interplay to delay geriatric diseases in ES³⁵. Iowa EPESE was conducted in a fairly homogenous population with relatively little variability with regards to ethnic, religious and occupational composition of the study group. This probably limits the generalizability of this study to other populations comprising of many different ethnic and occupational groups. In addition, we did not have measures of potentially

important factors, including diet and medical care. This may partially have limited our power to detect the effects of some potential predictors. In this analysis we have examined associations for 22 'a priori' predictors, and found significant associations for 10 (at $p < 0.05$): multiple statistical testing would typically account for only one false positive association. Nevertheless it is important that our findings are replicated in an independent study population. It is now necessary to analyze the predictors of exceptional longevity in other cohorts nearing extinction, to extend the findings presented here. Prospective analyses of claimed genetic and blood measures are also needed, to extend the accumulating evidence from comparisons of long lived survivors with younger controls.

CONCLUSIONS

Seniors who achieve exceptional longevity differ in several domains compared to contemporaneous controls. Classical health risks such as smoking and obesity are important. Possibly genetic factors such as parental longevity and birth order are less important in men. Associations with positive attitude towards life may be primarily due to better disease status in later life.

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Fig 1.
Odds Ratios of Accumulated Survival Advantage Scores for Extraordinary Survival

Table 1

Basic characteristics of participants * in Established Population for the Epidemiological Study of the Elderly (EPESE), Iowa

	Male	Female
Longevity		
Age at baseline		
Median (inter-quartile range)	72 (8)	74 (8)
Years lived beyond baseline		
Median (inter-quartile range)	11 (10)	14 (11)
Age at death		
Median (Inter-quartile range)	85 (9)	89 (9)
Extraordinary survival (approximately top 10% longest-lived members in respective groups)		
Numbers of extraordinary survivors (cut-off age for extraordinary survival)	99 (94 yrs)	154 (97 yrs)
Demographic characteristics		
Birth order of participants among siblings		
Median (inter-quartile range)	3 (2)	3 (2)
Minimum-Maximum	1 to 19	1 to 15
Parents' age at death		
Both parents living 85 yrs (%)	57 (7%)	95 (7%)
One parent living 85 yrs (%)	285 (35%)	483 (35%)
Pregnancy		
At least one pregnancy (%)	NA	1319 (85%)
Social characteristics		
Marital status		
Never Married (%)	45 (4%)	104 (6%)
Spouse support		
Living with spouse (%)	783 (71%)	667 (39%)
Educational Status		
Less than 9 years (%)	499 (46%)	574 (34%)
9–12 years (%)	438 (40%)	759 (45%)
More than 12 years	154 (14%)	370 (22%)
Annual income (1981–83)		
< \$ 5,000 (%)	102 (12%)	339 (26%)
\$ 5000 – \$ 9999 (%)	277 (32%)	513 (39%)
> \$ 10, 000 (%)	488 (56%)	472 (36%)
Social network support from children, friends or relatives		
No support (%)	18 (2%)	16 (1%)
1 to 2 sources of support (%)	578 (66%)	1001 (69%)
3 sources of support (%)	279 (32%)	420 (29%)
Attitude towards life		
Negative attitude (%)	330 (37%)	563 (38%)
Intermediate attitude (%)	255 (29%)	433 (29%)

	Male	Female
Positive attitude (%)	306 (34%)	474 (32%)
General health and lifestyle characteristics		
Self-reported health		
Excellent (%)	208 (19%)	324 (19%)
Good (%)	580 (53%)	910 (54%)
Poor to very poor (%)	298 (27%)	465 (27%)
Systolic BP		
< 120 (%)	153 (17%)	252 (17%)
120 – 139 (%)	357 (42%)	565 (38%)
140 – 159 (%)	272 (30%)	464 (31%)
>159 (%)	117 (13%)	215 (14%)
Diastolic BP		
<80 (%)	608 (6%)	1056 (71%)
80 – 119 (%)	210 (23%)	326 (22%)
>119 (%)	81 (9%)	114(8%)
Sleep scores		
Maximum sleep difficulty (%)	365 (40%)	727 (48%)
Intermediate sleep difficulty (%)	366 (40%)	530 (35%)
Minimum sleep difficulty (%)	185 (20%)	267 (17%)
Smoking		
Never smoked (%)	437 (40%)	1462 (86%)
Ex-smokers (%)	503 (46%)	121 (7%)
Current smokers (%)	152 (14%)	115 (7%)
Cognition and Mental health		
Short Portable Mental Status Questionnaire		
Number (%) with less than full score	695 (47%)	786 (53%)
Self Assessed Memory Score		
Minimum (%)	270 (33%)	458 (33%)
Intermediate (%)	336 (41%)	611 (44%)
Maximum (%)	219 (26%)	328 (23%)
Numbers of words recalled		
Minimum (%)	374 (46%)	592 (33%)
Intermediate (%)	316 (39%)	612 (39%)
Maximum (%)	134 (16%)	442 (29%)
Physical Functional Assessment		
Activities of Daily Living (ADL)		
Numbers (%) with some difficulty	59 (6%)	152 (10%)
Gross mobility and physical ability		
Numbers (%) with difficulty in 2/7 activities	208 (23%)	387 (27%)
Numbers (%) with difficulty in 2/7 activities	80 (9%)	233 (16%)
Exercise score		
Minimum (%)	368 (33%)	643 (36%)

	Male	Female
Moderate (%)	598 (54%)	998 (56%)
Maximum (%)	144 (13%)	149 (8%)

*
age between 65–85 years and living for 3 years after baseline

Table 2

Associations of individual variables with extraordinary survival. Basic adjusted models (adjusted for age and smoking status, plus sex for all combined). Only significant associations ($p < 0.05$) are presented.

Variables	Male n= 1092		Female n= 1698		All combined		Gender interaction term	
	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p		p
Smoking *								
Current smoker	1	NA	1	NA	1	NA		
Ex-smoker	4.11 (0.97 – 17.47)	0.06	0.97 (0.16 – 6.05)	0.98	2.61 (0.9 – 7.5)	0.07		0.25
Never-smoker	8.87 (2.12 – 37.08)	0.003	3.03 (0.73 – 12.66)	0.13	5.86 (2.12 – 16.23)	0.001		0.34
Birth order								
Birth order among siblings	1.05 (0.95 – 1.16)	0.35	0.89 (0.81 – 0.98)	0.02	0.96 (0.89 – 1.02)	0.2		0.02
Parental age at death								
Parents not living 85	1	NA	1	NA	1	NA		NA
One parent living 85	1.22 (0.73 – 2.04)	0.43	1.80 (1.20 – 2.74)	0.005	1.60 (1.16 – 2.19)	0.004		0.16
Both parents living 85	1.16 (0.45 – 2.98)	0.75	3.55 (1.93 – 6.53)	0.00001	2.44 (1.48 – 4.01)	<0.0001		0.05
Attitude towards life								
Negative	1	NA	1	NA	1	NA		NA
Intermediate	0.93 (0.51 – 1.71)	0.83	1.59 (1.01 – 2.52)	0.05	1.31 (0.91 – 1.88)	0.15		0.17
Positive	1.36 (0.78 – 2.35)	0.28	1.68 (1.05 – 2.71)	0.02	1.54 (1.08 – 2.21)	0.02		0.73
Self-reported health								
Poor and very poor	1	NA	1	NA	1	NA		NA
Good to Fair	3.55 (1.80 – 6.99)	<0.0001	2.29 (1.42 – 3.69)	0.001	2.66 (1.80 – 3.92)	<0.0001		0.56
Excellent	3.71 (1.73 – 7.94)	<0.0001	3.19 (1.85 – 5.50)	<0.0001	3.31 (2.12 – 5.14)	<0.0001		0.48
Chronic medical condition								
Worst	1	NA	1	NA	1	NA		NA
Intermediate	1.04 (0.53 – 2.01)	0.92	1.42 (0.83 – 2.43)	0.21	1.25 (0.82 – 1.9)	0.29		0.47
Best	2.03 (1.11 – 3.71)	0.02	3.18 (1.91 – 5.28)	<0.0001	2.64 (1.79 – 3.89)	<0.0001		0.28
BMI at 50 years of age								
<20	0.6 (0.13 – 2.83)	0.52	1.35 (0.65 – 2.78)	0.42	1.12 (0.59 – 2.15)	0.72		0.33
20–25	1	NA	1	NA	1	NA		NA

Variables	Male n= 1092		Female n= 1698		All combined		Gender interaction term	
	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p		p
25–29.9	0.69 (0.41 – 1.15)	0.16	0.86 (0.56 – 1.32)	0.5	0.79 (0.57 – 1.1)	0.16		0.54
>30	0.58 (0.25 – 1.38)	0.22	0.44 (0.19 – 1)	0.05	0.5 (0.28 – 0.91)	0.02		0.61
Systolic BP								
90–119	1	NA	1	NA	1	NA	NA	NA
120–139	2.37 (1.1 – 5.13)	0.03	1.01 (0.61 – 1.67)	0.97	1.29 (2.03 – 0)	0.88		0.10
140–159	1.32 (0.57 – 3.02)	0.52	0.6 (0.35 – 1.04)	0.07	0.78 (0.5 – 1.23)	0.28		0.22
160	1.47 (0.57 – 3.84)	0.43	0.37 (0.18 – 0.75)	0.01	0.6 (0.35 – 1.05)	0.07		0.04
Numbers of words recalled								
Lowest numbers	1	NA	1	NA	1	NA	NA	NA
Intermediate numbers	1.41 (0.82 – 2.41)	0.21	1.92 (1.19 – 3.1)	0.01	1.66 (1.17 – 2.37)	0.01		0.50
Highest numbers	1.07 (0.49 – 2.32)	0.87	2.27 (1.33 – 3.87)	<0.0001	1.71 (1.12 – 2.62)	0.01		0.07
Gross mobility and physical ability								
Difficulty in >2/7 activities	1	NA	1	NA	1	NA	NA	NA
Difficulty in 2/7 activities	1.74 (0.6 – 5.1)	0.31	1.87 (1 – 3.49)	0.05	1.82 (1.06 – 3.13)	0.03		0.96
No difficulty	3 (1.12 – 8.08)	0.03	2.6 (1.43 – 4.7)	0.002	2.71 (1.64 – 4.49)	<0.0001		0.66

Note:

* estimates adjusted for age and sex

Table 3

Multi-variable model for earlier life predictors (adjusted for age at baseline, sex and smoking)

Variables	Male n= 1092		Female n= 1698		All Combined	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Birth order						
Birth order among siblings	1.05 (0.94–1.16)	0.38	0.89 (0.81–0.98)	0.02	0.96 (0.9–1.03)	0.27
Parental age at death						
Parents not living 85	1	NA	1	NA	1	NA
One parent living 85	1.24(0.74–2.07)	0.41	1.76(1.16–2.68)	0.008	1.52(1.1–2.1)	0.01
Both parents living 85	1.18(0.46–3.04)	0.73	3.33(1.79–6.19)	<0.0001	2.33(1.41–3.86)	0.001
BMI at 50 years of age						
<20	0.68 (0.14–3.29)	0.64	1.12 (0.52–2.43)	0.78	1 (0.51–1.98)	1
20–25	1	NA	1	NA	1	NA
25–29.9	0.73 (0.43–1.24)	0.25	0.87 (0.56–1.34)	0.52	0.81 (0.58–1.13)	0.22
>30	0.64 (0.27–1.52)	0.31	0.44 (0.18–1.07)	0.07	0.52 (0.28–0.96)	0.04

Table 4
Multi-variable model for variables related to baseline status (adjusted for age at baseline, sex and smoking)

Variables	Male n= 1080		Female n= 1683		All Combined	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Smoking						
Current smoker	1	NA	1	NA	1	NA
Ex-smokers	4.62 (1.07–19.92)	0.04	0.80 (0.13–5.15)	0.81	2.7 (0.94–7.8)	0.07
Never smoked	9.14 (2.16–38.4)	0.003	2.55 (0.60–10.8)	0.20	5.5 (1.97–15.4)	0.001
Attitude towards life						
Negative	1	NA	1	NA	1	NA
Intermediate	0.84 (0.44–1.6)	0.6	1.32 (0.81–2.14)	0.26	1.11 (0.776–1.61)	0.60
Positive	1.12 (0.61–2.03)	0.71	1.3 (0.79–2.16)	0.31	1.17 (0.80–1.72)	0.40
Self-reported health						
Poor and very poor	1	NA	1	NA	1	NA
Good	2.82 (1.37–5.78)	0.005	2.00 (1.19–3.34)	0.008	2.26 (1.50–3.41)	<0.0001
Excellent	2.80 (1.22–6.46)	0.01	2.17 (1.19–3.97)	0.01	2.42 (1.49–3.92)	<0.0001
Chronic medical condition						
Worst	1	NA	1	NA	1	NA
Intermediate	0.81 (0.40–1.62)	0.55	1.18 (0.67–2.06)	0.57	1.01 (0.65–1.55)	0.98
Best	1.47 (0.78–2.78)	0.24	2.38 (1.39–4.09)	0.002	1.93 (1.28–2.90)	0.002
Systolic BP						
90–119	1	NA	1	NA	1	NA
120–139	2.25 (1.02–4.97)	0.05	0.99 (0.58–1.67)	0.96	1.27 (0.83–1.94)	0.28
140–159	1.23 (0.53–2.90)	0.63	0.66 (0.37–1.17)	0.15	0.78 (0.49–1.25)	0.31
160	1.45 (0.54–3.9)	0.47	0.37 (0.17–0.78)	0.01	0.58 (0.33–1.05)	0.07
Numbers of words recalled						
Lowest numbers	1	NA	1	NA	1	NA
Intermediate numbers	1.38 (0.78–2.44)	0.27	1.95 (1.18–3.23)	0.01	1.65 (1.13–2.39)	0.008
Highest numbers	0.94 (0.41–2.13)	0.88	2.15 (1.22–3.78)	0.01	1.59 (1.01–2.48)	0.04
Gross mobility & physical ability						
Difficulty in >2/7 activities	1	NA	1	NA	1	NA

Variables	Male n= 1080		Female n= 1683		All Combined	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Difficulty in 2/7 activities	1.84 (0.58–5.80)	0.3	1.36 (0.7–2.66)	0.36	1.49 (0.84–2.64)	0.17
No difficulty	2.38 (0.81–6.97)	0.11	1.46 (0.75–2.83)	0.26	1.71 (0.99–2.97)	0.05