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Sex differences in healthy life expectancy among nonagenarians: A multistate survival model using data from the Vitality 90+ study

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ABSTRACT

Objectives: Little is known about sex differences in healthy life expectancy among the oldest old, the fastest growing segment of the older population. This study examines sex differences in total, healthy and unhealthy life expectancy among nonagenarians.

Methods: Longitudinal data of 884 older adults aged 90 and over participating in the Vitality 90+ study (Tampere, Finland) were used, including 2501 observations (health or death states) from 5 measurement waves between 2001 and 2014. Using the MSM and ELECT packages in R, multistate survival models were performed to estimate the transition probabilities of older adults through the different health states and to calculate life expectancies. The analyses were done separately for two health indicators (disability and multimorbidity) to see whether patterns were consistent.

Results: Women had higher total life expectancies than men (about 8 months), but also higher unhealthy life expectancies. Men had a higher disability-free life expectancy between the age of 90 and 95 compared to women. For multimorbidity, no sex differences in healthy life expectancy were found.

Conclusions: This study showed that the male-female health-survival paradox remains at very old age. Women aged 90+ live longer than men, and spend more time in poor health.

1. Introduction

The male-female health-survival paradox is well-established in many countries worldwide (Van Oyen et al., 2013; Oksuzyan et al., 2009; Lindahl-Jacobsen et al., 2013; Freedman et al., 2016). This is the phenomenon that higher life expectancy is accompanied by higher rates of poor health in women compared to men. This is seen as a paradox, since poor health is usually associated with lower survival. The fact that men die at younger ages than women, despite their better health, has been attributed to various biological, behavioral, social and contextual factors (Oksuzyan et al., 2008).

Despite the large number of studies focused on sex differences in health and mortality, relatively little is known about the male-female health-survival paradox at very old age, i.e. people aged 90 and over, for several reasons. First, although the oldest old constitute one of the fastest growing segments of the older population (Christensen et al., 2009), the increasing number of people in this age group is still a quite recent development (Jylhä et al., 2013). Second, population-based studies of older adults rarely include sufficient data on people aged 90 and over, to be able to calculate reliable estimates on healthy life expectancy. Therefore, little is known about the extent to which sex differences in healthy life expectancy continue to exist at very old age.

The few studies that have been conducted among the oldest old show that men have a higher risk of mortality than women in populations aged 85 years and older (Kingston et al., 2014; Tiainen et al., 2013). These studies also found that disability increases the risk of mortality more in men than in women (Kingston et al., 2014; Tiainen et al., 2013). However, what this exactly means for the number of years

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lived in good and poor health at very old age remains unclear. The only longitudinal study that provides detailed insight into healthy life years among people aged 90 years and older was conducted in Denmark (Bronnum-Hansen et al., 2009). This study calculated average lifetimes of Danish oldest old between 1998 and 2005, and observed between the ages of 92 and 100 an average life time of 2.7 years for men and 3.3 years for women. This study also indicated that a large proportion of the remaining years was spent in good health, and that this did not differ much between men and women (Bronnum-Hansen et al., 2009). These results have not been replicated so far.

Multistate models facilitate a better understanding of transitions between health states and death among the oldest old. Recent developments in multistate modeling make it possible to study the role of risk factors, such as sex, in transitions between these states (Robitaille et al., 2018). Moreover, based on multistate models, overall, healthy, and unhealthy life expectancies (LEs) may be estimated for specific groups (Van den Hout, 2016). The objective of this study was to examine sex differences in total, healthy and unhealthy life expectancy in a population of nonagenarians (i.e., people aged 90 years and over). First, we investigate the role of sex in transitions between health states and death, using two different health indicators. Then, we estimate LEs for men and women to gain insight into the male-female health-survival paradox at very old age.

2. Methods

2.1. Study sample and design

For this longitudinal study, data were used from the Vitality 90+ Study, a population-based study of nonagenarians in the city of Tampere, Finland (Jylhä et al., 2013; Tiainen et al., 2013). At baseline in 2001, all individuals aged 90 and older, irrespective of health or place of living, were included in a mailed survey. The data collection was repeated in 2003, 2007, 2010, and 2014, every time including the whole age group in the area. As all those who participated once were also included in the next waves, longitudinal data is available for all people who entered the study in 2001. At baseline, a questionnaire was mailed to all inhabitants aged 90 years and over (n = 1129), of which 892 (79%) returned the questionnaire. The response rate was 86% among those still alive during the data collection, as 87 individuals had died between sampling and sending out of the questionnaires.

In the current study, we included participants that returned the mailed questionnaire in 2001, and who had at least one health state at baseline (2001) and one health or death state at follow-up available (2003–2014). That was the case for 884 people, who provided a maximum of 2501 observations. The frequencies of number of observations were: two observations (n = 354), three observations (n = 399), four observations (n = 89) and five observations (n = 48). If persons were not able to fill out the questionnaire, they were instructed to ask help from a family member, caregiver, or friend. In certain cases, when participants were not able to select answers, these helpers participated as proxy. In this study, the percentage of proxy participants was 23.6%. Proxy rates were 15.3% for men and 25.6% for women (p difference < 0.01).

The ethics committee of the Pirkanmaa Hospital District or the ethics committee of the Tampere Health Center, depending on the study year, approved the study. All participants or their legal representatives provided written informed consent.

2.2. Measures

Two health indicators were used in the current study, disability and multimorbidity, to see whether results were consistent across health indicators. Health indicators were identically measured at each follow-up. Disability was measured with five mobility activities and activities of daily living (ADL): to move about indoors, to walk 400 m, to use stairs, to dress and undress and to get in and out of bed. For each item, identical questions were asked in the mailed questionnaire: “Are you able to…?”. Response categories were “Yes, without difficulty”, “Yes, with difficulty”, “Only if someone helps”, and “No”. Disability was defined as being dependent for two or more activities, where dependence was considered present if a participant was not able to perform a certain activity or only with help (Lisko et al., 2017; Tiainen et al., 2015).

Morbidity was measured by self-report. Participants were asked in the mailed questionnaire whether a doctor had told them that they had any of the following ten conditions: hypertension, atherosclerosis, heart disease, cancer, dementia, stroke, diabetes, rheumatic disorder, osteoarthritis, and Parkinson's disease. Multimorbidity was considered present if two or more diseases were reported (Salive, 2013).

2.3. Mortality

All-cause mortality status, including date of death, was retrieved from the Finnish National Population Register until May 2014, and linked to the dataset with personal identifier codes.

2.4. Statistical analysis

At baseline, characteristics of the study population were reported for the total sample and by sex, with means and standard deviation for continuous variables and percentages for categorical variables. Baseline differences between men and women were determined using Chi square tests and t-tests.

Multistate modeling was used to assess transitions between health states and death during 13 years of follow-up. With multistate modeling it is possible to simultaneously model transitions between health states and to examine the role of covariates on all transitions. A three-state model was applied, where state 1 was the healthy state (absence of disability or multimorbidity), state 2 was the unhealthy state (disability or multimorbidity present), and state 3 was death as absorbing state (Fig. 1). Multistate survival models with age and sex as covariates were estimated separately for disability and multimorbidity. Age was included as time-varying covariate. Date of death was used to calculate the exact age of death. When participants had missing states between two known states, interval censoring was applied. Right censoring was applied when the last state was missing and the participant was known to be still alive. However, this was done for very few cases (n = 8), as most people had died at the end of the study period (May 2014). Initially, we allowed backward transitions from state 2 to 1, but due to low numbers of backward transitions we had to fix this transition in the analyses on multimorbidity for both covariates, and we had to fix the sex parameter for this transition in the analyses on disability. Hazard ratios and 95% confidence intervals for state transitions are reported for age and sex.

The multistate survival models were estimated using the MSM package for R (Jackson, 2011). Based on the parameters of the multistate models, LEs were calculated using the ELECT (Estimating Life

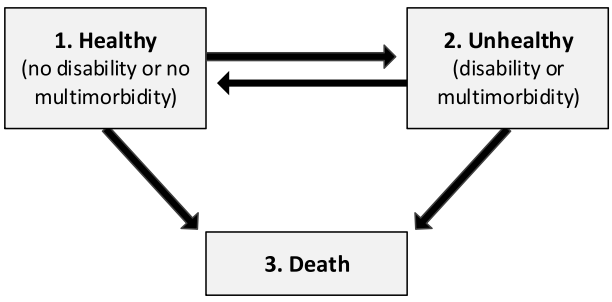

Fig. 1. Design: three-state model.

Table 1
Baseline characteristics of the study population.

	Total	Men	Women	p^*
	$n = 884$	$n = 172$	$n = 712$	
Age, mean (SD)	92.2 (2.5)	91.9 (2.3)	92.3 (2.6)	0.11
Multimorbidity, % 2 or more diseases	67.3	53.5	70.6	< 0.001
Hypertension, %	31.8	18.2	35.1	< 0.001
Atherosclerosis, %	16.7	19.4	16.1	0.29
Heart disease, %	53.4	49.4	54.4	0.24
Cancer, %	11.0	16.5	9.7	< 0.05
Dementia, %	42.9	38.8	43.9	0.23
Stroke, %	7.9	6.5	8.2	0.44
Diabetes, %	10.9	7.6	11.6	0.13
Rheumatic disorder, %	8.5	7.1	8.1	0.46
Osteoarthritis, %	35.8	25.9	38.2	< 0.01
Parkinson's disease, %	2.4	1.2	2.7	0.25
Disability, % dependence for 2 or more mobility or ADL activities	43.3	27.9	47.0	< 0.001
To move about indoors, % dependence	19.5	11.7	21.4	< 0.01
To walk 400 m, % dependence	49.5	33.5	53.8	< 0.001
To use stairs, % dependence	49.3	33.5	53.1	< 0.001
To dress and undress, % dependence	28.3	19.8	30.4	< 0.01
To get in and out of bed, % dependence	19.5	10.5	21.7	< 0.01
Respondent				
Participant, %	76.4	84.7	74.4	< 0.01
Proxy, %	23.6	15.3	25.6	

* *t*-Test or chi-square test.

Expectancies in Continuous Time) package for R (Van den Hout, 2016). ELECT estimates total and marginal LEs based on multinomial regression models for state prevalence. Total, unhealthy, and healthy LEs were estimated for men and women separately, for both disability and multimorbidity as health variables. LEs were estimated for individuals aged 90 to 100 years. To examine sex differences in total, unhealthy, and healthy life expectancy, 95% confidence intervals for LEs were estimated. All statistical analyses were performed using R version 3.4.2.

3. Results

Table 1 shows the characteristics at baseline for the total sample and by sex. The sample included 172 men and 712 women. The mean age was 92.2 years (SD = 2.5), with a range from 90 to 106 years. In the total sample, multimorbidity prevalence at baseline was 67.3%, with heart disease (53.4%), dementia (42.9%), osteoarthritis (35.8%), hypertension (31.8%) and atherosclerosis (16.7%) as the most common conditions. Multimorbidity was higher in women (70.6%) than in men (53.5%). Hypertension and osteoarthritis were more often present among women, whereas cancer was more frequently observed among men. Disability was present in 43.3% of the sample at baseline. All disability items showed a higher prevalence in women than in men ($p < 0.01$).

During 13 years of follow-up, 98.9% of the sample died ($n = 874$). Among the 48 observations at the last follow-up measurement (in 2014), there were two valid health state observations, 8 were right-censored and 38 were death states (deceased between 2010 and 2014). The results of the multistate models are presented in Table 2. Age and sex were not associated with transitioning from a healthy state to an unhealthy state, for both health indicators. In the analyses using disability as health indicator, a higher age was associated with an increased risk of transitioning from a healthy state to death (HR = 1.15, 95% CI = 1.03–1.28) and with transitioning from an unhealthy state to death (HR = 1.04, 95% CI = 1.02–1.07). Female sex was associated with a lower likelihood to transition from an unhealthy state to death (HR = 0.52, 95% CI = 0.40–0.67), but not with transitioning from a healthy state to death (HR = 0.52, 95% CI = 0.23–1.16). When using multimorbidity as health indicator, a higher age was again associated with a higher risk of transitioning from a healthy state to death (HR = 1.14, 95% CI = 1.08–1.21) and from an unhealthy state to death (HR = 1.08, 95% CI = 1.06–1.11). For females, there was a lower risk of transitioning from a healthy state to death (HR = 0.51, 95% CI = 0.31–0.84) and from an unhealthy state to death (HR = 0.73, 95% CI = 0.58–0.92).

LEs were calculated for the ages 90 to 100 (Table 3 and Fig. 2). The estimates for total life expectancy slightly differ between the two health indicators, due to small differences in the parameters and observations included in the analyses for each indicator. However, this does not affect the interpretation of results, as sex differences for total life expectancy are consistent across health indicators. Total life expectancy at age 90 was around 3.7 years for women and 3 years for men, corresponding with a difference of 8 months in total life expectancy. This decreased to 1.8 years (women) and 1.3 years (men) at the age of 100, which is still a difference of 6 months in total life expectancy.

For both health indicators, sex differences in unhealthy life expectancy were observed, showing that women spend more time in poor health, in both absolute (years) and relative (proportion) terms. The average life expectancy with disability for women was 2 years at age 90, 1.7 years at age 95 and 1.5 years at age 100, which corresponds to 53%, 66%, and 78% of the total life expectancy, respectively. For men, life expectancy with disability at the age of 90, 95 and 100 was 26%, 36% and 48% of total life expectancy, respectively. Fig. 2 provides an illustration of these differences. Similar patterns were observed for life expectancy with multimorbidity, although sex differences were a bit smaller when using this health indicator. Table 3 also provides healthy life expectancy estimates. Between the age of 90 and 95, men had higher disability-free life expectancy than women. For example, at the age of 90 the sex difference in disability-free life expectancy was 6 months, in favor of men. At the age of 100, sex differences in disability-free life expectancy were no longer observed. For multimorbidity, no sex differences in healthy life expectancy were found.

4. Discussion

The main aim of this study was to examine sex differences in total, healthy, and unhealthy life expectancy among nonagenarians, using estimates based on multistate survival models. The results indicated that sex differences in LEs were present up to very high age. Differences

Table 2
Hazard ratios and 95% confidence intervals for the effect of age and sex on transitions through the different health states.

Transitions	Disability		Multimorbidity	
	Age	Sex	Age	Sex
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
State 1 – state 2	1.07 (0.99, 1.14)	1.37 (0.82, 2.27)	0.97 (0.91, 1.04)	1.61 (0.97, 2.70)
State 1 – death	1.15 (1.03, 1.28)*	0.52 (0.23, 1.16)	1.14 (1.08, 1.21)*	0.51 (0.31, 0.84)*
State 2 – state 1	0.89 (0.74, 1.08)	–	–	–
State 2 – death	1.04 (1.02, 1.07)*	0.52 (0.40, 0.67)*	1.08 (1.06, 1.11)*	0.73 (0.58, 0.92)*

State 1 = healthy (no disability or no multimorbidity); state 2 = unhealthy (disability or multimorbidity); sex (0 = men, 1 = women); *$p < 0.05$; N observations disability = 2501; N observations multimorbidity = 2488.

Table 3
Life expectancy estimates for men and women by health indicator.

		Disability		Multimorbidity	
		Men	Women	Men	Women
Age 90	Total life expectancy in years (95% CIs)	3.13 (2.68, 3.51)	3.77 (3.53, 3.99)*	2.96 (2.60, 3.34)	3.70 (3.46, 3.92)*
	Unhealthy life expectancy in years (95% CIs)	0.84 (0.64, 1.06)	2.01 (1.81, 2.18)*	1.68 (1.41, 1.98)	2.66 (2.46, 2.85)*
	Healthy life expectancy in years (95% CIs)	2.28 (1.84, 2.66)	1.76 (1.58, 1.95)*	1.28 (0.99, 1.26)	1.04 (0.89, 1.19)
Age 95	Total life expectancy in years (95% CIs)	2.01 (1.57, 2.30)	2.64 (2.42, 2.91)*	1.98 (1.69, 2.28)	2.62 (2.41, 2.83)*
	Unhealthy life expectancy in years (95% CIs)	0.72 (0.52, 0.92)	1.74 (1.54, 1.94)*	1.05 (0.86, 1.27)	1.78 (1.60, 1.96)*
	Healthy life expectancy in years (95% CIs)	1.29 (0.96, 1.54)	0.91 (0.76, 1.08)*	0.93 (0.72, 1.17)	0.85 (0.69, 1.00)
Age 100	Total life expectancy in years (95% CIs)	1.27 (0.87, 1.56)	1.91 (1.63, 2.22)*	1.25 (0.98, 1.59)	1.78 (1.55, 2.05)*
	Unhealthy life expectancy in years (95% CIs)	0.62 (0.44, 0.83)	1.49 (1.22, 1.78)*	0.63 (0.47, 0.85)	1.14 (0.95, 1.38)*
	Healthy life expectancy in years (95% CIs)	0.64 (0.34, 0.89)	0.42 (0.29, 0.59)	0.62 (0.39, 0.90)	0.64 (0.47, 0.84)

* Sex difference = $p < 0.05$.

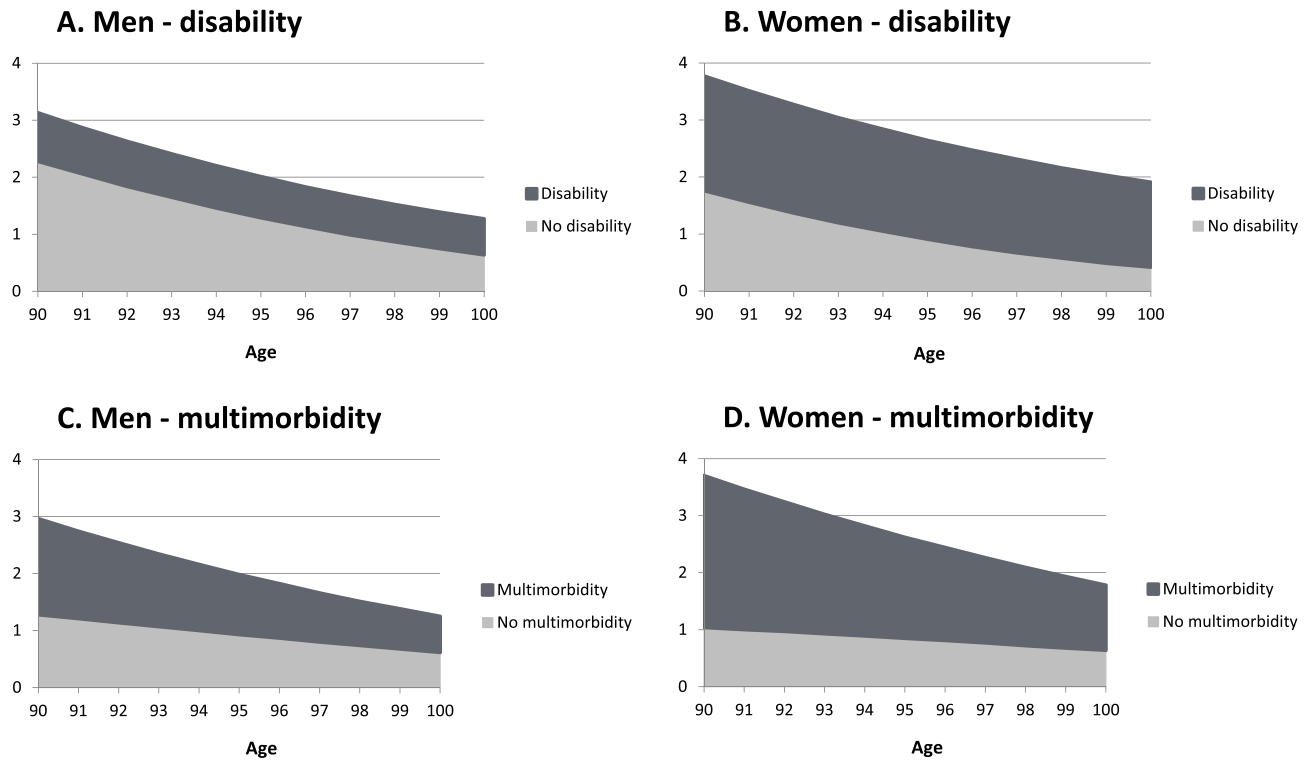

Fig. 2. Life expectancy in good and poor health by gender and health indicator (in years).

were mainly observed in total and unhealthy life expectancy: women aged 90 years and over live longer than men, and spend more time in poor health, for both disability and multimorbidity as health indicator. Based on these results we conclude that the male-female health-survival paradox is still present in the very old.

The results of this study revealed that the total life expectancy at the age of 90 was 3.7 years for women and 3 years for men. This is not very different from a previous study in a Danish population, that found an average lifetime among nonagenarians of 3.3 years for women and 2.7 years for men (Bronnum-Hansen et al., 2009). However, this study only provided averages for the total group aged 90 and over, and did not calculate LEs for specific ages. Our findings provide a more detailed

insight into decreases in life expectancy with advancing age. For a person aged 100 years, the total life expectancy decreased to 1.8 years for women and 1.3 years for men.

Patterns with regard to unhealthy life expectancy were similar to those previously observed in younger age groups (Van Oyen et al., 2013), as we found that women live more years with disability and multimorbidity than men. At the age of 90, women spend on average 14 months more with disability and 12 months more with multimorbidity than men. A large proportion of the total life expectancy between the ages of 90 and 100 is estimated to be in the unhealthy state. These findings are contrary to those from the previously mentioned study in Denmark, where nonagenarians were estimated to spend 75% of their remaining lifetime in physical independence. Moreover, this Danish study did not find substantial sex differences in unhealthy life expectancy. This suggests that estimates should be interpreted in the context of the country where the research is conducted. With regard to healthy life expectancy, we observed between the age of 90 and 95 that men had a higher disability-free life expectancy of about 5 to 6 months. This is line with results from the Newcastle 85+ study, in which men were estimated to live 6 months longer without disability compared to women (Kingston et al., 2014).

Women were less likely to transition from a healthy or unhealthy state to death than men. This is probably just an expression of the lower mortality rates among female nonagenarians (Tiainen et al., 2013). The finding that age and sex were not associated with transitioning from a healthy state to an unhealthy state in the multistate models, may be due to the fact that prevalence of disability and multimorbidity was already high at baseline. It is known that among nonagenarians the prevalence of disability and multimorbidity is high (Formiga et al., 2013; Nybo et al., 2001).

This was one of the first studies to use longitudinal data to estimate LEs in the oldest old. Strengths of the study include the large sample of nonagenarians, the use of an entire age cohort from one area, the long follow-up period, and the novel analytical approach. The multistate survival model approach is among the few statistical methods that does not require national life table data to calculate LEs (Van den Hout, 2016; Strauss et al., 2004), as opposed to the commonly used Sullivan method (Mathers and Robine, 1997). Using the ELECT package in R, LEs may be calculated in any longitudinal dataset with information on health states and mortality. Nevertheless, some limitations should be considered when interpreting the results of this study. First, the number of men included in this study is small as compared to the number of women. However, this reflects that mortality rates are higher among men. The percentage of men corresponds with their share in the total population. In the Vitality 90+ study, there were no differences in participation rates between men and women (Tiainen et al., 2013). Second, it is possible that mortality rates among nonagenarians have declined in recent years. These possible cohort effects were not considered in this study, and should be addressed in future research. Finally, most measures included in our analyses – except mortality – were based on self-report. It is well-known that self-reported data may lead to bias. The same may be true for reporting by proxy. However, previous research with data from the Vitality 90+ study indicated that for disability and disease proxy answers are sufficiently reliable (Tiainen et al., 2013; Vuorisalmi et al., 2012).

There are several potential explanations for our findings that should be addressed in future research. First, there may be sex differences in self-reporting or proxy-reporting of disease and disability, that may explain higher rates of poor health among women. Second, various explanatory factors could be considered in the analyses, such as life course experiences prior to age 90 and living arrangements. For example, among nonagenarians women are more likely than men to be widow or to live alone. Finally, more research could be devoted to biological differences between men and women, in order to explain sex differences in longevity.

The increasing number of oldest old in the population is a major challenge for healthcare systems, as the prevalence of diseases and disability among nonagenarians is very high (Nybo et al., 2001). Yet, much more research in the oldest old is needed to better understand why women live longer with multimorbidity and disability than men, even in this selective group at very old age. The field would also benefit from comparative research in multiple countries (Robine et al., 2010), to see whether life expectancy patterns in nonagenarians are consistent across countries. Most studies among the oldest old have been conducted in one country or setting (Collerton et al., 2009; van Houwelingen et al., 2014), and it is likely that LEs in the oldest old reflect the specific conditions in each of these countries and settings. Finally, other health indicators than disability and multimorbidity may be considered in future life expectancy research, for example physical performance measures and risk indicators such as frailty (Granic et al., 2016; Legrand et al., 2014; Dent et al., 2016). Ultimately, findings from these studies may be used to inform public health policy, and to develop interventions focused on maintaining independence among the oldest old. For example, the high prevalence of mobility disability in the current study sample would call for interventions focused on mobility and physical activity (Pahor et al., 2014).

In conclusion, this longitudinal study showed that sex differences in total and unhealthy life expectancy were present in a sample of people aged 90 and over. Therefore, the results provide support for the male-female health-survival paradox at very old age. Women aged 90+ live longer than men, and spend more time in poor health.

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Conflict of interest

The authors declare that they have no conflict of interest.

References

Bronnum-Hansen, H., Petersen, I., Jeune, B., Christensen, K., 2009. Lifetime according to health status among the oldest olds in Denmark. Age Ageing 38, 47–51.
Christensen, K., Doblhammer, G., Rau, R., Vaupel, J.W., 2009. Ageing populations: the challenges ahead. Lancet 374, 1196–1208.
Collerton, J., Davies, K., Jagger, C., Kingston, A., Bond, J., Eccles, M.P., et al., 2009. Health and disease in 85 year olds: baseline findings from the Newcastle 85+ cohort study. BMJ b4904, 339.
Dent, E., Kowal, P., Hoogendijk, E.O., 2016. Frailty measurement in research and clinical practice: a review. Eur. J. Intern. Med. 31, 3–10.
Formiga, F., Ferrer, A., Sanz, H., Marengoni, A., Alburquerque, J., Pujol, R., 2013. Patterns of comorbidity and multimorbidity in the oldest old: the Octabaix study. Eur J Intern Med 24, 40–44.
Freedman, V.A., Wolf, D.A., Spillman, B.C., 2016. Disability-free life expectancy over 30 years: a growing female disadvantage in the US population. Am. J. Public Health 106, 1079–1085.
Granic, A., Jagger, C., Davies, K., Adamson, A., Kirkwood, T., Hill, T.R., et al., 2016. Effect of dietary patterns on muscle strength and physical performance in the very old: findings from the Newcastle 85+ study. PLoS One 11, e0149699.
van Houwelingen, A.H., Cameron, I.D., Gussekloo, J., Putter, H., Kurrle, S., de Craen, A.J., et al., 2014. Disability transitions in the oldest old in the general population. The Leiden 85-plus study. Age 36, 483–493.
Jackson, C.H., 2011. Multi-state models for panel data: the msm package for R. J. Stat. Softw. 38, 1–29.
Jylhä, M., Enroth, L., Luukkaala, T., 2013. Trends of functioning and health in non-agenarians: the vitality 90+ study. Ann. Rev. Gerontol. Geriatr. 33, 313–332.
Kingston, A., Davies, K., Collerton, J., Robinson, L., Duncan, R., Bond, J., et al., 2014. The contribution of diseases to the male-female disability-survival paradox in the very old: results from the Newcastle 85+ study. PLoS One 9, e88016.
Legrand, D., Vaes, B., Mathei, C., Adriaensen, W., Van Pottelbergh, G., Degryse, J.M.,

2014. Muscle strength and physical performance as predictors of mortality, hospitalization, and disability in the oldest old. J. Am. Geriatr. Soc. 62, 1030–1038.
Lindahl-Jacobsen, R., Hanson, H.A., Oksuzyan, A., Mineau, G.P., Christensen, K., Smith, K.R., 2013. The male-female health-survival paradox and sex differences in cohort life expectancy in Utah, Denmark, and Sweden 1850–1910. Ann. Epidemiol. 23, 161–166.
Lisko, I., Tiainen, K., Raitanen, J., Jylhava, J., Hurme, M., Hervonen, A., et al., 2017. Body mass index and waist circumference as predictors of disability in nonagenarians: the vitality 90+ study. J. Gerontol. A Biol. Sci. Med. Sci. 72, 1569–1574.
Mathers, C.D., Robine, J.M., 1997. How good is Sullivan's method for monitoring changes in population health expectancies? J. Epidemiol. Community Health 51, 80–86.
Nybo, H., Gaist, D., Jeune, B., McGue, M., Vaupel, J.W., Christensen, K., 2001. Functional status and self-rated health in 2,262 nonagenarians: the Danish 1905 cohort survey. J. Am. Geriatr. Soc. 49, 601–609.
Oksuzyan, A., Juel, K., Vaupel, J.W., Christensen, K., 2008. Men: good health and high mortality. Sex differences in health and aging. Aging Clin. Exp. Res. 20, 91–102.
Oksuzyan, A., Petersen, I., Stovring, H., Bingley, P., Vaupel, J.W., Christensen, K., 2009. The male-female health-survival paradox: a survey and register study of the impact of sex-specific selection and information bias. Ann. Epidemiol. 19, 504–511.
Pahor, M., Guralnik, J.M., Ambrosius, W.T., Blair, S., Bonds, D.E., Church, T.S., et al., 2014. Effect of structured physical activity on prevention of major mobility disability in older adults: the LIFE study randomized clinical trial. JAMA 311, 2387–2396.
Robine, J.M., Cheung, S.L., Saito, Y., Jeune, B., Parker, M.G., Herrmann, F.R., 2010. Centenarians today: new insights on selection from the 5-COOP study. Curr. Gerontol. Geriatr. Res., 120354. https://doi.org/10.1155/2010/120354.
Robitaille, A., van den Hout, A., Machado, R.J.M., Bennett, D.A., Cukic, I., Deary, I.J., et al., 2018. Transitions across cognitive states and death among older adults in relation to education: a multistate survival model using data from six longitudinal studies. Alzheimers Dement. 14, 462–472.
Salive, M.E., 2013. Multimorbidity in older adults. Epidemiol. Rev. 35, 75–83.
Strauss, D., Ojdana, K., Shavelle, R., Rosenbloom, L., 2004. Decline in function and life expectancy of older persons with cerebral palsy. NeuroRehabilitation 19, 69–78.
Tiainen, K., Luukkaala, T., Hervonen, A., Jylha, M., 2013. Predictors of mortality in men and women aged 90 and older: a nine-year follow-up study in the vitality 90+ study. Age Ageing 42, 468–475.
Tiainen, K., Raitanen, J., Vaara, E., Hervonen, A., Jylha, M., 2015. Longitudinal changes in mobility among nonagenarians: the vitality 90+ study. BMC Geriatr. 15, 124.
Van den Hout, A., 2016. ELECT: Estimation of life expectancies using continuous-time multi-state survival models. In: ELECT Version 0.2.Vignette.
Van Oyen, H., Nusselder, W., Jagger, C., Kolip, P., Cambois, E., Robine, J.M., 2013. Gender differences in healthy life years within the EU: an exploration of the "health-survival" paradox. Int. J. Public Health 58, 143–155.
Vuorisalmi, M., Sarkeala, T., Hervonen, A., Jylha, M., 2012. Among nonagenarians, congruence between self-rated and proxy-rated health was low but both predicted mortality. J. Clin. Epidemiol. 65, 553–559.