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10-Year Follow-up of the Original Faroese Septuagenarian Cohort: Focus on Frailty and Association With All-cause Mortality

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Abstract

Little is known about the health status of Faroese people reaching high age. The purpose of this study was to elucidate the health status of older adults in a small-scale society with emphasis on frailty and all-cause mortality. In this 10-year follow-up study, 347 Faroese citizens aged 80 to 84 from the Faroese Septuagenarian cohort participated. A detailed health examination was conducted, in addition to self-reported questionnaire. We constructed a 40-item Frailty Index (FI) to assess frailty. Survival and mortality risks were analyzed using Kaplan-Meier curves and Cox proportional hazard model. Median FI score was 0.28 ranging from 0.09 to 0.7; 71 (21%) individuals were least frail, 244 (67%) moderately frail, and 41 (12%) were most frail. Frailty and sex were statistically significantly associated with mortality; being male was associated with hazard ratio (HR) of 4.05 [CI 1.73, 9.48], and being most frail with HR of 6.2 [CI 1.84, 21.3]. Classification of octogenarians as least/moderately frail may be an opportunity to initiate interventions to prevent or delay frailty in this population stratum.

Keywords

frailty, health status, mortality, octogenarians, older adults

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Introduction

Older adults' health varies greatly. Differences are primarily observed between subgroups of older adults such as "the young-old" (65–74 years), "the old" (75–84 years), and "the old-old" (>85 years) (Crews & Zavotka, 2006). In general, the old-old have poorer health outcomes, for example, worse physical and mental health, institutionalization and hospitalization (Cohen-Mansfield et al., 2013; Lee et al., 2018). Nevertheless, variation in health is also observed amongst older individuals of same age, as some individuals seemingly appear to age faster than their peers.

The health status of older adults can be assessed by measuring frailty. The level of frailty has an impact on older persons' resilience to negative health changes and the ability to recover from illness (Clegg et al., 2013). Frail people are at increased risk of adverse health outcomes such as disability, hospitalization, need for health- and social care, and mortality (Clegg et al., 2013; Shi et al., 2021). Frailty prevalence varies in different populations (O'Caoimh et al., 2018). Among European octogenarians, the prevalence varied from 18% in Luxemburg to 48% among Portuguese; in Denmark, 22% were characterized as frail individuals, while 59% were pre-frail (Manfredi et al., 2019).

Two well-known methods to measure frailty are Fried's frailty phenotype (Fried et al., 2001) and Rockwood and Mitnitski's Frailty Index (Dent et al., 2016; Searle et al., 2008). The phenotype approach defines frailty based on five criteria: weight loss, weakness, exhaustion, slowness, and low physical activity (Fried et al., 2001), while Frailty Index (FI) defines frailty as the accumulation of age-related health deficits (e.g., symptoms, signs, diseases, disabilities, laboratory abnormalities) (Searle et al., 2008). The deficits are

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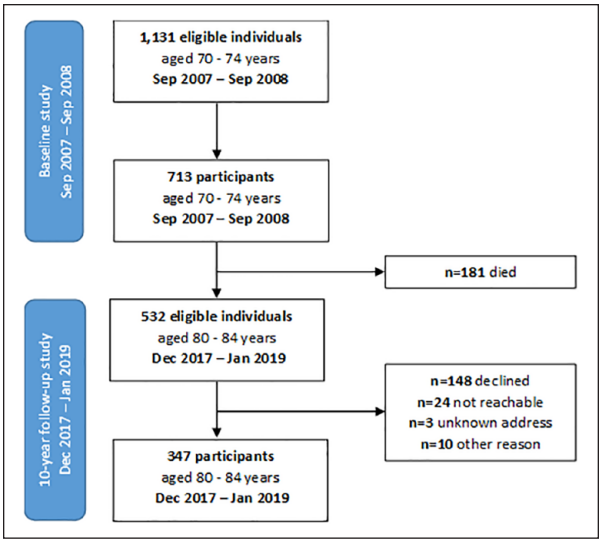

Figure 1. Flowchart of the Faroese Septuagenarian cohort.

combined into a FI score—the more deficits a person has, the frailer that person is (Searle et al., 2008).

The Faroe Islands, a self-governing part of the Kingdom of Denmark, located in the North Atlantic Ocean (population of approximately 54,000) are experiencing an aging population. Life expectancy has gradually increased to 83.9 years (82.1 years for men and 85.6 years for women), and the Faroe Islands are among countries with highest life expectancy (Hagstova, 2022a). The Faroe Islands are characterized as a small-scale society. Although there are similarities to other Nordic countries in terms of welfare system, access to health services, and lifestyle, the Faroe Islands are a fishing- and rural community with close social relations and a tradition of eating Faroese food (e.g., fish, whale meat, seabird). Though life expectancy is increasing, little is known about the health status of older Faroese people reaching high age and the variability within this group. This study aims to elucidate the health status of older adults in the Faroe Islands with comprehensive measures of major areas of function that decline during aging with emphasis on frailty and all-cause mortality.

Methods

Study Design and Sample

This population-wide study is a 10-year follow-up of the Faroese Septuagenarian cohort established in 2007/2008. Baseline study procedures have been described elsewhere (Petersen et al., 2019). With no prior follow-up, all living cohort members ($n=532$) were invited to a 10-year follow-up from December 2017 to January 2019; 347 cohort members participated (65%) (Figure 1). Participation involved a clinical examination, self-reported questionnaire and a blood sample. Participants unable to attend the clinic were offered a home visit. The study has been approved by the Faroese Scientific Ethics Committee and the Data Protection Agency Faroe Islands. Participation was voluntary and written informed consent was obtained from each participant or next of kin.

Data Collection

Self-Reported Questionnaire Information Collected. Sociodemographic data, smoking status and alcohol consumption were obtained from self-reported questionnaire. Daily prescription medicine consumption (yes/no) and disease burden based on 20 health conditions (Supplemental File 1 Table 1) were likewise collected.

Ten basic and instrumental activities of daily living were reported: dressing, bathing, using the telephone, transportation, meal preparation, shopping, housekeeping, medication management, walking stairs, and managing paperwork/finances (Lawton & Brody, 1969; Mahoney & Barthel, 1965).

The general subjective health status was assessed using three self-rated health (SRH) items: "In general, how would you rate your health?"; "Compared to 1 year ago, how would you rate your health now?"; "Compared to other people your age, how would you rate your health?" Moreover, we assessed participants' subjective memory with two items: "In general, how would you rate your memory?"; "Compared to other people your age, how would you rate your memory?"

Objective Health Measures. The objective health measures presented rely on biomarkers proposed by Lara et al. of physiological functions, physical capability and cognitive functions (Lara et al., 2015).

Physiological function: The following parameters were measured to assess participants' cardiovascular function (CV): blood lipids (total cholesterol, low-density lipoprotein [LDL], high-density lipoprotein [HDL], triglycerides) and blood pressure (BP) measured at rest horizontally. Lung function was measured as forced expiratory volume in 1 s (FEV1), predicted value for FEV1 and % predicted value for FEV1 with a Vitalograph device model 6800 Pneumotrac (Ireland). Glycated hemoglobin (HbA1C) and non-fasting blood glucose were measured and height, weight, waist (WC), and hip circumference were measured without shoes and overgarments. BMI was calculated (kg/m^2) and was classified as <18.5 underweight, 18.5 to 24.9 normal range, 25.0 to 29.9 overweight, and ≥ 30 obese (WHO, 2000). Waist-hip ratio (WHR) was calculated by WC divided by the hip measurement and cut-off points were WC normal range ≤ 102 cm for men and ≤ 88 cm for women, WHR normal range <0.90 cm for men and <0.85 cm for women (WHO, 2008). Body fat distribution was measured with bioelectrical impedance analysis (BIA) (Imp SFB7 System medical device, ImpediMed Ltd). Reference value was classified according to manufacturer: women $\geq 31.0\%$=high, men $\geq 25.8\%$=high (ImpediMed, 2021).

Physical capability: Handgrip strength was measured (kg) with a Hand Dynamometer model 78010

(Lafayette, 2004), and maximum grip strength out of three trials on dominant/non-dominant hands was reported. Walking speed was measured in seconds using the Timed Up- and Go test (TUG) (Podsiadlo & Richardson, 1991) and we used the 30-Second Chair Rising Stand test to measure lower body strength (Jones et al., 1999). Participants' dexterity was assessed with the Purdue Pegboard Test (Lafayette, 2015) and postural sway was measured with CATSYS system (Despres et al., 2000), a computer-based test, where a force plate was used for recording balance with eyes open and closed, respectively. Cognitive function: Cognitive function was assessed with Mini-Mental State Examination (MMSE) (Folstein et al., 1975). Moreover, we used a test battery assessing verbal comprehension and incidental memory with the Boston Naming Test (BNT) (Kaplan et al., 1983), non-verbal reasoning with Raven Colored Matrices (Raven, 1958), immediate and delayed recall verbal memory with 10-word list learning with Selective Reminding Test (Buschke, 1973). Speed of processing and immediate and delayed visual perceptual and spatial memory were assessed with a computerized version of Warrington's Recognition Memory for Faces test (series B) set up in DMDX Display Software (Psychology, 2002). Further, we used the Neurobehavioral Evaluation System 2 (NES2) to assess visuospatial skills (Pattern Recognition Test), attention (Continuous Performance test and Symbol Digit Modalities test), and motor function (Finger Tapping test) (Dahl et al., 1996; Letz & Baker, 1988; White et al., 1996).

Mortality. Mortality was recorded and mean follow-up time from day of examination to date of death/date of latest follow-up (16 December 2021) was 39 months. None of the 347 participants were lost to follow-up.

Construction of Frailty Index (FI). To assess frailty, we developed a FI in line with the accumulation of deficits model (Searle et al., 2008) including 40 deficits. Our FI comprised clinical measurements and laboratory tests related to physiological functions (five items), cognitive function (one item), body composition (three items), and physical capability (three items), in addition to self-reported data on ADL/IADL (10 items), history of health conditions (15 items), polypharmacy (one item), and self-rated health and memory (two items). The FI score was calculated by the number of deficits present in a person divided by the total number of deficits considered with a higher value indicating worse, frailer health (Searle et al., 2008). Besides the total FI score ranging from 0.0 to 1.0, we categorized individuals with FI scores of 0.0 to 0.2 as least frail, 0.2 to 0.4 as moderately frail and >0.4 as most frail based on previously reported cut-off scores of ≥0.2 indicating frailty (Gilmour & Ramage-Morin, 2021; Jiang et al., 2017; Zhang et al., 2021). (See Supplemental File 2 for detailed information on construction of the FI).

Statistical Analysis

For continuous variables, the independent *t*-test or Mann–Whitney was used for sex comparison and Kruskal–Wallis test to compare frailty groups. For categorical variables, Chi-square or Fisher's exact test, as appropriate was used. For the neuropsychological test battery, we calculated *z*-scores to compare individuals to a mean standard score indicating a *z*-score >1.5 as above average, −1.5 and 1.5 as average and <−1.5 as below average.

Univariate logistic regression was used to estimate the likelihood of mortality for each deficit in the FI with a mean follow-up of 39 months. Survival analysis was performed with Kaplan–Meier curves stratified by sex and by frailty levels. Further, we used Cox proportional hazards regression model to calculate the hazard ratio (HR) and 95% CI for the association between frailty and all-cause mortality in a crude model and adjusted for sociodemographic data. The statistical analysis was performed using IBM SPSS Statistics for windows v28 (IBM Corp., Armonsk, NY) and R version 4.1.1 (RCoreTeam, 2021), survival package 3.2-11 (Therneau, 2021) and survminer package 0.4.9 (Kassambara et al., 2021).

Results

Characteristics of the study population by sex are depicted in Supplemental File 1 Table 1.

Of the 532 invited octogenarians, 347 participated (51% women). Complete data collection on all items was not obtained from all 347 participants mainly due to reasons such as cognitive state, physical inability and lack of equipment during home visits (Supplemental File 1 Table 1). In 13 cases, proxy reporting was used to answer the questionnaire due to the cognitive state of the participant.

A total of 148 cohort members declined participation, while 37 were not reachable/unknown addresses or other reasons. Non- participants were to a greater extent women ($p = .02$) and median 1 year older compared to those who participated ($p = .006$). The mean age of participants was 82.5 years. More than half of the women were widowed (54%) and lived alone (48%) compared to men, where 14% were widowers and 17% lived alone ($p < .001$). Almost half of the participants had less than or 10-year primary school and men had higher education than women ($p < .001$).

More women were never-smokers (54% vs. 34%) and teetotalers (61% vs. 37%) compared to men ($p < .001$). Hypertension was the most common self-reported health condition (80%) followed by hypercholesterolemia (56%) and myocardial infarction (MI)/

Table 1. Demographic Characteristics of the Sample by Frailty Status.

	Least frail 0.0–0.2	Moderately frail 0.2–0.4	Most frail >0.4	*p*-Value
n (%)	71 (21.1)	224 (66.7)	41 (12.2)	—
Sex, *n* (%)				.37*
Female	38 (22.5)	107 (63.3)	24 (14.2)	
Male	33 (19.8)	117 (70.1)	17 (10.2)	
Age, mean ± *SD*	82.3 (1.3)	82.4 (1.2)	82.8 (1.2)	.157**
Marital status, *n* (%)				.073***
Married/partner	46 (64.8)	141 (62.9)	19 (46.3)	
Divorced/separated	3 (4.2)	3 (1.3)	3 (7.3)	
Never married/single	1 (1.4)	7 (3.1)	0 (0.0)	
Widow/widower	21 (29.6)	73 (32.6)	19 (46.3)	
Education, *n (%)*				.207***
10-year primary school/less	33 (46.5)	104 (46.4)	25 (61.0)	
Upper secondary	5 (7.0)	13 (5.8)	1 (2.4)	
Vocational education	7 (9.9)	42 (18.8)	9 (22.0)	
Diploma/Bachelor's degree	21 (29.6)	53 (23.7)	6 (14.6)	
Master/PhD degree	5 (7.0)	12 (5.4)	0 (0.0)	
Living arrangement,[a] *n (%)*				**<.001*** **
Alone	27 (38.0)	73 (32.6)	9 (22.0)	
With partner/family	44 (62.0)	150 (67.0)	19 (46.3)	
Nursing home	0 (0.0)	1 (0.4)	13 (31.7)	

*Chi-Square Test, **Kruskal Wallis Test, ***Fisher exact test.
[a]Living arrangement: Participants who reported living in a basement apartment in their children's home are categorized as living with a partner/family.
Statistically significant values shown in bold.

coronary heart disease (CHD)/other heart disease (50%). Osteoporosis, arthritis, and mental illness occurred statistically significantly more often among women ($p = .05$), while MI/CHD/other heart disease and cancer were more prevalent among men. The majority (94%) took daily medication and polypharmacy was observed amongst half of the participants (51%).

Most could perform ADL/IADL without assistance ranging from 61% in managing paperwork/finance to 91% in dressing. However more women than men needed help regarding transportation (26% vs. 13%) and shopping (30% vs. 17%), while the opposite was true with meal preparation (11% vs. 23%).

Half of the octogenarians rated their health as good (51%) with more women (56%) than men (46%) ($p = .04$). On the other hand, more men reported their health to be excellent or very good (16%) compared to women (8%). Approximately the same proportion of the study population rated their memory to be good (39%) and fair (40%) and most rated their memory to be about the same as others of their age (78%).

The blood biomarkers, cholesterol, triglycerides and blood glucose, were within normal values for the total study population. The diastolic BP was within normal range while the systolic BP was elevated and slightly higher in women than men. The respiratory function was better in women compared to men; the result showed for women 4% higher FEV1 than predicted and for men 5% lower than predicted ($p < .001$).

Approximately three-quarters of the participants were overweight or obese according to BMI. Obesity was also confirmed by high body fat percentage, high WHR, and in women high WC. While men had a statistically significantly stronger handgrip, women performed better in dexterity in the Purdue Pegboard test, but there was no sex difference in lower body strength and walking speed. Postural sway was lower for women than men in all postural sway parameters ($p < .001$). For both sexes, we observed an increase in postural sway, when eyes closed compared to eyes open. The median MMSE score was 28 and the majority (90%) scored between 24 and 30 with no difference between the sexes. However, women performed statistically significantly better in incidental, immediate, and delayed memory ($p < .001$).

Frailty Index (FI)

Median FI was 0.28 and showed a slightly right-skewed distribution ranging from 0.09 to 0.7 (Supplemental File 1 Figure 1). The least frail group consisted of 71 individuals (21%), while 41 people (12%) were categorized as most frail (FI > 0.4). Thus, the majority of participants (67%) had a FI score between 0.2 and 0.4 corresponding to moderately frail. Participants with higher FI values were more often living in nursing homes ($p < .001$) (Table 1). The univariate logistic regressions showed that half of the included FI deficits were statistically significantly associated with mortality and more often in men than women. Some of the deficits were associated with mortality in both sexes, while some only in men or only in women (Supplemental File 1 Table 2).

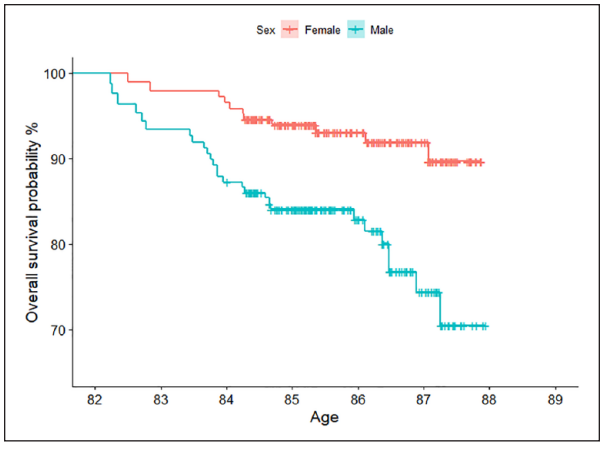

Figure 2. Kaplan-Meier overall survival probability % by sex.

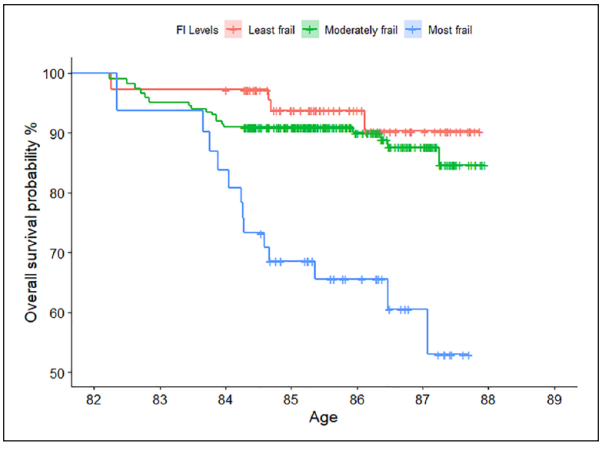

Figure 3. Kaplan-Meier overall survival probability % by FI levels.

Kaplan Meier Survival Curves by Sex and FI Levels

Survival curves plotted against sex and FI levels are displayed in Figures 2 and 3. During a mean follow-up of 39 months, 38 (11%) persons died, 27 (8%) males, and 11 (3%) females with a statistically significant sex difference, as the survival probability for women was higher compared to men at all ages ($p = .004$). Increasing grades of frailty were associated with decreased survival. The survival probability was highest among least frail and lowest among participants in the frailest group ($p < .001$). The survival probability decreased by 33% from age 83 to 87 (94%–61%) in the frailest group, compared to 7% (95%–88%) (97%–90%) in the moderately frail and least frail categories.

Cox Regression Analysis of the Impact of FI on Mortality Risk

Being most frail was associated with higher mortality risk (HR 6.58 [CI 2.14, 20.18]). After adjustment for demographic variables, this association remained statistically significant. Of the tested variables (frailty, sex, marital status, education, and living situation) only frailty and sex remained statistically significantly associated with mortality; being male was associated with an increased HR of 4.05 [CI 1.73, 9.48] compared to females (Figure 4).

Discussion

In this study, we found that the health profile of older Faroese people was comparable to the pattern in other countries. At the age of 80+, Faroese women outlived men. We found that women suffered more often from disabilities and health conditions that may affect daily life, while men suffered from more lethal diseases. We identified every fifth person to be least frail and 67% were moderately frail. Being male or most frail was associated with higher mortality risk compared to women and least frail.

Our results are in line with other studies. The sociodemographic characteristics with more women being widowed, living alone and having lower education were similar to a large cohort of 85-year-olds from the Newcastle 85+ Study (Collerton et al., 2007).

We found that men more often suffer from diseases such as heart disease and cancer, while women have higher rates of less life-threatening health conditions related to disabilities such as osteoporosis, arthritis, and mental health. This sex difference has also been reported in other studies (Carmel, 2019) and presumably contributes to women living longer than men. Even when both sexes survive to 80+ years, women outlive men ($p = .004$), as seen in this study.

For both sexes, nearly all anthropometric measurements were outside normal range and 77% of the participants were characterized as overweight/obese according to BMI. However, studies indicate that present BMI categories and interpretations may be inappropriate for older adults (Javed et al., 2020), while a BMI between 25 and 35 may be optimal for health (Kıskaç et al., 2022). Still, both WC, WHR and body fat percent were outside normal range. This suggests that the trend with an increasing part of overweight or obese people worldwide and in all age groups recognized as an obesity pandemic (Boutari & Mantzoros, 2022) also exists among Faroese octogenarians.

As found at baseline (Petersen et al., 2019), women performed significantly better in memory assessments than men at the 10 years-follow-up. This may seem peculiar since a higher proportion of women than men develop dementia, as observed in the Faroese Septuagenarian cohort, where women had a greater incidence of all-cause dementia (IRR 1.58 [CI 0.93, 2.71]) (Paul et al., 2021). Nevertheless, our findings are consistent with previous studies suggesting that women have better memory function even at old ages (Golchert et al., 2019; Olaya et al., 2017). A recent study indicates that

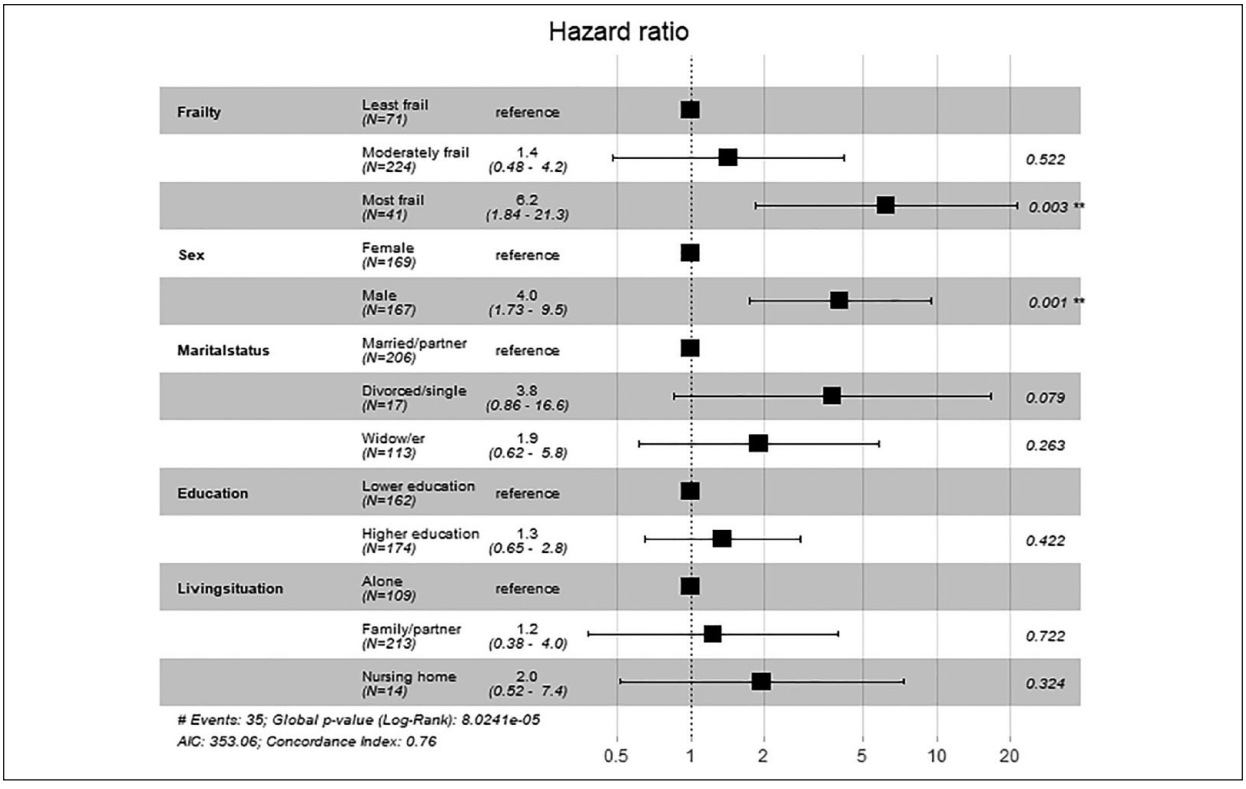

Figure 4. Mortality risk during the mean of 39 months of follow-up.

the female advantage exists amongst persons with none-to-one modifiable dementia risk factors, while no difference between the sexes was observed, when multiple risk factors were present, suggesting that women are cognitively more vulnerable to the accumulation of dementia risk factors (LaPlume et al., 2022).

A systematic review including 62 countries worldwide found a frailty prevalence of 32% amongst older adults aged 80 to 89 from studies using a FI approach (O'Caoimh et al., 2021). Compared to this review, our frailty prevalence is high with a defined cut-point of 0.2. indicating frailty.

The median FI score in this study was 0.28. Frailty score appears to be higher in FI combining self-reported data and objective measurements, as constructed in this study, compared to FI including self-reported data solely (Theou et al., 2015). A Dutch study found a mean FI score of 0.27 in older people aged ≥82 and an overall prevalence of 50% with a cut-point of ≥0.25 indicating frailty (Hoogendijk et al., 2017). Likewise, our findings are similar with a mean FI score of 0.26 found among community-dwelling octogenarians from 12 different European countries (Romero-Ortuno & Kenny, 2012). We included residents in long-term care and this probably contributes to a slightly higher FI score compared to studies only including community-dwelling older adults (O'Caoimh et al., 2018).

Comparing frailty geographically and between studies is a challenge mainly due to methodological differences. Besides, various FI cut-points have been reported to identify frailty, from 0.12 to 0.45 with 0.21 and 0.25 being used most frequently (Gordon et al., 2021).

Our findings are in line with other studies where FI is associated with adverse outcomes. We observed that being most frail was significantly associated with six times higher mortality risk regardless of sex, marital status, education, and living situation. Likewise, our findings support a "male-female health-survival paradox" (Gordon et al., 2017); although women accumulate more deficits, by having higher FI median scores than men, the deficits are more lethal in men; our results showed being male was associated with higher mortality (HR 4.0 [CI 1.73, 9.5]), and individual FI deficits were more often associated with mortality in men than women.

Frailty is a threatening condition affecting a person's quality of life, independence, and aging in place. The stratification into frailty categories of a cohort of Faroese octogenarians, corresponding to approximately every fourth person in the age group 80 to 84 years in the Faroe Islands as of August 2022 (Hagstova, 2022b), revealed that a majority are moderately frail (67%) while 21% were least frail. The identification of least and moderate frail long-living adults could be useful to prevent and/or postpone further deterioration to a most frail state with preventive interventions, as some studies report a reduced level of frailty amongst older adults participating in such courses (Puts et al., 2017).

Our study has several strengths. The participation rate is high (65%), considering the high age of the

participants and we included residents in long-term care. The sample is considered representative of this age group of older adults in a small-scale society with 28% of the Faroese population aged 80 to 84 (as of August 2022) participating. Additional strengths are the comprehensive health examinations undertaken, allowing objective measurements and self-reported data in the construction of FI covering a wide range of health deficits compared to FI with only self-reported data (Theou et al., 2015).

This study has its limitations. Although the strength is the extensive data collection, this is also a key limitation, as some participants have incomplete data, because of health problems, and thus not able to complete all tasks. Another methodological challenge is death and loss to follow-up (Hardy et al., 2009). In this cohort, 181 had died and 185 were non-participants. Thus, both healthy participation bias and survivor bias may be of potential concern and results must be interpreted with this caution. On the other hand, we set up examination clinics in the participants' vicinity. Hence, traveling far was not an obstacle to participation limiting bias.

Conclusion

In conclusion, we found a sex difference in health status, with women showing higher rates of health conditions related to disability, while men more often have heart diseases and cancer and even at older ages a lower life expectancy than women. Moreover, the most frail individuals had six times higher mortality risk compared to people least frail and were more often living in nursing homes. Further, the identification and possibility to classify octogenarians as least and moderately frail may be an opportunity to initiate national preventive interventions in this age group, to slow down the process of frailty and preserve independence and aging in place as long as possible.

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Declaration of Conflicting Interests

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Supplemental Material

Supplemental material for this article is available online.

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