

**Chronic conditions and multimorbidity in population aged 90 years and over: associations with mortality and long-term care admission**

**Introduction**

by Halonen, Pauliina; Raitanen, Jani; Jämsen, Esa; Enroth, Linda; Jylhä Marja

Increases in longevity along with improved management of chronic conditions have led to more people living to very old ages with one or more chronic conditions [1]. The prevalence of most chronic conditions is projected to increase; by 2035, over half the population aged over 85 years will have four or more chronic conditions [2]. Consequently, interest is increasing in the associations of chronic conditions and multimorbidity with different health outcomes.

The prevalence of multimorbidity, defined as having more than one chronic condition, peaks around age 85, with reported prevalence rates ranging from 82% to 95% [3–5]. In studies mostly concerning younger people, multimorbidity has been associated with declining functional ability, lower quality of life and high need for health care services [6].

Most studies have shown higher mortality for people with several chronic conditions, but in old age, this association is thought to be mediated by functional ability [7]. Disability and chronic conditions are closely related and often co-occur in old age, reflecting the severity of chronic conditions. However, functioning seems to decrease in old age irrespective of a person's disease status [8]. Currently, knowledge about the predictors of mortality among the oldest old is limited. In a Danish study, chronic conditions had little effect on mortality [9], whereas in another study low baseline comorbidity was associated with low 5-year mortality [10].

The need for long-term care (LTC) rises during the last years or months of life. Time spent in LTC during the end of life seems to have increased, possibly since people are living longer and suffering from more chronic conditions than before [11]. In younger old people, dementia and Parkinson's disease, as well as multimorbidity, have been associated with the need for LTC [12, 13]. Prior research is scarce on chronic conditions or multimorbidity as predictors of LTC use in the oldest old population.

The study examines to what extent chronic conditions and multimorbidity predict mortality and LTC admission in the population aged 90 and over, and assesses the population attributable fractions of mortality and LTC admission for individual chronic conditions.

## **Methods**

### *Sample*

The data were based on four cross-sectional waves of the Vitality 90+ Study conducted in 2001, 2003, 2007 and 2010 [14]. Each study year the mailed survey included both community-dwelling and institutionalized residents aged 90 years and over in the city of Tampere, Finland (in 2017 with 231,853 inhabitants, of whom 19% were aged over 65 and 0.9% aged over 90 [15]). The response rate varied between 79% and 86%. Due to high mortality, most participants ( $n = 1,650$ ) responded to only one survey. Of the remainder, 1,004 participated in two surveys, 176 three surveys and 32 all four surveys. The sample used in the analysis concerning mortality included 2,862 participants (79.5% women). The LTC analysis used a subsample of 1,954 respondents living in their own homes at baseline. Proxy answers were included for participants who could not answer the questionnaire themselves.

### *Chronic conditions*

Information on chronic conditions was based on self-reports. Participants were asked whether a doctor had told them they had any of nine chronic conditions: hypertension, heart disease, dementia, stroke, diabetes, arthritis, Parkinson's disease, hip fracture, and depression. To describe multimorbidity, the respondents were categorized as having 0, 1, 2, 3 and 4+ conditions.

### *Covariates*

Functional ability was included in the analysis as a sum of five variables measuring activities of daily living and mobility. Participants were asked "Are you able to..." move indoors, walk at least 400 meters, use stairs, dress, and get in and out of bed. The answer choices were "Yes, without difficulty," "Yes, but it's difficult," "Not without help" and "Unable." Answers were scored from 1 (able without difficulty) to 4 (unable). Hence, the total score for functional ability ranged from 5 (i.e., able to perform all activities without difficulty) to 20 (unable for all activities).

Occupational class was used as a covariate since multimorbidity and certain chronic conditions tend to be more prevalent in people with lower socioeconomic status [3, 16]. The participant's main occupation during working life was coded according to the Statistics Finland occupation classification [17] as upper non-manual, lower non-manual, skilled manual, unskilled manual, housewives and unknown occupation.

Other covariates used in the analysis were age and year entering the study. Additionally, living alone vs. with others was included as a covariate in LTC analysis.

### *Outcomes*

The main outcomes in this study were death and entering LTC. LTC was defined as an approval for LTC admission from the municipal authorities or being at least 90 days in a residential home, service home with 24-hour assistance or inpatient ward of a health center or hospital. Data for mortality and LTC were retrieved from the Finnish Population Register and the National Care Registers for Health and Social Welfare and were linked to the survey data using unique personal identity codes. The follow-up began on the index date of every study year and ended on December 31, 2012 at the latest.

Permission to use pseudonymized register data was obtained from the National Institute for Health and Welfare and the data was formed with Statistics Finland. The ethics committees of Pirkanmaa Hospital District or the City of Tampere, depending on the study year, gave ethical statements for the Vitality 90+ Study.

### *Statistical analysis*

Cox proportional hazard regression was used to estimate risk of death. In the analysis concerning LTC admission, competing risk regression [18] with death as a competing risk was used. Chronic conditions, functional ability and living arrangements were considered as time-dependent covariates using data from each participants' all available survey rounds. Number of chronic conditions was also considered as a time-dependent covariate. However, if a participant reported fewer conditions on a later survey round, the former number (i.e., the higher number) of conditions remained unchanged.

First, the associations of each chronic condition and functional ability separately, with mortality, adjusted for age and year of entry, were analyzed. Second, all chronic conditions, functional ability, and occupational class, together with age and year of entry were included in the same model. The analyses concerning association between chronic conditions and entering LTC followed the same patterns but living alone was also included in the second model. Then similar analyses were performed to test the effects of multimorbidity. All analyses were conducted separately for men and women. Hazard ratios (HR) and sub-hazard ratios (SHR) with 95% confidence intervals are presented.

Population attributable fraction (PAF) was used to describe the burden of chronic conditions. PAF was computed based on the Cox and competing risk regression analyses [19]. These models, however, were adjusted only for age, year of entry and all conditions, in order to estimate purely the attribution of the chronic conditions. PAF takes into account not only the strength of a relationship between risk factor and outcome but also the prevalence of the risk factor in a population. Therefore, it describes the importance of certain risk factors at population level [20].

P-values <0.5 were considered significant. Stata version 15.1 was used in all analyses.

## **Results**

In total, 2,862 participants were included in the analyses concerning mortality. Of them 2,165 died (75.2% of women and 77.3% of men) during the follow-up. The average time to death was 2.5 years (range 9 days – 11.6 years). Of those living outside institutions at baseline ( $n = 1,954$ ), 46.1% of women and 33.8% of men moved to LTC. The average follow-up time to LTC admission was 2.1 years (range 4 days - 11 years). Characteristics of participants at baseline are shown in Table 1.

### *Chronic conditions and multimorbidity as predictors of mortality*

In the first model, dementia, stroke, diabetes, heart disease and depression increased the risk of death, whereas participants with arthritis had lower mortality. In addition, worse functional ability predicted mortality. The findings were similar for both genders (Table 2).

In the fully adjusted model, heart disease, dementia and diabetes, but not stroke, increased the risk of death for both genders. In addition, depression was associated with an increased risk of death in women. In men, arthritis and Parkinson's disease were associated with lower risk of death (Table 2).

In the model adjusted for age and year of entry, there was a graded association between the number of conditions and the risk of death in both genders. When functional ability and occupational class were added, HRs declined but women with 3 or 4+ conditions still had increased risk of death (53% and 59% respectively). In the final model, having three or more conditions predicted mortality in women whereas the association was found in men only for those with one condition compared to men with no conditions (Table 2).

### *Chronic conditions and multimorbidity as predictors of LTC admission*

Women with Parkinson's disease, dementia, hip fracture or depression had an increased risk of LTC admission in both the first and fully adjusted models. In men, none of the conditions was associated with LTC admission; the only significant predictor was worse functional ability (Table 3).

Having at least two conditions increased the risk of LTC admission in women when only age and year of entry were adjusted for. When functional ability, living alone and occupational class were taken into account, the risk of entering LTC increased by 64% for women having 3 conditions and 99% for women having 4+ conditions. In men, multimorbidity was not associated with LTC admission (Table 3).

### *PAF of mortality and LTC admission*

In women 16% of deaths, and in men 14%, were attributable to heart disease. Corresponding numbers for dementia were 19% for women and 20% for men, and for diabetes, 3% for women and 5% for men. Depression accounted for 5% and stroke for 3% of deaths in women and hip fracture for 3% of deaths in men.

In both genders, dementia had the highest PAF for entering LTC (8% in women and 9 % in men). In women, Parkinson's disease had the lowest PAF (0.6%), though it was the strongest predictor of LTC admission in regression model (Table 3). PAF for hip fracture was 5% and for depression 4% (Supplementary table 1).

## Discussion

This follow-up study describes the associations of chronic conditions and multimorbidity with mortality and LTC admission in the fastest growing population segment in Europe: people aged over 90 years. The results show that certain individual conditions, as well as multimorbidity, predict mortality and LTC admission in this population independent of functional ability, age, living arrangements, socioeconomic status and cohort effect. Furthermore, a notable fraction of deaths is attributed to dementia, which also has the greatest effect on LTC admission. In men, chronic conditions and multimorbidity had weaker effects on the outcomes, at least partly due to the small number of male participants.

In this study, heart disease in women and diabetes in men had the strongest association with mortality, in line with previous studies considering younger old people [21, 22]. Our findings support previous evidence that cardiovascular diseases are a significant cause of death still in old age [23]. However, in oldest old, dementia was a greater determinant of death than heart disease or diabetes at population level. An even greater PAF of dementia was observed in a previous study including people over 95 years old [24]. As advances in prevention and treatment of cardiovascular diseases improve survival and decrease cardiovascular mortality [23], increasing numbers of the oldest will be expected to suffer and die from dementia.

Besides dementia and cardiovascular disease, depression was associated with mortality in women. Such an association has not been reported before in this age group. As causes of death were not studied, the mechanisms underlying the association between depression and mortality in the oldest old remain unknown. The lower risk of death for arthritis sufferers is not an unprecedented finding [22] yet contrasts with most studies on younger old people [25]. Both depression and arthritis in the oldest old should be studied further.

Previous evidence on the association between multimorbidity and mortality in nonagenarians has been inconsistent [9, 10]. In line with our findings, a study with younger old people indicated that having at least three diseases increases the risk of death, and the effect is more pronounced in those with five or more diseases [22]. Comparisons between studies are difficult because of different ways of defining and measuring multimorbidity. However, our findings suggest that multimorbidity should be considered a predictor of mortality in the oldest old population.

Due to their disabling effects, Parkinson's disease, dementia, hip fracture and depression understandably increased the need for LTC as they do in younger old people [12, 13]. Our results emphasize the importance of dementia as the most important condition leading to LTC in the oldest old. Certain conditions previously associated with institutionalization (stroke, diabetes, heart disease, arthritis) [12, 13] did not affect LTC admission in our study, reflecting the importance of more disabling conditions in this age group: dementia, Parkinson's disease and hip fracture. Multimorbidity as predictor of LTC admission [13] seems to hold in the oldest old women, as our results suggest. Consonant with previous studies [9, 13, 26, 27], our results also show that LTC admissions are more common in women than men whereas mortality is higher in men in this age group. This might be one reason why we did not find associations between chronic conditions or multimorbidity and LTC admission in men.

The strength of this study is the study design, rarely used in studying the oldest old. A maximum of over 11 years' follow-up and use of time-dependent covariates provided information on the changes in morbidity and functional status. PAF added to this information by describing the significance of analyzed conditions. It is also noteworthy that the sample included both community-dwelling and institutionalized participants.

Using proxy answers, data were available from those not able to answer themselves. The response rates in the Vitality 90+ Study have been very high.

The most important limitation is that the information was mostly self-reported and except for data about functional status, there was no way to estimate the severity of conditions. However, it has been shown that even the oldest old are able to give sufficiently reliable information on their health status [28]. Another restriction is that to maintain sufficient response rates, the number of questions, including the number of conditions, was limited.

Our findings indicate that even though baseline mortality in very old people is high, certain chronic conditions, such as heart disease, diabetes, dementia and depression, in addition to multimorbidity, are still significant predictors of mortality in nonagenarians. In general, morbidity is associated with disability, but in this study, multimorbidity, dementia, hip fracture and depression increased the risk of LTC admission in women independent of functioning. Future research should focus on comorbidities with dementia since its prevalence is expected to increase [23]. In addition, updated information on the progression of the prevalence and incidence of other chronic conditions in the oldest old population is needed.

**Conflict of interest:**

No conflict of interests.

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**Table 1.** Baseline characteristics of the study population. % (*n*) of each variable if not stated otherwise.

Baseline	All		Home at baseline		
	Women	Men	Women	Men	
Total number of participants	2,276	586	1,489	465	
Proxy answers	20.1 (456)	13.2 (77)	4.1 (60)	4.3 (20)	
Missing <i>n</i>	11	4	7	3	
Median age (range)	91 (90-107)	91 (90-102)	91 (90-107)	91 (90-102)	
Year of entry					
	2001	31.6 (720)	29.4 (172)	27.5 (409)	28.8 (134)
	2003	16.3 (370)	18.1 (106)	16.7 (249)	16.8 (78)
	2007	23.9 (543)	24.6 (144)	24.0 (358)	24.7 (115)
	2010	28.3 (643)	28.0 (164)	31.8 (473)	29.7 (138)
Occupation					
	Upper non-manual	5.5 (125)	17.9 (105)	5.4 (80)	17.9 (83)
	Lower non-manual	28.6 (651)	25.6 (150)	30.4 (452)	27.1 (126)
	Skilled manual	33.3 (758)	44.5 (261)	34.6 (515)	43.7 (203)
	Unskilled manual	9.6 (219)	2.2 (13)	8.9 (132)	1.7 (8)
	Housewives	11.2 (254)		12.6 (188)	
	Unknown occupation	11.8 (269)	9.7 (57)	8.2 (122)	9.7 (45)
Living arrangements					
	Living alone	53.1 (1,203)	37.6 (220)	78.3 (1,160)	47.2 (219)
	Living with someone	11.7 (264)	39.7 (232)	21.7 (321)	52.8 (245)
	in LTC	35.2 (797)	22.7 (133)		
	Missing <i>n</i>	12	1	8	1
Functional ability score median (IQR)		9 (6-13)	7 (5-11)	8 (6-14)	6 (5-14)
	Missing <i>n</i>	69	21	40	16
Chronic conditions					
	Hypertension	45.9 (1,030)	31.5 (182)	51.3 (753)	33.2 (152)
	Heart disease	54.1 (1,213)	51.6 (298)	53.8 (790)	51.3 (235)
	Dementia	41.6 (932)	38.6 (223)	26.7 (392)	32.2 (148)
	Stroke	7.1 (158)	6.1 (35)	4.4 (64)	4.4 (20)
	Diabetes	11.7 (262)	10.7 (62)	10.4 (153)	9.8 (45)
	Arthritis	41.3 (926)	28.0 (162)	45.8 (672)	28.6 (131)
	Parkinson's disease	2.1 (47)	1.0 (6)	1.2 (18)	0.7 (3)
	Hip fracture	17.6 (395)	11.1 (64)	14.4 (212)	10.0 (46)
	Depression	23.3 (522)	18.3 (106)	16.8 (246)	15.5 (71)
	Missing <i>n</i>	32	8	21	7
Number of conditions					
	0	6.0 (134)	13.2 (76)	8.0 (117)	15.3 (70)
	1	19.7 (442)	26.6 (154)	22.1 (324)	28.2 (129)
	2	28.2 (633)	26.5 (153)	29.9 (439)	26.4 (121)
	3	24.9 (559)	23.0 (133)	23.8 (350)	21.2 (97)
	4+	21.1 (474)	10.7 (62)	16.2 (238)	9.0 (41)
	Median (range)	2 (0-7)	2 (0-7)	2 (0-7)	2 (0-7)
	Missing <i>n</i>	32	8	21	7

Functional ability score ranges from 5 to 20, higher score representing worse functional ability

**Table 2.** Associations of chronic conditions, multimorbidity and functional ability with mortality. Hazard ratios (HR) and 95% confidence intervals (CI) from Cox regression models

	Women				Men			
	Model 1 <sup>a</sup>		Model 2 <sup>b</sup>		Model 1 <sup>a</sup>		Model 2 <sup>b</sup>	
	(n=2,216-2,255)		(n=2,216)		(n=566-581)		(n=566)	
	HR	95 % CI	HR	95 % CI	HR	95 % CI	HR	95 % CI
Functional ability	1.12	1.10-1.13	1.10	1.09-1.12	1.15	1.13-1.17	1.15	1.12-1.18
Hypertension	0.91	0.82-1.01	0.93	0.84-1.04	1.06	0.85-1.32	1.03	0.82-1.30
Heart disease	1.34	1.21-1.48	1.35	1.22-1.50	1.46	1.20-1.77	1.25	1.02-1.54
Dementia	1.68	1.52-1.86	1.20	1.07-1.33	1.75	1.44-2.12	1.30	1.05-1.61
Stroke	1.66	1.40-1.98	1.18	0.98-1.41	1.59	1.08-2.33	0.90	0.60-1.36
Diabetes	1.39	1.20-1.61	1.27	1.09-1.48	1.64	1.23-2.20	1.67	1.24-2.25
Arthritis	0.84	0.76-0.93	0.80	0.72-0.90	0.78	0.62-0.97	0.68	0.53-0.85
Parkinson's disease	1.26	0.91-1.76	1.02	0.73-1.43	1.11	0.52-2.36	0.37	0.17-0.82
Hip fracture	1.12	0.99-1.26	0.91	0.80-1.03	1.24	0.94-1.63	0.94	0.70-1.27
Depression	1.41	1.26-1.58	1.15	1.02-1.29	1.30	1.02-1.65	0.96	0.74-1.25
		Model 3 <sup>a</sup>		Model 4 <sup>c</sup>		Model 3 <sup>a</sup>		Model 4 <sup>c</sup>
		(n=2,255)		(n=2,216)		(n=581)		(n=566)
Functional ability	1.12	1.10-1.13	1.11	1.10-1.12	1.15	1.13-1.17	1.15	1.12-1.18
Multimorbidity								
0 diseases	ref.		ref.		ref.		ref.	
1 disease	1.64	1.20-2.24	1.38	1.01-1.90	1.63	1.10-2.43	1.56	1.03-2.35
2 diseases	1.69	1.25-2.29	1.32	0.96-1.79	1.85	1.25-2.74	1.42	0.94-2.14
3 diseases	2.27	1.68-3.07	1.53	1.12-2.08	2.08	1.40-3.08	1.40	0.92-2.12
4+ diseases	2.64	1.95-3.57	1.59	1.16-2.16	3.06	2.00-4.69	1.57	0.99-2.49

<sup>a</sup>Separate model for each variable, adjusted for age and year of entry

<sup>b</sup>All conditions and functional ability adjusted for age, year of entry and occupational status

<sup>c</sup>Multimorbidity and functional ability adjusted for age, year of entry and occupational status

**Table 3.** Associations of chronic conditions, multimorbidity and functional ability with entering LTC. Regression models with mortality as a competing risk for LTC. Subhazard ratios (SHR) and 95% confidence intervals (CI)

	Women				Men			
	Model 1 <sup>a</sup>		Model 2 <sup>b</sup>		Model 1 <sup>a</sup>		Model 2 <sup>b</sup>	
	(n=1,458-1,476)		(n=1,444)		(n=450-461)		(n=447)	
	SHR	95% CI	SHR	95% CI	SHR	95% CI	SHR	95% CI
Functional ability	1.08	1.06-1.11	1.07	1.04-1.10	1.14	1.08-1.20	1.11	1.05-1.18
Hypertension	0.98	0.84-1.15	0.98	0.83-1.17	0.97	0.64-1.45	1.07	0.68-1.68
Heart disease	0.90	0.77-1.06	0.86	0.73-1.02	1.33	0.93-1.91	1.31	0.90-1.92
Dementia	1.58	1.33-1.87	1.50	1.25-1.79	1.44	1.01-2.06	1.23	0.80-1.89
Stroke	1.11	0.74-1.67	0.97	0.63-1.50	0.93	0.36-2.36	0.68	0.24-1.93
Diabetes	1.01	0.78-1.32	1.01	0.77-1.34	0.82	0.43-1.55	0.74	0.36-1.50
Arthritis	1.16	0.99-1.35	1.08	0.91-1.27	1.40	0.96-2.06	1.34	0.90-2.00
Parkinson's disease	3.05	1.92-4.82	2.36	1.40-3.97	0.41	0.48-3.49	0.51	0.05-4.88
Hip fracture	1.52	1.24-1.86	1.42	1.14-1.75	1.21	0.71-2.06	1.27	0.72-2.24
Depression	1.56	1.27-1.91	1.27	1.01-1.59	1.21	0.76-1.92	1.05	0.65-1.70
	Model 3 <sup>a</sup>		Model 4 <sup>c</sup>		Model 3 <sup>a</sup>		Model 4 <sup>c</sup>	
	(n=1,458-1,476)		(n=1,444)		(n=450-461)		(n=447)	
Functional ability	1.08	1.06-1.11	1.08	1.05-1.11	1.14	1.08-1.20	1.10	1.04-1.17
Multimorbidity								
0 diseases	ref.		ref.		ref.		ref.	
1 disease	1.32	0.92-1.91	1.34	0.91-1.97	0.84	0.48-1.49	0.90	0.49-1.66
2 diseases	1.46	1.03-2.08	1.43	0.98-2.08	1.51	0.88-2.60	1.52	0.82-2.78
3 diseases	1.76	1.23-2.51	1.64	1.12-2.40	1.52	0.84-2.74	1.57	0.83-3.00
4+ diseases	2.21	1.53-3.20	1.99	1.34-2.95	1.78	0.88-3.59	1.56	0.72-3.37

<sup>a</sup> Separate model for each variable, adjusted for age and year of entry

<sup>b</sup> All conditions and functional ability adjusted for age, year of entry, occupational status and living arrangements

<sup>c</sup> Multimorbidity and functional ability adjusted for age, year of entry, occupational status and living arrangements