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# Fatigability in Basic Indoor Mobility in Nonagenarians

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# Abstract

**OBJECTIVES**—Older adults' subjective feelings of fatigue have been considered an important indicator of functional decline in old age. However, fatigue in the fastest growing segment of the older population, the oldest old, has not been reported in previous studies. The aim of this study was to evaluate the prevalence and associated health factors of indoor mobility related fatigability among nonagenarians.

**DESIGN**—A cross-sectional observational study of all Danes born 1905 assessed in 1998.

**SETTING**—Community, sheltered housing and nursing homes.

**PARTICIPANTS**—92-93-year old persons (n=1181) who were independent of help in basic indoor mobility.

**MEASUREMENTS**—Fatigability in basic indoor mobility was defined as a subjective feeling of fatigue when transferring or walking indoors. Other standardized assessments include self-report measures of medical history, as well as performance-based assessments of walking speed and maximum hand grip strength.

**RESULTS**—In total, every fourth (26%) of the participants reported fatigability when transferring or walking indoors and fatigability was more common among participants living in

#### **Conflict of Interest:**

The authors declare no conflict of interest.

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Mänty had full access to all the data gathered for the study and takes full responsibility for the integrity of the data and the accuracy of the data analyses. Concept and design: Mänty, Christensen, Avlund. Acquisition of data: Christensen, Thinggaard. Statistical analysis: Mänty. Interpretation of data: Mänty, Ekmann, Thinggaard, Christensen, Avlund. Drafting the manuscript: Mänty. Critical revision of the manuscript for important intellectual content: Mänty, Ekmann, Thinggaard, Christensen, Avlund

sheltered housing as compared to those living independently (32% vs. 23%, p<.001). Cardiovascular diseases, musculoskeletal pain, medications, walking speed and depressive symptoms were independently associated with fatigability.

**CONCLUSION**—Fatigability in very basic everyday mobility is relatively common in nondisabled nonagenarians. The results also indicate important associations between fatigability and potentially modifiable health factors.

## Keywords

Fatigue; Aging; Nonagenarians; Health; Mobility limitation

# INTRODUCTION

The oldest old, those aged 85 years and older, is the fastest growing segment of the older population in the western world, mainly due to a reduction in mortality rates in this population.<sup>1</sup> To date, it has been well shown that physical functioning declines with increasing age and studies including the oldest-old have suggested that for the individual, long life brings an increasing risk of declining physical abilities and loss of independence.<sup>2-4</sup> For example, a previous study of the Danish 1905 cohort survivors showed that the proportion of individuals with independent basic daily functioning declined from 70% to 33% between age 92 and 100 years.<sup>3</sup>

Older adults' subjective feelings of fatigue have been considered an important early indicator of functional decline in old age.<sup>5;6</sup> Many previous cross-sectional as well as longitudinal observational studies have shown that fatigue is associated with poorer functional performance,<sup>7-10</sup> increased disability,<sup>11;12</sup> use of social and health services,<sup>13</sup> and higher mortality.<sup>14-16</sup> Although the information on the physical functioning of the oldest old is gradually accumulating, fatigue in this population segment has not been reported in previous literature.

It has recently<sup>6</sup> been suggested to make a distinction between the terms fatigue and fatigability. Fatigue is considered as a general feeling of fatigue or tiredness irrespective of the specific context, whereas fatigability is a characteristic of an individual that describes how fatigued he or she gets in relation to defined activities, such as, walking indoors or climbing stairs.<sup>6</sup> The term fatigability used in this current paper is also distinct from the same term used in the exercise literature describing the endurance characteristics of individual muscles. The aim of this study was to evaluate the prevalence and associated factors of fatigability in basic indoor mobility among Danish nonagenarians aged 92 to 93 years.

# METHODS

#### Study population

This observational study is based on baseline data of the nationwide Danish 1905 cohort study.<sup>17</sup> The cohort members were traced through the Danish Civil Registration System and the whole Danish 1905 cohort was contacted in 1998. A total of 3600 persons aged 92 to 93 years were alive at the beginning of the survey, and of these, 2262 (63%) participated in the study. In this current study, we included only 1814 participants with non-proxy interview on indoor mobility related fatigability. Of these, 271 were unable to transfer or walk indoors independently and 362 did not have full information on all variables used, leaving a total of 1181 participants for the final analyses. Two-thirds (68%, n=807) of the selected sample lived independently in a house or an apartment and one-third (32%, n=374) in sheltered

housing, e.g. in supportive housing or nursing home. The regional Scientific Ethical Committees of Denmark approved the study (19980073PMC).

#### Data collection and methods

Face-to-face interviews were conducted at participants' homes and included structured questions on mobility related fatigability and other health factors. In addition, maximum handgrip strength and walking speed were measured during the interview.

#### Fatigability

Fatigability was defined as "a subjective feeling of fatigue in basic indoor mobility tasks". It was measured using two items of the Avlund Mobility-Tiredness Scale (MOB-T).<sup>18</sup> Participants were first asked whether they were able to 1) transfer from a chair or a bed and 2) walk indoors without help of another person. Participants who were able to manage the tasks independently were further asked if they felt fatigued after performing them. Individuals reporting fatigue in either one or both of the tasks were categorized as having fatigability in basic indoor mobility. Participants who were unable to manage the tasks independently (n=271) were excluded from the current study.

#### Independent factors

**Pathology**—Information on self-reported physician diagnosed diseases and prescription medication was collected during the face-to-face interview. The total sum of reported diseases was used for descriptive purposes. For the main analyses the following disease groups were identified: musculoskeletal diseases (osteoarthritis, rheumatoid arthritis, gout, and/or spinal disc herniation), cardiovascular diseases (myocardial insufficiency, ischemic heart disease, hypertension, and/or cardiac arrhythmia), lung diseases (chronic obstructive pulmonary disease, asthma, and/or pulmonary edema), and eye diseases or conditions affecting vision (cataract, glaucoma, and/or age related macular degeneration). The used medicine was coded according to the Anatomical Therapeutic Chemical (ATC) classification system by a physician and the total number of medications was used in this study. Body mass index (BMI, kg/m<sup>2</sup>) was calculated using self-reported data on height and weight. Categories of BMI were created using gender-specific tertiles (low-middle-high) and the lowest tertile was used as a reference category in the analyses. Musculoskeletal pain was measured with questions: "Do you have pain in your hips/knees/back when you move?" and "Do you have pain in your hips/knees/back when you sit/rest/sleep?" Participants reporting movement or rest pain in one or more locations were considered as having musculoskeletal pain.

**Impairments**—Maximum isometric grip strength was measured using a handheld dynamometer. The best performance of three measurements with the preferred hand was used as a measure of grip strength<sup>17</sup> and weight adjusted grip strength was used in the analyses.

**Functional limitations**—Habitual walking speed was measured over a 3-meter (n=1094) or a 4-meter (n=87) distance.<sup>17</sup> Participants wore walking shoes or sneakers and use of a walking aid was allowed if needed. Walking time was measured with a stopwatch and walking speed was calculated as meters per second (m/s). The fastest time of two trials was used for the present analyses. There were no significant differences in the walking speed regarding the distance of the test.

**Psychological factors**—Depressive symptoms were assessed using the depression section from the Cambridge Mental Disorders of the Elderly Examination (CAMDEX)

diagnostic interview, <sup>19</sup> comprising 17 items concerning depressive symptoms (total score range from 0 -34 points), with a higher score indicating higher level of depressive symptoms. Cognitive performance was assessed with the Mini-Mental State Examination (MMSE, score range 0-30)<sup>20</sup> with a higher score indicating higher levels of cognition.

#### **Statistical analyses**

Comparisons between groups with and without fatigability were examined with chi-square test for categorical variables, and one-way analysis of variance (ANOVA) for continuous variables. The association between health factors and fatigability was analyzed using bivariate and multivariate logistic regression models with stepwise forward selection. Variables that were associated with fatigability at the bivariate level (p<.10) were included in the following order: pathology (6 variables in three consecutive groups), impairment (1 variable), functional limitation (1 variable), and psychological factors (2 variables). For each step, variables which were related to the outcome measure with p-value of <.10 were included in the next model and only the significant (p<.05) associations were included in the final regression model. The Hosmer-Lemeshow goodness-of-fit tests showed that there were no differences between the observed and predicted values. Analyses were performed using SAS software version 9.2 (SAS Institute Inc., Cary, NC).

# RESULTS

In total, every fourth (26%) of the participants reported fatigability when transferring or walking indoors and fatigability was more common among participants living in sheltered housing as compared to those living independently (32% vs. 23%, p<.001). In addition, a larger proportion of independently living women than men reported fatigability (26% vs. 15%, p<.001) but there were no gender differences among those living in sheltered housing (33% vs. 29%, p>.05). We did not find any significant interactions between gender and studied health factors on fatigability (all p values >.05). However, significant interactions between housing type (independent / sheltered housing) and some of the health factors (medications and diseases) on fatigability were found (p values <.05). Therefore all results are presented stratified by housing type.

Descriptive data of the study population are presented in Table 1. Around two-thirds (68%) of the participants lived independently and 71% were women. Persons reporting fatigability had more diseases, medications, musculoskeletal pain and depressive symptoms, as well as poorer grip strength and slower walking speed compared to those without fatigability (Table 1).

Table 2 shows the estimated odds ratios for the associations between different health factors and fatigability among independently living nonagenarians. In the bivariate analyses, body mass index was the only variable that was not significantly (p>.05) associated with fatigability. Cardiovascular diseases, musculoskeletal pain, number of medications, walking speed and depressive symptoms remained significantly associated with fatigability in the final multivariate model. Participants with one or more cardiovascular disease(s) were over 1.5 times more likely (odds ratio (OR) 1.55, 95% confidence interval (CI) 1.04-2.32) and those reporting musculoskeletal pain almost two times more likely (OR 1.83, 95% CI 1.24-2.69) to report fatigability as compared to those without cardiovascular disease(s) or pain. In addition, each reported medication and one point increase in the depression score were associated with around 10% increase in the odds for fatigability (OR 1.10, 95% CI 1.01-1.19 and OR 1.09, 95% CI 1.05-1.13, respectively). On the contrary, one standard deviation faster walking speed decreased the odds with 43% (OR 0.57, 95% CI 0.45-0.71).

Table 3 shows the estimated odds ratios for associations between different health factors and fatigability among nonagenarians living in sheltered housing. In bivariate analyses, musculoskeletal pain, number of medications, grip strength, walking speed and depressive symptoms were significantly (p<.05) associated with reported fatigability. Pain, walking speed and depressive symptoms remained significantly associated with fatigability in the final multivariate model. Participants with musculoskeletal pain were almost two times more likely to report fatigability (OR 1.84, 95% 1.14-2.98) as compared to those without pain, and one point increase in the depression score was associated with almost 10% increase in the odds for fatigability (OR 1.09, 95% CI 1.05-1.13). Furthermore, one standard deviation faster walking speed decreased the odds with 44% (OR 0.56, 95% CI 0.42-0.74).

# DISCUSSION

In the present sample of non-disabled nonagenarians, cardiovascular diseases, musculoskeletal pain, medications, walking speed and depressive symptoms were independently associated with fatigability in basic indoor mobility. During recent years, there has been a growing interest in fatigue as a marker of aging-related declines in health and functional abilities.<sup>5;6</sup> However, fatigue in the fastest growing population segment, the oldest-old, has not been reported in previous studies.

Although this study included only nonagenarians who managed indoor mobility without help, feelings of fatigability in very basic everyday mobility was relatively high; almost every fourth of the independently living and every third of those living in sheltered housing reported fatigability when transferring or walking indoors. The results regarding the associated factors are comparable to those reported earlier in younger populations,<sup>7;9</sup> indicating that underlying factors for subjective feelings of fatigue are similar in younger older adults and in the oldest-old. For example a study<sup>9</sup> by Avlund et al. showed that social position, number of comorbidities, muscle impairment, pain and depressive mood were independently associated with fatigability in daily activities among 75-year-old community living older adults. Further, the fact that subjective feelings of fatigability in very basic indoor mobility reflect declines in objectively measured physical function also among the oldest old population strengthens the validity of the self-reported measure of fatigability.

Few studies have indicated that fatigue is more prevalent among older women than men,<sup>5;7;21</sup> and it has been suggested that there might be some gender differences in underlying factors for fatigue.<sup>10:22</sup> In this study, independently living nonagenarian women reported more indoor mobility related fatigability as compared to men. However, we did not observe any significant interaction between gender and associated health factors for fatigue, indicating that the factors contributing to feelings of fatigability are similar for men and women.

In this study, cardiovascular diseases were the most evident disease group that was associated with fatigability. However, it is worth to note that also musculoskeletal diseases and eye diseases seemed to be strongly associated with reported fatigability (Table 1). Musculoskeletal pain appeared to be an important variable explaining the association between musculoskeletal disease and fatigability among independently living participants (Table 1: Model 2 and model 3) as well as those living in sheltered housing (Table 2: Model 1 and Model 2). Pain is a common symptom of most musculoskeletal diseases and it is strongly associated with decreased physical performance, such as poor muscle strength and slow walking speed, in older adults.<sup>23;24</sup> Low physical performance, in turn, can be reflected as increased fatigability in mobility related tasks.<sup>9;10</sup> Respectively, vision plays an important role in balance, gait and orientation, and therefore diseases affecting vision may have detrimental effects on physical function,<sup>25;26</sup> potentially leading to increased feelings of

fatigue when performing mobility related tasks. It is also possible, that the association between eye diseases and mobility related fatigability is due to the increased efforts that an individual has to make in order to be able to observe the physical environment when performing the task. However, the association between vision and fatigue is not known and merit further investigation.

An interesting finding was that in the final multivariate model, diseases and medications remained significant correlates with fatigability only among independently living participants but not among those living in sheltered housing. Muscle strength and walking speed seemed to be important factors explaining the association between medications and fatigability among those living in sheltered housing (Table 2, Model 4 and Model 5). These findings indicate that physical manifestations, such as pain and poor functional performance, rather than diseases and medications themselves are important factors contributing to fatigability among nonagenarians living in sheltered housing. One hypothesis for these observations can be derived from the sufficient-component cause model, which refers to a minimal set of conditions that are sufficient for the outcome to occur.<sup>27</sup> It is possible that due to lower physical function in those living in sheltered housing, pain, functional limitation and depressive symptoms are sufficient components to result in feelings of fatigability, whereas among community living participants with better physical capacity, additional effect from diseases and medications are needed to cause fatigability in indoor mobility. However, the results of this paper are based on cross-sectional analyses and no causal inference can be made.

Our findings also supported the previously found associations between depressive symptoms and fatigue<sup>9;28;29</sup> and underline that the nature of the relationship may be reciprocal; fatigue is known to be a symptom of depression, but on the other hand, chronic fatigue has been shown to cause depression.<sup>28;29</sup> It is also possible that fatigue and depression are conditions that arise concurrently as a result of common underlying pathophysiological process. Further, the association between fatigue and depression might partly be explained by the way these two entities have been conceptualized.<sup>30</sup> Especially, measures emphasizing general or mental fatigue may have problems with overlapping criteria as they are often included in measures of depressive symptoms. This problem may be less evident when using mobility related measures of fatigue due to their strong association with specific physical tasks. In this current study, self-reported fatigability in basic indoor mobility was significantly associated with depressive symptoms as well as with objectively measured walking speed, indicating that mobility related fatigability reflects both, mental and physical dimensions in this very old cohort. Nevertheless, the exact causal associations between fatigue and depression are likely to be complex and more studies are needed to delineate the causal mechanisms between fatigue and depressive symptoms.

This is the first time to apply the Mobility-Tiredness Scale (MOB-T) for the oldest old population. This scale has been previously validated and used with younger older populations, showing good reliability, validity and predictive value.<sup>5;10;18</sup> Specifically it has been tested<sup>18</sup> by the Rasch model for item analysis that the separate items are expression of the same underlying uni-dimensional scale. The MOB-T scale thus fulfills the demands for construct validity and scalability in terms of objectivity, sufficiency and strongly homogeneous items. It is thus acceptable to remove items from the original scale, even though a full item scale is preferred. Due to high prevalence of inability in the more advanced tasks of the scale, that is, climbing stairs and walking outdoors, a modified scale was utilized in this current study. Ability to transfer and walk indoors can be considered as minimal requirements for independent daily functioning, and therefore using these two essential tasks can be regarded as a sound measure of fatigability in this population.

When interpreting the results, some limitations and strengths of the study should be considered. The results of this study are based on cross-sectional analyses and longitudinal studies are needed to examine the causal inference between fatigability and associated health factors. The strengths of the study are a well-characterized nationwide cohort with standardized measures of fatigability, physical function and health related factors.

## CONCLUSION

Fatigability in very basic everyday mobility is relatively common in non-disabled nonagenarians. The results also indicate important associations between fatigability and potentially modifiable health factors.

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(N=1181)
Participants
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	Independent	living (n=807)		Sheltered ho	using (n=374)	
	Fatig	ability		Fatig	ability	
	No (n=622)	Yes (n=185)	Ρ	No (n=254)	Yes (n=120)	Ρ
Formal education 7 years, n (%)	495 (80)	133 (72)	.027	200 (79)	87 (73)	.182
Women, n (%)	415 (67)	149 (81)	<.001	184 (72)	92 (77)	.386
Body Mass Index, mean $\pm$ SD	23.1 (3.3)	23.4 (3.8)	.396	23.3 (3.5)	22.8 (3.2)	.148
Number of diseases, mean $\pm$ SD	3.1 (2.2)	4.3 (2.5)	<.001	3.3 (2.4)	3.8 (2.6)	.115
Number of medications, mean $\pm$ SD	2.6 (2.6)	3.9 (2.8)	<.001	3.4 (2.7)	4.2 (2.9)	600.
Musculoskeletal pain, n (%)	286 (46)	131 (71)	<.001	116 (46)	78 (65)	<.001
Grip strength (kg), mean $\pm$ SD	18.4 (6.8)	16.0 (6.1)	<.001	15.9 (5.9)	13.7 (5.9)	<.001
Walking speed (m/s), mean $\pm$ SD	0.6(0.3)	0.5 (0.2)	<.001	0.6 (0.2)	0.4 (0.2)	<.001
$MMSE^{a}$ score , mean ± SD (range 0-30)	23.8 (4.5)	22.9 (4.6)	.015	21.3 (5.9)	20.7 (5.8)	.404
CAMDEX <sup>b</sup> score, mean $\pm$ SD (range 0-29)	6.2 (4.8)	10.1 (5.9)	<.001	7.5 (5.9)	11.5 (6.4)	<.001
SD = Standard deviation						

<sup>a</sup>Mini-Mental State Examination, score range 0-30.

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 $b \hspace{-0.5mm}$  Modified Cambridge Mental Disorders of the Elderly Examination, score range 0-29.

:	Model 1 <sup>a</sup>	Model 2 <sup><i>p</i></sup>	Model 3"	Model 4"	Model 5"	Model 6"	Model 7"	Final model
Variables	<b>UR</b> (95% CI)	OR (95% CI)	<b>UR (95% CI)</b>	<b>UR (95% CI)</b>	OR (95% CI)	<b>UR (95% CI)</b>	<b>UR (95% CI)</b>	<b>UR (95% CI)</b>
Anthropometry								
Body Mass Index <sup><math>c</math></sup> :								
Low (Ref.)	1			·	ı		ı	
Middle	1.34(0.88-2.03)							
High	1.31 (0.87-1.98)	ı	ı	ı		ı	ı	
Pathology								
Musculoskeletal disease	1.88 (1.35-2.64)	1.65 (1.17-2.34)	1.34 (0.93-1.92)	ı	ı	·		
Cardiovascular disease	2.28 (1.62-3.21)	1.93 (1.36-2.75)	1.88 (1.31-2.69)	1.50 (1.02-2.20)	1.58 (1.08-2.32)	1.62 (1.10-2.41)	1.55 (1.03-2.32)	1.55 (1.04-2.32)
Lung disease	2.05 (1.36-3.10)	1.65 (1.07-2.53)	1.64 (1.06-2.55)	1.45 (0.92-2.27)				
Eye disease	1.79 (1.23-2.59)	1.63 (1.12-2.38)	1.53 (1.04-2.24)	1.43 (0.97-2.11)	1.49 (1.01-2.19)	1.51 (1.01-2.24)	1.43 (0.96-2.16)	
Musculoskeletal pain	2.76 (1.93-3.94)		2.32 (1.59-3.34)	2.31 (1.59-3.34)	2.21 (1.53-3.21)	1.94 (1.33-2.85)	1.80 (1.22-2.66)	1.83 (1.24-2.69)
Number of medications	1.26 (1.17-1.35)			1.16 (1.07-1.26)	1.17 (1.08-1.26)	1.12 (1.03-1.21)	1.10 (1.01-1.19)	1.10 (1.01-1.19)
Impairment								
Grip strength <sup>d</sup>	0.77 (0.64-0.91)				0.79 (0.67-0.96)	0.92 (0.76-1.11)	ı	ı
Functional limitation								
Walking speed $^{e}$	0.46 (0.37-0.56)					0.53 (0.42-0.67)	0.57 (0.46-0.72)	0.57 (0.45-0.71)
Psychological factors								
Cognitive function $^{f}$	0.96 (0.93-0.99)						0.98 (0.95-1.03)	
Depressive symptoms $^{\mathcal{G}}$	1.13 (1.10-1.17)						1.09 (1.05-1.12)	1.09 (1.05-1.13)
OR = Odds Ratio								
CI = Confidence Interval								

Estimated Odds Ratios (ORs) And 95% Confidence Intervals (CIs) for Associations between Health Factors and Fatigability in Basic Indoor Mobility among *Independently Living* Nonagenarians (N=807) Table 2

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cGender specific Body Mass Index (kg/m<sup>2</sup>) tertiles: low – middle – high.

 $^{a}\mathrm{Gender}$  and education adjusted bivariate associations  $^{b}\mathrm{Gender}$  and education adjusted multivariate associations

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dGender specific z score for continuous weight adjusted variable

 $^{e}$  Gender specific z score for continuous variable

fMini-Mental State Examination score, range 0-30.

 ${^{\cal B}}$  Modified Cambridge Mental Disorders of the Elderly Examination score, range 0-29.

Table 3

Estimated Odds Ratios (ORs) And 95% Confidence Intervals (CIs) for Associations between Health Factors and Fatigability in Basic Indoor Mobility among Nonagenarians Living in *Sheltered Housing* (N=374)

VariableOR (95%, CI)OR (95%, CI) <th></th> <th>Model 1<sup>a</sup></th> <th>Model 2<sup>b</sup></th> <th>Model <math>3^b</math></th> <th>Model <math>4^b</math></th> <th>Model <math>5^b</math></th> <th>Model <math>6^b</math></th> <th>Final model <math>^{b}</math></th>		Model 1 <sup>a</sup>	Model 2 <sup>b</sup>	Model $3^b$	Model $4^b$	Model $5^b$	Model $6^b$	Final model $^{b}$
Autropometry           Body Muss Index <sup>C</sup> :         1         - <td< th=""><th>Variables</th><th>OR (95% CI)</th><th>OR (95% CI)</th><th>OR (95% CI)</th><th>OR (95% CI)</th><th>OR (95% CI)</th><th>OR (95% CI)</th><th>OR (95% CI)</th></td<>	Variables	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Body Mass Indec <sup>5</sup> :         1         ·	Anthropometry							
Low (ref.)       1       - <th< td=""><td>Body Mass Index <math>^{c}</math>:</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></th<>	Body Mass Index $^{c}$ :							
Middle $0.77 (0.45-1.32)$ $   -$ <td>Low (ref.)</td> <td>1</td> <td></td> <td>ı</td> <td></td> <td></td> <td></td> <td>ı</td>	Low (ref.)	1		ı				ı
High1.24 (0.73-2.10)	Middle	0.77 (0.45-1.32)		ı				ı
Pathology       Pathology       -	High	1.24 (0.73-2.10)		ı				
Musculoskeletal disease         149 (0.96.2.31)         1.19 (0.74.1.89)         -	Pathology							
Cardiovascular disease       101 (0.56-1.81)       -	Musculoskeletal disease	1.49 (0.96-2.31)	1.19 (0.74-1.89)					
Lung disease $101(0.56-1.81)$ $   -$	Cardiovascular disease	1.01 (0.64-1.60)		ı				
Eye disease1.32 (0.83-2.14) <td>Lung disease</td> <td>1.01 (0.56-1.81)</td> <td></td> <td>ı</td> <td></td> <td></td> <td></td> <td>ı</td>	Lung disease	1.01 (0.56-1.81)		ı				ı
Musculoskeletal pain $2.76(1.93-3.94)$ $2.09(1.30-3.36)$ $2.38(1.65-3.44)$ $2.02(1.27-3.11)$ $1.80(1.10-2.93)$ $1.84(1.14-2.13)$ Number of medications $1.11(1.02-1.20)$ $1.22(1.14-1.31)$ $1.08(0.99-1.17)$ $1.06(0.97-1.15)$ $-$ Impairment $\overline{Crip}$ strength $d$ $0.70(0.56-0.88)$ $1.22(1.14-1.31)$ $1.08(0.99-1.15)$ $ -$ Turbuilding $0.70(0.56-0.88)$ $0.70(0.56-0.88)$ $0.27(0.60-0.94)$ $0.87(0.68-1.11)$ $ -$ Functional limitation $0.70(0.56-0.88)$ $    -$ Valking speed $e$ $0.49(0.37-0.65)$ $  0.75(0.60-0.94)$ $0.87(0.68-1.11)$ $ -$ Pychological factors $0.99(0.37-0.65)$ $    -$ Pychological factors $0.99(0.95-1.02)$ $                       -$ <td< td=""><td>Eye disease</td><td>1.32 (0.83-2.14)</td><td></td><td>ı</td><td></td><td></td><td></td><td>ı</td></td<>	Eye disease	1.32 (0.83-2.14)		ı				ı
Number of medications       1.11 (1.02-1.20)       1.22 (1.14-1.31)       1.08 (0.99-1.17)       1.06 (0.97-1.15)       -       -         Impairment       Grip strength <sup>d</sup> 0.70 (0.56-0.88)       0.75 (0.60-0.94)       0.87 (0.68-1.11)       -       -       -         Functional limitation       0.70 (0.56-0.88)       0.75 (0.60-0.94)       0.87 (0.68-1.11)       -       -       -         Walking speed $^{e}$ 0.49 (0.37-0.65)       0.49 (0.37-0.65)       0.55 (0.41-0.73)       0.55 (0.41-0.74)       0.56 (0.42-0.74)         Walking speed $^{e}$ 0.49 (0.37-0.65)       0.99 (0.37-0.65)       0.55 (0.41-0.73)       0.55 (0.41-0.74)       0.56 (0.42-0.74)         Psychological factors        0.55 (0.41-0.73)       0.55 (0.41-0.73)       0.56 (0.42-0.74)       0.56 (0.42-0.74)         Depressive symptoms $^{e}$ 1.11 (1.07-1.15)         1.01 (0.97-1.06)          OR = Odds Ratio       1.11 (1.07-1.15)         1.09 (1.05-1.13)       1.09 (1.05-1.13)       1.09 (1.05-1.13)       1.09 (1.05-1.13)       1.09 (1.05-1.13)       1.09 (1.05-1.13)       1.09 (1.05-1.13)       1.09 (1.05-1.13)       1.09 (1.05-1.13)       1.09 (1.05-1.13)       1.09 (1.05-1.13)       1.09 (1.05-1.13)       1.09 (1.05-1.13)       1.09 (1.05-1.13)       1.09 (1.05-1.13)	Musculoskeletal pain	2.76 (1.93-3.94)	2.09 (1.30-3.36)	2.38 (1.65-3.44)	2.02 (1.27-3.21)	1.94 (1.20-3.11)	1.80 (1.10-2.93)	1.84 (1.14-2.98)
Impairment $0.70 (0.56-0.88)$ $0.70 (0.56-0.88)$ $0.70 (0.56-0.88)$ $0.70 (0.56-0.88)$ $0.70 (0.56-0.88)$ $0.70 (0.56-0.88)$ $0.70 (0.56-0.88)$ $0.70 (0.56-0.88)$ $0.70 (0.56-0.88)$ $0.70 (0.56-0.88)$ $0.70 (0.56-0.88)$ $0.70 (0.56-0.88)$ $0.70 (0.56-0.88)$ $0.70 (0.56-0.88)$ $0.70 (0.56-0.86)$ $0.70 (0.56-0.74)$ $0.55 (0.41-0.74)$ $0.56 (0.42-0.76)$ Walking speed $e$ $0.49 (0.37-0.65)$ $0.49 (0.37-0.65)$ $0.55 (0.41-0.73)$ $0.55 (0.41-0.74)$ $0.56 (0.42-0.76)$ Psychological factors $0.99 (0.95-1.02)$ $0.99 (0.95-1.02)$ $0.55 (0.41-0.73)$ $0.55 (0.41-0.74)$ $0.56 (0.42-0.76)$ Depressive symptoms $f$ $1.11 (1.07-1.15)$ $1.01 (0.97-1.06)$ $1.00 (1.05-1.13)$ $1.09 (1.05-1.13)$ </td <td>Number of medications</td> <td>1.11 (1.02-1.20)</td> <td></td> <td>1.22 (1.14-1.31)</td> <td>1.08 (0.99-1.17)</td> <td>1.06 (0.97-1.15)</td> <td></td> <td></td>	Number of medications	1.11 (1.02-1.20)		1.22 (1.14-1.31)	1.08 (0.99-1.17)	1.06 (0.97-1.15)		
Grip strength <i>Functional limitation</i> $0.70 (0.56-0.88)$ $0.75 (0.60-0.94)$ $0.87 (0.68-1.11)$ $-$ <i>Functional limitation</i> $0.49 (0.37-0.65)$ $0.49 (0.37-0.65)$ $0.55 (0.41-0.74)$ $0.56 (0.42-0.74)$ <i>Rychological factors</i> $0.99 (0.95-1.02)$ $0.90 (0.95-1.02)$ $0.55 (0.41-0.73)$ $0.55 (0.41-0.74)$ $0.56 (0.42-0.74)$ <i>Psychological factors</i> $0.99 (0.95-1.02)$ $0.99 (0.95-1.02)$ $1.01 (0.97-1.06)$ $-$ Depressive symptoms $1.11 (1.07-1.15)$ $1.01 (0.97-1.06)$ $-$ OR = Odds Ratio $  0.90 (0.95-1.02)$ $1.09 (1.05-1.13)$ $1.09 (1.05-1.13)$ OR = Confidence Interval $    a^2$ $     a^3$ $     a^4$ <td>Impairment</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td>	Impairment							
Functional limitation       0.49 (0.37-0.65)       0.55 (0.41-0.73)       0.55 (0.41-0.74)       0.56 (0.42-0         Psychological factors       0.99 (0.95-1.02)       0.99 (0.95-1.02)       1.01 (0.97-1.06)       -         Depressive symptoms       1.11 (1.07-1.15)       1.01 (0.97-1.06)       -       -         OR = Odds Ratio $C = Confidence Interval       1.09 (1.05-1.13)       1.09 (1.05-1.13)       1.09 (1.05-1.13)   $	Grip strength <sup>d</sup>	0.70 (0.56-0.88)			0.75 (0.60-0.94)	0.87 (0.68-1.11)		·
Walking speed $e$ 0.49 (0.37-0.65)       0.55 (0.41-0.74)       0.56 (0.42-0)         Psychological factors       0.99 (0.95-1.02)       0.95 (0.41-0.74)       0.56 (0.42-0)         Cognitive function $f$ 0.99 (0.95-1.02)       1.01 (0.97-1.06)       -         Depressive symptoms $g$ 1.11 (1.07-1.15)       1.09 (1.05-1.13)       1.09 (1.05-1.13)       1.09 (1.05-1.13)         OR = Odds Ratio $T$ <	Functional limitation							
Psychological factors1.01 (0.97-1.06)-Cognitive function $f$ 0.99 (0.95-1.02)1.01 (0.97-1.06)-Depressive symptoms $g$ 1.11 (1.07-1.15)1.09 (1.05-1.13)1.09 (1.05-1.13)OR = Odds RatioCI = Confidence Interval3.00 (1.05-1.13)1.09 (1.05-1.13)	Walking speed $^{e}$	0.49 (0.37-0.65)				0.55 (0.41-0.73)	0.55 (0.41-0.74)	0.56 (0.42-0.74)
Cognitive function f       0.99 (0.95-1.02)       1.01 (0.97-1.06)       -         Depressive symptoms f       1.11 (1.07-1.15)       1.09 (1.05-1.13)       1.09 (1.05-1.13)         Depressive symptoms f       1.11 (1.07-1.15)       1.09 (1.05-1.13)       1.09 (1.05-1.13)         OR = Odds Ratio       I       I       II.01 (0.97-1.15)       IIII (1.07-1.15)         OR = Odds Ratio       IIII (1.07-1.15)       IIII (1.07-1.15)       IIIII (1.07-1.13)       IIIII (1.07-1.13)         OR = Odds Ratio       IIIII (IIIIIIIIIIIIIIIIIIIIIIIIIIIIIII	Psychological factors							
Depressive symptoms <sup>g</sup> 1.11 (1.07-1.15)         1.09 (1.05-1.13)         1.09 (1.05-1.13)           OR = Odds Ratio         CI = Confidence Interval         1.09 (1.05-1.13)         1.09 (1.05-1.13)	Cognitive function $^{f}$	0.99 (0.95-1.02)					1.01 (0.97-1.06)	
OR = Odds Ratio CI = Confidence Interval a	Depressive symptoms $\mathcal{G}$	1.11 (1.07-1.15)					1.09 (1.05-1.13)	1.09 (1.05-1.13)
CI = Confidence Interval	OR = Odds Ratio							
$a_{r-1}$	CI = Confidence Interval							
	<sup>d</sup> Gender and education adiu	etad hivariata accor	iatione					

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cGender specific Body Mass Index (kg/m<sup>2</sup>) tertiles: low - middle - high.

 $\boldsymbol{b}_{\mbox{Gender}}$  and education adjusted multivariate associations

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dGender specific z score for continuous weight adjusted variable

 $^{e}$  Gender specific z score for continuous variable

fMini-Mental State Examination score, range 0-30.

 ${^{\cal B}}$  Modified Cambridge Mental Disorders of the Elderly Examination score, range 0-29.