Determinants of physical and cognitive health transitions among Danish nonagenarians

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Abstract

At older ages, deteriorating of physical and cognitive health is very likely. This study investigates whether (1) transitions in physical and cognitive health are driven by the same demo-socio-economic characteristics and lifestyle habits; (2) these transitions follow the same patterns and how do physical or cognitive dimensions affect the transitions in the other dimension.
Using the 1905 Danish Cohort survey, we applied Multi State Models – with Markov chain assumption - for panel data to evaluate physical and cognitive deterioration of the oldest-old.
This study highlights a "one-step" worsening pattern in both physical and cognitive health. Both types of transitions were associated with similar socio-demographic and behavioral characteristics but not with emotional factors. The two health dimensions were related to each other in terms of transitions: being in a better health condition according to one dimension lowered the probability of worsening the other one or dying.

Introduction

The proportion of oldest old people has increased during the last decades as a consequence of the decline in old-age mortality [1, 2, 3]. The share of nonagenarians in Denmark increased from around 0.08% in 1950 to 0.75% in 2015 and seems to keep growing, according to World Population Prospects [4], during the next years, reaching 1.87% in 2040. This phenomenon affected most of the developed countries, driving the attention on the health conditions in which people reach very old ages, considered as a major public health challenge nowadays. In particular at older ages, the deterioration of both physical and cognitive health conditions is very likely [5, 6]. The relationship between these two aspects (physical and cognitive) has been widely investigated during the last years since more longitudinal data suitable for this purpose became available. A systematic review assessing the longitudinal relationship between physical and cognitive change was published in 2013 by Clouston et al. [7]. They found that physical functioning at baseline was associated with longitudinal changes in cognition while the opposite relationship was inconsistent. Nevertheless, articles studying the determinants of health transitions and analyzing the longitudinal relationship between physical and cognitive dimensions among the oldest-old are lacking in the literature [8]. This study aims to partly fill this gap by analyzing the 1905 Danish Cohort Data to determine whether (1) transitions in physical and cognitive health are driven by the same demographic and socio-economic characteristics and lifestyle habits; (2) transitions in physical and cognitive health follow the same patterns and how does each dimension (physical or cognitive) affect the transitions of the other dimension.

Methods

Study population and measures

The study population comes from the nationwide survey - with no exclusion criteria - described in the article by Nybo et al. (2001) [9]. It includes many information at individual level on people born in Denmark in 1905. The first data collection was in 1998: according to the Danish National Registry, the identified participants were 3,738. Since 138 people died before being contacted, potential participants were 3,600 but only 62.8% of them became participants (2,626 individuals). Questions have been answered by a proxy if needed. Studies on this cohort showed that high level of disability and poor physical and cognitive performance are predictors of mortality in the oldest old [10, 11]. This work takes advantage of the first two waves of "The Danish 1905 Cohort Survey" because it is part of a research project that includes a comparison with two waves of an Italian survey on nonagenarians. Cognitive function was measured with the Mini-Mental State Examination

(MMSE): the higher the score (0-30) the better the cognitive status [12]. We grouped it into three categories in order to distinguish people with severe (0-17), mild (18-23) and no cognitive impairment. Physical function was assessed by Chair-Stand Test: elderly who can raise from a chair have better functional status than who needs to use hands or can not do it [13]. For computational reasons, both health indicators were dichotomized for the multi state analysis.
The analysis controlled for demographic and socio-economic characteristics (sex, education and living conditions), emotional characteristics (loss of a close person, self-rated health and depression) and health behaviors (smoking habits, body mass index, physical activity and use of medications).
All these variables were selected and categorized according to the literature about oldest old mortality and health-transitions predictors. Detailed information about their classification are available into the Appendix S1. The main reference for variables' selection and classification is the Appendix S1 of the article by Thinggaard et al. (2016) on the same study population [14].

Statistical analysis

Multi-State Model for panel data - with Markov chain assumption - [15, 16] was applied to assess the association between the many potential factors measured on the Danish nonagenarians and the transition probabilities through different states.
The Multi-State Model is based on a stochastic multi-state process $(X(t), t \in T)$ with a finite state-space $S = 1, ..., N$ where $T = [0, \tau], \tau < \infty$ represents the time (continuous or discrete for panel data). It is fully characterized through transition probabilities between states h and j:

$$p_{hj}(s,t) = P(X(t) = j | X(s) = h) \tag{1}$$

for $h, j \in S,\ t, s \in T$ or through transition intensities:

$$\alpha_{hj}(t) = \lim_{\Delta t \to 0} \frac{p_{hj}(t, t + \Delta t)}{\Delta t} \tag{2}$$

representing the instantaneous hazard of progression to state j conditionally on occupying state h at the previous time. According to the Markov assumption, the probability of the next transition depends only on the state occupied at the time t.
The effect of the explanatory variables z_{it} on the transition intensity for individual i at time t is modeled using proportional intensities, replacing α_{hj} with:

$$\alpha_{hj}(z_{it}) = \alpha_{hj}^{(0)} exp(\beta_{hj}^T z_{it}) \tag{3}$$

Participants in the first wave have been separated into people in good and in bad health conditions, first differentiated by their physical status and

then by cognitive health. The transitions into four states (good health, bad health, non-participant but alive and non-participant because of death) have been estimated through transition probabilities and the effect of the covariates on the transition intensities has been evaluated.
Multiple imputation was necessary to deal with missing values (MAR) in order to avoid loss of precision in the analysis. K-nearest neighbor imputation method has been used for its high performance with survey data [17]. Taking advantage of all the variables available in the dataset except for the one analyzed, five neighbors have been used to calculate the aggregated values to impute.
Statistical analysis was performed using R version 3.5.0 [18].

Results

Descriptive results

Of the 2262 participants to the study, one forth were male (25.8%) while the rest of the people were female (74.2%).
Men were more educated than women, especially in terms of vocational education (32.9% of male vs 14.2% of female). Fewer men were living alone (50.5% of male vs 64.4% of female).
More men experienced the loss of a close person due to death during the last five years (71.7% of male vs 66.9% of female) but they did not declare better health conditions and they reported lower rates of depression (39% of male vs 32.3% of female were not depressed) than women as a testimony of a better emotional profile.
Except for the higher share of smokers (78.8% of male vs 32.4% of female are past or current smoker), men had higher BMI (73.1% of male vs 55.3% of female had a BMI higher than 22) and practiced more physical activity (43.8% of male vs 28.9% of female perform some physical activity) than women - as a testimony of better health behaviors. More details about baseline characteristics of the population are shown in Table 1.
Men shown a better physical (52.1% of male vs 41.5% of female are able to stand up from the chair without any aid) and cognitive (48.5% of male vs 40.6% of female were not cognitive impaired) health conditions than women as reported in Table 2.

Table 1: Characteristics of the population in the first wave

Characteristics	Sex						p*
	M		F		T		
	n	%	n	%	n	%	
Sample	584	25.8	1678	74.2	2262	100	
Education							
elementary	292	50.0	1254	74.7	1546	68.3	<0.001
vocational	192	32.9	238	14.2	430	19.0	
higher	100	17.1	186	11.1	286	12.6	
Living alone							
no	289	49.5	598	35.6	887	39.2	<0.001
yes	295	50.5	1080	64.4	1375	60.8	
Loss of a close person							
no	165	28.3	556	33.1	721	31.9	0.033
yes	419	71.7	1122	66.9	1541	68.1	
Self-rated health							
(very) poor	307	52.6	886	52.8	1193	52.7	0.013
acceptable	204	34.9	553	33.0	757	33.5	
good or excellent	73	12.5	239	14.2	312	13.8	
Depression							
29-52	184	31.5	591	35.2	775	34.3	0.008
23-28	172	29.5	545	32.5	717	31.7	
17-22	228	39.0	542	32.3	770	34.0	
Smoking status							
current smoker	144	24.7	171	10.2	315	13.9	<0.001
past smoker	316	54.1	372	22.2	688	30.4	
never smoked	124	21.2	1135	67.6	1259	55.7	
Body-Mass Index							
<22	157	26.9	750	44.7	907	40.1	<0.001
22 - 28	348	59.6	785	46.8	1133	50.1	
>28	79	13.5	143	8.5	222	9.8	
Physical activity							
none/irrelevant	328	56.2	1193	71.1	1521	67.2	<0.001
light	177	30.3	390	23.2	567	25.1	
heavy	79	13.5	95	5.7	174	7.7	
Medications							
4+	228	39.0	714	42.6	942	41.6	0.057
2 3	153	26.2	423	25.2	576	25.5	
0 1	203	34.8	541	32.2	744	32.9	

*Men vs Women from Pearson χ^2 test

Table 2: Health conditions of the population in the first wave

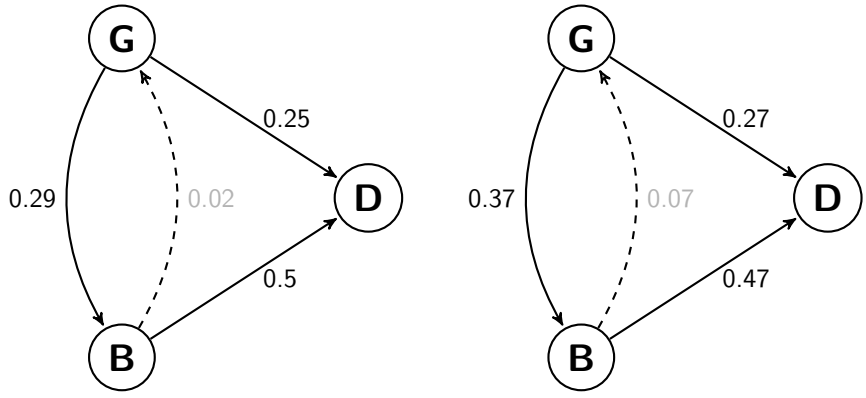
Characteristics	Sex						p*
	M		F		T		
	n	%	n	%	n	%	
Chair stand							
not able	70	12.0	293	17.5	363	16.0	<0.001
with use of hands	210	36.0	689	41.1	899	39.7	
without use of hands	304	52.1	696	41.5	1000	44.2	
MMSE							
0-17	124	21.2	472	28.1	596	26.3	<0.001
18-23	177	30.3	524	31.2	701	31.0	
24-30	283	48.5	682	40.6	965	42.7	

*Men vs Women from Pearson χ^2 test

Multi state analysis results

The probability of passing from a good to a bad physical health condition was higher than dying directly (29% vs 25%). People in bad physical health condition have a 50% probability of dying from that condition.
Similar results have been obtained when considering the cognitive health condition to define the states. People in good cognitive health condition have a higher probability to worsen the health condition instead of experiencing the death directly (37% vs 27%). People in bad health condition have a 47% probability of dying from that condition as shown in Figure 1.
More details about transition probabilities are available in the Appendix S2.

Figure 1: Transition probabilities of the multi state model where states are defined according to:

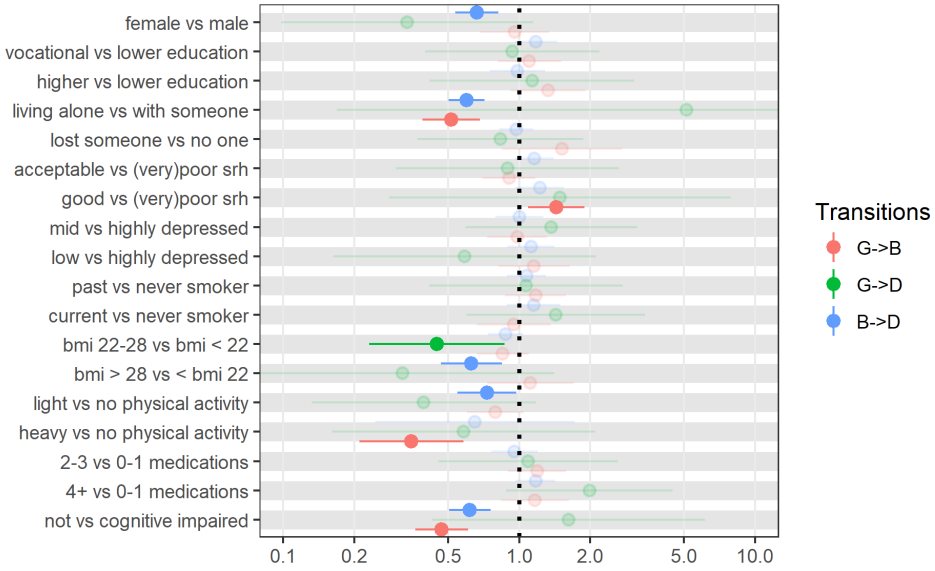


(a)Physical health condition (b)Cognitive health condition

G: good; B: bad; D: dead.

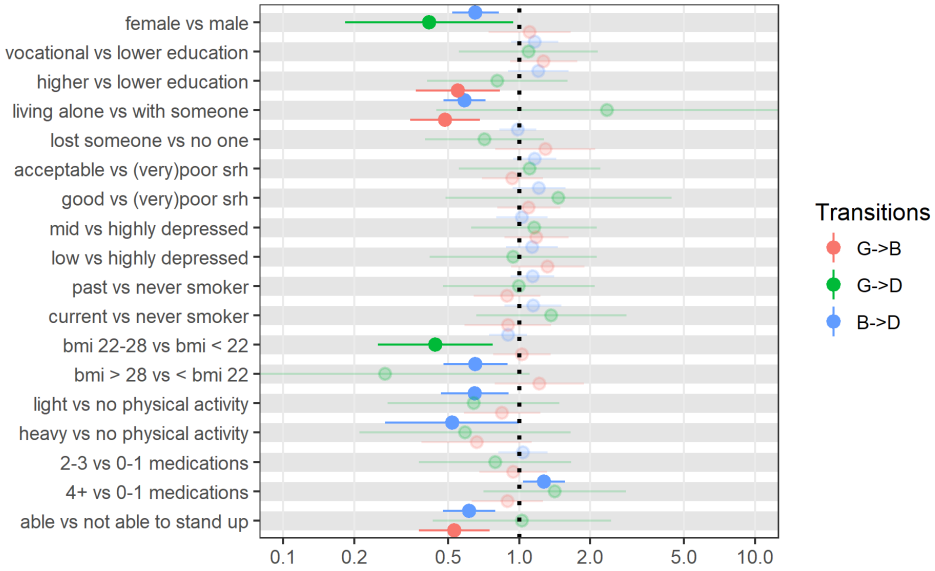
The effect of potential modifiers on some of the transition intensities (transition from good to bad, good to dead and bad to dead) are described in Figure 2 and 3 for the model in which states are defined according to physical and cognitive health condition respectively.
More details are available in the tables (S3 and S4) in Appendix S2.
With respect to the transitions in physical health, being female and living alone were statistically associated with a slightly lower probability of dying for people in bad health conditions (HR respectively of 0.66 and 0.6). Living alone was also significantly associated with lower probability of passing from a good to a bad health condition (HR = 0.52). Having a BMI higher than 22 was statistically associated with lower probability of dying, both from a good (BMI 22-28 vs <22: HR = 0.45) and a bad (BMI >28 vs <22: HR = 0.63) health condition. Doing physical activity was significantly related to the transition from good to bad (heavy vs no physical activity: HR = 0.35) and bad to death (light vs no physical activity: HR = 0.73). Finally, being not cognitive impaired was statistically associated with a lower probability of worsening the health condition (HR = 0.47) and dying from a bad one (HR = 0.62).
Regarding the transitions in cognitive health, being a woman was associated with a lower probability of death (from good health: HR = 0.42; from bad health: HR = 0.65). Being more educated results in a lower probability of worsening the health condition (HR = 0.55). Living alone is significantly associated with lower probability of worsening the health condition (HR = 0.49) and dying from a bad one (HR = 0.59). Having a BMI higher than 22 is statistically associated with lower probability of dying from a good (BMI 22-28 vs <22: HR = 0.44) and a bad (BMI >28 vs <22: HR = 0.65) health condition. Doing physical activity is significantly related to lower transition rates from bad to death (light vs no physical activity: HR = 0.65, heavy vs no physical activity: HR = 0.52). Using more than four medications per day is associated with higher probability of dying from a bad health condition (HR = 1.27). Finally, being able to stand up from the chair without any aid is statistically associated with a lower probability of worsening the health condition (HR = 0.53) and dying from a bad one (HR = 0.61).

Figure 2: Multivariate predictions (hazard ratios) of transitions in physical health



Highlighted hazard ratios are significant; G: good; B: bad; D: dead.

Figure 3: Multivariate predictions (hazard ratios) of transitions in cognitive health



Highlighted hazard ratios are significant; G: good; B: bad; D: dead.

Discussion

The increasing proportion of oldest old people experienced during the last decades, in most of the developed countries, drove the attention of policy makers on elderly's health [2, 3]. Finding the determinants of physical and cognitive health conditions and analyzing their longitudinal relationship are, nowadays, two of the major public health challenges [19, 20]. Deterioration of physical and cognitive health is also becoming widely investigated among old people [6, 21, 22, 23]. Despite this , only few studies analyzed such deterioration on the oldest old [7, 8, 24]. Studying the determinants of worsening transitions in physical and cognitive health among very old people and the relationship between these two conditions will help policy makers understanding when and how intervene.

This study uses the first two waves of The 1905 Danish Cohort survey [9] to study the transitions in physical and cognitive health among people aged 93 years old at the baseline (1998) and 95 at the second wave (2000). To our knowledge, this is the first study that analyzes the relationship between physical and cognitive decline and the determinants of transitions in these two health aspects (physical and cognitive) among the oldest old.

Our results confirm the trends shown in the literature for both physical and cognitive health over the years [22, 24, 25, 26, 27]. Even at very old ages, the probability of worsening the health condition resulted higher than dying for people in good status at the baseline. These results suggest that both physical and cognitive health follow a "one-step" worsening pattern even among the oldest old.

The analysis of potential drivers of the health decline shown similar results for physical and cognitive health.

Demographic and socio-economic variables in both cases resulted associated with health transitions. In particular, being female was associated with lower probability of dying from a bad physical and cognitive health condition and also from a good cognitive one, confirming the so called gender paradox [21, 23, 24, 28, 25, 26]. Being more educated resulted in lower probability of cognitive decline, confirming the results found among younger adults [23, 26, 29, 30] but it did not affect the physical status, as it appears in literature [24, 25]. To the best of our knowledge, living alone is widely used as potential driver for physical [21, 22, 24] but not for cognitive health transitions. In our study it was associated with lower probability of worsening the physical and cognitive health status and dying from a good one. Anyway, it is not possible to disentangle the causal effect of this association: people who are able to live alone are in better health conditions or living alone helps to protect the health condition.

Emotional characteristics did not display any effect, despite other scholars found that self-rated health and depression have an active role in explaining transitions in physical and cognitive health [24, 31, 32, 27].
For both health conditions, having a lower BMI resulted in lower probability of dying from a good and a bad health status, confirming previous findings on younger adults [33, 34] and in mortality research [35]. Doing some light physical activity was significantly associated with lower probability of dying from a bad physical and cognitive status, while doing heavy physical activity resulted in lower probability of worsening the good physical health condition and dying from a bad cognitive status. Other studies reported this association in terms of frailty [5, 21, 22] for physical transitions and few discussed it about cognitive transitions [36]. Again, it was not possible to understand the causal relationship of the two aspects.
The main novelty of this paper was to understand the relationship between physical and cognitive conditions from a transition prospective. The transitions in the two health status (physical and cognitive) were statistically associated with the other health measure in both cases, confirming what have been observed by other scholars among younger adults.
The strength of this study is the sample size and the numerous information available about this unique group of oldest-old. This allowed us to include many potential confounders together in the analysis despite the complexity of the model. The weakness of this study is that it is not possible to clearly identify the causal relationship of the associations even if data are longitudinal.
To conclude, this study highlights a "one-step" worsening pattern in both physical and cognitive health among the oldest old which has not been shown before. Transitions in both physical and cognitive health were related with similar socio-demographic and behavioral characteristics but not with emotional factors. The two health dimensions resulted associated with each other in terms of transitions: being in a better health condition according to one of the two health measures resulted in a lower probability of worsening the other health status or dying from a bad condition. This confirms what have been discussed by the extensive systematic review by Clouston and colleagues [7] about the role of the physical condition at baseline on the transitions in cognitive health and brings new evidence on the role of the cognitive status on the transitions in physical health for which the literature so far has not found consistent evidence.

References

[1] J. W. Vaupel. Biodemographic Trajectories of Longevity. *Science*, 280(5365):855–860, May 1998.

[2] Kaare Christensen, Gabriele Doblhammer, Roland Rau, and James W Vaupel. Ageing populations: The challenges ahead. *The Lancet*, 374(9696):1196–1208, October 2009.

[3] J. W. Vaupel. Biodemography of human ageing. *Nature*, 464(7288):536–542, March 2010.

[4] World Population Prospects - Population Division - United Nations. https://esa.un.org/unpd/wpp/.

[5] S. E. Hardy, J. A. Dubin, T. R. Holford, and T. M. Gill. Transitions between States of Disability and Independence among Older Persons. *American Journal of Epidemiology*, 161(6):575–584, March 2005.

[6] Ardo van den Hout and Fiona E. Matthews. Multi-state analysis of cognitive ability data: A piecewise-constant model and a Weibull model. *Statistics in Medicine*, 27(26):5440–5455, November 2008.

[7] S. A. P. Clouston, P. Brewster, D. Kuh, M. Richards, R. Cooper, R. Hardy, M. S. Rubin, and S. M. Hofer. The Dynamic Relationship Between Physical Function and Cognition in Longitudinal Aging Cohorts. *Epidemiologic Reviews*, 35(1):33–50, January 2013.

[8] Clifford Qualls, D. L. Waters, B. Vellas, D. T. Villareal, P. J. Garry, A. Gallini, and S. Andrieu. Reversible states of physical and/or cognitive dysfunction: A 9-year longitudinal study. *The journal of nutrition, health & aging*, 21(3):271–275, March 2017.

[9] Hanne Nybo, David Gaist, Bernard Jeune, Lise Bathum, Matt Mcgue, James W. Vaupel, and Kaare Christensen. The Danish 1905 Cohort: A Genetic-Epidemiological Nationwide Survey. *Journal of Aging and Health*, 13(1):32–46, February 2001.

[10] Hanne Nybo, David Gaist, Bernard Jeune, Matt McGue, James W. Vaupel, and Kaare Christensen. Functional Status and Self-Rated Health in 2,262 Nonagenarians: The Danish 1905 Cohort Survey. *Journal of the American Geriatrics Society*, 49(5):601–609, May 2001.

[11] Hanne Nybo, Hans Chr Petersen, David Gaist, Bernard Jeune, Kjeld Andersen, Matt McGue, James W. Vaupel, and Kaare Christensen. Predictors of Mortality in 2,249 Nonagenarians—The Danish 1905-Cohort Survey. *Journal of the American Geriatrics Society*, 51(10):1365–1373, October 2003.

[12] Marshal F. Folstein, Susan E. Folstein, and Paul R. McHugh. "Mini-mental state": A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*, 12(3):189–198, November 1975.

[13] Jack M. Guralnik, Luigi Ferrucci, Eleanor M. Simonsick, Marcel E. Salive, and Robert B. Wallace. Lower-Extremity Function in Persons over the Age of 70 Years as a Predictor of Subsequent Disability. *New England Journal of Medicine*, 332(9):556–562, March 1995.

[14] Mikael Thinggaard, Matt McGue, Bernard Jeune, Merete Osler, James W. Vaupel, and Kaare Christensen. Survival Prognosis in Very Old Adults. *Journal of the American Geriatrics Society*, 64(1):81–88, January 2016.

[15] Philip Hougaard. Multi-state Models: A Review. page 26.

[16] Christopher H. Jackson. Multi-State Models for Panel Data: The **msm** Package for *R*. *Journal of Statistical Software*, 38(8), 2011.

[17] Jiahua Chen and Jun Shao. Nearest Neighbor Imputation for Survey Data. page 19.

[18] R Core Team. R: The R Project for Statistical Computing. https://www.r-project.org/, 2017.

[19] Francesc Orfila, Montserrat Ferrer, Rosa Lamarca, Cristian Tebe, Antonia Domingo-Salvany, and Jordi Alonso. Gender differences in health-related quality of life among the elderly: The role of objective functional capacity and chronic conditions. *Social Science & Medicine*, 63(9):2367–2380, November 2006.

[20] Caterina Rosano, Eleanor M. Simonsick, Tamara B. Harris, Steven B. Kritchevsky, Jennifer Brach, Marjolein Visser, Kristine Yaffe, and Anne B. Newman. Association between Physical and Cognitive Function in Healthy Elderly: The Health, Aging and Body Composition Study. *Neuroepidemiology*, 24(1-2):8–14, 2005.

[21] Thomas M. Gill, Heather G. Allore, Susan E. Hardy, and Zhenchao Guo. The Dynamic Nature of Mobility Disability in Older Persons: Mobility disability in older persons. *Journal of the American Geriatrics Society*, 54(2):248–254, February 2006.

[22] Thomas M. Gill, Heather G. Allore, Evelyne A. Gahbauer, and Terrence E. Murphy. CHANGE IN DISABILITY AFTER HOSPITALIZATION OR RESTRICTED ACTIVITY IN OLDER PERSONS. *JAMA : the journal of the American Medical Association*, 304(17):1919–1928, November 2010.

[23] Arnold B Mitnitski, Nader Fallah, Charmaine B Dean, and Kenneth Rockwood. A multi-state model for the analysis of changes in cognitive scores over a fixed time interval. *Statistical Methods in Medical Research*, 23(3):244–256, June 2014.

[24] Anne H. van Houwelingen, Ian D. Cameron, Jacobijn Gussekloo, Hein Putter, Susan Kurrle, Anton J. M. de Craen, Andrea B. Maier, Wendy P. J. den Elzen, and Jeanet W. Blom. Disability transitions in the oldest old in the general population. The Leiden 85-plus study. *AGE*, 36(1):483–493, February 2014.

[25] Rossitza Nikolova, Louise Demers, François Béland, and Francine Giroux. Transitions in the functional status of disabled community-living older adults over a 3-year follow-up period. *Archives of Gerontology and Geriatrics*, 52(1):12–17, January 2011.

[26] Hong-mei Yu, Shan-shan Yang, Jian-wei Gao, Li-ye Zhou, Rui-feng Liang, and Cheng-yi Qu. Multi-state Markov model in outcome of mild cognitive impairments among community elderly residents in Mainland China. *International Psychogeriatrics*, 25(05):797–804, May 2013.

[27] Kala M. Mehta, Kristine Yaffe, and Kenneth E. Covinsky. Cognitive Impairment, Depressive Symptoms, and Functional Decline in Older People. *Journal of the American Geriatrics Society*, 50(6):1045–1050.

[28] Karine Pérès, Catherine Verret, Ahmadou Alioum, and Pascale Barberger-Gateau. The disablement process: Factors associated with progression of disability and recovery in French elderly people. *Disability and Rehabilitation*, 27(5):263–276, March 2005.

[29] Riccardo E. Marioni, Michael J. Valenzuela, Ardo van den Hout, Carol Brayne, Fiona E. Matthews, and MRC Cognitive Function and Ageing Study. Active Cognitive Lifestyle Is Associated with Positive Cognitive Health Transitions and Compression of Morbidity from Age Sixty-Five. *PLoS ONE*, 7(12):e50940, December 2012.

[30] Shaoceng Wei, Liou Xu, and Richard J. Kryscio. Markov transition model to dementia with death as a competing event. *Computational Statistics & Data Analysis*, 80:78–88, December 2014.

[31] Andreas E Stuck, Jutta M Walthert, Thorsten Nikolaus, Christophe J Büla, Christoph Hohmann, and John C Beck. Risk factors for functional status decline in community-living elderly people: A systematic literature review. *Social Science & Medicine*, 48(4):445–469, February 1999.

[32] Joshua Chodosh, Deborah Kado, Teresa E Seeman, and Arun S Karlamangla. Depressive Symptoms as a Predictor of Cognitive Decline: MacArthur Studies of Successful Aging. *The American journal of geriatric psychiatry : official journal of the American Association for Geriatric Psychiatry*, 15:406–15, May 2007.

[33] Flávia Cristina Drumond Andrade, Ahmad Iqmer Nashriq Mohd Nazan, Maria Lúcia Lebrão, and Yeda Aparecida de Oliveira Duarte. The Impact of Body Mass Index and Weight Changes on Disability Transitions and Mortality in Brazilian Older Adults. *Journal of Aging Research*, 2013:1–11, 2013.

[34] Benjamin B. Cronk, David K. Johnson, and Jeffrey M. Burns. Body Mass Index and Cognitive Decline in Mild Cognitive Impairment. *Alzheimer disease and associated disorders*, 24(2):126–130, 2010.

[35] M. Thinggaard, R. Jacobsen, B. Jeune, T. Martinussen, and K. Christensen. Is the Relationship Between BMI and Mortality Increasingly U-Shaped With Advancing Age? A 10-Year Follow-up of Persons Aged 70-95 Years. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences*, 65A(5):526–531, May 2010.

[36] Danielle Laurin, René Verreault, Joan Lindsay, Kathleen MacPherson, and Kenneth Rockwood. Physical Activity and Risk of Cognitive Impairment and Dementia in Elderly Persons. *Archives of Neurology*, 58(3), March 2001.

[37] John E. Ware, Jr., Mark Kosinski, and Susan D. Keller. A 12-Item Short-Form Health Survey: Construction of Scales and Preliminary Tests of Reliability and Validity. *Medical Care*, 34(3):220–233, 1996.

[38] M. Roth, E. Tym, C. Q. Mountjoy, F. A. Huppert, H. Hendrie, S. Verma, and R. Goddard. CAMDEX: A Standardised Instrument for the Diagnosis of Mental Disorder in the Elderly with Special Reference to the Early Detection of Dementia. *The British Journal of Psychiatry*, 149(6):698–709, December 1986.

Supplemental Material

Appendix S1: Covariates into analysis

Education and living condition were used to measure the socio-economic situation of the participants. Education was grouped into three categories: (1) elementary school; (2) vocational and (3) higher education. Living condition was divided into people living (1) alone and (2) with someone.
The loss of a close-person, self-rated health and depression were used to assess the general health perception of the participant and the feelings related to it. The loss of a close-person was categorized into two classes: (1) lost someone and (2) no people lost due to death within the last five years. Self-rated health was assessed with the first question of Short Form 12 (SF12) questionnaire [37]: "How do you consider your health in general?". It was grouped in three categories: (1) (very)poor; (2) acceptable and (3) good or excellent. Depression was assessed using an adaptation of the depression section of the Cambridge mental disorders of the elderly examination [38]. It has a scale from 17 to 52 and it was grouped into three equal-size categories: (1) 17-22; (2) 23-28 and (3) 29-52.
The health behaviors taken into account are: smoking habits, body Mass Index (BMI), physical activity and use of medications. Smoking habits was categorized into (1) never smoked; (2) past and (3) current smoker. BMI was calculated on the basis of the reported height and weight at the interview and categorized into three groups: (1) <22; (2) 22-28 and (3) >28. Physical activity was assessed by asking how often participants were performing light or heavy exercises at the time of the interview. It was grouped into three categories: (1) never or not able; (2) light and (3) heavy physical activity. The number of medications was coded according to the Anatomical Therapeutic Chemical classification system and it was grouped into three equal-size categories: (1) 0-1; (2) 2-3 and (3) 4+.

Appendix S2: Multi state analysis

Table S1: Transition probabilities of the multi state model where states are defined according to the physical health condition

From/To	Good	Bad	Dropout	Dead
Good	0.34	0.29	0.13	0.25
Bad	0.02	0.34	0.14	0.50
Dropout	0.00	0.00	1.00	0.00
Dead	0.00	0.00	0.00	1.00

*Health status according to Chair Stand test

Table S2: Transition probabilities of the multi state model where states are defined according to the cognitive health condition

From/To	Good	Bad	Dropout	Dead
Good	0.37	0.24	0.12	0.27
Bad	0.07	0.31	0.14	0.47
Dropout	0.00	0.00	1.00	0.00
Dead	0.00	0.00	0.00	1.00

*Health status according to Mini-Mental State Examination

Table S3: Multivariate predictions (hazard ratios) of transitions in physical health

Covariates	From	Good						Bad		
	To	Bad			Dead			Dead		
		HR	IC95%L	IC95%U	HR	IC95%L	IC95%U	HR	IC95%L	IC95%U
Sex		0.96	0.68	1.34	0.34	0.10	1.15	0.66	0.54	0.82
Education	Vocational	1.10	0.81	1.50	0.93	0.40	2.19	1.18	0.96	1.45
(Ref. lower)	Higher	1.32	0.92	1.91	1.13	0.42	3.07	0.98	0.75	1.29
Living alone (Ref. No)	Yes	0.52	0.39	0.68	5.11	0.17	154.80	0.60	0.50	0.71
People lost (Ref. No)	Yes	0.91	0.70	1.17	0.83	0.37	1.88	0.97	0.82	1.15
Self-Rated Health	Acceptable	1.44	1.09	1.89	0.89	0.30	2.65	1.16	0.96	1.40
(Ref. Poor)	Good	1.52	0.85	2.73	1.49	0.28	7.85	1.22	0.97	1.55
Depression	23-28	0.98	0.73	1.32	1.37	0.59	3.16	1.00	0.79	1.26
(Ref. 29-52)	17-22	1.16	0.82	1.63	0.59	0.16	2.11	1.12	0.89	1.42
Smoke	Past	1.17	0.87	1.58	1.07	0.42	2.75	1.08	0.89	1.30
(Ref. Never smoked)	Current	0.95	0.66	1.36	1.43	0.60	3.42	1.15	0.89	1.49
Body-Mass Index	22-28	0.85	0.66	1.10	0.45	0.23	0.87	0.88	0.74	1.04
(Ref. ¡22)	28	1.11	0.73	1.70	0.32	0.07	1.41	0.63	0.47	0.85
Physical activity	Light	0.79	0.60	1.04	0.39	0.13	1.18	0.73	0.55	0.97
(Ref. None)	Heavy	0.35	0.21	0.58	0.58	0.16	2.10	0.65	0.25	1.72
Medications	2-3	1.19	0.90	1.58	1.09	0.45	2.61	0.96	0.76	1.20
(Ref. 0-1)	4+	1.17	0.84	1.62	1.99	0.88	4.47	1.18	0.97	1.42
MMSE (Ref. 0-23)	24-30	0.47	0.36	0.61	1.62	0.43	6.13	0.62	0.50	0.76

Table S4: Multivariate predictions (hazard ratios) of transitions in cognitive health

Covariates	From	Good						Bad		
	To	Bad			Dead			Dead		
		HR	IC95%L	IC95%U	HR	IC95%L	IC95%U	HR	IC95%L	IC95%U
Sex		1.11	0.74	1.65	0.42	0.18	0.94	0.65	0.52	0.82
Education	Vocational	1.27	0.92	1.76	1.10	0.56	2.16	1.16	0.93	1.46
(Ref. Lower)	Higher	0.55	0.36	0.83	0.81	0.41	1.60	1.21	0.90	1.62
Living alone (Ref. No)	Yes	0.49	0.35	0.68	2.36	0.45	12.45	0.59	0.48	0.72
People lost (Ref. No)	Yes	0.94	0.69	1.26	0.71	0.40	1.27	0.99	0.83	1.18
Self-Rated health	Acceptable	1.10	0.81	1.49	1.11	0.55	2.21	1.17	0.95	1.44
(Ref. Poor)	Good	1.29	0.79	2.10	1.47	0.49	4.42	1.21	0.94	1.57
Depression	23-28	1.18	0.87	1.62	1.16	0.63	2.13	1.03	0.80	1.32
(Ref. 29-52)	17-22	1.32	0.92	1.89	0.94	0.42	2.13	1.13	0.88	1.46
Smoke	Past	0.89	0.64	1.23	1.00	0.48	2.09	1.14	0.92	1.41
(Ref. Never smoked)	Current	0.90	0.59	1.37	1.37	0.66	2.85	1.15	0.87	1.51
Body Mass Index	22-28	1.03	0.78	1.36	0.44	0.25	0.77	0.90	0.75	1.08
(Ref. ¡22)	28	1.22	0.79	1.89	0.27	0.07	1.11	0.65	0.48	0.89
Physical activity	Light	0.85	0.58	1.23	0.64	0.28	1.48	0.65	0.47	0.90
(Ref. None)	Heavy	0.66	0.39	1.13	0.59	0.21	1.65	0.52	0.27	1.00
Medications	2-3	0.94	0.68	1.31	0.79	0.38	1.66	1.04	0.82	1.32
(Ref. 0-1)	4+	0.89	0.63	1.26	1.42	0.71	2.84	1.27	1.04	1.56
Chair stand (Ref. Not able)	Able	0.53	0.38	0.75	1.03	0.43	2.45	0.61	0.48	0.79