FACTORS AFFECTING FUNCTIONAL IMPAIRMENT AMONG ELDERLY GERMANS – RESULTS OF A LONGITUDINAL STUDY

A. HAJEK¹, T. LUCK², C. BRETTSCHNEIDER¹, T. POSSELT³, C. LANGE³, B. WIESE⁴, S. STEINMANN⁴, S. WEYERER⁵, J. WERLE⁵, M. PENTZEK⁶, A. FUCHS⁶, J. STEIN², H. BICKEL⁷, E. MÖSCH⁷, M. WAGNER^{8,9}, K. HESER⁸, W. MAIER^{8,9}, M. SCHERER³, S.G. RIEDEL-HELLER^{2*}, H.-H. KÖNIG^{1*} FOR THE AGECODE STUDY GROUP

1. Department of Health Economics and Health Services Research, Hamburg Center for Health Economics, University Medical Center Hamburg-Eppendorf, Germany; 2. Department of Primary Medical Care, Center for Psychosocial Medicine, University Medical Center, Hamburg-Eppendorf, Germany; 3. WG Medical Statistics and IT-Infrastructure, Institute of General Practice, Hannover Medical School, Germany; 4. Central Institute of Mental Health, Medical Faculty Mannheim/Heidelberg University, Germany; 5. Institute of General Practice, Medical Faculty, Heinrich-Heine-University Düsseldorf, Germany; 6. Institute of Social Medicine, Occupational Health and Public Health, University of Leipzig, Germany; 7. Department of Psychiatry, Technical University of Munich, Germany; 8. Department of Psychiatry, University of Bonn, Germany; 9. German Center for Neurodegenerative Diseases (DZNE), Bonn, Germany; *These authors contributed equally to this work. Corresponding author: Dr. André Hajek, University Medical Center, Hamburg-Eppendorf, Hamburg Center for Health Economics, Department of Health Economics and Health Services Research, Telephone +49 40 7410 52877; Fax +49 40 7410 40261, E-mail: a.hajek@uke.de

Abstract: Objective: To investigate causal factors of functional impairment in old age in a longitudinal approach. Design: A population-based prospective cohort study. Setting: Elderly individuals were recruited via GP offices at six study centers in Germany. They were observed every 1.5 years over six waves. Participants: Three thousand two hundred fifty-six people aged 75 years and older at baseline. Measurements: Functional impairment was quantified by the Lawton and Brody Instrumental Activities of Daily Living scale (IADL) and the Barthel-Index (BI). Results: Fixed effects regressions revealed that functional impairment (IADL; BI) increased significantly with ageing (β =-.2; β =-1.1), loss of a spouse (β = .5; β =-3.1), not living alone in private household (β =-1.2; β =-5.5), depression (solely significant for IADL: β = .6) and dementia (β =-2.3; β =-18.2). The comorbidity score did not affect functional impairment. Conclusion: Our findings underline the relevance of changes in sociodemographic variables as well as the occurrence of depression or dementia for functional impairment. While several of these causal factors for functional decline in the oldest old are inevitable, some may not be, such as depression. Therefore, developing interventional strategies to prevent depression might be a fruitful approach in order to delay functional impairment in old age.

Key words: Functional impairment, depression, dementia, older people, longitudinal study.

Introduction

Functional impairments refer to limitations in basic activities of daily living, such as bathing, dressing or even more complex activities, e.g. using a telephone, taking medication or preparing meals. These functional impairments are associated with numerous negative outcomes, including risk of institutionalization (1, 2) and mortality (3). Due to demographic changes (4, 5) it is expected that the number of individuals with functional impairments will increase, underlining the need for interventions.

Several cross-sectional studies have investigated factors associated with functional impairment in old age (6, 7), including predictors such as depression or physical morbidity. Yet, however, only a few studies (8–13) have examined factors affecting functional impairments in old age longitudinally. Most of these studies used static models. This means that they used a static set of baseline indicators in their analysis and therefore could not account for changes in baseline characteristics. Thus, only a few studies (14–19) examined how changes in independent variables affect functional impairments.

We analysed time-dependent variables which might be relevant for functional impairments, such as sociodemographic (20–22), psychological (6, 8, 15) as well as cognitive factors (11, 23) and comorbidity (6, 11, 12). Thus, we hypothesize that *Received November 9, 2015*

increasing chronic conditions increase functional impairment since the onset of chronic conditions may lead to the inability to perform daily activities. Furthermore, we hypothesize that the occurrence of dementia increases functional impairment. For instance, the onset of dementia might lead to the inability to deal with financial matters or to use the telephone. Moreover, we hypothesize that the onset of depression increases functional impairment. This might be explained by decreased social ties and physical activities. Moreover, we hypothesize that age has an independent effect on functional impairment (24). Additionally, we hypothesize that predictors differ by gender.

We aimed at determining time-dependent factors affecting functional impairment in old age in a longitudinal setting. This knowledge is crucial in order to understand the factors leading to functional decline (causality). In a further step, this might open up possibilities for prevention or delay of functional decline.

Methods

Sample

This longitudinal study used data from the German Study on Ageing, Cognition and Dementia in Primary Care Patients (AgeCoDe). It is a population based prospective cohort study. General practitioners' (GP) offices recruited individuals at

six study centers in Germany (Leipzig, Hamburg, Dusseldorf, Mannheim, Bonn and Munich) in 2003/2004 (baseline). From this time onwards trained staff interviewed individuals and their proxies every 1.5 years, with follow-up (FU) wave 5 taking place in 2011/2012.

Only if they met three conditions at baseline, individuals were included in the sample: (i) aged 75 years or older, (ii) absence of dementia and (iii) at least one contact with the GP during the last 12 months.

Individuals were excluded if they fulfilled at least one of the following conditions: insufficient knowledge of the German language, consultations solely by home visits, residence in a nursing home, severe illness the GP would deem fatal within 3 months, deafness, blindness, lack of ability to provide informed consent and not being a regular patient of the participating practice. More details regarding the sampling frame have been reported by Luck et al. (25). The study has been approved by the local ethics boards of all participating centers and written informed consent was obtained from all patients.

While we draw on three waves (FU wave 3: n=1,940; FU wave 4: n=1,605; FU wave 5: n=1,310) in main analyses for reasons of data availability, we draw on six waves (baseline: n=3,256) in additional analyses. Main reasons for lack of follow-up data were death (n=763) and refused participation (n=828).

Dependent variables

Functional impairment (assessed from baseline upwards) was quantified by means of the Instrumental Activities of Daily Living (26) scale (IADL, 0 = worst score, 8 = best score). The IADL scale is widely used and has good psychometric properties (27). By using the IADL scale, we focused on rather complex instrumental activities of daily living.

In contrast to the IADL scale, the Barthel-Index (BI) (28) (assessed from FU wave 3 upwards) assesses impairments in more basic activities of daily living, ranging from 0 (worst score) to 100 (best score). All estimates were performed using both, IADL and BI, as outcome variable.

Independent variables

Age, sex, educational level (CASMIN classification (29): primary, secondary and tertiary education), family status (Ref.: married; others (single, widowed, divorced)) and living situation (Ref.: living alone in private household; others (with spouse/partner, with other relatives, nursing home, assisted living, retirement home, other)) were used as sociodemographic variables. It is worth mentioning that the time-invariant independent variables sex and education were only used to describe our dataset and cannot be included as independent variables in FE regressions since they are time-constant.

Depressive symptoms were quantified by means of the 15-item version of the Geriatric Depression Scale (30). We dichotomized the Geriatric Depression Scale (1 if Geriatric Depression Scale \geq 10; 0 otherwise). Hence, we concentrate

on the occurrence of severe depression. Moreover, dummy variables for region were included in all regressions (for the sake of space results for region dummies are not shown in tables but are available upon request from the authors).

Dementia was assessed by using the Global Deterioration Scale (1 = no impairment, 7 = severe dementia) (assessed from baseline upwards) (31). The scale was dichotomized into dementia (Global Deterioration Scale \geq 4) and absence of dementia (otherwise).

The GP recorded (assessed from FU wave 2 upwards) the presence of 28 chronic conditions: Diabetes, hypertension, cardiac arrhythmia, coronary heart disease, myocardial infarction, hyperlipidemia, hypercholesteremia, chronic heart failure, peripheral arterial disease, Parkinson's disease, epilepsy, alcohol abuse, stenosis, transient ischaemic attack, stroke, hyperthyroidism, hypothyroidism, renal insufficiency, chronic liver disease, traumatic brain injury, back pain, arthrosis, obesity, gout, varicose veins, chronic obstructive pulmonary disease, asthma and gastritis. These comorbidities were selected to reflect chronic conditions which are frequent in old age.

If a chronic condition was present, the GP rated the severity (1 = mild up to 4 = severe). A weighted count comorbidity score was computed. For this purpose, the sum of severity ratings for conditions scored as present was calculated. It was done to account for the severity of the chronic conditions.

In all variables the proportion of missing values was below

In total, variables included from baseline upwards were: IADL, age, sex, educational level, family status, living situation, Geriatric Depression Scale, Global Deterioration Scale. Variable included from FU wave 2 upwards was: Comorbidity score. Variable included from FU wave 3 upwards was: Barthel-Index.

Statistical Analysis

Linear fixed effects (FE) regressions were used to estimate the effects of our time dependent variables on functional impairment (IADL or BI). Consequently, we suppose that the unobserved heterogeneity such as genetic predisposition is correlated with the predictors. Random effects (RE) regressions would be inconsistent in such a case (32). Cluster-robust standard errors were computed (33) (please see the Appendix (section: Statistical Analysis) for more details).

In our main models, as already stated earlier, we concentrated on changes between FU waves 3-5 in the IADL scale and the BI for reasons of data availability. In order to test the robustness of our results (in terms of effect size and significance), we estimated an additional model where intraindividual changes from all waves (from baseline to FU wave 5) were used (please see the Appendix (section: Alternate models)). Consequently, solely IADL were used as outcome variable because BI was assessed from FU wave 3 upwards.

JNHA: CLINICAL NEUROSCIENCES

Moreover, comorbidity (assessed from FU wave 2 upwards) was removed as a covariate. To further check the robustness of these findings, we also applied FE poisson models with cluster-robust standard errors.

The level of significance was set at $\alpha = .05$. All statistical analyses were performed using Stata 13.1 (Stata Corp., College Station, Texas).

Results

Sample characteristics

Sociodemographic variables, depression, dementia and comorbidity are depicted over time (FU waves 3-5) in table 1 (please see the Appendix (Tables S1 and S2) for more details).

At FU wave 3, mean age was 84 years (± 3.3 years), ranging from 79-97 years. The majority was female (66.1%), had low education (59.4%), was either single, widowed, or divorced (65.2%) and was living alone in private household (50.7%).

Most of these individuals had no depression (98.4%) and no dementia (91.8%). The mean comorbidity score was 4.5 (\pm 3.8). Moreover, mean IADL was 6.6 (\pm 2.0) and mean BI was 95.1 (\pm 13.2).

After 3 years (FU wave 5) the proportion of single, widowed, or divorced individuals increased to 71.9% due to the death of many spouses. Other sociodemographic variables remained almost constant. Furthermore, the mean comorbidity score decreased to 3.9 (±3.8), while functional impairment increased (IADL: 5.9±2.4; BI: 90.7±19.2).

Table 1Descriptive Statistics over Time (Waves 3-5)

Variables	Follow-Up Wave 3 (n=1,940)	Follow-Up Wave 4 (n=1,605)	Follow-Up Wave 5 (n=1,310)
Age: Mean (SD)	84.0 (3.3)	85.4 (3.2)	86.9 (3.1)
Female: N (%)	1282 (66.1)	1074 (66.9)	896 (68.4)
Education: N (%)			
Low Education	1152 (59.4)	930 (57.9)	755 (57.6)
Middle Education	555 (28.6)	480 (29.9)	390 (29.8)
High Education	233 (12.0)	195 (12.2)	165 (12.6)
Unmarried: N (%)	1263 (65.2)	1075 (67.0)	941 (71.9)
Living alone in private household: N (%)	984 (50.7)	808 (50.4)	641 (48.9)
Absence of depression: N (%)	1865 (98.4)	1510 (98.0)	1212 (97.4)
Absence of dementia: N (%)	1780 (91.8)	1449 (90.3)	1152 (87.9)
Comorbidity (Weighted count score): Mean (SD)	4.5 (3.8)	4.5 (3.9)	3.9 (3.8)
IADL: Mean (SD)	6.6 (2.0)	6.2 (2.3)	5.9 (2.4)
BI: Mean (SD)	95.1 (13.2)	93.2 (15.9)	90.7 (19.2)

Regression analysis

Table 2 presents the results of FE regressions for the IADL scale. Table 3 presents the results of FE regressions for the BI

scale (FU waves 3-5). Gender-specific regressions were also included (columns 2-3). It is worth mentioning that an increase in functional impairment corresponds to a decrease in the IADL scale.

In the total sample, functional impairment (IADL) increased with each additional year. Moreover, functional impairment significantly increased with loss of a spouse (β = 0.5) and not living alone in private household (β =-1.2). Furthermore, functional impairment significantly increased with the occurrence of depression (β = 0.6) and the occurrence of dementia (β =-2.3). The comorbidity score did not achieve statistical significance.

While transitions in marital status affected the IADL scale in women, transitions in marital status did not affect the IADL scale in men (with a significant interaction term, p=.01). Furthermore, the occurrence of depression affected solely functional impairment in women. However, the interaction term was not significant (p=.15).

Moreover, we repeated all estimates with the BI as dependent variable, focusing on more basic activities of daily living. In contrast to our analyses with the IADL scale as dependent variable, the occurrence of depression did not affect functional impairment.

In the total sample, the occurrence of dementia considerably reduced functional impairment (β = 18.2). Additionally, functional impairment significantly increased with loss of a spouse (β =-3.1), not living alone in private household (β =-5.5) and increasing age (β =-1.1). Again, comorbidity score did not achieve statistical significance.

While changes in marital status and living situation affected the BI in women, changes in these factors did not affect the BI in men. However, the interaction terms (marital status x sex, p=.34; living situation x sex, p=.07) were not significant (please see the Appendix (Table S3) for more details).

Discussion

Main findings

Longitudinal regressions revealed that functional impairment (IADL; BI) increased significantly with ageing (β =-.2; β =-1.1), loss of a spouse (β = .5; β =-3.1), not living alone in private household (β =-1.2; β =-5.5), depression (solely significant for IADL: β =-.6) and dementia (β =-2.3; β =-18.2). The comorbidity score did not affect functional impairment.

Previous research

In sum, our data corroborate the hypothesis, that depression and dementia are causal factors for functional impairment, and thus extend previous knowledge (depression: (8, 16, 34, 35); cognitive functioning: (23, 36–40) about an association of these factors.

Nevertheless, it is surprising that the occurrence of depression did not affect the BI which is in contrast to most previous longitudinal studies (41–43). The effect of depression

 Table 2

 Longitudinal Predictors of IADL: Results of Fixed Effects Regressions (Waves 3-5)

Independent variables	(1) IADL – All Beta-Coefficients (Cluster-robust standard errors in parentheses)	(2) IADL – Women Beta-Coefficients (Cluster- robust standard errors in parentheses)	(3) IADL – Men Beta-Coefficients (Cluster- robust standard errors in parentheses)
Ageing	-0.245***	-0.247***	-0.233***
	(0.0127)	(0.0141)	(0.0254)
Loss of spouse	0.476***	0.884***	0.0592
	(0.144)	(0.192)	(0.201)
Transitions from living alone to other living arrangements	-1.180***	-1.324***	-0.734**
	(0.131)	(0.155)	(0.228)
Occurrence of depression	-0.574*	-0.683**	0.0279
	(0.224)	(0.245)	(0.499)
Occurrence of dementia	-2.334***	-2.479***	-1.797***
	(0.212)	(0.246)	(0.387)
Changes in comorbidity (Weighted count score)	-0.00739	-0.0149	0.00759
	(0.0100)	(0.0115)	(0.0185)
Constant	27.14***	27.56***	25.45***
	(1.120)	(1.242)	(2.182)
Observations	4,674	3,119	1,555
\mathbb{R}^2	0.323	0.409	0.166
Number of Individuals	1,902	1,257	645

Comments: Regressions are controlled for region; *** p<0.001, ** p<0.01, * p<0.05, + p<0.10; Observations with missing values were dropped (listwise deletion).

on functional impairment might be explained by decreased physical activity and social interaction (42, 44). Non-significant effects were only occasionally found in longitudinal studies (44, 45)

With regard to chronic medical conditions, our findings based on a weighted count comorbidity score are hard to compare to previous literature since several studies (11, 22, 39, 45) examined the predictive value of numerous specific chronic conditions mostly separately. In contrast to our study, studies using chronic conditions scores including Geerlings et al. (physical chronic conditions score) (34) or Hybels et al. (12) (chronic conditions score) found significant associations between chronic conditions and functional impairment. These differences might be explained by differences in model specification, statistical methods and a large variety in chronic conditions used to calculate comorbidity scores. Moreover, it is assumed that the occurrence of dementia is a key driver of functional impairment. Other emerging chronic diseases, such as diabetes, might be irrelevant for functional decline. This assumption should be investigated in future studies.

As for age and marital status, our findings correspond to the previous literature (8, 20–22, 39). However, regarding living situation, literature is inconclusive (8, 13, 46, 47). For example, living alone was a risk factor for functional decline among Japanese community-dwelling older adults (8). This was confirmed by Gill et al. (older adults in the US) (47). Another longitudinal study among older people (13) did not reveal a significant association between living with spouse and functional decline. In our study the changes in living situation (transitions from living alone to other living arrangements) most likely reflect the emerging need for help in activities in daily living. Other findings using the baseline predictor 'living alone' as risk factor for subsequent functional impairment may be explained by the fact that this living situation reflect other risk factors including lower physical activity or multiple falls (48).

Strength and Limitations

This is one of few longitudinal studies aimed at determining factors affecting functional impairment in old age. Moreover, unlike other studies, the present study investigated the effect of time-dependent variables. Consequently, evidence for causality can be provided, even though with some limitations (since we did not have a controlled stimulus).

A further strength is that the study population was an almost representative sample of old age individuals in Germany because individuals were recruited via GP offices and almost every individual of this age bracket has regular GP visits.

JNHA: CLINICAL NEUROSCIENCES

 Table 3

 Longitudinal Predictors of BI: Results of Fixed Effects Regressions (Waves 3-5)

Independent variables	(1) BI – All Beta-Coefficients (Cluster- robust standard errors in parentheses)	(2) BI –Women Beta-Coefficients (Cluster- robust standard errors in parentheses)	(3) BI – Men Beta-Coefficients (Cluster- robust standard errors in parentheses)
Ageing	-1.085***	-1.099***	-1.003***
	(0.0831)	(0.103)	(0.138)
Loss of spouse	3.096**	4.471**	1.446
	(1.021)	(1.551)	(1.337)
Transitions from living alone to other living arrangements	-5.483***	-6.536***	2.420
	(1.111)	(1.364)	(1.584)
Occurrence of depression	-3.135	-4.400	1.988
	(2.583)	(2.863)	(5.340)
Occurrence of dementia	-18.19***	-17.92***	-17.98***
	(2.377)	(2.665)	(4.890)
Changes in comorbidity (Weighted count score)	-0.0494	-0.0317	-0.0545
	(0.0748)	(0.0935)	(0.124)
Constant	189.3***	189.7***	180.4***
	(7.301)	(9.022)	(11.72)
Observations	4,673	3,119	1,554
\mathbb{R}^2	0.233	0.263	0.170
Number of Individuals	1,902	1,257	645

Comments: Regressions are controlled for region; *** p<0.001, ** p<0.01, ** p<0.05, + p<0.10; Observations with missing values were dropped (listwise deletion).

Moreover, we draw on a long-running dataset (up to 6 waves) and time intervals between waves were relatively short (1.5 years)

On the other side, we cannot rule out the possibility that our estimates are biased downwards due to panel attrition (endogenous selection bias). Consequently, the true effects might be underestimated. To this end, we investigated whether there were differences at baseline between individuals with complete follow-up data and individuals who dropped out sometime after baseline. Initially the latter group was more severely functionally (IADL and BI) as well as cognitively (Global Deterioration Scale) impaired. Furthermore, the latter group was older, more depressed and had a higher comorbidity score (results are not shown, but are available upon request from the authors).

Even though model fit was acceptable, there might exist factors that also affect functional impairment, such as income (49), loneliness (50) or stress symptoms (51). Future studies should clarify the impact of these predictors.

Moreover, even though the IADL scale showed good psychometric properties, it should be noted that it is insensitive to small changes in functional status. Furthermore, due to the self-report method (rather than a demonstration of functional abilities), the functional abilities might be slightly overestimated (27) - or underestimated if the person wants

attention.

We also cannot rule out the possibility that there might be a simultaneity bias (endogeneity) between depression and functional impairments (52). From a theoretical perspective, endogeneity bias can be solved by Panel-IV-estimator (32). Nevertheless, we rejected this idea as we had a problem of weak instruments.

Conclusion

Our findings stress the importance of changes in sociodemographic factors as well as the occurrence of depression or dementia for functional impairment. While several of these causal factors for functional decline in the oldest old are inevitable, some may not be, such as depression. Therefore, developing interventional strategies to prevent depression might be a fruitful approach in order to delay functional impairment in old age.

Furthermore, with the growing old age population it is most likely that the number of old age individuals with dementia (53) and depression (54) will increase considerably in the upcoming decades. Consequently, it is expected that the number of functional impaired elderly individuals will increase. This in turn will probably increase the need for care in the next decades. These future challenges should be taken into

consideration.

Moreover, it is worth emphasizing that it is important to control for time-constant unobserved factors in functional impairment research. Therefore, in order to receive unbiased estimates, future studies should exploit longitudinal data and consequently use FE regressions to estimate the longitudinal predictors of functional decline.

Ethics statement: The ethics committees of the participating centers approved the study (reference numbers: 050/02 (University of Bonn), 2079 (Faculty of Medicine, University of Düsseldorf), 2817/2007 (Hamburg Medical Association), 309/2007 (Faculty of Medicine, University of Leipzig), 2007-253E-MA (Medical Ethics Commission II, University of Heidelberg at the University Medical Center of Mannheim), 713/02 (Faculty of Medicine, Technical University of Munich)). The study was conducted according to the principles expressed in the Declaration of Helsinki. All participants gave written informed consent prior to study entry.

Acknowledgements: We thank two anonymous reviewer who provided insightful comments. Funding sources: This publication is part of the German Research Network on Dementia (KNDD), the German Research Network on Degenerative Dementia (KNDD), and the Study on Needs, Health Service Use, Costs and Health-related Quality of Life in a large Sample of Oldest-old Primary Care Patients (85+) (AgeQualiDe) and was funded by the German Federal Ministry of Education and Research (grants KND 01GI0102, 01GI0420, 01GI0422, 01GI0423, 01GI0429, 01GI0431, 01GI0433 and 01GI0434; grants KNDD 01GI0710, 01GI0711, 01GI0712, 01GI0713, 01GI0714, 01GI0715, 01GI0716; and grants AgeQualiDe 01GY1322A, 01GY1322B, 01GY1322C, 01GY1322D, 01GY1322E, 01GY1322F, 01GY1322G).

Members of the AgeCoDe Study Group: Principal Investigators*: Wolfgang Maier, Martin Scherer.

Heinz-Harald Abholz, Cadja Bachmann, Horst Bickel, Wolfgang Blank, Hendrik van den Bussche, Sandra Eifflaender-Gorfer, Marion Eisele, Annette Ernst, Angela Fuchs, Kathrin Heser, Frank Jessen, Hanna Kaduszkiewicz, Teresa Kaufeler, Mirjam Köhler, Hans-Helmut König, Alexander Koppara, Carolin Lange, Hanna Leicht, Tobias Luck, Melanie Luppa, Manfred Mayer, Edelgard Mösch, Julia Olbrich, Michael Pentzek, Jana Prokein, Anna Schumacher, Steffi Riedel-Heller, Janine Stein, Susanne Steinmann, Franziska Tebarth, Michael Wagner, Klaus Weckbecker, Dagmar Weeg, Jochen Werle, Siegfried Weyerer, Birgitt Wiese, Steffen Wolfsgruber, Thomas Zimmermann. *Hendrik van den Bussche (2002-2011) We want to thank both all participating patients and their general practitioners for their good collaboration.

Conflict of Interest: The authors declare that they have no conflict of interest.

References

- Luppa M, Luck T, Weyerer S et al. Prediction of institutionalization in the elderly. A systematic review. Age Ageing 2010;39(1): 31–38. doi: 10.1093/ageing/afp202
- Hajek A, Brettschneider C, Lange C et al. Longitudinal Predictors of Institutionalization in Old Age. PLOS ONE 2015;10(12): e0144203. doi: 10.1371/ iournal.pone.0144203
- Reuben DB, Rubenstein LV, Hirsch SH et al. Value of functional status as a predictor of mortality: Results of a prospective study. Am J Med 1992;93(6): 663–669. doi: 10.1016/0002-9343(92)90200-U
- Talegawkar SA, Tanaka T, Maras JE et al. Validation of nutrient intake estimates derived using a semi-quantitative FFQ against 3 day diet records in the Baltimore Longitudinal Study of Aging. J Nutr Health Aging 2015;19(10): 994–1002. doi: 10.1007/s12603-015-0518-8
- Gomez-Gallego M, Gomez-Garcia J, Ato-Lozano E. Addressing the bias problem in the assessment of the quality of life of patients with dementia: Determinants of the accuracy and precision of the proxy ratings. J Nutr Health Aging 2015;19(3): 365–372.
- Chiu H, Chen C, Huang C et al. Depressive symptoms, chronic medical conditions and functional status: a comparison of urban and rural elders in Taiwan. Int J Geriatr Psychiatry 2005;20(7): 635–644
- Friedman B, Heisel MJ, Delavan RL. Psychometric Properties of the 15-Item Geriatric Depression Scale in Functionally Impaired, Cognitively Intact, Community-Dwelling Elderly Primary Care Patients. J Am Geriat Soc 2005;53(9): 1570–1576
- Iwasa H, Yoshida Y, Kumagai S et al. Depression status as a reliable predictor of functional decline among Japanese community-dwelling older adults: a 12-year population-based prospective cohort study. Int J Geriatr Psychiatry 22009;4(11): 1192–1200
- Fujiwara Y, Yoshida H, Amano H et al. Predictors of improvement or decline in instrumental activities of daily living among community-dwelling older Japanese.

- Gerontology 2008;54(6): 373-380
- Kelley-Moore JA, Ferraro KF. A 3-D model of health decline: Disease, disability, and depression among black and white older adults. J Health Soc Behav 2005;46(4): 376–391
- Wang L, van Belle G, Kukull WB et al. Predictors of functional change: a longitudinal study of nondemented people aged 65 and older. J Am Geriat Soc 2002;50(9): 1525–1534
- Hybels CF, Pieper CF, Blazer DG. The complex relationship between depressive symptoms and functional limitations in community-dwelling older adults: the impact of subthreshold depression. Psychol Med 2009;39(10): 1677–1688
- Shinkai S, Kumagai S, Fujiwara Y et al. Predictors for the onset of functional decline among initially non-disabled older people living in a community during a 6-year follow-up. Geriatr Gerontol Int 2003;3(s1): S31-S39
- Yang Y. Is old age depressing? Growth trajectories and cohort variations in late-life depression. J Health Soc Behav 2007;48(1): 16–32
- Chen C, Mullan J, Su Y et al. The longitudinal relationship between depressive symptoms and disability for older adults: a population-based study. J Gerontol A Biol Sci Med Sc 2012;67(10): 1059–1067. doi: 10.1093/gerona/gls074
- Ormel J, Rijsdijk FV, Sullivan M et al. Temporal and Reciprocal Relationship Between IADL/ADL Disability and Depressive Symptoms in Late Life. J Gerontol B Psychol Sci Soc Sci 2002;57(4): P338 -P347. doi: 10.1093/geronb/57.4.P338
- Fujiwara Y, Chaves PHM, Yoshida H et al. Intellectual activity and likelihood
 of subsequently improving or maintaining instrumental activities of daily living
 functioning in community-dwelling older Japanese: a longitudinal study. Int J Geriatr
 Psychiatry 2009;24(6): 547–555
- Yang Y, George LK. Functional disability, disability transitions, and depressive symptoms in late life. J Aging Health 2005;17(3): 263–292. doi: 10.1177/0898264305276295
- Hajek A, König H. Longitudinal Predictors of Functional Impairment in Older Adults in Europe – Evidence from the Survey of Health, Ageing and Retirement in Europe. PLOS ONE 2016; 11(1): e0146967. doi: 10.1371/journal.pone.0146967
- Guralnik JM, LaCroix AZ, Abbott RD et al. Maintaining mobility in late life. I. Demographic characteristics and chronic conditions. Am J Epidemiol 1993;137(8): 845–857
- 21. Boult C, Kane RL, Louis TA et al. Chronic conditions that lead to functional limitation in the elderly. J Gerontol 1994;49(1): M28-M36
- Dunlop DD, Semanik P, Song J et al. Risk factors for functional decline in older adults with arthritis. Arthritis Rheum 2005;52(4): 1274–1282
- McGuire LC, Ford ES, Ajani UA. Cognitive functioning as a predictor of functional disability in later life. Am J Geriatr Psychiatry 2006;14(1): 36–42
- Hajek A, Brettschneider C, Posselt T et al. Predictors of frailty in old age-results of a longitudinal study. J Nutr Health Aging: 2015;1-6. doi: 10.1007/s12603-015-0634-5
- Luck T, Riedel-Heller SG, Luppa M et al. Risk factors for incident mild cognitive impairment—results from the German Study on Ageing, Cognition and Dementia in Primary Care Patients (AgeCoDe). Acta Psychiatr Scand 2010;121(4): 260–272. doi: 10.1111/i.1600-0447.2009.01481.x
- Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. Gerontologist 1969;9(3): 179–186
- Graf C. The Lawton instrumental activities of daily living scale. AM J NURS 2008;108(4): 52-62
- Mahoney FI, Barthel DW. Functional Evaluation: The Barthel Index. Md State Med J 1965;14: 61–65
- Brauns H, Steinmann S. Educational Reform in France, West-Germany and the United Kingdom. Updating the CASMIN Educational Classification. ZUMA-Nachrichten 1999:44: 7–44
- Yesavage JA, Sheikh JI. Geriatric Depression Scale (GDS) Recent Evidence and Development of a Shorter Version. Clin Gerontol 1986;5(1-2): 165–173
- Reisberg B, Ferris SH, de Leon, Mony J et al. The Global Deterioration Scale for assessment of primary degenerative dementia. Am J Psych 1982;139(9): 1136–1139
- Cameron AC, Trivedi PK. Microeconometrics: methods and applications. Cambridge University Press, New York, 2005
- Stock JH, Watson MW. Heteroskedasticity-robust standard errors for fixed effects panel data regression. Econometrica 2008;76(1): 155–174
- Geerlings SW, Beekman AT, Deeg DJ et al. The longitudinal effect of depression on functional limitations and disability in older adults: an eight-wave prospective community-based study. Psychol Med 2001;31(8): 1361–1371
- Liang J, Shaw BA, Bennett JM et al. Intertwining courses of functional status and subjective health among older Japanese. J Gerontol B Psychol Sci Soc Sci 2007;62(5): S340-S348
- Bruce ML, Seeman TE, Merrill SS et al. The impact of depressive symptomatology on physical disability: MacArthur Studies of Successful Aging. Am J Public Health 1994;84(11): 1796–1799
- Vaughan L, Giovanello K. Executive function in daily life: Age-related influences
 of executive processes on instrumental activities of daily living. Psychol Aging
 2010;25(2): 343–355
- Jefferson AL, Paul RH, Ozonoff A et al. Evaluating elements of executive functioning as predictors of instrumental activities of daily living (IADLs). Arch Clin Neuropsychol 2006;21(4): 311–320

JNHA: CLINICAL NEUROSCIENCES

- Li LW. Predictors of ADL disability trajectories among low-income frail elders in the community. Res Aging 2005;27(6): 615–642
- Gill TM, Williams CS, Richardson ED et al. A predictive model for ADL dependence in community-living older adults based on a reduced set of cognitive status items. J Am Geriatr Soc 1997;45(4): 441–445
- Schillerstrom JE, Royall DR, Palmer RF. Depression, disability and intermediate pathways: a review of longitudinal studies in elders. J Geriatr Psychiatry Neurol 2008;21(3): 183–197
- Penninx BW, Leveille S, Ferrucci L et al. Exploring the effect of depression on physical disability: longitudinal evidence from the established populations for epidemiologic studies of the elderly. Am J Public Health 1999;89(9): 1346–1352
- Pohjasvaara T, Vataja R, Leppavuori A et al. Depression is an independent predictor of poor long-term functional outcome post-stroke. Eur J Neurol 2001;8(4): 315–319. doi: 10.1046/j.1468-1331.2001.00182.x
- Xue Q, Fried LP, Glass TA et al. Life-space constriction, development of frailty, and the competing risk of mortality: the Women's Health And Aging Study I. Am. J. Epidemiol. 2008;167(2): 240–248. doi: 10.1093/aje/kwm270
- Dunlop DD, Manheim LM, Sohn M et al. Incidence of functional limitation in older adults: The impact of gender, race, and chronic conditions. Arch Phys Med Rehabil 2002;83(7): 964–971. doi: 10.1053/apmr.2002.32817
- Hébert R, Brayne C, Spiegelhalter D. Factors associated with functional decline and improvement in a very elderly community-dwelling population. Am J Epidemiol 1999;150(5): 501–510
- Gill TM, Allore HG, Holford TR et al. Hospitalization, restricted activity, and the development of disability among older persons. J Am Med Assoc 2004;292(17):

- 2115-2124
- 48. Kharicha K, Iliffe S, Harari D et al. Health risk appraisal in older people 1: are older people living alone an 'at-risk' group? British Journal of General Practice 2007;57(537): 271–276
- Arber S, Ginn J. Gender and inequalities in health in later life. Soc Sci Med 1993;36(1): 33–46. doi: 10.1016/0277-9536(93)90303-L
- Perissinotto CM, Cenzer IS, Covinsky KE. Loneliness in older persons: a predictor of functional decline and death. Arch Intern Med 2012;172(14): 1078–1084
- Kulmala J, von Bonsdorff, Mikaela B, Stenholm S et al. Perceived stress symptoms in midlife predict disability in old age: a 28-year prospective cohort study. J Gerontol A Biol Sci Med Sc 2013;68(8): 984–991
- Hajek A, Brettschneider C, Ernst A et al. Complex coevolution of depression and health-related quality of life in old age. Qual Life Res 2015;24(11): 2713–2722
- Bickel H. Epidemiologie und Gesundheitsökonomie. In: Wallesch C (ed) Demenzen,
 überarbeitete und erweiterte Auflage. Thieme, Stuttgart, 2012;pp 18–35
- Moussavi S, Chatterji S, Verdes E et al. Depression, chronic diseases, and decrements in health: results from the World Health Surveys. Lancet 2007;370(9590): 851–858

Appendix

Statistical analysis

To test whether FE regressions are necessary or the more efficient RE models can be used instead, we performed Sargan-Hansen test, resulting in the need to control for unobserved time-constant factors. Thus, FE regressions are the preferred regressions.

Alternate models

We repeated estimates (IADL as criterion) without comorbidity score (assessed from FU 2 upwards) as a covariate. Thus, intraindividual changes from baseline up to FU wave 5 were used. Findings were almost the same (in terms of significant predictors and effect sizes) and the interaction term between depression and sex was significant (p=.001).

Furthermore, all analyses were repeated with FE poisson models, leading to similar results (in terms of significance) (results of alternate models are not shown, but are available upon request from the authors).

Sample characteristics

Table S1Descriptive Statistics over Time (Baseline – Wave 2)

Variables	Baseline (n=3,217)	Follow-Up Wave 1 (n=2,738)	Follow-Up Wave 2 (n=2,403)
Age: Mean (SD)	79.7 (3.6)	81.2 (3.5)	82.5 (3.4)
Female: N (%)	2,106 (65.5)	1,783 (65.1)	1,583 (65.9)
Education: N (%)	, , ,	, , ,	
Low Education	1,991 (61.9)	1,673 (61.1)	1,453 (60.5)
Middle Education	883 (27.4)	748 (27.3)	669 (27.8)
High Education	343 (10.7)	317 (11.6)	281 (11.7)
Unmarried: N (%)	1,848 (57.4)	1,638 (59.8)	1,477 (61.4)
Living alone in private household: N (%)	1,648 (51.2)	1,407 (51.4)	1,227 (51.1)
Absence of depression: N (%)	3,170 (98.7)	2,678 (98.2)	2,332 (98.2)
Absence of dementia: N (%)	3,217 (100)	2,663 (97.3)	2,289 (95.3)
Comorbidity (Weighted count score): Mean (SD)	-	-	4.5 (3.9)
(ADL: Mean (SD)	7.3 (1.2)	6.8 (1.7)	6.7 (1.7)
BI: Mean (SD)	-	-	-

 Table S2

 Descriptive Statistics at Baseline (Gender-specific)

Variables	Baseline	Baseline	
	(n=2,106) - Women	(n=1,111) - Men	
Age: Mean (SD)	79.8 (3.6)	79.4 (3.5)	
Education: N (%)			
Low Education	1,379 (65.5)	612 (55.1)	
Middle Education	613 (29.1)	270 (24.3)	
High Education	114 (5.4)	229 (20.6)	
Unmarried: N (%)	1,562 (74.2)	286 (25.7)	
Living alone in private household: N (%)	1,648 (51.2)	1,407 (51.4)	
Absence of depression: N (%)	2,072 (98.5)	1,098 (99.0)	
Absence of dementia: N (%)	2,106 (100)	1,111 (100)	
Comorbidity (Weighted count score): Mean	-	-	
(SD)			
IADL: Mean (SD)	7.8 (0.7)	6.3 (1.5)	
BI: Mean (SD)	-	-	

Additional models

 Table S3

 Longitudinal Predictors of Functional Impairment (with interaction terms): Results of Fixed Effects Regressions

Independent variables	(1) IADL	(2) IADL	(3) Barthel-Index	(4) Barthel-Index
Ageing	-0.244***	-0.245***	-1.083***	-1.073***
	(0.0127)	(0.0127)	(0.0829)	(0.0830)
Married (Ref.: No)	0.812***	0.483***	4.000**	2.850**
	(0.184)	(0.142)	(1.478)	(1.033)
Interaction: Sex x marital status	-0.638*		-1.721	
	(0.254)		(1.806)	
Living alone in private household (Ref.: No)	1.195***	1.181***	5.522***	6.321***
	(0.131)	(0.131)	(1.110)	(1.342)
Interaction: Sex x living situation				-3.472+
Occurrence of depression	-0.572*	-0.733**	-3.129	-3.123
	(0.222)	(0.250)	(2.583)	(2.576)
Interaction: Sex x depression		0.785		
		(0.547)		
Occurrence of dementia	-2.343***	-2.319***	-18.21***	-18.06***
	(0.212)	(0.211)	(2.378)	(2.373)
Changes in comorbidity (Weighted count score)	-0.00782	-0.00700	-0.0504	-0.0426
	(0.0101)	(0.00999)	(0.0750)	(0.0747)
Constant	27.12***	27.13***	189.3***	188.7***
	(1.121)	(1.119)	(7.299)	(7.286)
Observations	4,674	4,674	4,673	4,673
R-squared	0.324	0.323	0.234	0.235
Number of Individuals	1,902	1,902	1,902	1,902

 $Comments: Beta-Coefficients \ were \ reported; Cluster-robust \ standard \ errors \ in \ parentheses; Regressions \ are \ controlled \ for \ region; \\ *** \ p<0.001, ** \ p<0.01, * \ p<0.05, + \ p<0.10. \\$