

Three-year trajectories in Functional Limitations and Cognitive Decline among Dutch 75+ year olds, using nine-month intervals

Maura Gardeniers (✉ m.k.m.gardeniers@vu.nl)

VU Amsterdam

Marjolein Broese van Groenou

VU Amsterdam

Erik Jan Meijboom

VU Amsterdam

Martijn Huisman

VU Amsterdam

Research Article

Keywords: Trajectories, functional limitations, cognitive decline, mortality, group-based trajectory modelling

Posted Date: January 11th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-142036/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License. [Read Full License](#)

Version of Record: A version of this preprint was published at BMC Geriatrics on February 1st, 2022. See the published version at <https://doi.org/10.1186/s12877-021-02720-x>.

Abstract

Background

Using longitudinal panel data, the aim of this study was to first identify three-year trajectories in cognitive and physical functioning among Dutch older adults. And second, to identify which main characteristics were associated with these trajectories.

Methods

Group-based Trajectory Modelling with mortality jointly estimated was used to identify trajectories, using a scale composed of 6 Activities of Daily Living (ADL) as a measure of physical functioning, and a short version of the mini mental status examination (sMMSE) or the IQCODE as a measure of cognitive functioning. Data came from 574 Dutch adults aged 75+, collected in five nine-month measurement waves conducted between 2015 and 2018 for the Longitudinal Aging Study Amsterdam.

Results

Five trajectories in physical functioning were identified: 'high', 'moderate', 'steeply declining', 'gradually declining', and 'continuously low'. People that were older, lower educated, living in an institution, or suffered from diabetes or cerebrovascular accidents were more likely to follow a low or declining physical trajectory. For cognitive functioning four trajectories were identified: a 'high', 'moderate', 'declining', and 'low' trajectory. Old age, low education, living in an institution, and heart- and lung diseases were associated with continuously low or declining cognitive functioning. Mortality risks were highest among those experiencing the continuously low functioning trajectories.

Conclusions

This study identified trajectories comparable to previous studies that used longer time intervals, showing the consistent presence of heterogeneity in both physical and cognitive trajectories. Co-modelling mortality resulted in bigger group sizes for the more adverse trajectories. The favourable trajectories, containing most of the participants, were mostly characterized by absence of disease, whereas trajectories showing decline did not share a common indicator. Specific chronic diseases were associated with different rates of decline, however there was no factor that was associated with all declining trajectories; future research could focus on finding such an indicator.

Background

Western societies are aging rapidly, showing both an increase in the number of young older adults (aged 65 to 75) and the number of oldest-old (aged 75 and older) (1). For some older adults this increased longevity goes hand in hand with chronic disease, functional limitations, and cognitive decline (2–6). But ageing does not appear to be debilitating to all, and some older adults reach high age while maintaining good physical and cognitive functioning (7). In other words, there is considerable heterogeneity in health and functioning in old age. Exploring this heterogeneity is a fundamental task of gerontological research.

Since levels of functioning are known to be dynamic and not static, information about trajectories of functioning is key for understanding how functioning is associated with ageing. Previous studies usually identified between two and nine trajectories of physical or cognitive functioning; depending on various aspects of study design, such as the chosen indicator of functioning, the sample size, and the density of observation points (7–20). Despite this wide variety in the number of trajectories observed, studies focussing on older populations tend to be consistent in that they often report high levels of functioning, mostly report decline, but do not report trajectories reflecting recovery of functioning (13, 21, 22).

The best approach to gain a more comprehensive understanding of the heterogeneity in trajectories of functioning in older adults may be to triangulate findings from multiple studies that vary in key aspects of study design. Existing studies of functional limitations in Dutch older adults focused on relatively young samples (~ mean age 70) and used relatively long time intervals of 3 years to assess trajectories of limitations (7, 9, 20, 21). In the current study, we investigate heterogeneity in functional limitations and cognitive functioning among Dutch older adults. Our approach stands out from previous work on a number of aspects of study design. Firstly, we examine changes in functioning across relatively short time intervals of nine months, which may be more sensitive to meaningful change than longer follow-up periods. Secondly, we focus on a sample of participants aged 75 years and older, which is where we expect relatively many changes in functioning to occur. Thirdly, we measure functional limitations as a continuous variable. This allows for more accurate descriptions than dichotomization, which severely compresses the range of the severity of ADL-limitations. Finally, we incorporate information on mortality risk in our estimates of trajectories to account for bias in estimated group sizes caused by nonselective attrition caused by mortality (23). This approach builds on the assumption that attrition due to mortality is related to the participant's previous health status and provides relevant information for classifying individuals into broader functioning categories, leading to more accurate classifications. Studies that did not account for mortality in their models implicitly made the assumption that decrease occurred at random (23). In addition, we explore differences in several key characteristics of older adults between each of the observed trajectories. Our research question is as follows: What trajectories in functional limitations and cognitive functioning can be identified in Dutch adults aged 75 and older in a period of three years? And how are age, gender, socioeconomic status, and chronic diseases associated with these trajectories?

Methods

Design and study sample

This study used data from the LASA 75-PLUS-study, an ancillary study of the Longitudinal Aging Study Amsterdam (LASA). LASA is an ongoing longitudinal population-based study of older adults (aged 55+) in the Netherlands (24). The baseline sample was drawn from eleven municipal registries in 1992, stratified by age and sex, and contained 3107 men and women aged 55–84 years (born between 1908 and 1937). In 2002 and 2012 additional cohorts were sampled of respectively 1002 and 1032 men and women born between either 1938 and 1947, or 1948 and 1957. The baseline cooperation rate was 62% for the first cohort, and 62% and 63% for the second and third cohort (24, 25). The data were mainly collected by trained interviewers in face-to-face, computer-assisted interviews. In cases where respondents refused or were not able to complete the full interview, either an abbreviated face-to-face interview, or a 15-minute telephone interview (with either a proxy or the respondent) was conducted. Further details concerning data collection are described in cohort profile papers (25, 26). Although previous studies excluded demented and institutionalized people (Comijs et al. 2004; Kok et al. 2015), we did not exclude participants based on these criteria.

For the ancillary 75-PLUS-study, three additional nine-monthly measurement waves were conducted between the regular measurement waves of 2015/16 and 2018/19. All LASA-participants born before 1941 were asked to participate in the ancillary study (N = 686), of whom 601 eventually participated in the LASA 75-PLUS study. For this study we used these three nine-monthly measurements: 75-PLUS I, 75-PLUS II (N = 550) and 75-PLUS III (N = 507), together with data from the

Table 1
Description of the 5 LASA measurement waves conducted between 2015 and 2019

	Wave 2015-16	Wave 75PLUS I	Wave 75PLUS II	Wave 75PLUS III	Wave 2018-19
Invited	686	686	601	550	473
Participated, n (%)	601	601 (87.6)	550 (91.5)	507 (92.2)	473
Age, mean (SD)	82.2 (5.4)	83.0 (5.4)	83.4 (5.2)	83.8 (4.9)	84.1 (4.8)
Female, n %	368 (61.2)	368 (61.2)	338 (61.5)	311 (61.3)	295 (62.4)
Face-to-face interview, n	453 (78.0)	442 (73.5)	410 (68.2)	364 (66.2)	326 (68.9)
Telephone interview proxy	53 (8.8)	61 (10.1)	55 (10)	59 (11.6)	50 (10.3)
Telephone interview respondent	86 (14.3)	98 (16.3)	85 (15.5)	84 (16.6)	93 (17.0)

preceding (2015/16) and subsequent (2018/19) regular LASA waves (N = 473). Table 1 shows the

number of participants included in each wave.

Dependent Variables

Functional Limitations

Functional limitations are restrictions in performing physical or mental tasks, that usually result in limitations in the performance of activities of daily living (ADL). We used ADL-indicators of respondents' ability to perform the following six tasks: 1) dressing or undressing themselves, 2) standing up from or sitting down in a chair, 3) cutting own toenails, 4) using own or public transport, 5) climbing a flight of stairs, and 6) walking 5 minutes outdoors without resting. The response categories ranged from '1' not able at all, to '5' very able. The responses to the ADL-items were summed to the 'functional-limitations-scale', that ranged from 0 to 30, with higher scores indicating higher levels of functioning.

Cognitive Decline

The degree of cognitive decline was assessed using either the sMMSE, a short 8-item version of the Mini-Mental State Examination (MMSE) (27), in which functioning in the following domains was tested: orientation in time and place, registration of words, attention and calculation (measured by either subtraction or spelling), and recall of three words (28). For participants that were unable to perform the test, cognition was assessed by interviewing a proxy, if possible. For these interviews an abbreviated form of the IQCODE (29) was used: a 6-item scale ranging from 18 to 30 concerning the decline in the last 10 years on remembering 1) conversations, 2) addresses, and 3) phone numbers, and handling 4) domestic appliances, 5) money for groceries, and 6) finances. Higher scores indicated worse decline. For those participants who switched to the IQCODE at some point during the study, we imputed sMMSE data based on the IQCODE-scores.

No guidelines have been published on how to harmonize the IQCODE with the sMMSE, so we tried various ways of harmonizing the two, based on two studies that used both scales and reported which scores indicated similar levels of cognition (8, 30). Since these values differed between these two studies, we estimated the trajectories using these various ways of harmonizing the two scales, to assess whether this affected the shapes of the estimated trajectories. This did not affect the estimated shapes substantially (see figure S1 in additional file 1). Because the choice of the different cut-off points did not rigorously affect the trajectory shapes, we chose the cut-off points based on a previous LASA-study (8), since this would likely reflect our sample best. The values of the IQCODE and sMMSE are reported in Table 2. Because an IQCODE-score of 18 indicated no change in the last years, this value either corresponded with the participants' previous sMMSE-score, or if that score was not available, an sMMSE-score of 16. The eventual 'cognition-scale' was constructed by summing all the points scored on the 8 sMMSE items (or by harmonizing the IQCODE to an sMMSE-score), resulting in a scale that ranged from 0 to 16, with 16 indicating the highest level of cognitive functioning.

Table 2
 Values used to harmonize IQCODE-scores with sMMSE-scores, based on cut-off values provided by Comijs et al. (2004).

IQCODE	sMMSE
18	16, or previous sMMSE-score
19	16
20–21	15
22–23	14
24–25	13
26–27	12
28–29	11
30	10

Despite there being indications of the IQCODE and MMSE not entirely measuring the same

construct (31), we argue that keeping the participants that were assigned the IQCODE at some point during the study in the analyses is better than excluding them. Since our study focusses on cognitive decline, and the IQCODE is more likely to be assessed when participants experience considerable decline, excluding these participants would have likely resulted in missing a considerable portion of the trajectories showing cognitive decline. Since the model aims to be descriptive and not explanatory, we decided that the occurrence of decline was more informative than the rate of decline. Even if the imputed data based on IQCODE-scores is an under- or overestimation of the “true” sMMSE-score, we expect the direction of cognitive decline to still be in accordance with the “true” direction.

Mortality

Mortality-data (date of decease) were obtained through the registration of municipalities (GBA), and were last updated in February 2020. It was included as a dichotomous variable, with '0' indicating being alive and '1' indicating being deceased, per wave.

Independent Variables

Age, gender, partner status (partner/ no partner), educational level, and chronic disease status were used to give a description of respondents in the identified trajectories. This selection of characteristics was chosen because they represent some of the main vectors of social and economic disadvantage in older populations and reflect vulnerable groups. They were all measured at baseline (2015/16). Educational level was divided into three categories: low (primary school), middle (secondary school or lower vocational training), and high (higher vocational training or higher). For chronic disease we grouped ten diseases into five categories: 1) heart- and lung disease (coronary-, pulmonary-, and vascular disease), 2) rheumatic disease (arthritic and osteopathic), 3) diabetes, 4) cancer, and 5) cerebrovascular accidents (CVA).

Sensitivity and Missing Data

Data was either missing at the item level (e.g. one of the six ADL-items missed), or at the wave level (e.g. not participating in one or two waves). When a respondent had less than ~ 50% missing at the item level, data were imputed with the mean of the non-missing items at that wave. When more than 50% of the items was missing that wave was imputed with the mean of the preceding and subsequent wave. For a more in depth review on the rationale for this imputation method see: Halpin (32). Data were imputed for 79 participants. Of the initial sample of 601 4.7% (N = 27) dropped out for other reasons than decease, and were thus excluded from the analysis. We conducted sensitivity checks, by estimating the models 1) stratified by gender, 2) only for survivors, and 3) for deceased (see figures S2, S3, and S4 in additional file 2). The models stratified for gender did not differ substantially in terms of shapes of the trajectories, so we performed the main analyses unstratified. The models only for survivors and deceased participants were comparably different, as expected, yet showing the importance of including the deceased participants in the analysis by jointly modelling mortality.

Method of Analysis

Group-Based Trajectory Modelling

The analyses were conducted using the STATA package Proc Traj (33). Building on the work of Kok et al. (7) we started with estimating an unconditional model, in which even chronological age was not included. This approach has the advantage of not allowing one covariate to have a disproportionately big influence on the model. The independent variable in the model was the time of the measurement waves. We fitted two group-based trajectory models with mortality jointly estimated, for physical and cognitive functioning. Because the dependent variables were continuous scales, we used the Tobit model, assuming a censored normal distribution (34). First, we determined the number of identified trajectories that fitted the data best, by using the Bayesian Information Criterion (BIC) and the posterior probabilities (33, 35). We also assessed whether an extra trajectory group revealed a relevantly different trajectory. After having identified the optimal number of trajectories, cognitive or physical limitations were estimated in a trajectory model, with the dropout-function accounting for dropout due to decease (36). The 27 participants who had missing data due to other reasons than death and could not have their data imputed, were excluded from the analysis, using the obsmar-function (37).

Subsequently we calculated the average marginal effects (AME). The AME are a variation on a multinomial logistic regression, and show the association between a certain characteristic (i.e. age) and a trajectory for a one-unit change of that characteristic. The AME's main advantage over the estimates of multinomial logistic regression lies in the fact that their provided estimates are more intuitive in terms of interpretation since they don't require a reference group during interpretation (38).

Results

Descriptive Statistics

Table 3 about here [included at the end of the document]

Table 3
Descriptive statistics per trajectory type of 574 Dutch adults aged 75+

	Total sample (N = 574)	Functional Limitations					Cognitive functioning		
		1: <i>Continuous low functioning. high mortality</i> (N = 127)	2: <i>Steep decline in functioning. low mortality</i> (N = 34)	3: <i>Steady decline. low mortality</i> (N = 151)	4: <i>Moderately high functioning. low mortality</i> (N = 174)	5: <i>Continuous high functioning. low mortality</i> (N = 88)	1: <i>Continuous low functioning. high mortality</i> (N = 63)	2: <i>Moderately high functioning. low mortality</i> (N = 254)	3: <i>Declining functioning. moderate mortality</i> (N = 85)
Mean age (sd)	82.18 (5.31)	85.37 (5.85)	82.34 (4.95)	83.47 (5.19)	80.36 (4.06)	78.87 (3.44)	84.70 (5.09)	81.86 (5.43)	84.11 (5.67)
Age range	74.86– 102.86	75.09– 102.86	75.2–94.26	75.07– 97.59	75.05– 98.23	74.86– 90.08	75.26– 95.73	75.00– 99.12	75.09– 102.86
<i>% in group is</i>									
Female	60.98	71.65	58.82	65.56		47.72	60.32	59.45	67.06
Low education	48.08	61.42	41.18	53.64	46.55	25.00	57.14	52.76	65.88
Middle education	29.97	26.77	29.41	29.14	28.16	39.77	22.22	29.53	23.53
High education	21.95	11.81	29.41	17.22	17.22	35.23	20.63	17.72	10.59
Has a partner	50.52	33.85	50.00	46.36	60.34	62.50	39.68	50.00	45.88
Lives in an institution	92.51	25.20	8.82	3.97	1.15	0	34.92	3.15	11.76
Lung/heart/vascular disease	48.78	51.12	38.24	55.63	50.00	35.23	36.51	51.97	55.29
Diabetes	15.68	22.83	17.64	17.88	11.49	9.09	15.87	15.35	27.06
CVA	10.10	17.32	2.94	13.91	6.32	3.41	11.11	11.42	18.82
Cancer	23.17	17.32	23.53	31.79	23.56	15.91	23.81	20.47	28.24
Rheumatic disease	62.89	70.87	61.76	70.86	57.47	48.86	55.55	63.39	57.65
Deceased	24.34	56.00	17.65	19.33	12.64	13.64	55.55	18.11	47.06

The baseline (wave 2015/16) characteristics of the 574 participants are shown in Table 3. The average age was 82.18 years, with 61% being female, 50% currently having a partner, and respectively 48%, 30%, and 22% having had low, middle, and high education. Over the three years of follow-up 24% (N = 139) deceased. For each wave, data was collected by proxy for 12.3–15.3% of the sample. Most participants suffered from rheumatic diseases (63%) and heart- and lung disease (49%), whereas less people had diabetes (16%), CVA (10%), or cancer (23%). Comorbidity was present for 18.5% of the participants, and 43.3% had three or more chronic diseases.

Functional limitations

A model with five trajectories proved to be the best fit for the data. The descriptive statistics per trajectory and the multivariate estimates are shown in Tables 3 and 4, and the trajectory plot and estimated mortality probability are shown in Fig. 1.

Table 4
Multivariate predicted probabilities for the functional limitation trajectories (N = 574)

	1: <i>Continuous low functioning. high mortality</i> (N = 127)			2: <i>Steep decline in functioning. low mortality</i> (N = 34)			3: <i>Steady decline. low mortality</i> (N = 151)			4: <i>Moderately high functioning. low mortality</i> (N = 174)			5: <i>Continuous functioning.</i> (N = 88)
	dy/dx	se.	P-value	dy/dx	se.	P-value	dy/dx	se.	P-value	dy/dx	se.	P-value	dy/dx
Age	0.015***	0.003	< 0.001	0.001	0.002	0.440	0.014***	0.003	< 0.001	-0.014**	0.004	0.001	-0.018***
Female	0.040	0.036	0.263	-0.004	0.023	0.878	0.044	0.041	0.281	-0.017	0.043	0.700	-0.064
Low education (ref.)													
Middle education	-0.039	0.036	0.278	0.004	0.022	0.850	-0.023	0.042	0.578	-0.042	0.043	0.323	0.100**
High education	-0.109**	0.038	0.004	0.031	0.029	0.293	-0.043	0.047	0.367	0.014	0.050	0.781	0.107**
Has a partner	-0.050	0.035	0.152	0.000	0.022	0.991	0.024	0.041	0.554	0.046	0.042	0.269	-0.020
Lung/heart/vascular disease	0.011	0.031	0.710	-0.023	0.020	0.259	0.047	0.036	0.192	0.022	0.038	0.566	-0.058*
Diabetes	0.118*	0.047	0.012	0.019	0.032	0.539	0.029	0.050	0.558	-0.096*	0.047	0.039	-0.071*
CVA	0.143*	0.058	0.013	-0.045*	0.022	0.036	0.081	0.063	0.199	-0.100	0.058	0.083	-0.078
Cancer	-0.080*	0.034	0.018	0.000	0.024	0.999	0.118**	0.045	0.008	0.021	0.044	0.639	-0.059
Rheumatic disease	0.026	0.033	0.435	0.002	0.021	0.913	0.078*	0.037	0.034	-0.045	0.039	0.248	-0.061*
Lives in an institution	0.461***	0.080	< 0.001	0.037	0.054	0.494	-0.117	0.064	0.066	-0.221***	0.063	< 0.001	-0.159***

* Significance at p < 0.05; ** significance at p < 0.01; ***significance at p < 0.001.
N = 574

Tables 3 and 4 about here [included at the end of the document]

The first group, containing 22.3% of the respondents, showed stable low levels of physical functioning: The trajectory started at a mean ADL-score of 15, and stayed at that level for the following waves. Such scores usually indicate that respondents were unable to perform 3 ADL-indicators, but were still able to perform 2 without help, although for some it meant that they had much difficulty performing all of the five ADL-indicators, and needed help with at least one of them. This group had the highest mortality probability per year: 14% at each wave. Older people (dy/dx = 0.015, p < 0.001) and people who lived in an institution (dy/dx = 0.461, p < 0.001) were relatively likely to follow this trajectory, as were people who suffered from diabetes (dy/dx = 0.118, p = 0.012), and CVA (dy/dx = 0.143, p = 0.013) (see Table 4). People with a high education were 10.9% (p = 0.004) less likely compared to those with a low level of education to have a stable level of many ADL disabilities. Participants who had cancer were less likely to follow this trajectory as well (dy/dx=-0.08, p = 0.018).

The second group showed a decline in functioning, followed by a slight recovery in which some of the initial functioning was regained. The decline was steep: over the course of nine months the ADL-score declined from 26 to 15, which is indicative of gaining two severe limitations. At the end of the observation period, the average ADL-score was 17. Relatively few participants followed this trajectory (6.1%), and the mortality probability was stable at 3%. Having suffered a CVA decreased the probability of following this trajectory with 4.5% (p = 0.036), but none of the other covariates were significantly associated with this trajectory.

The third trajectory showed slight decline, and gradually decreased from an average ADL-score of 24 to 19. This trajectory contained 26.1% of the participants, and had a stable mortality probability of 3%. Older people were more likely to follow this trajectory, with 1.4% (p < 0.001) extra for each life year. Participants who suffered from cancer or rheumatic disease were respectively 11.8% (p = 0.008) and 7.8% (p = 0.034) more likely to follow this trajectory.

The fourth trajectory was stable, with an average ADL-score of 27, which indicated being able to perform all ADL-indicators with only a little or no help. The mortality probability was stable at 3%, and 31% of the participants followed this trajectory. Age decreased the probability of following this trajectory with 1.4% (p = 0.001) per year, as did having diabetes (dy/dx= -0.096, p = 0.039). Not living in an institution was statistically significantly associated with this trajectory as well (dy/dx=-0.221, p < 0.001).

The fifth trajectory was stable as well, and the participants (14.6%) in this trajectory experienced no ADL-limitations at all. Older people were less likely to follow this trajectory (dy/dx=-0.018, p < 0.001), as were people that suffered from heart- and lung disease (dy/dx=-0.058, p = 0.041), diabetes (dy/dx=-0.071, p = 0.033), or rheumatic disease (dy/dx=-0.061, p = 0.041). Living in an institution decreased the probability of this trajectory with 15.9% (p < 0.001).

Sensitivity analyses showed that not jointly modelling mortality resulted in different group sizes: 13.8% in the first, 6.6% in the second, 27.7% in the third, 35.4% in the fourth, and 16.5% in the fifth trajectory (see S4 additional file 2). This resulted in overestimations of 2%, 4%, 1.5%, and 0.5% of respectively the highest (G5), moderate (G4), gradual decline (G3), and rapid decline (G2) physical functioning trajectories, and an 8.5% underestimation of the low physical functioning trajectory (G1), compared to the solutions of the models that included mortality.

Cognitive limitations

For cognitive limitations a four-trajectory model, shown together with the mortality plot in Fig. 2, proved to be the best fit. The descriptive statistics per trajectory and the multivariate estimates are shown in Tables 3 and 5.

Table 5
Multivariate predicted probabilities for the cognitive functioning trajectories (N = 574)

	1: <i>Continuous low functioning. high mortality (N = 63)</i>			2: <i>Moderately high functioning. low mortality (N = 254)</i>			3: <i>Declining functioning. moderate mortality (N = 85)</i>			4: <i>Continuous high functioning. low mortality (N = 172)</i>		
	<i>dy/dx</i>	<i>se.</i>	<i>P-value</i>	<i>dy/dx</i>	<i>se.</i>	<i>P-value</i>	<i>dy/dx</i>	<i>se.</i>	<i>P-value</i>	<i>dy/dx</i>	<i>se.</i>	<i>P-value</i>
Age	0.004	0.002	0.060	-0.004	0.004	0.354	0.009**	0.003	0.001	-0.009*	0.004	0.012
Female	-0.022	0.029	0.459	-0.067	0.048	0.157	0.050	0.032	0.122	0.039	0.041	0.342
Low education (ref.)												
Middle education	-0.040	0.028	0.153	-0.048	0.048	0.321	-0.077*	0.033	0.022	0.164***	0.042	< 0.001
High education	-0.022	0.032	0.489	-0.137**	0.053	0.009	-0.113**	0.035	0.001	0.272***	0.050	< 0.001
Has a partner	-0.020	0.028	0.473	-0.050	0.047	0.280	0.023	0.033	0.487	0.047	0.041	0.249
Lung/heart/vascular disease	-0.055*	0.025	0.027	0.039	0.041	0.347	0.015	0.029	0.613	0.001	0.036	0.977
Diabetes	0.021	0.038	0.572	-0.047	0.055	0.399	0.124**	0.047	0.008	-0.098*	0.046	0.034
CVA	0.014	0.043	0.739	0.084	0.068	0.221	0.094	0.053	0.079	-0.192***	0.050	< 0.001
Cancer	0.003	0.030	0.929	-0.068	0.048	0.154	0.044	0.036	0.229	0.022	0.043	0.612
Rheumatic disease	-0.035	0.027	0.193	0.023	0.043	0.587	-0.064*	0.032	0.048	0.076*	0.037	0.039
Lives in an institution	0.373***	0.082	< 0.001	-0.228**	0.075	0.002	0.061	0.063	0.333	-0.205**	0.059	0.001
												N = 574
* Significance at $p < 0.05$; **significance at $p < 0.01$; ***significance at $p < 0.001$.												
N = 574												

Table 5 about here [included at the end of the document]

The first group showed very low cognitive functioning across time, the trajectory started at the threshold for dementia (11) with a mean sMMSE of 11. The trajectory showed no further decline, but it could be argued that given the low baseline scores, there was little further decline possible for this group. Containing 10.8% of the sample, this group was the smallest of the four trajectories. The mortality probability was continuously high at 14%. Age, although showing a positive direction, was not significantly statistically associated with this trajectory ($dy/dx = 0.004$, $p = 0.060$, which might be explained by the low power of this study. Suffering from heart- and lung disease decreased the probability of this trajectory with 5.5% ($p = 0.027$), while living in an institution increased the probability with 37.3% ($p < 0.001$).

The second group, containing 43% of the participants, started at a mean sMMSE of 14, slightly increased to 15, and then decreased to 14. It had a stable mortality probability of 4%. People with a high education, or people that lived in an institution were respectively 13.7% ($p = 0.009$) and 22.8% ($p = 0.002$) significantly less likely to follow this trajectory.

The third trajectory (16%) showed decline, decreasing from probable mild cognitive impairment (sMMSE = 13) to probable dementia (sMMSE = 11). The mortality probability was quite high: 9%. Being older increased the probability of this trajectory ($dy/dx = 0.009$, $p = 0.001$), as did having diabetes ($dy/dx = 0.124$, $p = 0.008$). Having had a middle or high education decreased the probability of this trajectory with 7.7% ($p = 0.022$) and 11.3% ($p = 0.001$), as did having rheumatic disease ($dy/dx = -0.064$, $p = 0.048$).

The last trajectory showed continuous high cognitive functioning combined with a low mortality probability (2%), and contained 30.3% of the participants. Older age decreased the probability of this trajectory ($dy/dx = -0.009$, $p = 0.012$), as did having diabetes ($dy/dx = -0.098$, $p = 0.034$), CVA ($dy/dx = -0.192$, $p < 0.001$), or living in an institution ($dy/dx = -0.205$, $p = 0.001$). People with a middle or high education respectively had a 16.4% ($p < 0.001$) and 27.2% ($p < 0.001$) higher probability of following this trajectory, and people with rheumatic disease were 7.6% ($p = 0.039$) more likely to experience continuous high cognitive functioning.

Not jointly modelling mortality resulted in the following group sizes: 5.7% in the first, 47.5% in the second, 8.9% in the third, and 37.9% in the fourth trajectory. The high (G4) and moderate (G2) cognitive functioning trajectories would have been overestimated with 7.2% and 4.5%, while the declining (G3) and low (G1) trajectories would have been underestimated with 7% and 5%. In the analysis with mortality jointly estimated the declining trajectory (G3) was also steeper, with similar starting scores at wave 1 (sMMSE-score of 14), but slightly different end scores: 12 for the survivors and 11 for the whole sample.

Overlap between the trajectories

Figures 3 and 4 show overlap between the trajectories of functioning. A certain coherence is visible: people in the adverse physical functioning trajectories experience low cognitive functioning more often, and people experiencing high physical functioning often experience high cognitive functioning. However, there is also still substantial variation, since 22% of people with high cognitive function experience a trajectory with severe ADL-limitations. The picture for the declining physical trajectory shows little correlation with cognition: the percentages of the cognitive trajectories are distributed almost evenly over this group.

Discussion

This study identified trajectories in both physical and cognitive functioning among Dutch older adults aged 75 and older. Using the innovative methodology of Group-Based Trajectory Modelling, modelling trajectories jointly with mortality, we were able to estimate more precise group sizes. We identified five trajectories in functional limitations and four trajectories in cognitive decline. A considerable proportion of the Dutch 75+ experienced high levels of functioning over the course of three years. For physical functioning, 15% of the sample experienced continuous high levels of physical functioning, and 31% of the sample experienced high moderate physical functioning. As for cognitive functioning, 30% of the sample experienced high cognitive functioning and 43% experienced moderately high cognitive functioning. But, adverse trajectories were present as well. For the physical functioning trajectories, 26% of the participants experienced moderate decline and 6% experienced steep decline followed by slight recovery. For cognitive functioning 16% experienced rapid cognitive decline. The most adverse trajectories showed continuous low physical functioning with at least 2 severe ADL-limitations (22%), and continuous low cognitive functioning (11%) with probable dementia. These trajectories had high mortality levels (~14%). The declining and low functioning trajectories are the trajectories where the requirement for care is probably highest.

Despite our study using shorter time intervals, examining older participants, and incorporating mortality risk, the trajectories seem to reflect patterns that were also identified in previous studies on trajectories of functioning in old age. Among populations of the same age group similar trajectories were identified (10, 13). Whereas our relatively old study sample resulted in a low trajectory for cognition, that is not identified among younger study samples (7, 8), but is also identified among older study samples (39, 40). It can be concluded that our study corroborates that there is considerable diversity in health trajectories among the 75-plus.

Taking mortality into account resulted in bigger group sizes for the more adverse trajectories, while it led to smaller group sizes for the more favourable trajectories, which is in line with what could be expected based on the studies conducted by Haviland et al. (23) and Zimmer et al. (41), who used the same methodology. However, although we expected that modelling mortality would result in bigger group sizes for the trajectories that showed decline, this was only the case for cognitive decline, but not modelling mortality only resulted in a very slight underestimation of the declining functional limitation trajectories. This is in line with previous studies reporting very low mortality probabilities for people with increasing functional limitations (18).

The second aim of our study was to explore how the trajectories varied for several background variables (gender, age, level of education and partner status) and types of diseases. What is clear from these results is that the persons following the three most favourable trajectories (with either high or high moderate levels of physical functioning, or high levels of cognitive functioning) had rather favourable characteristics. They were younger, middle or high educated, lived independently, and did not have diabetes or heart- and lung disease.

Yet, there was no common denominator between the people following the three declining trajectories. Older age, having cancer, or rheumatic disease increased the probability of the steady declining physical functioning trajectory, which is understandable as these chronic diseases in more advanced stages limit mobility. Older age also increased the chance of cognitive decline, as did having a low education, or diabetes. The link with diabetes can be explained by the adverse effects of hyperglycaemia, inflammatory cytokines, and neuropathic processes (42). Having suffered a stroke reduced the chance of steep decline in physical functioning, but increased the chance of continuous functional limitations. This shows the severe debilitating effects of CVA, since it reduces the level of functioning in such a severe way that the chance of following a trajectory that starts with high functioning is rather low (18). The finding that CVA is only (negatively) associated with high cognitive functioning is in line with previous findings that CVA does not necessarily lead to dementia, but reduces cognitive functioning, thereby resulting in mild cognitive impairment for most (43, 44). People experiencing mild cognitive impairment are likely to be found in all other three cognition trajectories (45), which probably leads to the absence of other associations.

While rheumatic diseases increased the chance of gradually declining physical functioning, a finding also reported by for example Botes et al. (46), they also increased the probability of high levels of cognitive functioning. This positive relation between rheumatic diseases and cognition has been widely studied, and despite the growing body of evidence suggesting that aspirin does not have a protective effect on cognition (47, 48), studies do indicate that non-steroidal anti-inflammatory drugs (NSAIDs) decrease the risk of cognitive decline (49).

As expected based on previous studies, living in an institution, having diabetes and/or CVA were significantly associated with the two trajectories of poor functioning: with severe functional limitations, and with severe cognitive problems (45, 46, 50). In addition, people who suffered from heart- and lung disease were more likely to have continuous cognitive dysfunction. Also, being older or low educated increased the probability of having a continuously high number of functional limitations, but not of low cognitive functioning. This might be due to the inclusion of 'being institutionalized' as an explanatory variable. This variable might have led to a stronger attenuation of the associations of age and education for severe cognitive decline than for severe functional limitations, since severe cognitive decline leads to institutionalization more often than severe functional limitations do. All in all, these trajectories seem to contain

persons that experienced the deleterious effects of chronic diseases, and about half of them had to be taken into residential care due to the resulting limitations.

Associations for sex were not present. Although previous studies stratified by sex a priori (7, 41), stratifying by sex would have reduced our statistical power substantially due to our small sample. However, analysis stratified by sex showed comparable trajectories for men and women (see figures S2 and S3 in additional file 2). The absence of sex differences might be explained by the finding that these differences are most pronounced in the level of functional impairment, while rates of change are similar for men and women (51). It could be possible that due to our shorter measurement intervals the rate of change has had a bigger impact in defining the trajectories. On the other hand, the absence of sex differences is not entirely anomalous; for functional limitations Bolano et al. (52) and Holstein et al. (53) do not report any statistically significant sex differences, and Comijs et al. (8) do not always identify sex differences for trajectories in cognition. Moreover, our analyses included mortality, various diseases, age and level of education, which are all factors that differ by sex, which may have decreased the effect of sex itself to non-significance.

Low education being associated with low levels of physical functioning is a finding also reported by Boyd et al. (54) and Kingston et al. (13). The finding that education is negatively associated with moderate or declining levels of cognitive functioning, and positively associated with high cognitive functioning, corroborates the link between education and cognition. Furthermore, it is partly in line with the MMSE being less sensitive for cognitive decline among higher educated people (55), but also in line with education having a protective effect on cognitive decline (56), and people having more cognitive capacities having pursued more education.

Associations for partner status were absent. This might have been caused by not differentiating between coresiding and noncoresiding partners. Second, it is possible that the protective effect of having a partner diminishes with age, since this usually results in the partner requiring more care as well. Lastly, studying a population that could be either institutionalized or community-dwelling might have resulted in absent associations for partner status.

Strengths and Limitations

The main strength of this study was the use of the 75PLUS LASA-data, containing a representative sample of the Dutch oldest old: the study has a high response and cooperation rate, and enabled for studying both community dwelling and institutionalized people. Accounting for attrition by jointly modelling mortality is a strength as well, enabling us to estimate the group sizes correctly. Third, defining ADL as a scale forms a strength in opposition to previous studies that compressed the range of the severity of ADL-limitations by dichotomizing ADL. Because the overall degree of limitations decides the need for care, it is precisely this degree that is of vital importance for policymakers, and by measuring ADL as a scale we were better at capturing the existence and the range of need for care that follow from functional limitations.

The first limitation of the study was not being able to conduct a multi-trajectory model to study the interconnectedness between cognitive decline and ADL-limitations that is implied by previous studies (57, 58). We instead decided to report the estimates of the trajectories separately, since jointly modelling mortality in a multi-trajectory model was not possible, and accounting for decease is necessary in a very old population. Second, although the use of proxy data allowed us to also include severely cognitively impaired respondents, this resulted in two different measurements for cognition (the sMMSE and the IQCODE) (31). Although different ways of harmonizing did not affect the trajectories much, the absence of guidelines on how to harmonize the sMMSE and IQCODE leaves some uncertainty on whether the eventual scores are an accurate reflection of cognitive functioning among our participants. Although we did not have a considerable amount of missing items for ADL or sMMSE, we are mindful of the slight overestimation of both cognitive and ADL-levels in which the imputation of these items might have resulted. On the flip side, not including these participants in the analysis would have likely resulted in an overestimation of favourable trajectories as well. Third, although our sample size was sufficient for performing analyses, analysing a bigger sample size would have allowed for performing all of the analysis stratified by sex, and would have increased statistical power.

Implications

This study has implications for policymakers in health and long term care. Despite this study showing that a considerably large group experiences little to no functional limitations and/ or cognitive decline, this study also identifies groups that, based on their low or declining levels of physical and cognitive functioning, have a high or increasing care need. The trajectories corresponding to the highest requirements of care are the two stable low trajectories (11–22%), and part of those groups are already living in residential care. This simultaneously shows how half of these people apparently have a high requirement of care, but do still live in independent housing, probably with a large demand on care from informal and formal caregivers. The declining trajectories (6%, 16%, 26%) are of most interest due to the increasing care need over time. This increase makes this group vital for policies aimed at future care planning, since they require more adjustments in care provision than the stable trajectories do. Our study does not provide one indicator to target all these groups, but shows old age, low education, diabetes, and CVA as the best indicators for targeting risk groups. Previous studies and policymakers should aim at finding indicators to identify the people that experience declines in functioning.

Conclusions

Our study underscores the diversity in health trajectories among the older old. Most Dutch 75-plus had high levels of functioning. Yet, about a quarter of the respondents experienced moderate functional decline, while 6% and 16% experienced rapid functional and cognitive decline. A small part experienced very low levels of functioning: 22% and 11% experienced severe functional limitations or cognitive limitations with probable dementia and high mortality probabilities. The findings show that chronic diseases impact physical and cognitive functioning differently, with diabetes mostly contributing to decline. Older age, low education, diabetes and CVA should be the predictors policymakers use for future care planning and identifying people at risk for adverse functioning. A small percentage of the Dutch oldest old lives independently while having a high care requirement, and a considerable number of people has an increasing care need. It is important to identify whether the groups with currently high and an increasing care requirement get the care they need.

Abbreviations

ADL: Activities of daily living; AME: Average marginal effects; CVA: Cerebrovascular accidents; GBA: Gemeentelijke basisadministratie; LASA: Longitudinal Aging Study Amsterdam; sMMSE: short Mini Mental State Examination

Declarations

Ethics approval and consent to participate

The LASA study was approved by The VU University Medical Centre's Medical Ethics Evaluation Committee, and was conducted in line with the Declaration of Helsinki. All participants gave written informed consent.

Consent for publication

Not applicable.

Availability of data and materials

Anonymized participant-level data can be requested from LASA using a standard analysis proposal form, available through http://www.lasa-vu.nl/data/availability_data/availability_data.htm.

Competing interests

The authors declare that they have no competing interest.

Funding

The Longitudinal Aging Study Amsterdam was supported by a grant from the Dutch Ministry of Health, Welfare and Sports, Directorate of Long-Term Care. *The first author (MG) was supported by a research grant of the Wetenschappelijk Instituut 50PLUS in the Netherlands.*

Authors' contributions

All authors made substantial contributions to conception (MH, MB, EM, MG), design (MH, MB, EM, MG), interpretation of the data (MH, MB, EM, MG), and preparation of the manuscript (MH, MB, EM, MG). MH was involved in the design of the Longitudinal Aging Study Amsterdam and was responsible for the data collection. MG prepared the data, performed statistical analyses, and wrote the first and final draft of the manuscript. All authors (MH, MB, EM, MG) contributed to and approved the final version.

Acknowledgements

The authors wish to thank Bobby Jones, Martijn Heymans, and Mariska van der Horst for their statistical advice.

Authors' information (optional)

Maura K.M. Gardeniers¹, Marjolein I. Broese van Groenou¹, Erik-Jan Meijboom¹, Martijn Huisman^{1,2}

¹Vrije Universiteit Amsterdam, Department of Sociology, De Boelelaan, 1081 Amsterdam, The Netherlands. ²Amsterdam UMC, Vrije Universiteit Amsterdam, Department of Epidemiology & Biostatistics, Amsterdam Public Health research institute, De Boelelaan, 1117 Amsterdam, Netherlands.

References

1. World Health Organization. World report on ageing and health. Geneva, Switzerland; 2015.
2. Centraal Bureau voor de Statistiek. Gezondheid en zorggebruik; persoonskenmerken [Internet]. Statline. 2019 [cited 2019 Nov 16]. Available from: <https://opendata.cbs.nl/statline/#/CBS/nl/dataset/83005ned/table?fromstatweb>
3. Crimmins EM, Beltrán-Sánchez H. Mortality and morbidity trends: Is there compression of morbidity? *J Gerontol - Ser B Psychol Sci Soc Sci.* 2011;66 B(1):75–86.
4. Deeg DJH, Comijs HC, Hoogendijk EO, Van Der Noordt M, Huisman M. 23-year trends in life expectancy in good and poor physical and cognitive health at age 65 years in the Netherlands, 1993-2016. *Am J Public Health.* 2018;108(12):1652–8.

5. Heger D, Kolodziej I. Changes in Morbidity over Time - Evidence from Europe [Internet]. 2016 [cited 2020 Apr 29]. Available from: <http://nbn-resolving.de/urn:nbn:de:101:1-201609219272>
6. Rijksinstituut voor Volksgezondheid en Milieu. Volksgezondheid Toekomst Verkenning [Internet]. VTV-2018. 2018. Available from: <https://www.rivm.nl/bibliotheek/rapporten/270241002.pdf>
7. Kok AAL, Aartsen MJ, Deeg DJH, Huisman M. Capturing the Diversity of Successful Aging: An Operational Definition Based on 16-Year Trajectories of Functioning. *The Gerontologist*. 2015 Sep 1;53(5):927–937.
8. Comijs HC, Dik MG, Deeg DJH, Jonker C. The Course of Cognitive Decline in Older Persons: Results from the Longitudinal Aging Study Amsterdam. *Dement Geriatr Cogn Disord*. 2004;17(3):136–42.
9. Deeg DJ. Longitudinal characterization of course types of functional limitations. *Disabil Rehabil*. 2005 Mar;27(5):253–61.
10. Gill TM, Gahbauer EA, Lin H, Han L, Allore HG. Comparisons Between Older Men and Women in the Trajectory and Burden of Disability Over the Course of Nearly 14 Years. *J Am Med Dir Assoc*. 2013 Apr;14(4):280–6.
11. Han L, Allore H, Murphy T, Gill T, Peduzzi P, Lin H. Dynamics of functional aging based on latent-class trajectories of activities of daily living. *Ann Epidemiol*. 2013 Feb 1;23(2):87–92.
12. Hu X, Gu S, Sun X, Gu Y, Zhen X, Li Y, et al. Cognitive ageing trajectories and mortality of Chinese oldest-old. *Arch Gerontol Geriatr*. 2019 May 1;82:81–7.
13. Kingston A, Davies K, Collerton J, Robinson L, Duncan R, Kirkwood TBL, et al. The enduring effect of education-socioeconomic differences in disability trajectories from age 85 years in the Newcastle 85+ Study. *Arch Gerontol Geriatr*. 2015 May 1;60(3):405–11.
14. Martin LG, Zimmer Z, Lee J. Foundations of Activity of Daily Living Trajectories of Older Americans. *J Gerontol B Psychol Sci Soc Sci*. 2017 Jan;72(1):129–39.
15. Min JW. A longitudinal study of cognitive trajectories and its factors for Koreans aged 60 and over: A latent growth mixture model. *Int J Geriatr Psychiatry*. 2018;33(5):755–62.
16. Nusselder WJ, Looman CWN, Mackenbach JP. Nondisease factors affected trajectories of disability in a prospective study. *J Clin Epidemiol*. 2005 May;58(5):484–94.
17. Proust C, Jacqmin-Gadda H. Estimation of linear mixed models with a mixture of distribution for the random effects. *Comput Methods Programs Biomed*. 2005 May;78(2):165–73.
18. Taylor MG, Lynch SM. Cohort Differences and Chronic Disease Profiles of Differential Disability Trajectories. *J Gerontol B Psychol Sci Soc Sci*. 2011 Nov 1;66B(6):729–38.
19. Terrera GM, Brayne C, Matthews F, CC75C Study Collaboration Group. One size fits all? Why we need more sophisticated analytical methods in the explanation of trajectories of cognition in older age and their potential risk factors. *Int Psychogeriatr*. 2010 Mar;22(2):291–9.
20. Timmermans EJ, Huisman M, Kok AAL, Kunst AE. Smoking Cessation and 16-year Trajectories of Functional Limitations Among Dutch Older Adults: Results from the Longitudinal Aging Study Amsterdam. *J Gerontol Ser A*. 2018 Nov 10;73(12):1722–8.
21. van Houwelingen AH, Cameron ID, Gussekloo J, Putter H, Kurlle S, de Craen AJM, et al. Disability transitions in the oldest old in the general population. The Leiden 85-plus study. *AGE*. 2014 Feb;36(1):483–93.
22. Lafortune L, Béland F, Bergman H, Ankrj J. Health status transitions in community-living elderly with complex care needs: a latent class approach. *BMC Geriatr*. 2009 Feb 3;9(1):6.
23. Haviland AM, Jones BL, Nagin DS. Group-Based Trajectory Modeling Extended to Account for Nonrandom Participant Attrition. In 2011.
24. Hoogendijk EO, Deeg DJH, Poppelaars J, van der Horst M, Broese van Groenou MI, Comijs HC, et al. The Longitudinal Aging Study Amsterdam: cohort update 2016 and major findings. *Eur J Epidemiol*. 2016;31(9):927–45.
25. Hoogendijk EO, Deeg DJH, Breij S de, Klokgieters SS, Kok AAL, Stringa N, et al. The Longitudinal Aging Study Amsterdam: cohort update 2019 and additional data collections. *Eur J Epidemiol* [Internet]. 2019 Jul 25 [cited 2020 Jun 14]; Available from: <https://research.vumc.nl/en/publications/the-longitudinal-aging-study-amsterdam-cohort-update-2019-and-add>
26. Huisman M, Poppelaars J, van der Horst M, Beekman AT, Brug J, van Tilburg TG, et al. Cohort Profile: The Longitudinal Aging Study Amsterdam. *Int J Epidemiol*. 2011 Aug 1;40(4):868–76.
27. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". *J Psychiatr Res*. 1975 Nov;12(3):189–98.
28. Tombaugh TN, McIntyre NJ. The Mini-Mental State Examination: A comprehensive review. *J Am Geriatr Soc*. 1992;40(9):922–35.
29. Jorm AF. The Informant Questionnaire on cognitive decline in the elderly (IQCODE): a review. *Int Psychogeriatr*. 2004 Sep;16(3):275–93.
30. Chiriboga DA, McHugh D, Sweeney MA. The Mini-Mental Exam (Mini-ME). *Clin Gerontol* [Internet]. 2008 Oct 3 [cited 2020 May 6]; Available from: https://www.tandfonline.com/doi/pdf/10.1300/J018v27n01_02
31. Mackinnon A, Khalilian A, Jorm AF, Korten AE, Christensen H, Mulligan R. Improving screening accuracy for dementia in a community sample by augmenting cognitive testing with informant report. *J Clin Epidemiol*. 2003 Apr;56(4):358–66.
32. Halpin B. Multiple Imputation for Life-Course Sequence Data [Internet]. 2012 [cited 2020 Jun 4]. (University of Limerick Department of Sociology Working Paper Series;WP2012-01). Available from: </paper/Multiple-Imputation-for-Life-Course-Sequence-Data-Halpin/332bc1aa1a4dd97ae65dbb8824d4921a0a0cd39b>
33. Jones BL, Nagin DS, Roeder K. A SAS Procedure Based on Mixture Models for Estimating Developmental Trajectories: *Sociol Methods Res* [Internet]. 2001 [cited 2020 Jun 15];29(3). Available from: <https://journals.sagepub.com/doi/10.1177/0049124101029003005>

34. Jones BL, Nagin DS. A Note on a Stata Plugin for Estimating Group-based Trajectory Models: *Sociol Methods Res* [Internet]. 2013 Sep 30 [cited 2020 Jun 15]; Available from: <https://journals.sagepub.com/doi/10.1177/0049124113503141>
35. Raftery AE. Bayesian Model Selection in Social Research. *Sociol Methodol*. 1995;25:111–63.
36. Jones BL, Nagin DS. Advances in group-based trajectory modeling and an SAS procedure for estimating them. *Sociol Methods Res*. 2007;35(4):542–71.
37. Jones BL. traj: group-based modeling of longitudinal data [Internet]. [cited 2020 Aug 29]. Available from: <https://www.andrew.cmu.edu/user/bjones/documentation.htm>
38. Jann B. Predictive Margins and Marginal Effects in Stata. In *Potsdam*; 2013. p. 65.
39. Han ES, Lee Y, Kim J. Association of cognitive impairment with frailty in community-dwelling older adults. *Int Psychogeriatr*. 2014 Jan;26(1):155–63.
40. Hu X, Gu S, Sun X, Gu Y, Zhen X, Li Y, et al. Cognitive ageing trajectories and mortality of Chinese oldest-old. *Arch Gerontol Geriatr*. 2019 May 1;82:81–7.
41. Zimmer Z, Martin LG, Nagin DS, Jones BL. Modeling Disability Trajectories and Mortality of the Oldest-Old in China. *Demography*. 2012 Feb;49(1):291–314.
42. Chiu C-J, Wray LA, Ofstedal MB. Diabetes-related change in physical disability from midlife to older adulthood: Evidence from 1996–2003 Survey of Health and Living Status of the Elderly in Taiwan. *Diabetes Res Clin Pract*. 2011 Mar 1;91(3):413–23.
43. Levine DA, Galecki AT, Langa KM, Unverzagt FW, Kabeto MU, Giordani B, et al. Trajectory of Cognitive Decline After Incident Stroke. *JAMA*. 2015 Jul 7;314(1):41–51.
44. Tham W, Auchus AP, Thong M, Goh M-L, Chang H-M, Wong M-C, et al. Progression of cognitive impairment after stroke: One year results from a longitudinal study of Singaporean stroke patients. *J Neurol Sci*. 2002 Nov 15;203–204:49–52.
45. Comijs HC, Kriegsman DMW, Dik MG, Deeg DJH, Jonker C, Stalman WAB. Somatic chronic diseases and 6-year change in cognitive functioning among older persons. *Arch Gerontol Geriatr*. 2009 Apr;48(2):191–6.
46. Botes R, Vermeulen KM, Correia J, Buskens E, Janssen F. Relative contribution of various chronic diseases and multi-morbidity to potential disability among Dutch elderly. *BMC Health Serv Res*. 2018 Dec;18(1):24.
47. Ryan J, Storey E, Murray AM, Woods RL, Wolfe R, Reid CM, et al. Randomized placebo-controlled trial of the effects of aspirin on dementia and cognitive decline. *Neurology*. 2020 Jul 21;95(3):e320–31.
48. Veronese N, Stubbs B, Maggi S, Thompson T, Schofield P, Muller C, et al. Low-Dose Aspirin Use and Cognitive Function in Older Age: A Systematic Review and Meta-analysis. *J Am Geriatr Soc*. 2017 Aug;65(8):1763–8.
49. Wang W, Sun Y, Zhang D. Association Between Non-Steroidal Anti-Inflammatory Drug Use and Cognitive Decline: A Systematic Review and Meta-Analysis of Prospective Cohort Studies. *Drugs Aging*. 2016 Jul;33(7):501–9.
50. Marengoni A, Angleman S, Melis R, Mangialasche F, Karp A, Garmen A, et al. Aging with multimorbidity: A systematic review of the literature. *Ageing Res Rev*. 2011 Sep 1;10(4):430–9.
51. Liang J, Bennett JM, Shaw BA, Quiñones AR, Ye W, Xu X, et al. Gender Differences in Functional Status in Middle and Older Age: Are There Any Age Variations? *J Gerontol Ser B*. 2008 Sep 1;63(5):S282–92.
52. Bolano D, Berchtold A, Bürge E. The Heterogeneity of Disability Trajectories in Later Life: Dynamics of Activities of Daily Living Performance Among Nursing Home Residents. *J Aging Health*. 2019 Aug 1;31(7):1315–36.
53. Holstein BE, Due P, Almind G, Avlund K. Eight-year change in functional ability among 70- to 95-year-olds. *Scand J Public Health*. 2007 May 1;35(3):243–9.
54. Boyd CM, Ricks M, Fried LP, Guralnik JM, Xue Q-L, Bandeen-Roche K. Functional Decline and Recovery of Activities of Daily Living among Hospitalized, Disabled Older Women: The Women's Health and Aging Study I. *J Am Geriatr Soc*. 2009 Oct;57(10):1757–66.
55. Aevarsson Ó, Skoog I. A Longitudinal Population Study of the Mini-Mental State Examination in the Very Old: Relation to Dementia and Education. *Dement Geriatr Cogn Disord*. 2000;11(3):166–75.
56. Anstey K, Christensen H. Education, activity, health, blood pressure and apolipoprotein E as predictors of cognitive change in old age: a review. *Gerontology*. 2000 Jun;46(3):163–77.
57. Braungart Fauth E, Zarit SH, MalMBERG B, Johansson B. Physical, Cognitive, and Psychosocial Variables From the Disablement Process Model Predict Patterns of Independence and the Transition Into Disability for the Oldest-Old. *The Gerontologist*. 2007 Oct 1;47(5):613–24.
58. Mansbach WE, Mace RA. Predicting Functional Dependence in Mild Cognitive Impairment: Differential Contributions of Memory and Executive Functions. *The Gerontologist*. 2019 Sep 17;59(5):925–35.

Figures

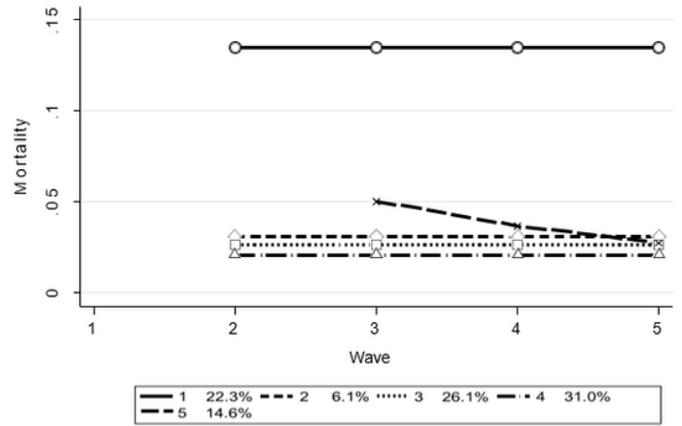
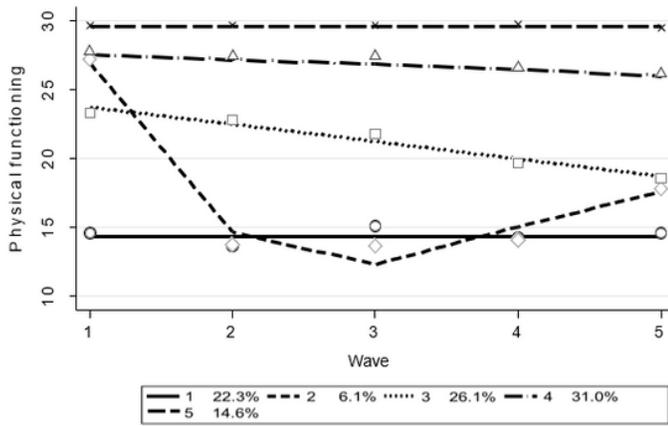


Figure 1

Trajectories in functional limitations (left, and mortality probability (right) by age (N=574).

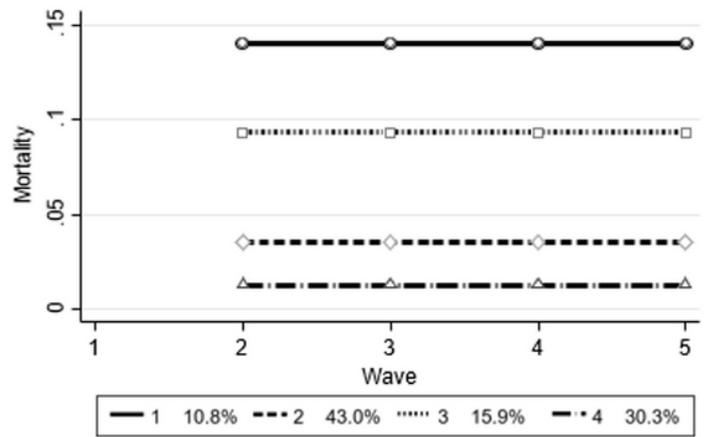
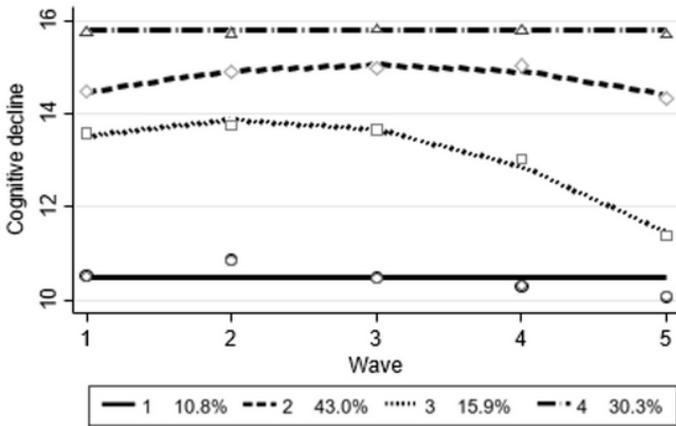


Figure 2

Trajectories in cognitive decline (left, and mortality probability (right) by age (N=574).

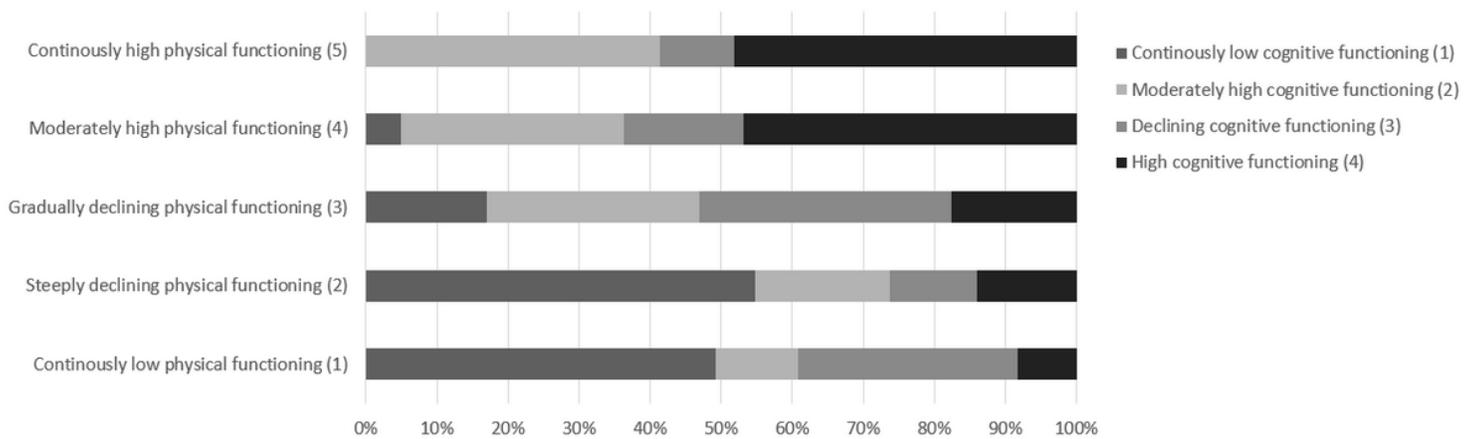


Figure 3

Overlap between functional limitations trajectories and cognitive trajectories: percentage of people in cognitive functioning trajectory per functional limitations trajectory.

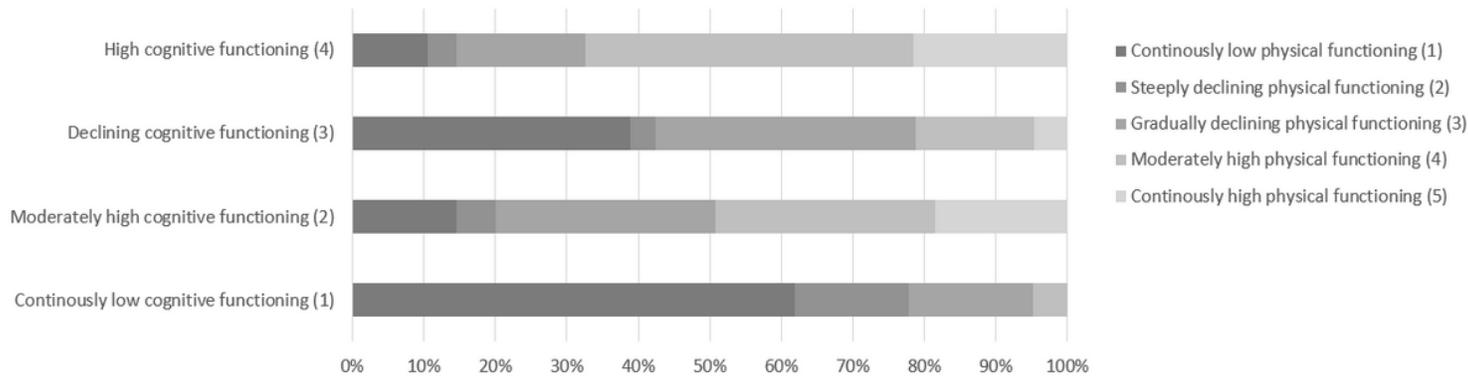


Figure 4
 Overlap between functional limitations trajectories and cognitive trajectories: percentage of people in functional limitations trajectory per cognitive functioning trajectory

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Additionalfile1Threeyeartrajectoriesinfunctionallimitationsandcognitivedecline.docx](#)
- [Additionalfile2Threeyeartrajectoriesinfunctionallimitationsandcognitivedecline.docx](#)