Supplementary Material

Distinct Cognitive Trajectories in Late Life and Associated Predictors and Outcomes: A Systematic Review

Methods

Protocol registration

The protocol of this systematic review was registered with the International Prospective Register of Systematic Reviews (PROSPERO) (registration ID: CRD42020156754). The study was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement and followed the PRISMA checklist [1] (Supplementary Table 5).

Eligibility criteria

Any studies involving human adults (18 years or above) in the general population were eligible. Studies exclusively involving participants at high risk of unfavorable health outcomes or specific patient samples (e.g., individuals with dementia, cognitive impairment, cancer, vascular or psychiatric diseases) were not eligible. There were no selection criteria related to gender or ethnicity.

Studies were eligible if they investigated trajectories of cognitive function with a prospective/longitudinal design. A cognitive trajectory was defined as the course of cognitive function over time or age, including assessing cognitive function using three or more waves of data. Eligible studies must also have two or more classes of cognitive trajectories identified with a hypothesis-free and data-driven approach, rather than based on any pre-specified factor (i.e.,

male versus female). There was no restriction on the cognitive domain, which was assessed, nor the test used for the assessment.

For studies that investigated the association between cognitive trajectories and specific predictive factors, there was no restriction on what factors were included. The predictive factors to be analyzed could range from demographics, socioeconomic factors, lifestyle and health behaviors, to genetic factors and biomarkers.

Search strategies

A systematic search was conducted in two databases via Ovid, MEDLINE and EMBASE, from inception until 6 November 2019. After consultation with a professional librarian, a wide range of keywords and subject headings were used including 1) cognition, cognitive function, 2) trajectory, classification, subgroup, maintain or pattern, 3) longitudinal, prospective, longitudinal or follow-up. The literature search was restricted to human studies published in English. The detailed search strategies are presented in Supplementary Table 1.

Study selection

Three reviewers (ZW, AZZP, and TA) independently conducted initial screening based on the titles and abstracts. ZW screened all the identified articles. AZZP and TA screened a subsample of 60% and 40% respectively in parallel. Articles preliminarily meeting the selection criteria were further assessed by full-text reading. Discrepancies of the screening results between the three reviewers were resolved through discussion and consultation with a fourth reviewer (JR).

Information extraction

Three reviewers independently extracted the relevant information from each eligible article using a standardized data extraction form. This included information on 1) place of recruitment and name of the study, 2) the characteristics of the study sample (size, age, gender, ethnicity), 3) inclusion criteria of the studies and their source cohorts, 4) methods of cognitive assessment, 5) number of waves cognitive function was assessed, 6) maximum length of follow-up, 7) statistical methods, 8) number and description of trajectory classes, 9) factors considered, 10) predictors or outcomes associated with the patterns of trajectories. Discrepancies were resolved by discussion and consultation.

Quality assessment

Quality of each selected study was assessed using a modified version of the Newcastle-Ottawa Scale (NOS) for cohort studies [2]. The NOS is a star-based scale commonly used to assess the risk of bias in terms of several aspects including the selection of participants, accuracy of exposure ascertainment and outcome measurement, comparability between subgroups, demonstration of temporality, and follow-up and attrition. A higher number of stars indicates higher quality and lower risk of bias. A modified NOS was used for quality assessment so that it would be more applicable to the types of studies included in this review.

Data synthesis

There was high heterogeneity across the included studies, especially in terms of the tools used for cognitive assessment (over 10 different cognitive tests and 17 composite scores, measured at different time-points), methodology used to determine the trajectories (the latent class growth

analysis follows a flexible framework in which the modelling parameters are pre-specified and largely dependent on the research assumptions), as well as the predictors and outcomes associated with cognitive trajectories. Therefore, a meta-analysis could not be undertaken and a narrative synthesis of the main findings is presented.

Supplementary Table 1. Search strategies

MEDLINE
1. exp Cognition/ or exp Cognition Disorders/ or cognit*.mp.
2. ((((((((((trajector* adj5 cognit*) or classif*) adj4 cognit*) or class$2) adj4 cognit*) or subgroup*) adj4 cognit*) or maintain*) adj3 cognit*) or pattern*) adj3 cognit*).mp.
3. exp Longitudinal Studies/ or exp Prospective Studies/ or exp Cohort Studies/ or exp Follow-Up Studies/ or (longitudinal or prospective or cohort or follow up).mp.
4. (infant* or infancy or child or children or pregnant wom#n or pregnancy or perinatal or pediatric).mp.
5. 1 and 2 and 3
6. 5 not 4
7. exp animals/ not humans.sh.
8. 6 not 7
9. limit 8 to English language

EMBASE
1. exp cognition/ or exp cognitive defect/ or cognit*.mp.
2. ((((((((((trajector* adj5 cognit*) or classif*) adj4 cognit*) or class$2) adj4 cognit*) or subgroup*) adj4 cognit*) or maintain*) adj3 cognit*) or pattern*) adj3 cognit*).mp.
3. exp longitudinal study/ or exp prospective study/ or exp cohort analysis/ or exp follow up/ or (longitudinal or prospective or cohort or follow up).mp.
4. (infant* or infancy or child or children or pregnant wom#n or pregnancy or perinatal or pediatric).mp.
5. 1 and 2 and 3
6. 5 not 4
7. (exp animal/ or nonhuman/) not exp human/
8. 6 not 7
9. limit 8 to English language

Supplementary Table 2. Studies excluded from full-text assessment

Reason for exclusion	Study
Not trajectory analysis (n=12)	
	Clouston SAP et al. [3]
	Huang F et al. [4]
	Newman AB et al. [5]
	Bott NT et al. [6]
	Aiken-Morgan AT et al. [7]
	Zammit AR et al. [8]
	Zammit AR et al. [9]
	Zammit AR et al. [10]
	Seil K et al. [11]
	Hayden KM et al. [12]
	de Frias CM et al. [13]
	Burns RA et al. [14]
No classification of the participants (n=7)	
	Luo Y et al. [15]
	Clarke PJ et al. [16]
	MacDonald SW et al. [17]
	Yamada M et al. [18]
	Beydoun MA et al. [19]
	Murayama H et al. [20]
	Sweet RA et al. [21]
Classification based on pre-specified factor(s) (n=9)	
	Tampubolon G et al. [22]
	Dodge HH et al. [23]
	Hill TD et al. [24]
	Armstrong JJ et al. [25]
	Aiken-Morgan AT et al. [26]
	Racine AM et al. [27]
	Stephan BCM et al. [28]
	Okereke OI et al. [29]
	Li G et al. [30]
Not trajectory of cognitive function (n=2)	
	Hughes TF et al. [31]
	Liang J et al. [32]
Non-general population (n=7)	
	Sun N et al. [33]
	Laukka EJ et al. [34]
	Molsberry SA et al. [35]
	Popov M et al. [36]
	Baker E et al. [37]
	Hulur G et al. [38]
	Agrinier N et al. [39]

Supplementary Table 3. Associated factors of cognitive trajectories

Authors	Association analysis	Factors considered	Associated factors
Terrera et al. [40]	n.s.	Baseline coefficient estimates: age, gender, education, mobility Follow-up covariates: dropout and death	• Coefficient estimates (class-specific) Good performers with smooth decline: older age (-), female (-), higher education (+) Moderate cognitively impaired with constant sharp decline: older age (-) Cognitively impaired with sharp and changing decline: older age (-), good mobility (+)
Howrey et al. [41]	Logistic regression models	Baseline class membership: age, gender, education, language of interview, nativity, diabetes, overweight, obese, hypertension Baseline coefficient estimates: social support, married status, financial strain, depression, ADLs, heart attack, stroke, church attendance	• Class membership Stable: reference group Slow decline: older age (+), vision impairment (+), female (-), higher education (-), obese (-) Rapid decline: older age (+), vision impairment (+), female (-), higher education (-), overweight (-), obese (-) • Coefficient estimates (class-specific) Stable: married (+), church attendance (+), physical limitation (-), depression (-), strain (-) Slow decline: married (+), church attendance (+), physical limitation (-), depression (-), heart attack (+), stroke (+) Rapid decline: being married (+), church attendance (+), physical limitation (-), depression (+), strain (+), social support (+)
Downer et al. [42]	Logistic regression models	Baseline class membership: age, gender, education, nativity, marital status, living arrangement, hearing problem, depression, ADLs, heart diseases Baseline + follow-up coefficient estimates: stroke, PD, AD or other dementia	• Class membership Persistent high: older age (-), physical limitation (-), hearing problem (-), higher education (+), not married and living alone (-), depression (-) Decline but high: older age (-), physical limitation (-), hearing problem (-), higher education (+), not married and living alone (+) Decline to low: reference group • Coefficient estimates (class-specific) General cognitive function Persistent high: AD/dementia (-), PD (-); Decline but high: AD/dementia (-); Decline to low: AD/dementia (-) Memory Persistent high: AD/dementia (-); Decline but high: AD/dementia (-); Decline to low: AD/dementia (-) Non-memory Persistent high: AD/dementia (-); Decline but high: AD/dementia (-); Decline to low: AD/dementia/stroke (-)
Yu et al. [43]	ANOVA, χ^2 test, Kruskal-Wallis test	Baseline class membership: age, gender, education, cognition, depression, social engagement, life purpose, physical activity Follow-up class membership: tangle density, macroscopic infarcts, neocortical Lewy bodies, hippocampal sclerosis, pathologic AD, neuronal density in brainstem	• Class membership (univariate comparison) Compared to other classes, non-decliners had: • Younger age at baseline and death, and higher baseline cognitive function • Fewer depressive symptoms, more cognitive activity, social activity, physical activity and purpose in life • Lower proportion of pathologic AD, macroscopic infarcts, neocortical Lewy bodies and hippocampal sclerosis, and higher neural density in locus ceruleus
Chen et al. [44]	Logistic regression models; mixed models	Baseline + follow-up class membership: BMI, self-rated health, depression, mobility, ADLs, IADLs, social interaction,	• Class membership High stable: reference group Starting high and declining: depression (+), physical limitation (+), smoking (+), diabetes (+)

		emotional support, hypertension, diabetes, heart disease, physical activity, smoking, drinking Baseline covariates: age, gender, education	Starting low and declining: depression (+), physical limitation (+), physical activity (-), emotional support (-) • Associated time-varying variables (of cognitive trajectory class) High stable: reference group Starting high and declining: mobility (-), physical limitation (+), depression (+), social interaction (-), emotional support (-), physical activity (-), diabetes (+), heart disease (+) Starting low and declining: mobility (-), physical limitation (+), depression (+), social interaction (-), emotional support (-), physical activity (-), diabetes (+), BMI (-), self-rated health (-) Note: (+) indicates factors being higher/more prevalent at last timepoint versus reference group, (-) indicates the opposite.
Min et al. [45]	Logistic regression models	Baseline class membership: age, gender, education, marital status, depression, ADLs, IADLs, social activities, exercise, smoking, drinking	• Class membership Stable: reference group Sharp cognitive decline: older age (+), depression (+), female (+), higher education (-), social activity (-), physical activity (-)
Lee et al. [46]	Logistic regression models	Baseline class membership: social activity, education, household income, employment status, depression, self-rated health, ADLs, IADLs, interaction with children Baseline covariates: age, gender, marital status	• Class membership (gender-specific) Male (n=1711) High-Maintaining: social activity (+), friendship activity (+), religious activity (+), volunteering (+), depression (-), self-rated health (+), baseline cognitive function (+), higher education (+) Moderate-Stable: reference group Low-Decreasing: friendship activity (-), higher education (-), baseline cognitive function (-) Moderate declined to severe impairment: None Females (n=2018) High-Maintaining: baseline cognitive function (+), higher education (+) Moderate-Stable: reference group Low-Decreasing: social activity (-), religious activity (-), baseline cognitive function (-), higher education (-) Moderate decline-severe impairment: social activity (-), baseline cognitive function (-), higher education (+)
Park et al. [47]	Logistic regression models	Baseline class membership: parent & own education, poor family, self-rated health, income, marital status, nursing home admission, relocation, chronic condition, ADLs, IADLs, social engagement Baseline covariates: age, gender, ethnicity	• Class membership Stable High: volunteering & become volunteering (+), self-rated health (-), higher education (+), higher income (+), chronic condition (-), increased physical limitation (-), decreased social activity (-) High-to-Moderate: social activity & increased activity (+), volunteering & becoming volunteer (+), higher parent & own education (+), higher income (+), nursing home admission (-), chronic condition (-) Stable Moderate: reference group Moderate-to-Low: volunteering & become volunteering (-), higher education (-), nursing home admission (+), chronic condition (-), physical limitation (+), increased physical limitation (+) Stable low: volunteering & become volunteering (-), higher education (-), higher income (-), physical limitation (+), increased chronic condition (+)

Espeland et al. [48]	Logistic regression model	Baseline class membership: education, type 2 diabetes, *APOE* 4, AD-PS	• Class membership Consistently high: reference group Relative improvement: higher education (-) Decline to median: *APOE* 4 (+) Decline to low: higher education (-), *APOE* 4 (+) Consistently low: higher education (-), AD-PS score (+), *APOE* 4 (+), type 2 diabetes (+)
Elovainio et al. [49]	Logistic regression model	Baseline class membership: social contacts, marital status Baseline covariates: age, gender, ethnicity, occupation, blood measures, alcohol, BMI	• Class membership High: reference group Medium: social activity (-) Low: social activity (-), being married (-)
McFall et al. [50]	Random forest analysis	Baseline class membership: age, gender, education, living status, depression, subjective health, vision, hearing, pulse pressure, peak expiratory flow, grip strength, BMI, heart rate, gait, balance, physical activity, social activity, novel cognitive activity, self-maintenance activity	• Class membership • Young old (<72.5 years) Stable memory: female (+), higher education (+), social activity (+), don't live alone (+), higher BMI (+) Normal memory aging: reference group Declining memory aging: novel cognitive activity (-), self-maintenance activity (-), older age (-), higher heart rate (+), higher grip strength (+) Stable memory aging: female (+), higher education (+), novel cognitive activity (+), self-maintenance activity (+), lower grip strength (+), living with someone (+), higher BMI (+), lower heart rate (+) Declining memory aging: reference group • Old age (>=72.5 years) Stable memory aging: female (+), higher education (+), higher heart rate (+), depression (-) Normal memory aging: reference group Declining memory aging: novel cognitive activity (-), social activity (-), faster gait speed (-) Stable memory aging: female (+), higher education (+), novel cognitive activity (+), social activity (+), lower peak expiratory flow (+), faster gait speed (+) Declining memory aging: reference group
Hayden et al. [51]	ANOVA, chi-squared test	Baseline class membership: age, gender, ethnicity, education, *APOE* 4, MMSE Follow-up associated outcomes: visits, follow-up, amyloid burden, tangle density	• Class membership (univariate comparison) The class of slow decline, moderate decline and rapid decline had progressively increased age, higher education, lower baseline MMSE and higher proportion of *APOE* 4 carriers. • Associated outcomes (of cognitive trajectory class) Slow decline: reference group Moderate decline: mortality risk (+) Rapid decline: mortality risk (+), amyloid burden (+), tangle density (+)
Ding et al. [52]	Logistic regression models	Baseline class membership: age, gender, education, BMI Baseline covariates: ethnicity, diabetes, hypertension, sleep apnea, smoking, *APOE* 4	• Class membership Norm 12.9-Stable: female (+) Norm 9.4-Curvilinear decline: reference group Norm 9.1-Curvilinear decline: none Norm 6.9-Stable: higher education (-) Norm 6.2-Linear decline: older age (+), higher education (-) Norm 3.3-Linear decline: none
Tampubolon et al. [53]	Logistic regression models	Baseline covariates: age, gender, education, marital status, wealth, occupation, social, various health,	• Associated outcome (of cognitive trajectory class) High-Decline (advantaged): risk of incident dementia (-) Medium (higher)-Decline: risk of incident dementia (-)

		physical activity, smoking, drinking	Medium (lower)-Decline (disadvantaged): risk of incident dementia (-) Low-Decline: reference group
Han et al. [54]	Generalized estimating equation Poisson models	Baseline covariates: age, gender, education, ethnicity, living status Baseline + follow-up covariates: depression, chronic conditions	• Associated outcomes (of cognitive trajectory class) No decline: reference group Minimal decline: ADL disability (+), IADL disability (+), hospitalization (+), nursing home admission (+), mortality risk (+) Moderate decline: same as above Progressive decline: same as above Rapid decline: same as above
Zahodne et al. [55]	Cox regression models, ANOVA	Baseline covariates: age, gender, education, ethnicity, intracranial volume Baseline + follow-up associated outcomes: total hippocampal volume, mean entorhinal cortical thickness	• Associated outcome (of cognitive trajectory class) Stable-High: risk of incident dementia (-) Stable-Low: reference group Decline: risk of incident dementia (+), rate of hippocampal atrophy (+) Rapid decline: risk of incident dementia (+), rate of hippocampal atrophy (+), hippocampal volume (-), entorhinal cortical thickness (-) Note: rapid decliners smallest hippocampal volume & entorhinal cortical thickness at baseline & follow-up.
Zahodne et al. [56]	Logistic regression models; Cox regression	Baseline class membership + follow-up associated outcomes: age, gender, education, ethnicity, depression, *APOE* 4, stroke hypertension, diabetes, heart disease	• Class membership Stable-High: female (+), Hispanic (-), African American (-) Stable-Low: reference group Decline: older age (+), *APOE* 4 (+), heart disease (+) Decliners: reference group Rapid decliners: older age (+), diabetes (+) • Predictors of incident dementia in each cognitive trajectory class Stable-High: older age (+), higher education (-), Hispanic (+), hypertension (-), stroke (+) Stable-Low: older age (+), higher education (-), depression (+), heart disease (-) Decliners: higher education (-), hypertension (-) Rapid decliners: stroke (+), *APOE* 4 (+)
Kim et al. [57]	Cox regression models	Baseline covariates: age, gender, education, various health, BMI, smoking, drinking, physical activity	• Associated outcomes (of cognitive trajectory class) Consistently high: reference group Decreased: none Increased: none Consistently low: mortality risk (+)
Teipel et al. [58]	Logistic regression models	Baseline class membership: age, gender, education, *APOE* 4, global amyloid load, basal forebrain volume, total intracranial volume	• Class membership MMSE High-Stable: global amyloid load (-), basal forebrain volume (+), higher education (+) Medium-Stable: older age (-), higher education (+) Low-Decline: reference group MBT-BS High-Stable: global amyloid load (-), female (+) Medium (higher)-Stable: global amyloid load (-) Medium (lower)-Stable: global amyloid load (-) Low-Stable: reference group MBT-List1/2 High-Stable: global amyloid load (-), basal forebrain volume (+), female (+)

			Medium (higher)-Stable: global amyloid load (-), basal forebrain volume (+) Medium (lower)-Stable: basal forebrain volume (+) Low-Decrease: reference group	
Lin et al. [59]	Logistic regression models; Cox regression models	Baseline class membership: age, gender, ethnicity, education, amyloid-β, t-tau, *APOE* 4, hypertension, obesity Follow-up associated outcome: global cognitive function, depression, daily cognitive function, physical function	• Class membership High-Stable/High-Increase: reference group High-Major decline: t-tau positive (+) Medium-Stable/Low-Minor decline: female (-), *APOE* 4 (+), amyloid-β (+) • Associated outcomes (of cognitive trajectory class) High-Stable/High-Increase: reference group High-Major decline: impaired general cognitive function (+) Medium-Stable/Low-Minor decline: impaired general cognitive function (+), deficits in daily cognitive function (+), depression (+), physical limitation (+)	
Graziane et al. [60]	Logistic regression models	Baseline covariates: age, gender, education, ethnicity, Baseline + follow-up class membership: depression	• Class membership (association with trajectories of depressive symptoms, ref. is rare) Non-persistently low (for each cognitive domain): reference group Persistently low (attention): low decreasing (-), low increasing (+), Persistently low (EF): low decreasing (+), low increasing (+), moderate (+) Persistently low (language): low decreasing (+), low increasing (+), moderate (+), high (+) Persistently low (memory): moderate (+), high (+) Persistently low (visuospatial skills): low decreasing (+), moderate (+), high (+)	
Sha et al. [61]	Logistic regression models	Baseline class membership: night-time sleep duration, post-lunch napping duration, sleep disturbances Baseline covariates: age, gender, education, marital status, residence, weight, height, BMI, depression, ADLs, smoking, drinking, hypertension, diabetes, high blood sugar, heart problems, dyslipidemia, other diseases	• Class membership EF, Male: High-Decline: reference group Medium-Stable: 5-7 days sleep disturbances (+) Low-Increase: 5-9 h night-time sleep (-), 3-7 days sleep disturbances (+), EF, Female: High-Decline: reference group Medium-Stable: ≥30 min. post-lunch sleep (+), 5-7 days sleep disturbances (-) Low-Increase: 0-90 mins post-lunch sleep (+),	• Class membership EM, Male: High-Decline: 5-9 h night sleep (+), ≥90 minutes post-lunch sleep (+) Medium (higher)-Increase: 5-9 h night sleep (+) Medium (lower)-Decline: no post-lunch sleep (-), ≥30 min post-lunch sleep (+) Low-Decline: reference group EM, Female: High-Decline: <7 h night sleep (-), ≥9 hours night sleep (+), ≥30 min post-lunch sleep (+) Medium (higher)-Decline: <7 h night sleep (-), ≥90 min post-lunch sleep (+) Medium (lower)-Decline: <7 h night sleep (-), ≥9 h night sleep (+), no post-lunch sleep (+), 3-7 days sleep disturbances (+) Low-Decline: reference group
Marioni et al. [62]	n.s.	Baseline class membership + follow-up associated outcomes: gender, education, occupation, social engagement	• Class membership High baseline cognition: reference group Low baseline cognition: higher education (-), intellectual occupation (-), social engagement (-) Slow decliners: female (-), higher education (-), social engagement (-) Immediate decline: female (-), higher education (-), intellectual occupation (-), social engagement (-)	

			• Predictors of mortality risk in each cognitive trajectory class High baseline cognition: female (-), higher education (+), social engagement (-) Low baseline cognition: female (-), social engagement (-) Slow decliners: female (-), social engagement (-) Immediate decliners: female (-)
Marioni et al. [63]	Chi-squared test and ANOVA	Baseline class membership: age, gender, education, marital status, depression; IADL, stroke, diabetes, cognitive tests (6), social network & satisfaction	• Class membership (univariate comparison) • Non-decliners, moderate decliners & fast decliners progressively decreasing cognitive scores • Fast decliners class was younger than the other two classes. • Associated outcomes (of cognitive trajectory class) Non-decliners, moderate decliners & fast decliners progressively ↑ risk of dementia & mortality.
Robitaille et al. [64]	Logistic regression models	Baseline class membership + coefficient estimates: age, gender, education, height, physical activity, cognitive activity	• Class membership High functioning: cognitive activity (+) Moderate functioning: physical activity (+) Low functioning: reference group • Coefficient estimates (class-specific) High functioning: None Moderate functioning: older age (-) Low functioning: higher education (+)
Hu et al. [65]	Logistic regression models	Baseline class membership: age, gender, education, marital status, job type, birthplace, residence	• Class membership Slow decline: reference group Moderate decline: female (+), higher education (-), rural residence (+) Progressive decline: female (+), higher education (-), being married (-), job of housework (+), rural birthplace (+) Rapid decline: female (+), higher education (-), being married (+), rural birthplace (+)
Liu et al. [66]	Generalized estimating equation	Baseline covariates: age, gender, education, ethnicity, living status; depression, chronic conditions	• Associated outcomes (of cognitive trajectory class) No cognitive frailty: reference group Slow cognitive decline: hospitalization (+), nursing home admission (+), ADL disability (+), IADL disability (+), mobility disability (+) Rapid cognitive decline: hospitalization (+), nursing home admission (+), ADL disability (+), IADL disability (+), mobility disability (+) Cognitive frailty: hospitalization (+), nursing home admission (+), ADL disability (+), IADL disability (+), mobility disability (+)
Hochstetler et al. [67]	Logistic regression models, ANOVA, CART	Baseline class membership + CART: age, gender, education, various health, amyloid disposition, large cognitive battery	• Class membership (univariate comparison) • Compared to the class of lowest baseline-minimal change, the 2 other classes were older, more amyloid positive & *APOE* 4 carriers, more alcohol abusers and lower scores on most cognitive tests • CART: FAQ was the most predictive variable of latent classes, with an accuracy of 82.3%.
Barnes et al. [68]	Logistic regression models	Baseline class membership: age, education, social network, physical function & activity, IADLs, health, smoking, drinking	• Class membership Cognitive maintainers: absence of diabetes (+), absence of hypertension (+), no smoking (+), no IADL difficulties (+), moderate alcohol consumption (+), moderate social networks (+) Minor decliners: reference group Major decliners: excluded from the analysis
Yaffe et al. [69]	Cox regression models	Baseline covariates: age, education, BMI, depression, hypertension, diabetes, smoking, drinking, physical activity	• Associated outcomes (of cognitive trajectory class) For both 3MS and TMTB trajectories: Best performers: all-cause mortality (-), CVD-cause mortality (-), other-cause mortality (-) Middle performers: reference group Worst performers: all-cause mortality (+), CVD-cause mortality (+), other-cause mortality (+)

Yaffe et al. [70]	Logistic regression models	Baseline class membership: age, gender, ethnicity, education, various social and health factors, *APOE*, CRP, IL-6, TNF-α, triglycerides, total cholesterol, fasting glucose	• Class membership Cognitive maintainers: older age (-), White (+), higher education (+), higher literacy level (+), physical activity (+), no smoking (+) Minor decliners: reference group Major decliners: older age (+), higher education (-), higher literacy level (-), enough social support (-), higher BMI (-), *APOE* 4 (+)	
Yaffe et al. [71]	Cox regression models	Baseline covariates: age, gender, ethnicity, education, self-rated health, depression, BMI, stroke, hypertension, diabetes, myocardial infarct, *APOE* 4	• Associated outcomes (of cognitive trajectory class) Cognitive maintainers: mortality risk (-), physical disability (-) Minor decliners: reference group Major decliners: mortality risk (+), physical disability (+)	
Rosano et al. [72]	Logistic regression models	Baseline covariates: age, gender, education, ethnicity, self-rated health, physical activity Follow-up class membership: medial temporal area, cingulate cortex, total brain	• Class membership Cognitive maintainers: medial temporal area (+), cingulate cortex (-) Cognitive decliners: reference group	
Casaletto et al. [73]	Logistic regression models	Baseline class membership: age, gender, education, depression, *APOE* 4, cytokine markers (5), MRI volumes (7), WMH volume, depression, EM, processing speed, general cognition, cognitive symptoms	• Class membership Processing speed Stable: reference group Decliners: slower processing speed (+), higher TNFα (+), more cognitive symptoms (+), EM Stable: reference group Decliners: better baseline EM (+), female (-), higher precuneus (-), higher WMH (-)	
Yokoyama et al. [74]	Logistic regression, linear models	Baseline nuisance variables: age, gender, education, total intracranial volume, scan type (1.5 T or 3 T), handedness, *APOE* 4	• Class membership 1. Intergenic SNP rs7109806 most significant with cognitive maintenance. 2. 4 of top 10 SNPs in high affinity melanocortin receptor 3. Top 10 SNPs (score) + with grey matter in 3 regions of right executive control network, & 6% greater volume with each additional cognitive maintenance allele.	
Proust et al. [75]	Not applicable	None	Sensitivity=30.9% Specificity=99.6%	Predictive positive value: 80.8% Predictive negative value: 96.6%
Small et al. [76]	Not applicable	Baseline Predictive accuracy: age, gender, education	Sensitivity=42.9% Specificity=94.5%	Predictive positive value=67.6% Predictive negative value=86.0%

n.s., not stated; ADL, activity of daily living; IADL, instrumental activity of daily living; PD, Parkinson's disease; AD, Alzheimer's disease; BMI, body mass index; *APOE*, Apolipoprotein E; AD-PS, Alzheimer's Disease Pattern Similarity; CRP, C-reactive protein; CVD, cardiovascular disease; ANOVA, analysis of variance; CART, classification and regression tree; FAQ, Functional Activities Questionnaire; MMSE, Mini-Mental State Examination; TIA, transient ischemic attack; IL-6, Interleukin 6; WMH, white matter hyperintensity; MRI, magnetic resonance imaging; EM, episodic memory; SNP, single-nucleotide polymorphism; TNF-α, tumor necrosis factor-α

1) For class membership, (+) indicates the factor is associated with increased odds of the corresponding class, (-) indicates the opposite. 2) For associated outcomes of trajectory class, (+) indicates that the class membership was associated with increased odds of the corresponding outcome, (-) indicates the opposite. 3) For class-specific coefficient estimates, (+) indicates that the factor is associated with better cognitive function in the corresponding class, (-) indicates the opposite. 4) For predicting outcomes in individual classes, (+) indicates that the factor is associated with increased odds of the outcome in the corresponding class, (-) indicates the opposite.

Supplementary Table 4. Quality assessment

			Selection		Comparability	Follow-up		
Authors	**Cohort**	**AHRQ standards**	**1. Representativeness of the cohort**	**2. Outcome of interest not present at start of study**	**1. Comparability of cohorts, e.g., design, control for confounders**	**1. Ascertainment of cognitive function**	**2. Sufficient follow-up for outcomes to occur (3 waves, 2 year)**	**3. Adequacy of follow-up (missing values in cognitive assessment)**
Terrera et al. [40]	CC75C	Moderate	b (*)	a (*)	a (*) b (*)	b (*)	a (*)	b
Howrey et al. [41]	HEPESE	Moderate	b (*)	a (*)	a (*) b (*)	b (*)	a (*)	b
Downer et al. [42]	HEPESE	Moderate	b (*)	a (*)	a (*) b (*)	b (*)	a (*)	c
Yu et al. [43]	ROS+MAP	**Good**	b (*)	a (*)	a (*) b (*)	b (*)	a (*)	a (*)
Chen et al. [44]	TLSA	Moderate	a (*)	a (*)	a (*) b (*)	b (*)	a (*)	b
Min et al. [45]	KLoSA	**Good**	b (*)	a (*)	a (*) b (*)	b (*)	a (*)	b (*)
Lee et al. [46]	KLoSA	**Good**	b (*)	a (*)	a (*) b (*)	b (*)	a (*)	b (*)
Park et al. [47]	Multiple cohorts	**Good**	a (*)	a (*)	a (*) b (*)	b (*)	a (*)	b (*)
Espeland et al. [48]	WHIMS	Moderate	c	a (*)	a (*) b (*)	b (*)	a (*)	b (*)
Elovainio et al. [49]	Whitehall II Study	Moderate	c	a (*)	a (*) b (*)	b (*)	a (*)	c
McFall et al. [50]	VLS	Moderate	b (*)	a (*)	a (*) b (*)	b (*)	a (*)	b
Hayden et al. [51]	ROS	Moderate	c	a (*)	a (*) b (*)	b (*)	a (*)	a (*)
Ding et al. [52]	ADNI	Moderate	b (*)	a (*)	a (*) b (*)	b (*)	a (*)	c
Han et al. [54]	PEP Study	**Good**	b (*)	a (*)	a (*) b (*)	b (*)	a (*)	a (*)
Tampubolon et al. [53]	ELSA	**Good**	a (*)	a (*)	a (*) b (*)	b (*)	a (*)	a (*)
Zahodne et al. [55, 56]	WHICAP	Moderate	b (*)	a (*)	a (*) b (*)	b (*)	a (*)	b
Kim et al. [57]	KLoSA	**Good**	a (*)	a (*)	a (*) b (*)	b (*)	a (*)	a (*)
Teipel et al. [58]	INSIGHT-PreAD	Moderate	c	a (*)	a (*) b (*)	b (*)	a (*)	b (*)
Graziane et al. [60]	MYHAT	**Good**	b (*)	a (*)	a (*) b (*)	b (*)	a (*)	a (*)
Lin et al. [59]	ADNI	Moderate	b (*)	a (*)	a (*) b (*)	b (*)	a (*)	c
Sha et al. [61]	CHARLS	**Good**	a (*)	a (*)	a (*) b (*)	b (*)	a (*)	a (*)
Marioni et al. [62]	PAQUID	**Good**	b (*)	a (*)	a (*) b (*)	b (*)	a (*)	a (*)
Marioni et al. [63]	PAQUID	Moderate	b (*)	a (*)	a (*) b (*)	b (*)	a (*)	b
Robitaille et al. [64]	OCTO-Twin	Moderate	c	a (*)	a (*) b (*)	b (*)	a (*)	b
Hu et al. [65]	CLHLS	**Good**	a (*)	a (*)	a (*) b (*)	b (*)	a (*)	a (*)
Liu et al. [66]	PEP Study	**Good**	b (*)	a (*)	a (*) b (*)	b (*)	a (*)	b (*)

Hochstetler et al. [67]	ADNI	Moderate	b (*)	a (*)	a (*) b (*)	b (*)	a (*)	c
Barnes et al. [68]	SOF	Moderate	b (*)	a (*)	a (*) b (*)	b (*)	a (*)	b
Yaffe et al. [69]	SOF	Moderate	b (*)	a (*)	a (*) b (*)	b (*)	a (*)	b
Yaffe et al. [70]	Health ABC	Moderate	b (*)	a (*)	a (*) b (*)	b (*)	a (*)	c
Yaffe et al. [71]	Health ABC	Moderate	b (*)	a (*)	a (*) b (*)	b (*)	a (*)	b
Rosano et al. [72]	Health ABC	**Good**	b (*)	a (*)	a (*) b (*)	b (*)	a (*)	a (*)
Casaletto et al. [73]	Healthy Aging Study	Moderate	b (*)	a (*)	a (*) b (*)	b (*)	a (*)	c
Yokoyama et al. [74]	SOF+MrOS	Moderate	b (*)	a (*)	a (*) b (*)	b (*)	a (*)	c
Proust et al. [75]	PAQUID	Moderate	b (*)	a (*)	N/A	b (*)	a (*)	c
Small et al. [76]	Kungsholmen Project	Moderate	b (*)	a (*)	N/A	b (*)	a (*)	c

Supplementary Table 5. PRISMA 2009 checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3-4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	Appendix
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	Appendix
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	Appendix
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	Appendix
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	Appendix
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	Appendix
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	Appendix
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	Appendix
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	N/A
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	Appendix
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	5
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	5
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	9
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	6-9
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	N/A
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	9
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	9-10
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	14-15
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	16-17
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	17

REFERENCES

[1] Moher D, Liberati A, Tetzlaff J, Altman DG, Group P (2010) Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Int J Surg* **8**, 336-341.

[2] Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, Tugwell P (2013) The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses, Ottawa Hospital Research Institute, http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp, Accessed on December 21, 2019.

[3] Clouston SAP, Smith DM, Mukherjee S, Zhang Y, Hou W, Link BG, Richards M (2019) Education and cognitive decline: An integrative analysis of global longitudinal studies of cognitive aging. *J Gerontol B Psychol Sci Soc Sci* **75,** e151-e160.

[4] Huang F, Zhang M, Wang S (2019) Changes in cognitive function among older adults: A latent profile transition analysis. *Arch Gerontol Geriatr* **80**, 12-19.

[5] Newman AB, Arnold AM, Sachs MC, Ives DG, Cushman M, Strotmeyer ES, Ding J, Kritchevsky SB, Chaves PH, Fried LP, Robbins J (2009) Long-term function in an older cohort--the cardiovascular health study all stars study. *J Am Geriatr Soc* **57**, 432-440.

[6] Bott NT, Bettcher BM, Yokoyama JS, Frazier DT, Wynn M, Karydas A, Yaffe K, Kramer JH (2017) Youthful processing speed in older adults: genetic, biological, and behavioral predictors of cognitive processing speed trajectories in aging. *Front Aging Neurosci* **9**, 55.

[7] Aiken-Morgan AT, Gamaldo AA, Wright RS, Allaire JC, Whitfield KE (2018) Stability and change in cognitive status classification of Black older adults. *J Am Geriatr Soc* **66**, 179-183.

[8] Zammit AR, Hall CB, Katz MJ, Muniz-Terrera G, Ezzati A, Bennett DA, Lipton RB (2018) Class-specific incidence of all-cause dementia and Alzheimer's disease: a latent class approach. *J Alzheimers Dis* **66**, 347-357.

[9] Zammit AR, Hall CB, Lipton RB, Katz MJ, Muniz-Terrera G (2018) Identification of heterogeneous cognitive subgroups in community-dwelling older adults: a latent class analysis of the Einstein Aging Study. *J Int Neuropsychol Soc* **24**, 511-523.

[10] Zammit AR, Muniz-Terrera G, Katz MJ, Hall CB, Ezzati A, Bennett DA, Lipton RB (2019) Subtypes based on neuropsychological performance predict incident dementia: findings from the Rush Memory and Aging Project. *J Alzheimers Dis* **67**, 125-135.

[11] Seil K, Yu S, Alper H (2019) A cognitive reserve and social support-focused latent class analysis to predict self-reported confusion or memory loss among middle-aged World Trade Center Health Registry enrollees. *Int J Environ Res Public Health* **16**, 1401.

[12] Hayden KM, Kuchibhatla M, Romero HR, Plassman BL, Burke JR, Browndyke JN, Welsh-Bohmer KA (2014) Pre-clinical cognitive phenotypes for Alzheimer disease: a latent profile approach. *Am J Geriatr Psychiatry* **22**, 1364-1374.

[13] de Frias CM, Dixon RA, Strauss E (2009) Characterizing executive functioning in older special populations: from cognitively elite to cognitively impaired. *Neuropsychology* **23**, 778-791.

[14] Burns RA, French D, Luszcz M, Kendig HL, Anstey KJ (2019) Heterogeneity in the health and functional capacity of adults aged 85+ as risk for mortality. *J Am Geriatr Soc* **67**, 1036-1042.

[15] Luo Y, Zhang L, Pan X (2019) Neighborhood environments and cognitive decline among middle-aged and older people in China. *J Gerontol B Psychol Sci Soc Sci* **74**, e60-e71.

[16] Clarke PJ, Weuve J, Barnes L, Evans DA, Mendes de Leon CF (2015) Cognitive decline and the neighborhood environment. *Ann Epidemiol* **25**, 849-854.

[17] MacDonald SW, Hultsch DF, Dixon RA (2011) Aging and the shape of cognitive change before death: terminal decline or terminal drop? *J Gerontol B Psychol Sci Soc Sci* **66**, 292-301.

[18] Yamada M, Landes RD, Mimori Y, Nagano Y, Sasaki H (2015) Trajectories of cognitive function in dementia-free subjects: Radiation Effects Research Foundation Adult Health Study. *J Neurol Sci* **351**, 115-119.

[19] Beydoun MA, Tajuddin SM, Shaked D, Beydoun HA, Evans MK, Zonderman AB (2019) One-carbon metabolism gene polymorphisms are associated with cognitive trajectory among African-American adults. *Neurobiol Aging* **84**, 238 e235-238 e218.

[20] Murayama H, Shinkai S, Nishi M, Taniguchi Y, Amano H, Seino S, Yokoyama Y, Yoshida H, Fujiwara Y, Ito H (2017) Albumin, hemoglobin, and the trajectory of cognitive function in community-dwelling older Japanese: a 13-year longitudinal study. *J Prev Alzheimers Dis* **4**, 93-99.

[21] Sweet RA, Seltman H, Emanuel JE, Lopez OL, Becker JT, Bis JC, Weamer EA, DeMichele-Sweet MA, Kuller LH (2012) Effect of Alzheimer's disease risk genes on trajectories of cognitive function in the Cardiovascular Health Study. *Am J Psychiatry* **169**, 954-962.

[22] Tampubolon G (2015) Cognitive ageing in Great Britain in the new century: cohort differences in episodic memory. *PLoS One* **10**, e0144907.

[23] Dodge HH, Wang CN, Chang CC, Ganguli M (2011) Terminal decline and practice effects in older adults without dementia: the MoVIES project. *Neurology* **77**, 722-730.

[24] Hill TD, Angel JL, Balistreri KS, Herrera AP (2012) Immigrant status and cognitive functioning in late-life: an examination of gender variations in the healthy immigrant effect. *Soc Sci Med* **75**, 2076-2084.

[25] Armstrong JJ, Godin J, Launer LJ, White LR, Mitnitski A, Rockwood K, Andrew MK (2016) Changes in frailty predict changes in cognition in older men: The Honolulu-Asia Aging Study. *J Alzheimers Dis* **53**, 1003-1013.

[26] Aiken-Morgan AT, Gamaldo AA, Sims RC, Allaire JC, Whitfield KE (2015) Education desegregation and cognitive change in African American older adults. *J Gerontol B Psychol Sci Soc Sci* **70**, 348-356.

[27] Racine AM, Koscik RL, Berman SE, Nicholas CR, Clark LR, Okonkwo OC, Rowley HA, Asthana S, Bendlin BB, Blennow K, Zetterberg H, Gleason CE, Carlsson CM, Johnson SC (2016) Biomarker clusters are differentially associated with longitudinal cognitive decline in late midlife. *Brain* **139**, 2261-2274.

[28] Stephan BCM, Muniz-Terrera G, Granic A, Collerton J, Davies K, Saxby BK, Wesnes KA, Kirkwood TBL, Jagger C (2018) Longitudinal changes in global and domain specific cognitive function in the very-old: findings from the Newcastle 85+ Study. *Int J Geriatr Psychiatry* **33**, 298-306.

[29] Okereke OI, Rosner BA, Kim DH, Kang JH, Cook NR, Manson JE, Buring JE, Willett WC, Grodstein F (2012) Dietary fat types and 4-year cognitive change in community-dwelling older women. *Ann Neurol* **72**, 124-134.

[30] Li G, Larson EB, Shofer JB, Crane PK, Gibbons LE, McCormick W, Bowen JD, Thompson ML (2017) Cognitive trajectory changes over 20 years before dementia diagnosis: a large cohort study. *J Am Geriatr Soc* **65**, 2627-2633.

[31] Hughes TF, Sun Z, Chang CH, Ganguli M (2018) Change in engagement in cognitive activity and risk for mild cognitive impairment in a cohort of older adults: The Monongahela-Youghiogheny Healthy Aging Team (MYHAT) Study. *Alzheimer Dis Assoc Disord* **32**, 137-144.

[32] Liang J, Shaw BA, Krause NM, Bennett JM, Blaum C, Kobayashi E, Fukaya T, Sugihara Y, Sugisawa H (2003) Changes in functional status among older adults in Japan: successful and usual aging. *Psychol Aging* **18**, 684-695.

[33] Sun N, Mormino EC, Chen J, Sabuncu MR, Yeo BTT, Alzheimer's Disease Neuroimaging Initiative (2019) Multi-modal latent factor exploration of atrophy, cognitive and tau heterogeneity in Alzheimer's disease. *Neuroimage* **201**, 116043.

[34] Laukka EJ, Macdonald SW, Fratiglioni L, Backman L (2012) Preclinical cognitive trajectories differ for Alzheimer's disease and vascular dementia. *J Int Neuropsychol Soc* **18**, 191-199.

[35] Molsberry SA, Lecci F, Kingsley L, Junker B, Reynolds S, Goodkin K, Levine AJ, Martin E, Miller EN, Munro CA, Ragin A, Sacktor N, Becker JT (2015) Mixed membership trajectory models of cognitive impairment in the multicenter AIDS cohort study. *AIDS* **29**, 713-721.

[36] Popov M, Molsberry SA, Lecci F, Junker B, Kingsley LA, Levine A, Martin E, Miller E, Munro CA, Ragin A, Seaberg E, Sacktor N, Becker JT (2019) Brain structural correlates of trajectories to cognitive impairment in men with and without HIV disease. *Brain Imaging Behav* **14**, 821-829.

[37] Baker E, Iqbal E, Johnston C, Broadbent M, Shetty H, Stewart R, Howard R, Newhouse S, Khondoker M, Dobson RJB (2017) Trajectories of dementia-related cognitive decline in a large mental health records derived patient cohort. *PLoS One* **12**, e0178562.

[38] Hulur G, Wolf H, Riese F, Theill N (2019) Cognitive change at the end of life in nursing home residents: differential trajectories of terminal decline. *Gerontology* **65**, 57-67.

[39] Agrinier N, Erpelding ML, Labat C, Gautier S, Guillemin F, Benetos A (2018) Prognostic association of major frailty domain trajectories with 5-year mortality in very old adults: results from the PARTAGE Cohort Study. *Am J Epidemiol* **187**, 1678-1685.

[40] Terrera GM, Brayne C, Matthews F, Group CCSC (2010) 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* **22**, 291-299.

[41] Howrey BT, Raji MA, Masel MM, Peek MK (2015) Stability in cognitive function over 18 years: prevalence and predictors among older Mexican Americans. *Curr Alzheimer Res* **12**, 614-621.

[42] Downer B, Chen NW, Raji M, Markides KS (2017) A longitudinal study of cognitive trajectories in Mexican Americans age 75 and older. *Int J Geriatr Psychiatry* **32**, 1122-1130.

[43] Yu L, Boyle PA, Segawa E, Leurgans S, Schneider JA, Wilson RS, Bennett DA (2015) Residual decline in cognition after adjustment for common neuropathologic conditions. *Neuropsychology* **29**, 335-343.

[44] Chen TY, Chang HY (2016) Developmental patterns of cognitive function and associated factors among the elderly in Taiwan. *Sci Rep* **6**, 33486.

[45] Min JW (2018) A longitudinal study of cognitive trajectories and its factors for Koreans aged 60 and over: A latent growth mixture model. *Int J Geriatr Psychiatry* **33**, 755-762.

[46] Lee Y, Jean Yeung WJ (2019) Gender matters: Productive social engagement and the subsequent cognitive changes among older adults. *Soc Sci Med* **229**, 87-95.

[47] Park S, Kwon E, Lee H (2017) Life course trajectories of later-life cognitive functions: Does social engagement in old age matter? *Int J Environ Res Public Health* **14**, 393.

[48] Espeland MA, Chen JC, Weitlauf J, Hayden KM, Rapp SR, Resnick SM, Garcia L, Cannell B, Baker LD, Sachs BC, Tindle HA, Wallace R, Casanova R, Women's Health Initiative Memory Study Magnetic Resonance Imaging Study Group (2018) Trajectories of relative performance with 2 measures of global cognitive function. *J Am Geriatr Soc* **66**, 1575-1580.

[49] Elovainio M, Sommerlad A, Hakulinen C, Pulkki-Raback L, Virtanen M, Kivimaki M, Singh-Manoux A (2018) Structural social relations and cognitive ageing trajectories: Evidence from the Whitehall II cohort study. *Int J Epidemiol* **47**, 701-708.

[50] McFall GP, McDermott KL, Dixon RA (2019) Modifiable risk factors discriminate memory trajectories in non-demented aging: precision factors and targets for promoting healthier brain aging and preventing dementia. *J Alzheimers Dis* **70**, S101-S118.

[51] Hayden KM, Reed BR, Manly JJ, Tommet D, Pietrzak RH, Chelune GJ, Yang FM, Revell AJ, Bennett DA, Jones RN (2011) Cognitive decline in the elderly: an analysis of population heterogeneity. *Age Ageing* **40**, 684-689.

[52] Ding X, Charnigo RJ, Schmitt FA, Kryscio RJ, Abner EL (2019) Evaluating trajectories of episodic memory in normal cognition and mild cognitive impairment: Results from ADNI. *PLoS One* **14**, e0212435.

[53] Tampubolon G, Nazroo J, Pendleton N (2017) Trajectories of general cognition and dementia in English older population: An exploration. *Eur Geriatr Med* **8**, 454-459.

[54] Han L, Gill TM, Jones BL, Allore HG (2016) Cognitive aging trajectories and burdens of disability, hospitalization and nursing home admission among community-living older persons. *J Gerontol A Biol Sci Med Sci* **71**, 766-771.

[55] Zahodne LB, Wall MM, Schupf N, Mayeux R, Manly JJ, Stern Y, Brickman AM (2015) Late-life memory trajectories in relation to incident dementia and regional brain atrophy. *J Neurol* **262**, 2484-2490.

[56] Zahodne LB, Schupf N, Brickman AM, Mayeux R, Wall MM, Stern Y, Manly JJ (2016) Dementia risk and protective factors differ in the context of memory trajectory groups. *J Alzheimers Dis* **52**, 1013-1020.

[57] Kim JH, Kim JM (2019) Association of cognitive impairment and grip strength trajectories with mortality among middle-aged and elderly adults. *Int Psychogeriatr* **31**, 723-734.

[58] Teipel SJ, Cavedo E, Lista S, Habert MO, Potier MC, Grothe MJ, Epelbaum S, Sambati L, Gagliardi G, Toschi N, Greicius MD, Dubois B, Hampel H, INSIGHT-preAD study group; Alzheimer Precision Medicine Initiative (APMI) (2018) Effect of Alzheimer's disease risk and protective factors on cognitive trajectories in subjective memory complainers: An INSIGHT-preAD study. *Alzheimers Dement* **14**, 1126-1136.

[59] Lin FV, Wang X, Wu R, Rebok GW, Chapman BP, Alzheimer's Disease Neuroimaging Initiative (2017) Identification of successful cognitive aging in the Alzheimer's Disease Neuroimaging Initiative study. *J Alzheimers Dis* **59**, 101-111.

[60] Graziane JA, Beer JC, Snitz BE, Chang CC, Ganguli M (2016) Dual trajectories of depression and cognition: a longitudinal population-based study. *Am J Geriatr Psychiatry* **24**, 364-373.

[61] Sha T, Cheng W, Yan Y (2019) Prospective association between sleep-related factors and the trajectories of cognitive performance in the elderly Chinese population across a 5-year period cohort study. *PLoS One* **14**, e0222192.

[62] Marioni RE, Proust-Lima C, Amieva H, Brayne C, Matthews FE, Dartigues JF, Jacqmin-Gadda H (2014) Cognitive lifestyle jointly predicts longitudinal cognitive decline and mortality risk. *Eur J Epidemiol* **29**, 211-219.

[63] Marioni RE, Proust-Lima C, Amieva H, Brayne C, Matthews FE, Dartigues JF, Jacqmin-Gadda H (2015) Social activity, cognitive decline and dementia risk: a 20-year prospective cohort study. *BMC Public Health* **15**, 1089.

[64] Robitaille A, Piccinin AM, Hofer SM, Johansson B, Muniz Terrera G (2018) An examination of the heterogeneity in the pattern and association between rates of change in grip strength and global cognition in late life. A multivariate growth mixture modelling approach. *Age Ageing* **47**, 692-697.

[65] Hu X, Gu S, Sun X, Gu Y, Zhen X, Li Y, Huang M, Wei J, Dong H (2019) Cognitive ageing trajectories and mortality of Chinese oldest-old. *Arch Gerontol Geriatr* **82**, 81-87.

[66] Liu Z, Han L, Gahbauer EA, Allore HG, Gill TM (2018) Joint trajectories of cognition and frailty and associated burden of patient-reported outcomes. *J Am Med Dir Assoc* **19**, 304-309.

[67] Hochstetler H, Trzepacz PT, Wang S, Yu P, Case M, Henley DB, Degenhardt E, Leoutsakos JM, Lyketsos CG (2016) Empirically defining trajectories of late-life cognitive and functional decline. *J Alzheimers Dis* **50**, 271-282.

[68] Barnes DE, Cauley JA, Lui LY, Fink HA, McCulloch C, Stone KL, Yaffe K (2007) Women who maintain optimal cognitive function into old age. *J Am Geriatr Soc* **55**, 259-264.

[69] Yaffe K, Peltz CB, Ewing SK, McCulloch CE, Cummings SR, Cauley JA, Hillier TA, Ensrud KE (2016) Long-term cognitive trajectories and mortality in older women. *J Gerontol A Biol Sci Med Sci* **71**, 1074-1080.

[70] Yaffe K, Fiocco AJ, Lindquist K, Vittinghoff E, Simonsick EM, Newman AB, Satterfield S, Rosano C, Rubin SM, Ayonayon HN, Harris TB (2009) Predictors of maintaining cognitive function in older adults: the Health ABC study. *Neurology* **72**, 2029-2035.

[71] Yaffe K, Lindquist K, Vittinghoff E, Barnes D, Simonsick EM, Newman A, Satterfield S, Rosano C, Rubin SM, Ayonayon HN, Harris T (2010) The effect of maintaining cognition on risk of disability and death. *J Am Geriatr Soc* **58**, 889-894.

[72] Rosano C, Aizenstein HJ, Newman AB, Venkatraman V, Harris T, Ding J, Satterfield S, Yaffe K (2012) Neuroimaging differences between older adults with maintained versus declining cognition over a 10-year period. *Neuroimage* **62**, 307-313.

[73] Casaletto KB, Elahi FM, Staffaroni AM, Walters S, Contreras WR, Wolf A, Dubal D, Miller B, Yaffe K, Kramer JH (2019) Cognitive aging is not created equally: differentiating unique cognitive phenotypes in "normal" adults. *Neurobiol Aging* **77**, 13-19.

[74] Yokoyama JS, Evans DS, Coppola G, Kramer JH, Tranah GJ, Yaffe K (2014) Genetic modifiers of cognitive maintenance among older adults. *Hum Brain Mapp* **35**, 4556-4565.

[75] Proust C, Jacqmin-Gadda H (2005) Estimation of linear mixed models with a mixture of distribution for the random effects. *Comput Methods Programs Biomed* **78**, 165-173.

[76] Small BJ, Backman L (2007) Longitudinal trajectories of cognitive change in preclinical Alzheimer's disease: a growth mixture modeling analysis. *Cortex* **43**, 826-834.