Trajectories of Verbal Episodic Memory in Middle-Aged and Older Adults: Evidence from the English Longitudinal Study of Ageing

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OBJECTIVES: To identify distinct latent groups of baseline levels and age-related decline in verbal episodic memory in middle-aged and older adults, and to identify factors associated with these trajectories.

DESIGN: Longitudinal study of six data collections over a period of 10 years.

SETTING: Population-based cohort in England.

PARTICIPANTS: 9,515 community-dwelling adults aged 50-79 years.

MEASUREMENTS: Six repeated measurements of immediate and delayed recall of 10 words over 10-year follow-up. Group-based trajectory modeling was used to identify patterns of baseline levels and subsequent decline in memory in two age categories (50-64 and 65-79 years), and to investigate associations between trajectories and baseline predictors of group membership (gender, education, household wealth, marital status, smoking and physical activity) and time-varying covariates (depressive symptoms and number of chronic conditions).

RESULTS: Four trajectories were identified and labelled according to baseline status and decline in memory: very low/decline (9.8%), low/stable (40.2%), average/stable (39.5%) and good/stable (10.5%) in the younger group, and very low/rapid decline (15.7%), low/decline (32.0%), average/stable (38.8%), and good/stable (13.5%) in older participants. In people with stable or declining trajectories, a higher number of depressive symptoms and the presence of cardiovascular diseases were associated with worse memory. Female sex, younger age, and higher education, wealth and physical activity were consistently associated with more favourable trajectories.

CONCLUSIONS: We identified four memory trajectories. Factors known to be associated with cognitive reserve (such as education, wealth and physical activity) were associated with better memory function while depressive symptoms and cardiovascular disease were associated with poorer memory. This suggests that interventions to reduce depressive symptoms and better manage cardiovascular risk factors and disease in midlife may help prevent or delay future memory decline. J Am Geriatr Soc 65:1274–1281, 2017.

Key words: verbal episodic memory; trajectories; longitudinal; community-dwelling; risk factors

The normal aging process is linked to cognitive decline, with dementia at the extreme end of the spectrum.1 Describing and characterizing cognitive decline is of special interest, because it places an immense burden on older adults, their families, and society in general.2

Longitudinal studies have consistently shown that age-related memory decline follows a curvilinear shape,3–5 and that it is around the age of 60 when cognitive decline is more likely to begin. They have also found that individual trajectories varied around the mean population trajectory in terms of both starting levels and rates of change6–7, indicating considerable heterogeneity. Analyses of latent classes of persons who follow similar cognitive function trajectories confirmed the heterogeneity within the general population.8–11 Two8, three9, and four10 different cognition trajectories have been described, distinguishing people with low starting performance and rapid decline from those with better baseline performance and a stable trajectory. Similar heterogeneity has also been observed in clinical samples of patients with Mild Cognitive Impairment12,13 and Alzheimer’s Disease (AD).14,15
The majority of previous studies focused on old or very old people. Less is known about what is happening in the earlier years, for instance in people aged 50–65, while it is at these earlier ages when preventive programs could be more effective in reverting or ameliorating cognitive deterioration.

The first objective of this study was to identify clusters of individuals who followed distinct trajectories of verbal episodic memory within a large cohort of persons aged 50–79 years over a 10-year follow up. The second aim was to investigate the influences of time-varying covariates on memory within the clusters (trajectories). Finally, we investigated potential baseline predictors of trajectory membership. Analyses were conducted separately for younger and older participants to determine whether cognitive trajectories differed between them and whether baseline predictors of group membership or time-varying factors are more important at younger ages and may thus be a potential target for preventive programs.

METHODS

Study Population

We used data from the English Longitudinal Study of Ageing (ELSA), a longitudinal, nationally representative survey of community-dwelling people aged 50 and older in England. Participants were recruited from households using a multistage stratified random probability design. The cohort was first assessed in 2002/03 and subsequent follow-up interviews took place approximately every 2 years. Ethical approval was obtained from the London Multicentre Research and Ethics Committee (MREC/01/2/91) and participants gave informed consent.

Data from cohort members who completed a non-proxy interview and were aged 50–79 at baseline were used (n = 10,026). Participants who were diagnosed by a doctor with dementia (including AD) at baseline were excluded (n = 82). Persons who had one or more missing values in immediate and/or delayed recall at baseline or in some of the baseline covariates used for the analysis were also excluded (4.31%), resulting in a final sample of 9,515 subjects.

Outcomes

Verbal episodic memory was assessed by word recall test. Participants listened to a list of 10 common words and were asked to recall as many as possible both immediately and after a short delay (during which other tests were performed). There were four alternative forms, so that different lists could be given in distinct waves. The number of words was added to obtain a total score (0–20), with higher scores indicating better memory.

Baseline Covariates

Sociodemographic characteristics at baseline included age, gender, marital status (never married, legally separated or divorced, married/remarried, and widowed), education (A-level or above recorded as “high”; O-level or secondary education recorded as “medium” level; and no qualifications recorded as “low” education), five quintiles of household wealth (including savings and investments, value of any property or business assets, net of debt, excluding pension assets), smoking status (never smoked, ex-smokers, and current smokers), and physical activity on a weekly basis (not at all, mild, moderate and vigorous).

Time-Varying Covariates

At each wave, participants’ self-reported medical diagnoses of cardiovascular diseases (blood pressure, heart attack or congestive heart failure, stroke, diabetes mellitus) and other chronic conditions (chronic lung disease, asthma, arthritis, osteoporosis, and cancer). The number of conditions at each wave was summed up, categorised as 0, 1, and two or more.

Depressive symptoms were measured using the 8-item Center for Epidemiologic Studies Depression Scale (CES-D). The response format was binary (yes, no). A total score was calculated (0–8), with higher scores indicating greater severity.

Statistical Analysis

Group-based trajectory models (GBTM) were calculated separately for people aged 50–64 and 65–79 years old at baseline. This method fits a semi-parametric mixture model to longitudinal data using a maximum-likelihood method. The time metric was years into the study (0–10). The outcome was memory scores assessed in waves 1-6, and modeled with a censored normal distribution using Stata Traj plug-in (Stata Corp., College Station, TX).

The number and shape (via polynomial functions) of trajectories were determined by analyzing 2-5 group models without covariates. We decided on the final number of trajectories using likelihood criteria such as Bayesian Information Criterion (BIC), while trying to be as parsimonious as possible. Average posterior probabilities above 70% also indicate optimal fit.

Covariates were simultaneously introduced in the model using two model extensions to determine: 1) how events that occur during follow-up (time-varying) affect the trajectories and 2) whether they predict group membership (covariates at baseline). Time-varying covariates (depression, numbers of CVDs and non CVDs) were included simultaneously with time. Adjustment for time-varying covariates can alter the degree and rate of change within each trajectory, therefore trajectories were presented after adjusting for these covariates. In the second part of the model, the probabilities of trajectory group membership (derived after including time and time-varying covariates) are treated as the dependent variable predicted by covariates assessed at baseline in a fashion similar to a multinomial analysis. Since the parameters defining the trajectories and probabilities of group membership are jointly estimated, group assignments based on the highest posterior probabilities are not used, thus reducing error assignment. Variables with multiple categories (education, marital status and smoking status) were introduced as dummy variables.
Table 1. Baseline Characteristics of the Sample by Age Category (N = 9,515)

| Characteristic               | 50–64, n = 5,523 | 65–79, n = 3,992 | P-value* |
|------------------------------|------------------|------------------|----------|
| Dropped out at Wave 6        | 2,144 (38.8)     | 2,164 (54.2)     | <.001    |
| Female                       | 2,651 (43.4)     | 2,154 (54)       | .61      |
| Marital status               |                  |                  |          |
| Single                       | 318 (5.8)        | 211 (5.3)        | <.001    |
| Married                      | 4,132 (74.8)     | 2,552 (63.9)     |          |
| Separated, divorced          | 788 (14.3)       | 314 (7.8)        |          |
| Widowed                      | 285 (5.2)        | 915 (22.9)       |          |
| Education                    |                  |                  |          |
| Low                          | 1,740 (31.5)     | 2,036 (51)       | <.001    |
| Medium                       | 1,790 (32.4)     | 1,115 (27.9)     |          |
| High                         | 1,993 (36.1)     | 841 (21.1)       |          |
| Quintile of wealth           |                  |                  |          |
| Low                          | 1,740 (31.5)     | 2,036 (51)       | <.001    |
| Medium                       | 1,790 (32.4)     | 1,115 (27.9)     |          |
| High                         | 1,993 (36.1)     | 841 (21.1)       |          |
| Physical activity            |                  |                  |          |
| None                         | 349 (6.3)        | 442 (4.1)        | <.001    |
| Mild                         | 624 (11.3)       | 638 (16.0)       |          |
| Moderate                     | 2,677 (48.5)     | 1,973 (49.4)     |          |
| Vigorous                     | 1,873 (33.9)     | 939 (23.1)       |          |
| Smoking status               |                  |                  |          |
| Never                        | 1,977 (35.8)     | 1,379 (34.5)     |          |
| Ex-smoker                    | 2,291 (41.5)     | 2,032 (50.9)     |          |
| Current smoker               | 1,255 (22.7)     | 581 (14.5)       |          |

Low education level included people with no formal education.

*Chi-square tests and one-way analysis of variance were performed to determine differences in baseline characteristics between age groups.

Table 2. Distribution of Outcome (Episodic Memory Score) and Time-Varying Covariates

| Covariate                  | Time 0 (baseline) | Time 1 (2 years) | Time 2 (4 years) | Time 3 (6 years) | Time 4 (8 years) | Time 5 (10 years) |
|----------------------------|-------------------|------------------|------------------|------------------|------------------|-------------------|
| 50–64                      |                   |                  |                  |                  |                  |                   |
| Episodic memory, mean ± SD*| 10.7 ± 3.5        | 11.1 ± 3.1       | 11.2 ± 3.2       | 11.2 ± 3.2       | 11.1 ± 3.4       | 11.2 ± 3.4        |
| CES-D sum, mean ± SDb      | 1.48 ± 1.99       | 1.47 ± 1.94      | 1.37 ± 1.93      | 1.25 ± 1.84      | 1.34 ± 1.87      | 1.16 ± 1.75       |
| Number of CVDs, n (%)      |                  |                  |                  |                  |                  |                   |
| 0                          | 3,598 (65.1)      | 3,192 (71.3)     | 2,690 (68.1)     | 2,325 (64.3)     | 2,216 (62.2)     | 2,088 (61.9)      |
| ≥2                         | 346 (6.3)         | 193 (4.3)        | 77 (1.9)         | 77 (2.1)         | 93 (2.6)         | 71 (2.1)          |
| Number of non-CVDs, n (%)  |                  |                  |                  |                  |                  |                   |
| 0                          | 3,304 (59.8)      | 2,660 (59.4)     | 2,259 (57.2)     | 1,963 (54.3)     | 1,823 (51.1)     | 1,661 (49.2)      |
| ≥2                         | 530 (9.6)         | 408 (9.1)        | 384 (9.7)        | 398 (11.0)       | 440 (12.3)       | 436 (12.9)        |
| 65–79                      |                   |                  |                  |                  |                  |                   |
| Episodic memory, mean ± SD*| 8.56 ± 3.34       | 8.93 ± 3.41      | 8.86 ± 3.50      | 8.72 ± 3.49      | 8.49 ± 3.63      | 8.51 ± 3.67       |
| CES-D sum, mean ± SDb      | 1.59 ± 1.93       | 1.59 ± 1.91      | 1.55 ± 1.94      | 1.51 ± 1.91      | 1.68 ± 1.97      | 1.48 ± 1.87       |
| Number of CVDs, n (%)      |                  |                  |                  |                  |                  |                   |
| 0                          | 1,865 (46.7)      | 1,822 (58.1)     | 1,461 (54.9)     | 1,162 (50.2)     | 993 (47.2)       | 867 (47.4)        |
| ≥2                         | 569 (14.2)        | 233 (7.44)       | 83 (3.1)         | 93 (4.0)         | 97 (4.6)         | 75 (4.1)          |
| Number of non-CVDs, n (%)  |                  |                  |                  |                  |                  |                   |
| 0                          | 1,851 (46.4)      | 1,433 (45.8)     | 1,173 (44.1)     | 968 (41.8)       | 844 (40.1)       | 690 (37.7)        |
| ≥2                         | 577 (14.4)        | 430 (13.7)       | 394 (14.8)       | 351 (15.2)       | 355 (16.9)       | 318 (17.4)        |

*Range 0–20.

bRange 0–8.

SD=standard deviation; CES-D=Center for Epidemiologic Studies Depression Scale; CVD=cardiovascular disease.

Missing data were handled using a maximum likelihood approach based on a missing-at-random assumption. In order to explore different attrition rates across trajectory groups and whether these differences could affect the main results, an extension of GBTM that accounts for non-random attrition was used. All analyses were performed using Stata software version 12.1 (Stata Corp., College Station, TX). A two-sided P < .05 was considered statistically significant.

RESULTS

A total of 4,238 persons (44.5%) had completed information on the outcome across all waves while 17% (n = 1,573) of participants had died by the end of the study. Tables 1 and 2 summarize the baseline characteristics of people (N = 9,515) and the distribution of the outcome and time-varying covariates across waves.

A 4-group model produced the best BIC values in both age groups. The average posterior probabilities were all above 0.70, indicating good fit. The four trajectory models were re-estimated including time-varying covariates, and the shape and probability of trajectory groups were similar to those identified without such an adjustment.

Trajectory groups were labeled according to baseline memory scores and decline (Figure 1). In the younger group, 9.8% (very low/decline) presented a negative linear term and a very low memory score at baseline (Table 3). The second group (40.2%) had low baseline memory score and a stable trajectory (low/stable). The third (39.5%) and the fourth (10.5%) presented also stable trajectories and were labelled as “average/stable” and “good/stable”, respectively.
In the older cohort, 15.7% had very poor scores at baseline and rapid cognitive decline (very low/rapid decline) and 32% had poor baseline memory and moderate cognitive decline (low/decline). The “average/stable” (38.8%) and the “good/stable” (13.5%) classes showed stability in memory function over time.

Table 3 displays the estimated coefficients for time and time-varying covariates within each group. In the younger cohort and at a given time point, each unit increase in depressive symptoms was associated with lower levels of memory in the very low/decline, low/stable, and average/stable groups but did not affect memory among people in the good/stable group. In the older cohort, each increase in depressive symptoms was related to worse memory function in the low/decline, average/stable, and good/stable but not in the very low/rapid decline group.

Each unit increase in the number of CVDs negatively affected the memory of middle-aged people belonging to the very low/decline, low/stable, and average/stable groups; in the older cohort, an association was only found in the low/decline group. Similarly, each unit increase in the number of other chronic conditions was associated with lower memory scores in the low/stable trajectory of the middle-aged category, while a significant improvement was observed in the low/decline and in the average/stable older cohort groups.

Table 4 displays the Odds Ratios (ORs) of group membership by baseline predictors. In the younger cohort, higher levels of wealth, medium or high level of education (vs low), female sex and younger age were associated with increased odds of membership of the three stable trajectories, relative to the very low/decline group. Higher levels of physical activity predicted the average/stable and good/stable trajectories. Being married, separated, or divorced at baseline predicted the low/stable trajectory, compared with the very low/decline group. Current smokers were less likely to be in the low/stable group, compared with the very low/decline group (OR = 0.92, 95% confidence interval (CI) = 0.89–0.95).

In the older cohort, higher levels of wealth, younger age and greater physical activity were significant predictors of the three more favourable trajectories, compared with the very low/rapid decline trajectory. Women were more likely than men to follow an average/stable (OR = 2.21, 95% CI = 1.51–2.87) and good/stable (OR = 4.62, 95% CI = 2.88–6.36) groups and smokers at baseline were less

Figure 1. Trajectories of verbal episodic memory according to age. Years indicate years since baseline. Verbal memory scores range from 0 to 20. These trajectories were calculated using a model including time-varying covariates (depression, cardiovascular disease, other chronic conditions) and predictors of group membership at baseline (age, gender, marital status, education level, wealth, smoking status, physical activity). 50–64: (1) very low/decline, (2) low/stable, (3) average/stable, (4) good/stable; 65–79: (1) very low/rapid decline, (2) low/decline, (3) average/stable, (4) good/stable.
Table 3: Parameter Estimations for Verbal Episodic Memory Trajectories (Model with Time-Varying Covariates) According to Age

| Parameter | 50–64 | 65–79 | 65–79 | 50–64 | 65–79 | 65–79 | 50–64 | 65–79 | 65–79 |
|-----------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Intercept | 7.09 (0.147) | 4.66 (0.174) | 9.93 (0.090) | 7.90 (0.143) | 12.15 (0.095) | 9.84 (0.115) | 14.38 (0.141) | 12.53 (0.153) |
| Years     | 0.16 (0.032)  | 0.17 (0.016)  | 0.17 (0.016)  | 0.17 (0.016)  | 0.17 (0.016)  | 0.17 (0.016)  | 0.17 (0.016)  | 0.17 (0.016)  |
| Years²    | 0.01 (0.003)  | 0.01 (0.003)  | 0.02 (0.003)  | 0.02 (0.003)  | 0.02 (0.003)  | 0.02 (0.003)  | 0.02 (0.003)  | 0.02 (0.003)  |
| Center for Epidemiologic Studies Depression Scale | 0.09 (0.08)  | 0.08 (0.08)  | 0.09 (0.08)  | 0.09 (0.08)  | 0.09 (0.08)  | 0.09 (0.08)  | 0.09 (0.08)  | 0.09 (0.08)  |
| Non-CVD   | 0.01 (0.015)  | 0.01 (0.015)  | 0.01 (0.015)  | 0.01 (0.015)  | 0.01 (0.015)  | 0.01 (0.015)  | 0.01 (0.015)  | 0.01 (0.015)  |

Time was measured as years into the study (0–10). Years since baseline, depressive symptoms, and number of cardiovascular diseases (CVDs; heart problems, diabetes mellitus, hypertension, stroke) and non-CVDs (asthma, cancer, osteoporosis, arthritis, chronic lung diseases) were simultaneously introduced into the models. Coefficient estimates for time-varying variables indicate the association between each unit of change in that particular covariate and an increase (or decrease) in the memory score at a given time point.

**Probability of Drop-Out**

The probability of attrition was higher for the very low/decline and very low/rapid decline trajectories in the youngest and oldest cohorts, respectively (Figure S1). However, trajectories in the models with and without the attrition extension and the probabilities of belonging to each trajectory group were similar (Figure 1, Figure S2).

**DISCUSSION**

Our findings suggest a presence of four distinct trajectories of verbal episodic memory in both age groups, although the shape and probabilities were different; in the younger cohort, three out of four latent groups showed a stable memory function over 10 years, whereas among older adults, memory decline is observed for two of the four groups.

Overall, these results confirm the heterogeneity in cognitive ageing reported by previous studies and are consistent with research into latent groups of cognitive decline, suggesting that rapid cognitive decline is not always observed in some older people. However, our findings suggest that this proportion depends on age. Only about 10% of middle-aged people (50–64) had some degree of memory decline, whereas 48% of older people (65–79) showed a memory decline.

Post mortem and neuroimaging studies in community-based samples have previously shown that persons with rapid cognitive decline and low performance were more likely than people with normal cognition to present underlying neuropathology and low hippocampal volume. Participants in the current study belonging to the very low/decline or very low/rapid decline groups might therefore present some degree of neuropathology associated with AD and dementia, although individuals with a diagnosis of dementia at baseline were excluded. Interventions to prevent progression to AD or other dementias should be delivered before disease symptoms are manifested.

Our results suggest that depressive symptomatology can negatively affect the memory of people who have stable trajectories. Depression has previously been associated with worse performance on cognitive tests in population-based samples of older adults. However, in our data depressive symptoms were not associated with memory decline in the older cohort, suggesting that, at this age, cognitive decline may depend on other underlying pathologies rather than depression.

Presence of CVD was also associated with lower memory scores in all trajectory groups of those aged 50–64 years. However, memory appears to be not affected by CVDs among the oldest cohort. This is consistent with previous studies showing that cardiovascular risk factors and CVD are related to cognitive decline in midlife. CVD may cause subtle brain damage at early stages that becomes more apparent at older ages. Thus, management of CVD in midlife could be an effective way to prevent future cognitive deterioration, regardless of level of
cognitive performance. Presence of non-cardiovascular chronic conditions was only associated with lower memory in the low/stable group for the younger cohort. This is in line with previous studies reporting an association between conditions such as musculoskeletal disease, lung disease or arthritis, and cognitive decline.\textsuperscript{31} Conversely, in two of the older groups, an improvement in memory function was associated with an increase in the number of chronic conditions. The reasons for this are unclear, and further epidemiological studies are needed to confirm our findings.

Results from baseline predictors of trajectory membership show that women are more likely to follow a stable trajectory with good memory function independently of other confounders (e.g., education). This might be explained by genuine differences in brain structures and the role of sex hormones affecting hippocampal structures involved in episodic memory,\textsuperscript{32} but may also reflect gender differences in behavioral and biological risk factors. In keeping with previous literature, people with low educational attainment were more likely to show a rapid decline in memory function. Education might have positive and profound effects on brain structures during the early stages of life,\textsuperscript{33} contributing to greater cognitive reserve.\textsuperscript{36,34} Cognitive reserve might help the brain to compensate for neuropathology and delay the onset of clinical symptoms. Wealth was also related to better trajectories of memory function, independently from education. Wealth might be related to intellectually demanding occupations, stimulating environments, or better access to health systems with a positive effect on cognitive function.\textsuperscript{35}

Physical activity is an important predictor of trajectories in midlife and older ages, and it increases the probability of being in stable groups. The literature suggests that physical activity is a powerful protective factor and constitutes part of the cognitive reserve.\textsuperscript{34} However, people in the unfavourable trajectory groups (poor cognitive performance and rapid decline) might present a lack of mobility and high levels of disability as a consequence of their cognitive status or of an underlying neuropathology.

Marital status predicted being in the low/stable group only for middle-aged people. Other studies have shown that being single, compared with being married, is associated with poorer cognitive function\textsuperscript{36} and faster rates of cognitive deterioration.\textsuperscript{16} A spouse could be an important source of emotional and social support,\textsuperscript{37} and thus offer protection against cognitive deterioration in later life. Smoking at baseline significantly predicted a poor memory trajectory, which is consistent with literature showing that smoking is a risk factor for cognitive decline.\textsuperscript{38}

Our findings should be considered in the light of limitations. First, people with a self-reported diagnosis of dementia were excluded from the analysis but we cannot rule out the possibility that persons with a current diagnosis were finally included in the sample. There is evidence that repeated memory tests might result in improved performance due to familiarity with the task\textsuperscript{39} and that the highest improvements are particularly evident at first re-assessments but diminish with subsequent waves.\textsuperscript{40} Statistical strategies to account for the practice effect may affect the estimated rates of cognitive change but not the estimated association of risk factors with change.\textsuperscript{40} The use of alternative list of words could help minimise the practice effect\textsuperscript{41}. Moreover, it is unlikely that the practice effect influenced the separation of study subjects into trajectory groups. Non-ignorable drop-out was addressed using a modeling extension designed to alleviate bias in the estimation of group membership probabilities.\textsuperscript{22} The shape of trajectories and size of latent groups were similar when using models with and without this extension, suggesting that attrition bias only minimally affected our results. It is difficult to confirm the equivalence between groups in distinct age categories. For example, people belonging to the very low/decline group in

### Table 4. Factors Associated with Trajectory Group Membership According to Age

| Baseline Variable | Low/Stable | Average/Stable | Good/Stable | Low/Decline | Average/Stable | Good/Stable |
|-------------------|------------|----------------|-------------|-------------|----------------|-------------|
| **50–64**         |            |                |             |             |                |             |
| Odds Ratio (95% CI) |            |                |             |             |                |             |
| Wealth            | 1.23 \(1.09–1.37\)* | 1.51 \(1.35–1.68\) \(b\) | 1.83 \(1.56–2.10\) \(a\) | 1.19 \(1.05–1.34\) \(a\) | 1.51 \(1.34–1.67\) \(b\) | 1.68 \(1.44–1.93\) \(c\) |
| Female            | 1.59 \(1.16–2.02\) \(b\) | 3.53 \(2.54–4.52\) \(a\) | 8.6 \(5.42–11.79\) \(b\) | 0.98 \(0.67–1.29\) \(c\) | 2.21 \(1.51–2.87\) \(c\) | 4.62 \(2.86–6.36\) \(a\) |
| **Education (reference low)** |            |                |             |             |                |             |
| Medium            | 1.99 \(1.32–2.62\) \(b\) | 4.7 \(3.18–6.23\) \(b\) | 14.71 \(4.4–25.03\) \(b\) | 1.82 \(1.15–2.49\) \(a\) | 2.98 \(1.96–4.01\) \(a\) | 8.15 \(4.47–11.83\) \(c\) |
| High              | 2.48 \(1.51–3.45\) \(b\) | 10.07 \(6.11–14.03\) \(b\) | 72.62 \(19.99–125.24\) \(b\) | 1.06 \(0.50–1.62\) \(b\) | 3.78 \(2.14–5.43\) \(b\) | 14.92 \(7.05–22.78\) \(b\) |
| **Age at baseline** | 0.92 \(0.89–0.95\) \(c\) | 0.84 \(0.81–0.87\) \(c\) | 0.77 \(0.74–0.81\) \(c\) | 0.92 \(0.89–0.96\) \(c\) | 0.81 \(0.78–0.84\) \(c\) | 0.72 \(0.69–0.76\) \(c\) |
| **Marital status (reference single)** |            |                |             |             |                |             |
| Married           | 2.48 \(1.35–3.62\) \(a\) | 1.75 \(0.93–2.57\) \(a\) | 1.47 \(0.55–2.39\) \(a\) | 1.32 \(0.62–2.04\) \(a\) | 1.96 \(0.86–3.07\) \(a\) | 1.36 \(0.34–2.38\) \(a\) |
| Separated         | 2.41 \(1.11–3.70\) \(a\) | 1.74 \(0.78–2.69\) \(a\) | 1.43 \(0.38–2.48\) \(a\) | 1.13 \(0.31–1.94\) \(a\) | 2.21 \(0.68–3.74\) \(a\) | 1.64 \(0.10–3.19\) \(a\) |
| Widowed           | 2.92 \(0.95–4.88\) \(a\) | 1.52 \(0.44–2.59\) \(a\) | 1.64 \(0.08–3.20\) \(a\) | 1.37 \(0.58–2.16\) \(a\) | 2.18 \(0.88–3.47\) \(a\) | 2.31 \(0.48–4.14\) \(a\) |
| Smoking status (reference never) |            |                |             |             |                |             |
| Ex-smoker         | 0.91 \(0.62–1.20\) \(b\) | 1.09 \(0.74–1.43\) \(b\) | 0.94 \(0.58–1.31\) \(b\) | 0.98 \(0.66–1.31\) \(b\) | 1.14 \(0.80–1.48\) \(b\) | 1.11 \(0.69–1.53\) \(b\) |
| Current smoker    | 0.72 \(0.48–0.96\) \(a\) | 0.76 \(0.50–1.02\) \(a\) | 0.72 \(0.38–1.06\) \(a\) | 0.87 \(0.5–1.25\) \(a\) | 0.67 \(0.4–0.94\) \(a\) | 0.86 \(0.41–1.31\) \(a\) |
| Physical activity | 1.07 \(0.91–1.22\) \(c\) | 1.18 \(1.00–1.36\) \(c\) | 1.35 \(1.06–1.64\) \(c\) | 1.39 \(1.16–1.61\) \(c\) | 1.55 \(1.32–1.78\) \(c\) | 1.97 \(1.57–2.38\) \(c\) |

The reference groups were very low/decline for the 50–64 age category and very low/rapid decline for the 65–79 age category. Models were calculated separately for each age group. Baseline covariates presented here were introduced simultaneously into the models. These models included time and time-varying covariates presented in Table 3 (depressive symptoms, number of cardiovascular diseases, and other chronic conditions). P < .05; \(b\) 0.01; \(c\) 0.001.
the middle-aged group, probably have poorer cognition than older adults in the very low group. Finally, trajectories of other cognitive domains (e.g., working memory) may have different patterns.

These findings suggest that there is substantial heterogeneity in how episodic memory evolves over time and identify four episodic memory trajectories. Memory deterioration is not restricted to older adults; a modest decline in memory can be observed as early as midlife. A subgroup of older adults can maintain optimal memory function, possibly due to a good cognitive reserve and health status. Risk factors such as depressive symptoms and cardiovascular diseases were strongly associated with lower memory function not only in persons with rapid decline, but also in those with optimal memory trajectories. Early interventions (e.g., at the age of 50) should be targeted to ameliorate the decline observed in persons with poor memory function and rapid deterioration. Targeting depressive symptoms and cardiovascular diseases, regardless of age and level of cognition, might help prevent memory decline, and both middle-aged and older adults might benefit from programs promoting healthy lifestyles.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

**Figure S1.** Drop-out probability within trajectory groups.

**Figure S2.** Trajectories of verbal episodic memory according to age using model with drop-out extension.

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