Association between healthy lifestyle and memory decline in older adults: 10 year, population based, prospective cohort study

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Supplementary data

20. Supplementary figure 3. Test of reverse causality between lifestyle and memory function

eMethods

1. Participant enrollment procedures

For random selection, we considered geographical regions, degree of urbanization, economic development status, and sex and age distribution for the site selection. In stage 1, we chose 12 provinces, metropolises, and autonomous areas that were representative of the socioeconomic status and lifestyles of the three major geographical regions in China (north, south, and west). In stage 2, we randomly selected one economically developed city (classified as urban, with >500000 residents, at or above the median provincial gross domestic product [GDP]) and one underdeveloped city (classified as urban, with >500000 residents, below the median provincial GDP) from each of the 12 provinces or autonomous areas. Meanwhile, we randomly selected one economically developed county (classified as rural, with ≤500000 residents, at or above the median provincial GDP) and one underdeveloped country (classified as rural, with ≤500000 residents, below the median provincial GDP). In stage 3, we randomly selected two districts from each city and two townships from each county. In stage 4, we randomly selected four communities from each district and four villages from each township; communities or villages usually have 600-1200 households. In brief, there were four levels of sampling units: the primary sampling unit was province or autonomous area, secondary was city (urban) or county (rural), tertiary was district (urban) or township (rural), and quaternary was community (urban) or village (rural).

2. China cognition and ageing study (COAST)-Healthy behavior questionnaire

The **Part I** in questionnaire is designed for participants to complete, and the **Part II** is for investigators to review and evaluate the information of **Part I**.

Part I

- **About your health conditions**

First, we would like to ask you about your medical problems. Please choose appropriate answers.

1.	**Have you ever been diagnosed with hypertension by a doctor?**	Yes ☐	No☐
	If yes, if you take anti-hypertensive medication regularly?	Yes☐	No☐
2.	**Have you ever been diagnosed with diabetes mellitus by a doctor?**	Yes☐	No☐
	If yes, if you take anti-diabetes mellitus medication regularly?	Yes☐	No☐
3.	**Have you ever been diagnosed with hyperlipidemia by a doctor?**	Yes☐	No☐
	If you know your total cholesterol levels in the past year, please write it in detail.	__ mmol/L	

4.	**Have you ever been diagnosed with a cardiovascular event or related cerebrovascular disease?**	Yes☐ No☐
5.	**Have you ever suffered a traumatic brain injury?**	Yes☐ No☐
6.	**Do you have depression diagnosed by a doctor or other health professionals?**	Yes☐ No☐
7.	**How about your body weight and height without your clothes and shoes on? Please measure your height and weight yourself on site.**	Weight (kg)___ Height (cm)___
8.	**How many education years did you receive?**	Education years___
9.	**Have you taken any alcoholic drinks in the past year?** **If yes, please write it in detail.** **Have you quitted drinking?**	Yes☐ No☐ Frequency__ (per week) and amount__(g) (per week) If yes, how long? __
10.	**Do you have a smoking habit?** **If yes, please write it in detail.** **Have you quitted smoking? If yes, how long?**	Yes☐ No☐ Frequency__ (per week) and amount__(per week) If yes, how long? __

- **About your diet**

Second, we would like to ask you about your diet in the past year. We will provide the recommended amount of food for reference in the picture below (we use the fist or hand of an adult man as a reference).

1. How much cereals did you take daily?	<250 g/day ☐ 250-400 g/day☐ >400 g/day ☐
2. How much legumes did you take daily?	<30 g/day ☐ 30-50 g/day ☐ >50 g/day ☐
3. How much vegetables did you take daily?	<300 g/day ☐ 300-500 g/day ☐ >500 g/day ☐
4. What was your daily fruit intake?	<200 g/day☐ 200-400 g/day☐ >400 g/day ☐
5. What was your daily meat intake?	<50 g/day☐ 50-75 g/day☐ >75 g/day☐
6. What was your daily egg intake?	<25 g/day☐ 25-50 g/day☐ >50 g/day☐
7. What was your daily salt intake?	≤5 g/day ☐ >5 g/day ☐
8. What was your daily oil intake?	≤30 g/day ☐

	>30 g/day☐
9. How often did you consume fish products per week?	≥2 times per week☐ <2 times per week☐
10. Did you have tea-drinking habits?	Yes☐ No☐
If yes, how many cups did you usually drink per week?	Number of cups per week __
11. What was your daily nuts intake?	≥50g per week☐ <50g per week☐
12. What was your daily dairy intake?	Far more than 300g per week☐ Far less than 300g per week☐ Approximately 300g per week☐

- **About your physical exercise**

These questions asked you about the time you spent being physically active in the past year.

1. Did you walk more than 10,000 steps each time?	Yes☐ No☐
If yes, how many times per week?	≥7 times per week☐ 6 times per week☐ 5 times per week☐ 4 times per week☐ 3 times per week☐ 2 times per week☐ 1 time per week☐
2. Did you often take Tai Chi exercise (exceeding 30 minutes each time)?	Yes☐ No☐
If yes, how many times per week?	≥7 times per week☐ 6 times per week☐ 5 times per week☐ 4 times per week☐ 3 times per week☐ 2 times per week☐ 1 time per week☐
3. Did you regularly participate in moderate-intensity physical exercise (requiring moderate effort and accelerating the heart rate)?	Yes☐ No☐
If yes, how many times per week?	

		≥7 times per week☐ 6 times per week☐ 5 times per week☐ 4 times per week☐ 3 times per week☐ 2 times per week☐ 1 time per week☐
	How long in total per week?	___minutes per week
4.	**Did you regularly participate in vigorous activity (requires a large amount of effort and causes rapid breathing and a substantial increase in heart rate), such as running, fast swimming, etc.?**	Yes☐ No☐
	If yes, how many times per week?	≥7 times per week ☐ 6 times per week☐ 5 times per week☐ 4 times per week☐ 3 times per week☐ 2 times per week☐ 1 time per week☐
	How long in total per week?	___minutes per week

- **About your cognitive activities**

These questions are about your cognitive activities in the past year.

1.	**Did you have a writing habit (diary, letters, emails, etc., including online)?**	Yes☐ No☐
	If yes, how often did you write for at least 30 minutes each time?	≥7 times per week ☐ 6 times per week☐ 5 times per week☐ 4 times per week☐ 3 times per week☐ 2 times per week☐ 1 time per week☐
2.	**Did you have a reading habit (newspaper, magazine, books, etc., including online)?**	Yes☐ No☐
	If yes, how often did you read for at least 30 minutes each time?	≥7 times per week ☐ 6 times per week☐

		5 times per week☐ 4 times per week☐ 3 times per week☐ 2 times per week☐ 1 time per week☐
3.	**Did you play chess or cards (go game, mah-jong, poker, etc., including online) regularly?** **If yes, how often did you usually play them (at least 30 minutes each time)?**	Yes☐ No☐ ≥7 times per week☐ 6 times per week☐ 5 times per week☐ 4 times per week☐ 3 times per week☐ 2 times per week☐ 1 time per week☐
4.	**Did you have any other hobbies (calligraphy, playing music, etc.)?** **If yes, how often did you play (at least 30 minutes each time?)**	Yes☐ No☐ ≥7 times per week☐ 6 times per week☐ 5 times per week☐ 4 times per week☐ 3 times per week☐ 2 times per week☐ 1 time per week☐

- **About your social contacts**

These questions about your social contact in the past year.

1.	**Did you attend meetings or parties regularly?** **If yes, how often did you attend?**	Yes☐ No☐ ≥7 times per week☐ 6 times per week☐ 5 times per week☐ 4 times per week☐ 3 times per week☐ 2 times per week☐ 1 time per week☐
2.	**Did you get together with friends or relatives regularly?** **If yes, how often did you get with them?**	Yes☐ No☐ ≥7 times per week☐

	6 times per week☐ 5 times per week☐ 4 times per week☐ 3 times per week☐ 2 times per week☐ 1 time per week☐
3. Did you participate in any other social activities (party, traveling, chatting online, etc.) regularly? **If yes, how often did you participate in these activities?**	Yes☐ No☐ ≥7 times per week☐ 6 times per week☐ 5 times per week☐ 4 times per week☐ 3 times per week☐ 2 times per week☐ 1 time per week☐

Part II

2.1 Risk factors[1-28]: Risk factors such as hypertension, hyperlipidemia, and diabetes are based on participants' self-reports, physical examinations, and medical records.

Risk factors	**Answers**	
Hypertension [a]	Yes☐	No☐
Diabetes mellitus [b]	Yes☐	No☐
Hyperlipidemia[c]	Yes☐	No☐
Cardiocerebrovascular disease[d]	Yes☐	No☐
Head injury	Yes☐	No☐
Depression [e]	Yes☐	No☐
Overweight or obesity [f]	Yes☐	No☐
Less education [g]	Yes☐	No☐
Heavy drinking [h]	Yes☐	No☐
Smoking	Yes☐	No☐
Number of Yes:__		

Notes：

a Hypertension: average of 2 or more systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg during at least two tests in different dates or regular use of antihypertensive medication.[29]

b Diabetes mellitus: fasting blood glucose ≥7.0 mmol/L or random blood glucose ≥1.1 mmol/L or regular hypoglycemic medication use.[30]

c Hyperlipidemia: including hypercholesterolaemia (total cholesterol ≥6.2 mmol/L or 240 mg/dL), low-density lipoprotein abnormalities (low-density lipoprotein-C ≥4.1 mmol/L or 160 mg/dL) or hypertriglyceridemia (triglyceride ≥2.3 mmol/L or 200 mg/dL).[31]

d Cardiocerebrovascular disease: heart and/or cerebrovascular diseases.

e Depression: Individuals who had a previous diagnosis of depression or a Geriatric Depression Scale score of ≥11 as an indicator of depression.[32]

f Overweight or obesity: Overweight is defined as body mass index (BMI, weight/height^2) 25.0-29.^{3} kg/m^2, and obesity is defined as BMI >30 kg/m.$^{2\ 15}$

g Less education: ≤6 years of education.

h Heavy drinking: daily alcohol consumption exceeds 60g.[33]

2.2 Diet[34-36]: The questionnaire for this part refers to the Chinese Dietary Guidelines (2007) and previous literature.

Whether participants' diet within the recommended amount	**Answers**	
Cereals (250-400 g/day)	Yes☐	No☐
Legumes (30-50 g/day)	Yes☐	No☐
Vegetables (≥300 g/day)	Yes☐	No☐
Fruits (≥200 g/day)	Yes☐	No☐
Meat (50-75 g/day)	Yes☐	No☐
Eggs (25-50 g/day)	Yes☐	No☐
Salt (≤5 g/day)	Yes☐	No☐
Oil (≤30 g/day)	Yes☐	No☐
Fish (≥2 times per week)	Yes☐	No☐
Tea drinking habits (have tea drinking habit)	Yes☐	No☐
Nuts (≥50 g/week)	Yes☐	No☐
Dairy (approximately 300 g/week)	Yes☐	No☐
Number of eligible diet items：__		

2.3 Physical exercise[37-39]: Please recheck and evaluate the frequency and time spent on the following activities

Whether participants have the following physical exercise habits	**Answers**
Walk more than 10000 steps	≥7 times per week☐ 6 times per week☐ 5 times per week☐ 4 times per week☐ 3 times per week☐ 2 times per week☐ 1 time per week☐ Never☐ ___minutes per week

Take Tai Chi exercise (exceeding 30 minutes each time)	≥7 times per week☐ 6 times per week☐ 5 times per week☐ 4 times per week☐ 3 times per week☐ 2 times per week☐ 1 time per week☐ Never☐ ___minutes per week
Regularly participate in moderate-intensity physical exercise	≥7 times per week☐ 6 times per week☐ 5 times per week☐ 4 times per week☐ 3 times per week☐ 2 times per week☐ 1 time per week☐ Never☐ __minutes per week
Regularly participate in vigorous activity	≥7 times per week☐ 6 times per week☐ 5 times per week☐ 4 times per week☐ 3 times per week☐ 2 times per week☐ 1 time per week☐ Never☐ __minutes per week
Physical exercise: __	

2.4 Cognitive activities[40-42]: Please record and evaluate the time and frequency of engaging the following activities

Whether participants have the following cognitive activities	**Answers**
Writing habits (diary, letters, emails, etc., including online) for at least 30 minutes each time	≥7 times per week☐ 6 times per week☐ 5 times per week☐ 4 times per week☐ 3 times per week☐ 2 times per week☐ 1 time per week☐ Never ☐

Reading habit (newspaper, magazine, books, online information etc.) for at least 30 minutes each time	≥7 times per week☐ 6 times per week☐ 5 times per week☐ 4 times per week☐ 3 times per week☐ 2 times per week☐ 1 time per week☐ Never ☐
Playing chess or cards (Go game, mah-jong, poker, etc., including online) for at least 30 minutes each time	≥7 times per week☐ 6 times per week☐ 5 times per week☐ 4 times per week☐ 3 times per week☐ 2 times per week☐ 1 time per week☐ Never ☐
Have any other hobbies (calligraphy, playing music, etc.) for at least 30 minutes each time	≥7 times per week☐ 6 times per week☐ 5 times per week☐ 4 times per week☐ 3 times per week☐ 2 times per week☐ 1 time per week☐ Never ☐
Cognitive exercise: __	

2.5 Social contacts[23,42,43-45]: Please record and evaluate the frequency of engaging the following activities

Whether participants have the following social contacts	**Answer**
Participation in meetings or parties	≥7 times per week☐ 6 times per week☐ 5 times per week☐ 4 times per week☐ 3 times per week☐ 2 times per week☐ 1 time per week☐ Never☐
Visiting friends or relatives	≥7 times per week☐ 6 times per week☐

	5 times per week☐ 4 times per week☐ 3 times per week☐ 2 times per week☐ 1 time per week☐ Never☐
Other social contacts	≥7 times per week☐ 6 times per week☐ 5 times per week☐ 4 times per week☐ 3 times per week☐ 2 times per week☐ 1 time per week☐ Never☐
Social contact: __	

3. Supplementary table 1. Distribution of missing values with different follow-up years

	2012			2014			2016			2019		
	N	Missing value	(%)	N	Missing value	(%)	N	Missing value	(%)	N	Missing value	(%)
BMI (kg/m^2)	28820	252	0.9	26551	302	1.1	24083	343	1.4	21221	372	1.7
MMSE	28948	124	0.4	26585	268	1	24141	285	1.2	21261	332	1.5
Hypertension	28839	233	0.8	26587	266	1	24102	324	1.3	21290	303	1.4
Diabetes	28789	283	1	26596	257	1	24087	339	1.4	21267	326	1.5
Heart attack	28860	212	0.7	26609	244	0.9	24127	299	1.2	21290	303	1.4
Head injury	28836	236	0.8	26589	264	1	24074	352	1.4	21250	343	1.6
Depression	28975	97	0.3	26546	307	1.1	24135	291	1.2	21273	320	1.5
Cerebrovascular disease	28960	112	0.4	26545	308	1.1	24116	310	1.3	21235	358	1.7
Never or former smoking	28792	280	1	26589	264	1	24076	350	1.4	21259	334	1.5
Never drinking	28945	127	0.4	26587	266	1	24078	348	1.4	21283	310	1.4
Active cognitive activity	28821	251	0.9	26534	319	1.2	24143	283	1.2	21257	336	1.6
Regular physical exercise	28946	126	0.4	26602	251	0.9	24092	334	1.4	21283	310	1.4
Active social contact	28893	179	0.6	26519	334	1.2	24112	314	1.3	21264	329	1.5
Healthy diet	28877	195	0.7	26597	256	1	24082	344	1.4	21238	355	1.6

4. Supplementary table 2. Demographic characteristics of APOE ε4 carriers and non-carriers at baseline

Characteristics	APOE ε4 status		P
	ε4 - (n=23133)	ε4 + (n=5939)	
	mean±SD /no.(%)	mean±SD /no.(%)	
Female	11246 (48.61)	2867 (48.27)	0.64
Age (years)	72.23±6.62	72.21±6.58	0.81
Place of residence			
Rural	10933 (47.26)	2809 (47.30)	0.96
Urban	12200 (52.74)	3130 (52.70)	
Region			
North	6897 (29.81)	1773 (29.85)	0.69
West	7603 (32.87)	1982 (33.37)	
South	8633 (37.32)	2184 (36.77)	
Marital status			
Widowed	2075 (8.97)	518 (8.72)	0.66
Divorced, separated, or single	2934 (12.68)	736 (12.39)	
Married	18124 (78.35)	4685 (78.89)	
Years of education			
< 1	3362 (14.53)	880 (14.82)	0.83
1-6	7667 (33.14)	1951 (32.85)	
7-12	9679 (41.84)	2503 (42.15)	
> 12	2425 (10.48)	605 (10.19)	
Monthly household income (Chinese Yuan)			
1000-2999	1743 (7.53)	465 (7.83)	0.60
3000-4999	6974 (30.15)	1741 (29.31)	
5000-10000	13797 (59.64)	3572 (60.14)	
>10000	619 (2.68)	161 (2.71)	
Occupation			
Manual laborer	9738 (42.10)	2533 (42.65)	0.51
Office worker	7216 (31.19)	1860 (31.32)	
Household	3948 (17.07)	965 (16.25)	
Others	2231 (9.64)	581 (9.78)	
BMI (kg/m^2)	23.28±4.08	23.35±4.08	0.25
MMSE score	27.52±1.30	27.53±1.30	0.59
Medical illnesses			
Hypertension	8745 (37.80)	2297 (38.68)	0.22
Diabetes	4627 (20.00)	1196 (20.14)	0.81
Hyperlipidemia	3079 (13.31)	4763 (80.20)	<0.001
Heart attack	1541 (6.66)	372 (6.26)	0.27
Head injury	1242 (5.37)	344 (5.79)	0.20
Depression	1378 (5.96)	362 (6.10)	0.69

Cerebrovascular disease	2375 (10.27)	643 (10.83)	0.21
Healthy lifestyle factors			
Never or former smoking	18470 (79.84)	4736 (79.74)	0.87
Never drinking	9164 (39.61)	2341 (39.42)	0.78
Active cognitive activity	5883 (25.43)	1268 (21.35)	<0.001
Regular physical exercise	5657 (24.45)	1119 (18.84)	<0.001
Active social contact	5686 (24.58)	1250 (21.05)	<0.001
Healthy diet	11420 (49.37)	2884 (48.56)	0.27
Number of healthy lifestyle factors			
0	837 (3.62)	258 (4.34)	<0.001
1	4528 (19.57)	1344 (22.63)	
2	7184 (31.06)	1944 (32.73)	
3	5992 (25.90)	1429 (24.06)	
4	3552 (15.35)	741 (12.48)	
5-6	1040 (4.50)	223 (3.75)	
Average follow-up period (years)	6.71 (2.28)	6.41 (2.25)	<0.001

Notes: Differences in covariates were compared among the two groups, using analyses of variance and chi-square tests for continuous and categorical variables, respectively. SD, standard deviation; no., number; BMI, body mass index; MMSE, Mini Mental State Examination; APOE, apolipoprotein E.

5. Supplementary table 3. Global cognition trajectory in the cognitively normal population using linear mixed effect model

	Estimate	Standard Error	P
(Intercept)	0.038	0.014	0.006
Age	0.002	0.001	0.011
Age^2	-0.000	0.001	0.161
Female	-0.006	0.008	0.491
Years of education			
1-6 years	0.011	0.013	0.395
7-12 years	-0.002	0.013	0.878
> 12 years	0.031	0.017	0.070
Region			
West	0.001	0.011	0.944
South	0.013	0.010	0.199

6. Supplementary table 4. Memory trajectory in the cognitively normal population using linear mixed effect model

	Estimate	Standard Error	P
(Intercept)	-9.852	0.149	<0.001
Baseline age	0.127	0.002	<0.001
Age	-0.161	0.002	<0.001
Baseline age^2	-0.000	0.000	<0.001
Age^2	0.001	0.000	<0.001
Female	-0.009	0.003	0.008
Years of education			
1-6 years	0.013	0.005	0.014
7-12 years	0.014	0.005	0.004
>12 years	0.011	0.007	0.086
Baseline memory	0.334	0.003	<0.001
Region			
West	-0.015	0.004	<0.001
South	-0.034	0.004	<0.001

7. Supplementary table 5. Longitudinal change in memory among APOE ε4 carriers and non-carriers

	Estimate	Standard Error	P
(Intercept)	-1.097	0.041	<0.001
APOE ε4 carriers	0.019	0.005	<0.001
Age	-0.034	0.000	<0.001
Age^2	0.001	0.000	<0.001
Female	-0.009	0.003	0.005
Years of education			
1-6 years	0.012	0.005	0.020
7-12 years	0.013	0.005	0.007
> 12 years	0.011	0.007	0.097
Region			
West	-0.016	0.004	<0.001
South	-0.033	0.004	0.001
Baseline memory	0.330	0.003	<0.001
APOE ε4 carriers: age	0.002	0.001	0.007
APOE ε4 carriers: age^2	-0.000	0.000	0.229

8. Supplementary table 6. Longitudinal change in memory associated with each lifestyle factor in the cognitively normal population

	Estimate	Standard Error	P
(Intercept)	-0.462	0.016	<0.001
Regular physical exercise	0.002	0.006	0.806
Active social contact	0.002	0.006	0.810
Healthy diet	0.016	0.005	0.004
Never or former smoking	0.021	0.007	0.002
Never drinking	-0.004	0.006	0.445
Active cognitive activity	0.013	0.006	0.045
Baseline memory score	-0.050	0.000	<0.001
Learning effect	0.334	0.017	<0.001
Age	-0.050	0.000	<0.001
Age^2	0.001	0.000	<0.001
Time	-0.134	0.003	<0.001
Female	-0.012	0.004	0.001
Years of education			
1-6 years	0.015	0.006	0.012
7-12 years	0.011	0.006	0.044
>12 years	0.002	0.007	0.797
Region			
West	-0.015	0.005	<0.001
South	-0.027	0.005	<0.001
Regular physical exercise: time	0.007	0.001	<0.001
Active social contact: time	0.004	0.001	<0.001
Healthy diet: time	0.016	0.001	<0.001
Never or former smoking: time	0.004	0.002	0.026
Never drinking: time	0.002	0.001	0.048
Active cognitive activity: time	0.010	0.001	<0.001

9. Supplementary table 7. Lifestyle effect on memory decline with age increasing in the cognitively normal population

	Estimate	Standard Error	P
(Intercept)	-1.327	0.032	<0.001
Average group	0.017	0.006	0.004
Favourable group	0.052	0.007	<0.001
Age	-0.040	0.003	<0.001
Age^2	0.001	0.000	<0.001
APOE ε4 non-carriers	0.051	0.012	<0.001
Female	-0.007	0.003	0.055
Years of education			
1-6 years	0.010	0.005	0.053
7-12 years	0.012	0.005	0.026
> 12 years	0.010	0.007	0.161
Region			
West	-0.010	0.004	0.021
South	-0.026	0.004	<0.001
Place of residence			
Urban	-0.002	0.003	0.620
Marital status			
Divorced, separated, or single	0.002	0.007	0.731
Married	0.081	0.005	<0.001
Monthly household income (Chinese Yuan)			
3000-4999	-0.005	0.007	0.473
5000-10000	-0.007	0.007	0.277
>10000	0.013	0.012	0.266
Occupation			
Office worker	0.007	0.004	0.095
Household	-0.001	0.005	0.777
Others	0.003	0.006	0.570
Learning effect	0.803	0.004	<0.001
Baseline memory score	0.231	0.003	<0.001
BMI (kg/m^2)	-0.004	0.000	<0.001
Medical illness			
No depression	0.000	0.008	0.966
No diabetes	0.026	0.004	<0.001

No head injury	0.144	0.005	<0.001
No hyperlipidemia	0.058	0.005	<0.001
No heart attack	0.079	0.006	<0.001
No hypertension	0.022	0.003	<0.001
No cerebrovascular disease	0.070	0.005	<0.001
Average group: age	-0.002	0.001	0.033
Favourable group: age	-0.007	0.001	<0.001
Average group: age^2	0.000	0.000	0.143
Favourable group: age^2	0.000	0.000	0.821
APOE ε4 non-carriers: age	0.006	0.002	<0.001
APOE ε4 non-carriers: age^2	0.000	0.000	0.685
Average group: APOE ε4 non-carriers	0.024	0.013	0.069
Favourable group: APOE ε4 non-carriers	0.014	0.016	0.392
BMI (kg/m^2): age	-0.000	0.000	<0.001
No depression: age	-0.003	0.001	0.008
No diabetes: age	0.000	0.001	0.762
No head injury: age	0.006	0.001	<0.001
No hyperlipidaemia: age	0.002	0.001	0.014
No heart attack: age	0.001	0.001	0.306
No hypertension: age	0.002	0.001	<0.001
No cerebrovascular disease: age	0.003	0.001	<0.001
Average group: age: APOE ε4 non-carriers	-0.002	0.002	0.295
Favourable group: age: APOE ε4 non-carriers	-0.001	0.002	0.733
Average group: age^2: APOE ε4 non-carriers	-0.000	0.000	0.231
Favourable group: age^2: APOE ε4 non-carriers	-0.000	0.000	0.740

10. Supplementary table 8. Hazard ratios for the onset of dementia and MCI in the unfavourable, average, and favourable groups for APOE stratified population

Time-dependent Cox regression model, HR of dementia and MCI in three lifestyle groups (95% CI)						
	Model 1	**P**	**Model 2**	**P**	**Model 3**	**P**
Unfavourable	Reference		Reference		Reference	
Average	0.705 (0.682-0.730)	<0.001	0.720 (0.707-0.733)	<0.001	0.725 (0.700-0.750)	<0.001
Favourable	0.112 (0.102-0.123)	<0.001	0.119 (0.109-0.129)	<0.001	0.120 (0.109-0.132)	<0.001
APOE ε4 non-carriers						
Unfavourable	Reference		Reference		Refences	
Average	0.687 (0.661-0.714)	<0.001	0.698 (0.671-0.726)	<0.001	0.704 (0.677-0.732)	<0.001
Favourable	0.102 (0.092-0.114)	<0.001	0.107 (0.096-0.119)	<0.001	0.108 (0.097-0.120)	<0.001
APOE ε4 carriers						
Unfavourable	Reference		Reference			
Average	0.780 (0.729-0.836)	<0.001	0.788 (0.736-0.845)	<0.001	0.790 (0.737-0.845)	<0.001
Favourable	0.163 (0.136-0.196)	<0.001	0.169 (0.141- 0.204)	<0.001	0.172 (0.143-0.207)	<0.001

*Unfavourable group as the reference group.

Model 1 unadjusted for covariates.

Model 2 adjusted for covariates.

Model 3 adjusted with the death as the competing risk

11. Supplementary table 9. Association between different lifestyle groups with cognitive impairment using the inverse probability weighting method

	Model 1	P	Model 2	P
Unfavourable	Reference		Reference	
Average	0.559 (0.541-0.577)	<0.001	0.559 (0.541-0.577)	<0.001
Favourable	0.052 (0.046-0.058)	<0.001	0.052 (0.046-0.057)	<0.001

*Unfavourable group as the reference group.

Model 1: Analyzed using the inverse probability weighting method, in which the variables were not adjusted.

Model 2: Analyzed using the inverse probability weighting method considering covariates.

12. Supplementary table 10. Longitudinal change in memory associated with the number of lifestyle factors in the cognitively normal population

	Estimate	Standard Error	P
(Intercept)	-0.400	0.023	<0.001
Number of healthy lifestyle factors			
1	-0.010	0.016	0.525
2	-0.011	0.015	0.485
3	0.003	0.015	0.833
4	0.025	0.016	0.126
5-6	0.023	0.019	0.210
Time	-0.150	0.005	<0.001
Age	-0.033	0.000	<0.001
Age^2	0.001	0.000	<0.001
Baseline memory score	0.328	0.003	<0.001
Learning effect	0.353	0.021	<0.001
Female	-0.009	0.003	0.004
Years of education			
1-6 years	0.012	0.005	0.018
7-12 years	0.013	0.005	0.010
>12 years	0.010	0.007	0.137
Region			
West	-0.015	0.004	<0.001
South	-0.032	0.004	<0.001
Number of lifestyle factors*time			
One healthy lifestyle factor: time	0.004	0.005	0.380
Two healthy lifestyle factors: time	0.016	0.004	<0.001
Three healthy lifestyle factors: time	0.020	0.004	<0.001
Four healthy lifestyle factors: time	0.028	0.004	<0.001
Five or six healthy lifestyle factors: time	0.037	0.005	<0.001

13. Supplementary table 11. Weighted scores of each health lifestyle factor based on β coefficient

	Estimate	P	Weighted Score
Never drinking			
No	0 (reference)		0
Yes	0.002	0.048	6
Never or former smoking			
No	0 (reference)		0
Yes	0.004	0.026	9
Healthy diet			
No	0 (reference)		0
Yes	0.016	<0.001	36
Regular physical exercise			
No	0 (reference)		0
Yes	0.007	<0.001	17
Active cognitive activity			
No	0 (reference)		0
Yes	0.010	<0.001	23
Active social contact			
No	0 (reference)		0
Yes	0.004	<0.001	10

Notes:

A healthy diet is defined as adherence to the appropriate amounts of at least 7 of the 12 dietary components. Regular physical exercise is defined as spending at least 150 or 75 min/week performing moderate or vigorous physical activity, respectively. Active cognitive activity is defined as participating in cognitive activities (including writing, reading, playing cards, mah-jong, and gaming) at least twice per week. Active social contact is defined as participating in social activities (including attending meetings or parties, visiting friends or relatives, traveling, and chatting online) at least twice per week. Never drinking and never or former smoking were also regarded as healthy factors.

14. Supplementary table 12. Longitudinal change in memory associated with the weighted lifestyle score in the cognitively normal population

	Estimate	Standard Error	P
(Intercept)	-0.414	0.017	<0.001
Intermediate score group	0.013	0.006	0.017
High score group	0.040	0.008	<0.001
Time	-0.144	0.003	<0.001
Age	-0.033	0.000	<0.001
Age^2	0.001	0.000	<0.001
Baseline memory score	0.327	0.003	<0.001
Learning effect	0.354	0.021	<0.001
Female	-0.010	0.003	0.003
Years of education			
1-6 years	0.012	0.005	0.017
7-12 years	0.013	0.005	0.009
>12 years	0.011	0.007	0.106
Region			
West	-0.014	0.004	<0.001
South	-0.031	0.004	<0.001
Intermediate score group: time	0.017	0.001	<0.001
High score group: time	0.029	0.002	<0.001

15. Supplementary table 13. Longitudinal change in memory after excluding each healthy lifestyle factor in the cognitively normal population

	Estimate	Standard Error	P
No diet			
(Intercept)	-0.483	0.003	<0.001
Average group*time	0.005	0.001	<0.001
Favourable group*time	0.016	0.002	<0.001
No cognitive activity			
(Intercept)	-0.480	0.003	<0.001
Average group*time	0.016	0.002	<0.001
Favourable group*time	0.025	0.002	<0.001
No physical exercise			
(Intercept)	-0.481	0.003	<0.001
Average group*time	0.016	0.002	<0.001
Favourable group*time	0.026	0.002	<0.001
No social contact			
(Intercept)	-0.480	0.003	<0.001
Average group*time	0.016	0.002	<0.001
Favourable group*time	0.027	0.002	<0.001
No smoking			
(Intercept)	-0.476	0.003	<0.001
Average group*time	0.011	0.001	<0.001
Favourable group*time	0.025	0.002	<0.001
No drinking			
(Intercept)	-0.476	0.003	<0.001
Average group*time	0.015	0.001	<0.001
Favourable group*time	0.028	0.002	<0.001

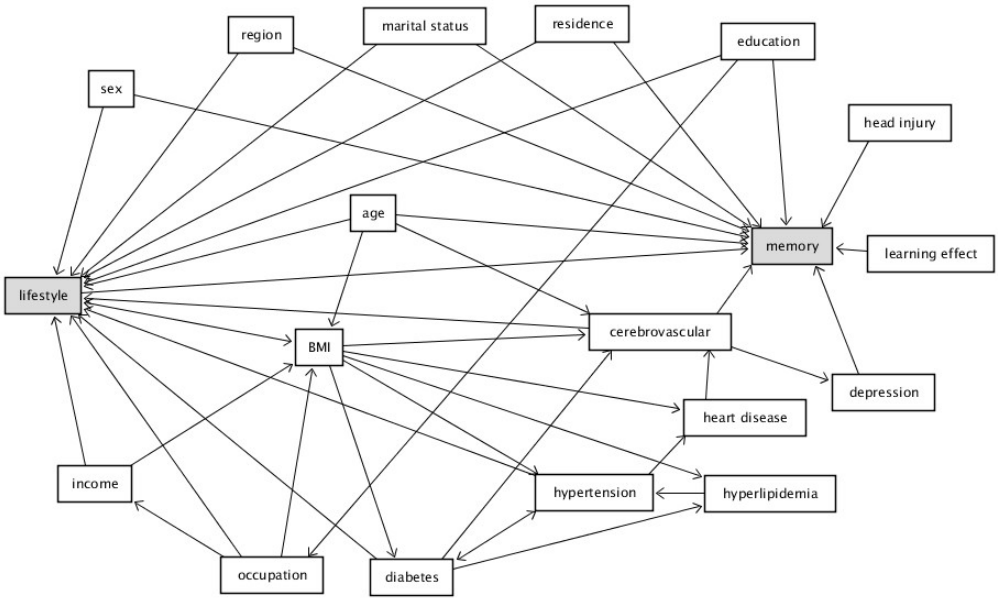
16. Supplementary table 14. Lifestyle effect on memory in participants without mild cognitive impairment or dementia throughout the follow-up

	Estimate	Standard Error	P
(Intercept)	-0.426	0.020	<0.001
Average group	0.017	0.014	0.206
Favourable group	0.051	0.014	<0.001
Time	-0.155	0.004	<0.001
Age	-0.036	0.001	<0.001
Age^2	0.001	0.000	<0.001
Baseline memory score	0.296	0.005	<0.001
Learning effect	0.342	0.018	<0.001
Female	-0.009	0.005	0.045
Years of education			
1-6 years	0.019	0.007	0.007
7-12 years	0.013	0.007	0.054
>12 years	0.007	0.009	0.464
Region			
West	-0.021	0.006	<0.001
South	-0.034	0.006	<0.001
Average group: time	0.017	0.003	<0.001
Favourable group: time	0.034	0.003	<0.001

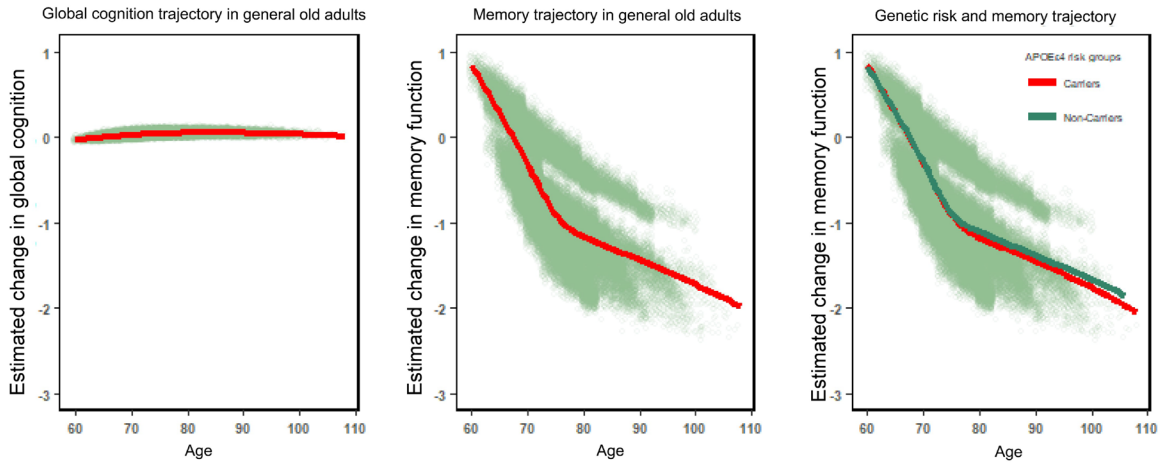
17.Supplementary table 15. Lifestyle effect on memory in participants without drop out or death throughout the follow-up

	Estimate	Standard Error	P
(Intercept)	-0.375	0.019	<0.001
Average group	0.009	0.008	0.240
Favourable group	0.059	0.010	<0.001
Time	-0.150	0.003	<0.001
Age	-0.035	0.000	<0.001
Age^2	0.001	0.000	<0.001
Baseline memory score	0.284	0.004	<0.001
Learning effect	0.300	0.021	<0.001
Female	-0.008	0.004	0.038
Years of education			
1-6 years	0.015	0.006	0.014
7-12 years	0.017	0.006	0.006
>12 years	0.019	0.008	0.021
Region			
West	-0.013	0.005	0.009
South	-0.035	0.005	<0.001
Average group: time	0.016	0.002	<0.001
Favourable group: time	0.025	0.002	<0.001

18.Supplementary figure 1. Directed acyclic graphs (DAG)

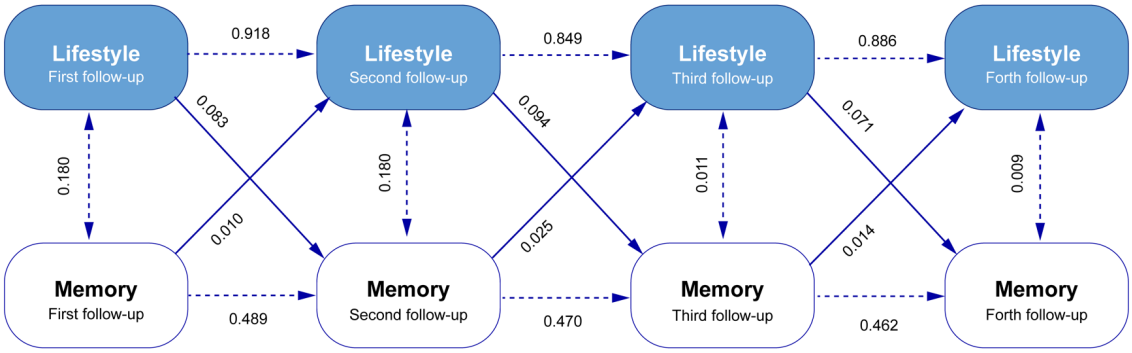


19. Supplementary figure 2. Global cognition and memory trajectories in the cognitively normal and APOE ε4 stratified populations



In cognitively normal older adults, global function (MMSE score) remains stable (left panel), memory performance (composite AVLT z score) declines rapidly (middle panel), and memory declines faster in APOE ε4 carriers than in non-carriers (right panel). Dots represent individuals' estimated z scores for MMSE or AVLT. Memory trajectories were calculated via linear mixed models, adjusted for covariates. MMSE, Mini-Mental State Examination; AVLT, auditory verbal learning test; APOE, apolipoprotein E.

20. Supplementary figure 3. Test of reverse causality between lifestyle and memory function



The cross-lagged models show the associations between the lifestyle profile and memory scores; Cross-lag pathways are used to show the results at the different follow-up time points. Path coefficients (the numbers in the figure e.g., 0.014, 0.010, etc.) are the standardized values.

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