Online Supplementary Materials

Association of combined healthy lifestyle factors with incident dementia in patients with type 2 diabetes

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eMethods.

Definitions of lifestyle factors in the UK Biobank study

During the baseline assessment (2006-2010) UK Biobank participants completed an extensive questionnaire that included information on lifestyle factors. Detailed questionnaires are available through the UK Biobank website (https://biobank.ndph.ox.ac.uk/showcase/).

i) Smoking behavior: The participants' current smoking status (current, previous, and never) was recorded, and no current smoking was defined as healthy.

ii) Alcohol consumption: Participants were asked about their drinking frequency and then further asked the amount of red wine (glasses), champagne plus white wine (glasses), beer plus cider (pints), spirits (measures), fortified wine (glasses), and other alcoholic drinks (glasses) they consumed on average in a week or a month. Alcohol intake in units per day was calculated by summing the average individual drinks per day according to alcohol unit reference (1). The units were then converted to grams assuming that one unit equals 8 g. Moderate alcohol consumption was defined as up to 1 drink (14 g)/day for women and up to 2 drinks (28 g)/day for men (2).

iii) Physical activity: The number of days of moderate/vigorous physical activity in a typical week and duration of moderate/vigorous physical activity on a typical day was recorded. The number of days was multiplied by the time duration per day to calculate the weekly total amount of moderate or vigorous physical activity. Regular physical activity was defined as ≥150 minutes of moderate activity or ≥75 minutes of vigorous activity per week or an equivalent combination.

iv) Diet: According to a previous UK Biobank study (3), we defined healthy diet as an adequate intake of at least 4 of the following 7 dietary components including increased consumption of fruits, vegetables, whole grains, (shell)fish, and reduced or no consumption of refined grains, processed and unprocessed meats following recommendations on dietary priorities for cardiometabolic health (4) (shown in Table S1).

v) Sleep duration: Total sleep duration was recorded by asking "About how many hours sleep do you get in every 24 hours? (Please include naps)". Adequate sleep duration was defined as sleep 7–8 h/day.

vi) Television watching time: Time spent watching television was recorded by asking "In a typical day, how many hours do you spend watching TV? (Put 0 if you do not spend any time doing it)". Less sedentary behavior was defined as the time spent watching television <4 h/day.

vii) Social contact: The social contact index used in the UK Biobank was constructed from three questions: question 1, including yourself, how many people are living together in your household (we assigned 1 point for living alone); question 2, how often do you visit friends or family or have them visit you (we assigned 1 point for answering less than once a month); question 3, which of the following (sports club or gym, pub or social club, religious group, adult education class, other group activity) do you engage in once a week or more often (we assigned 1point for answering none of the above). Individual scores were summed to obtain

an overall score ranging from 0 to 3 and categorized as active (score = 0), moderately active (score = 1), and isolated (scores ≥2), according to a previous UK Biobank study (5). Being active and moderately active was considered as having frequent social contact.

References

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3. Lourida I, Hannon E, Littlejohns TJ, Langa KM, Hyppönen E, Kuzma E, et al. Association of lifestyle and genetic risk with incidence of dementia. *JAMA*. 2019;322:430-437.

4. Mozaffarian D. Dietary and policy priorities for cardiovascular disease, diabetes, and obesity: a comprehensive review. *Circulation*. 2016;133:187-225.

5. Smith RW, Barnes I, Green J, Reeves GK, Beral V, Floud S. Social isolation and risk of heart disease and stroke: analysis of two large UK prospective studies. *Lancet Public Health*. 2021:6:e232-e239.

eTable 1. Diet component definitions used in the UK Biobank study.

Diet component	Intake goal	Field IDs
Fruit	≥3 servings/day	1309 (fresh fruit, pieces/day)
		1319 (dried fruit, pieces/day)
Vegetable	≥3 servings/day	1289 (cooked vegetables, tablespoons/day)
		1299 (salad/raw vegetables, tablespoons/day)
(Shell)fish	≥2 servings/week	1329 (oily fish [e.g. sardines, salmon, mackerel, herring]/week)
		1339 (non-oily fish [e.g. cod, tinned tuna, haddock]/week)
Processed meats	≤1 serving/week	1349 (processed meat [e.g. bacon, ham, sausages, meat pies, kebabs, burgers, chicken nuggets)/week or day)
Unprocessed meats	≤2 serving/week	1369 (beef/week or day)
		1379 (lamb or mutton/week or day)
		1389 (pork/week or day)
Whole grains	≥3 servings/day	1438 (slices of bread/week)
		1448 (type of bread, wholemeal or wholegrain)
		1458 (bowls of cereal/week)
		1468 (type of cereal, bran or oat or muesli cereal)
Refined grains	≤2 servings/day	1438 (slices of bread/week)
		1448 (type of bread, white or brown or other)
		1458 (bowls of cereal/week)
		1468 (type of cereal, biscuit or other)

Participants were considered to have an adequate intake of the diet component if they achieved the intake goal.

eTable 2. Codes used in the UK Biobank study to identify dementia cases.

Description	ICD-9 codes	ICD-10 codes	Self-reported code
Alzheimer's disease	331.0	F00, F00.0, F00.1, F00.2, F00.9, G30, G30.0, G30.1, G30.8, G30.9	Field 20002 Code 1263
Vascular dementia	290.4	F01, F01.0, F01.1, F01.2, F01.3, F01.8, F01.9, I67.3	
Frontotemporal dementia	331.1	F02.0, G31.0	
Other codes for all-cause dementia	290.2, 290.3, 291.2, 294.1, 331.2, 331.5	A81.0, F02, F02.1, F02.2, F02.3, F02.4, F02.8, F03, F05.1, F10.6, G31.1, G31.8	

All of the listed codes were used to identify all-cause dementia cases.

eTable 3. Baseline characteristics of participants by healthy lifestyle score.

	Healthy lifestyle score					
	0-2 (n=6709)	3 (n=18 106)	4 (n=37 668)	5 (n=50 611)	6 (n=39 858)	7 (n=14 994)
Age, years	64.0 (2.8)	64.1 (2.8)	64.1 (2.8)	64.1 (2.8)	64.1 (2.8)	64.1 (2.8)
Women	3256 (48.5)	8964 (49.5)	18 999 (50.4)	26 064 (51.5)	21 307 (53.5)	8304 (55.4)
White British	6540 (97.5)	17 663 (97.6)	36 822 (97.8)	49 545 (97.9)	39 116 (98.1)	14 790 (98.6)
Townsend index[a]	0.02 (3.49)	−0.97 (3.18)	−1.57 (2.92)	−1.88 (2.71)	−2.10 (2.60)	−2.27 (2.45)
College or university degree	815 (12.2)	3072 (17.0)	8316 (22.1)	14 576 (28.8)	13 906 (34.9)	6090 (40.6)
Body mass index, kg/m^2	28.9 (5.5)	28.7 (5.0)	28.1 (4.6)	27.4 (4.3)	26.7 (4.0)	26.0 (3.7)
HbA$_{1c}$, mmol/mol	39.1 (8.5)	38.0 (8.2)	37.4 (6.6)	36.9 (6.2)	36.4 (5.4)	36.2 (4.9)
HbA$_{1c}$, %	5.7 (0.8)	5.6 (0.8)	5.6 (0.6)	5.5 (0.6)	5.5 (0.5)	5.5 (0.4)
APOE ε4 carrier	1707 (25.4)	4859 (26.8)	10 288 (27.3)	14 240 (28.1)	11 403 (28.6)	4290 (28.6)
Morbidity count[b]						
None	1945 (29.0)	5902 (32.6)	13 849 (36.8)	20 199 (39.9)	17 611 (44.2)	6998 (46.7)
1	1813 (27.0)	5449 (30.1)	11 380 (30.2)	15 614 (30.9)	12 363 (31.0)	4621 (30.8)
2	1609 (24.0)	4031 (22.3)	7793 (20.7)	9685 (19.1)	6622 (16.6)	2296 (15.3)
≥3	1342 (20.0)	2724 (15.0)	4646 (12.3)	5113 (10.1)	3262 (8.2)	1079 (7.2)
Medication for BP, cholesterol or diabetes						
Antihypertensive	2631 (39.2)	6789 (37.5)	12 812 (34.0)	15 321 (30.3)	10 644 (26.7)	3659 (24.4)
Cholesterol lowering agents	2539 (37.8)	6025 (33.3)	11 337 (30.1)	13 597 (26.9)	9223 (23.1)	3210 (21.4)
Oral antidiabetic agents	546 (8.1)	1165 (6.4)	1890 (5.0)	1925 (3.8)	1125 (2.8)	335 (2.2)
Insulin	144 (2.2)	231 (1.3)	305 (0.8)	369 (0.7)	209 (0.5)	72 (0.5)
Reaction time, ms	603.5 (130.6)	594.2 (123.5)	587.6 (119.1)	585.1 (117.0)	583.2 (115.2)	582.7 (114.9)
Visual memory, no. of errors	4 (2-6)	4 (2-6)	4 (2-6)	4 (2-6)	4 (2-6)	4 (2-6)
Healthy lifestyle factors						
No current smoking	3609 (53.8)	14 411 (79.6)	33 971 (90.2)	48 536 (95.9)	39 376 (98.8)	—
Moderate alcohol consumption	689 (10.3)	3955 (21.8)	13 954 (37.0)	27 548 (54.4)	29 620 (74.3)	—
Regular physical activity	731 (10.9)	4208 (23.2)	14 584 (38.7)	28 819 (56.9)	30 794 (77.3)	—

Healthy diet	568 (8.5)	3261 (18.0)	11 876 (31.5)	25 754 (50.9)	30 415 (76.3)	—
Adequate sleep duration	1917 (28.6)	9051 (50.0)	24 921 (66.2)	40 006 (79.1)	35 791 (89.8)	—
Less sedentary behavior	869 (12.9)	4983 (27.5)	17 504 (46.5)	34 343 (67.9)	34 058 (85.4)	—
Frequent social contact	3698 (55.1)	14 449 (79.8)	33 862 (89.9)	48 049 (94.9)	39 094 (98.1)	—

Data are n (%), mean (SD), or median (IQR) unless otherwise stated. All *P* <0.001 for comparison across groups.

Abbreviations: *APOE* ε4, apolipoprotein ε4 allele; BP, blood pressure.

[a]Higher scores indicate higher levels of material deprivation.

[b]Prevalent diseases include hypertension, heart diseases, stroke, hyperlipidemia, head injury, depression, schizophrenia, Parkinson's disease, chronic obstructive pulmonary disease, chronic asthma, chronic liver diseases, and cancer.

eTable 4. Risk of incident dementia according to individual lifestyle factors.

	No. of cases/ total No.	Incidence rate per 1000 person-years	Model 1[a]		Model 2[b]	
			HR (95% CI)	*P* value	HR (95% CI)	*P* value
No current smoking						
No	410/13 049	2.76	1 (reference)		1 (reference)	
Yes	3941/154 897	2.14	0.77 (0.69-0.85)	<0.001	0.81 (0.73-0.90)	<0.001
Moderate alcohol consumption						
No	2180/77 186	2.39	1 (reference)		1 (reference)	
Yes	2171/90 760	2.01	0.86 (0.81-0.91)	<0.001	0.87 (0.82-0.92)	<0.001
Regular physical activity						
No	2031/73 816	2.33	1 (reference)		1 (reference)	
Yes	2320/94 130	2.07	0.87 (0.82-0.93)	<0.001	0.89 (0.84-0.94)	<0.001
Healthy diet						
No	2143/81 078	2.24	1 (reference)		1 (reference)	
Yes	2208/86 868	2.13	1.01 (0.95-1.08)	0.69	1.05 (0.98-1.12)	0.13
Adequate sleep duration						
No	1201/41 266	2.47	1 (reference)		1 (reference)	
Yes	3150/126 680	2.09	0.88 (0.82-0.94)	<0.001	0.89 (0.83-0.95)	<0.001
Less sedentary behavior						
No	1923/61 195	2.67	1 (reference)		1 (reference)	
Yes	2428/106 751	1.91	0.82 (0.77-0.88)	<0.001	0.84 (0.79-0.89)	<0.001
Frequent social contact						
No	515/13 800	3.24	1 (reference)		1 (reference)	
Yes	3836/154 146	2.09	0.70 (0.64-0.77)	<0.001	0.73 (0.67-0.81)	<0.001

Abbreviations: HR, hazard ratio.

[a]Model 1: adjusted for age, sex, education, ethnicity, Townsend index, morbidity count, diabetes status, body mass index, medication for hypertension and cholesterol, *APOE* ε4 carrier status, and cognitive performance at baseline.

[b]Model 2: additionally adjusted for other lifestyle factors.

eTable 5. Risk of Alzheimer's disease and vascular dementia according to diabetes and healthy lifestyle score[a].

		Alzheimer's disease				Vascular dementia			
		No. of cases	Incidence rate per 1000 person-years	HR (95% CI)[a]	*P* value	No. of cases	Incidence rate per 1000 person-years	HR (95% CI)	*P* value
No diabetes	**Healthy lifestyle score**								
	7	111	0.64	1 (reference)		52	0.30	1 (reference)	
	6	340	0.75	1.18 (0.95-1.46)	0.13	149	0.33	1.07 (0.78-1.46)	0.70
	5	497	0.88	1.38 (1.12-1.69)	0.002	209	0.37	1.13 (0.83-1.54)	0.43
	4	331	0.81	1.26 (1.02-1.57)	0.035	195	0.48	1.38 (1.02-1.88)	0.04
	3	164	0.87	1.35 (1.06-1.72)	0.017	99	0.52	1.46 (1.04-2.05)	0.03
	0-2	81	1.25	1.96 (1.47-2.63)	<0.001	36	0.55	1.48 (0.96-2.27)	0.076
Diabetes	**Healthy lifestyle score**								
	7	6	0.80	1.24 (0.54-2.82)	0.61	8	1.06	2.59 (1.22-5.47)	0.014
	6	30	1.18	1.70 (1.13-2.56)	0.011	27	1.06	2.31 (1.44-3.70)	<0.001
	5	73	1.76	2.50 (1.84-3.39)	<0.001	43	1.03	2.20 (1.45-3.32)	<0.001
	4	56	1.44	2.04 (1.46-2.84)	<0.001	45	1.16	2.37 (1.57-3.58)	<0.001
	3	33	1.48	2.21 (1.48-3.29)	<0.001	47	2.11	4.29 (2.84-6.48)	<0.001
	0-2	22	2.09	3.17 (1.99-5.06)	<0.001	21	2.00	4.01 (2.38-6.77)	<0.001

Abbreviations: HR, hazard ratio.

[a]Adjusted for age, sex, education, ethnicity, Townsend index, morbidity count, body mass index, medication for hypertension and cholesterol, *APOE* ε4 carrier status, and cognitive performance at baseline. Individuals without diabetes plus a healthy lifestyle score of 7 were used as the reference category.

P value for interaction between diabetes and healthy lifestyle score was 0.69 on Alzheimer's disease and 0.28 on vascular dementia.

eTable 6. Risk of incident dementia according to diabetes and weighted healthy lifestyle score category[a].

		No. of cases/ total No.	Incidence rate per 1000 person-years	HR (95% CI)[b]	*P* value
No diabetes	**Weighted lifestyle score**				
	7	249/14 355	1.44	1 (reference)	
	6 to <7	629/31 110	1.68	1.19 (1.03-1.38)	0.02
	5 to <6	1378/59 711	1.93	1.31 (1.14-1.50)	<0.001
	4 to <5	792/28 825	2.32	1.53 (1.32-1.76)	<0.001
	3 to <4	399/14 416	2.37	1.59 (1.35-1.86)	<0.001
	0 to <3	270/6760	3.54	2.27 (1.90-2.70)	<0.001
Diabetes	**Weighted lifestyle score**				
	7	21/639	2.81	1.74 (1.11-2.73)	0.015
	6 to <7	62/1702	3.14	1.86 (1.40-2.47)	<0.001
	5 to <6	195/4576	3.70	2.10 (1.73-2.55)	<0.001
	4 to <5	178/2997	5.26	2.96 (2.42-3.61)	<0.001
	3 to <4	106/1808	5.28	3.05 (2.42-3.86)	<0.001
	0 to <3	72/1047	6.47	3.80 (2.90-4.97)	<0.001

Abbreviations: HR, hazard ratio.

[a]The weighted lifestyle score was grouped into 6 categories based on the distribution of the unweighted score.

[b]Results were adjusted for age, sex, education, ethnicity, Townsend index, morbidity count, body mass index, medication for hypertension and cholesterol, *APOE* ε4 carrier status, and cognitive performance at baseline. Individuals without diabetes plus a weighted healthy lifestyle score of 7 were used as the reference category.

eTable 7. Risk of incident dementia according to diabetes and lifestyle profile with additional adjustment for employment status or income and after excluding incident dementia cases within 3 years of follow-up or participants with prevalent diseases.

		Additionally adjusting for employment status		Additionally adjusting for household income		Excluding cases in 3 years of follow-up (n=167 735)		Excluding prevalent diseases (n=66 504)	
		HR (95% CI)[a]	*P* value	HR (95% CI)[b]	*P* value	HR (95% CI)[c]	*P* value	HR (95% CI)[d]	*P* value
No diabetes	**Healthy lifestyle score**								
	7	1 (reference)		1 (reference)		1 (reference)		1 (reference)	
	6	1.24 (1.08-1.43)	0.003	1.24 (1.07-1.43)	0.003	1.23 (1.06-1.42)	0.006	1.51 (1.18-1.93)	0.001
	5	1.33 (1.16-1.53)	<0.001	1.32 (1.15-1.51)	<0.001	1.30 (1.13-1.50)	<0.001	1.52 (1.20-1.94)	<0.001
	4	1.47 (1.27-1.69)	<0.001	1.44 (1.25-1.66)	<0.001	1.45 (1.26-1.68)	<0.001	1.77 (1.38-2.28)	<0.001
	3	1.60 (1.37-1.87)	<0.001	1.57 (1.34-1.84)	<0.001	1.57 (1.34-1.85)	<0.001	1.67 (1.25-2.23)	<0.001
	0-2	2.07 (1.72-2.50)	<0.001	2.03 (1.68-2.45)	<0.001	2.04 (1.68-2.47)	<0.001	2.76 (1.95-3.90)	<0.001
Diabetes	**Healthy lifestyle score**								
	7	1.76 (1.12-2.75)	0.014	1.74 (1.11-2.73)	0.015	1.62 (1.01-2.59)	0.044	1.26 (0.18-9.09)	0.82
	6	1.84 (1.42-2.38)	<0.001	1.82 (1.41-2.35)	<0.001	1.82 (1.40-2.36)	<0.001	1.95 (0.71-5.33)	0.19
	5	2.40 (1.97-2.93)	<0.001	2.36 (1.93-2.88)	<0.001	2.38 (1.94-2.92)	<0.001	2.63 (1.31-5.25)	0.006
	4	2.42 (1.97-2.96)	<0.001	2.38 (1.94-2.91)	<0.001	2.33 (1.89-2.87)	<0.001	1.80 (0.73-4.47)	0.20
	3	3.19 (2.55-3.99)	<0.001	3.14 (2.51-3.93)	<0.001	3.11 (2.47-3.91)	<0.001	3.98 (1.83-8.65)[e]	<0.001
	0-2	3.89 (2.97-5.10)	<0.001	3.85 (2.94-5.04)	<0.001	4.05 (3.08-5.32)	<0.001		

Abbreviations: HR, hazard ratio.

[a]Adjusted for age, sex, education, ethnicity, Townsend index, morbidity count, employment (currently employed or not), body mass index, medication for hypertension and cholesterol, *APOE ε4* carrier status, and cognitive performance at baseline.

[b]Adjusted for age, sex, education, ethnicity, Townsend index, morbidity count, household income (in quintiles), body mass index, medication for hypertension and cholesterol, *APOE ε4* carrier status, and cognitive performance at baseline.

[c]Adjusted for age, sex, education, ethnicity, Townsend index, morbidity count, body mass index, medication for hypertension and cholesterol, *APOE* ε4 carrier status, and cognitive performance at baseline.

[d]Adjusted for age, sex, education, ethnicity, Townsend index, body mass index, *APOE* ε4 carrier status, and cognitive performance at baseline.

[e]Due to the limited number of cases, the category of lifestyle score 0-2 and score 3 was combined.

eTable 8. Risk of incident dementia according to diabetes and healthy lifestyle score after multiple imputation (n=201 930)[a].

		No. of cases/total No.	HR (95% CI)[b]	*P* value	HR (95% CI)[c]	*P* value
No diabetes	**Healthy lifestyle score**					
	7	292/15 844	1 (reference)		0.45 (0.38-0.53)	<0.001
	6	977/42 962	1.23 (1.07-1.41)	0.003	0.55 (0.48-0.63)	<0.001
	5	1369/55 277	1.30 (1.14-1.48)	<0.001	0.58 (0.51-0.67)	<0.001
	4	1211/42 198	1.49 (1.30-1.70)	<0.001	0.67 (0.59-0.76)	<0.001
	3	689/20 965	1.67 (1.45-1.94)	<0.001	0.76 (0.66-0.87)	<0.001
	0-2	354/8190	2.21 (1.88-2.61)	<0.001	1 (reference)	
Diabetes	**Healthy lifestyle score**					
	7	26/743	1.76 (1.15-2.70)	0.009	0.51 (0.32-0.83)	0.007
	6	110/2589	1.99 (1.55-2.54)	<0.001	0.59 (0.45-0.79)	<0.001
	5	234/4441	2.42 (2.01-2.90)	<0.001	0.71 (0.56-0.91)	0.007
	4	245/4450	2.52 (2.11-3.02)	<0.001	0.73 (0.57-0.94)	0.016
	3	197/2821	3.36 (2.78-4.06)	<0.001	0.94 (0.73-1.20)	0.60
	0-2	105/1450	3.69 (2.91-4.68)	<0.001	1 (reference)	

Abbreviations: HR, hazard ratio.

[a]Missing values for exposure (lifestyle) and covariates were imputed using multiple imputations by chained equations with 5 imputations.

[b]Adjusted for age, sex, education, ethnicity, Townsend index, morbidity count, body mass index, medication for hypertension and cholesterol, *APOE* ε4 carrier status, and cognitive performance at baseline.

[c]Among participants with diabetes, models were additionally adjusted for HbA_{1c} level (<53 or ≥53 mmol/mol [7.0%]), diabetes duration (<5, 5-9, or ≥10 years), and diabetes medication use (oral antidiabetic drugs only, insulin use, or neither).

eTable 9. Risk of incident dementia according to diabetes and healthy lifestyle score using a competing risk analysis.

		HR (95% CI)[a]	*P* value	HR (95% CI)[b]	*P* value
No diabetes	**Healthy lifestyle score**				
	7	1 (reference)		0.53 (0.44-0.64)	<0.001
	6	1.23 (1.07-1.42)	0.004	0.65 (0.56-0.76)	<0.001
	5	1.30 (1.14-1.50)	<0.001	0.69 (0.60-0.81)	<0.001
	4	1.43 (1.24-1.65)	<0.001	0.76 (0.65-0.89)	<0.001
	3	1.52 (1.30-1.77)	<0.001	0.81 (0.69-0.95)	0.011
	0-2	1.88 (1.56-2.26)	<0.001	1 (reference)	
Diabetes	**Healthy lifestyle score**				
	7	1.70 (1.09-2.64)	0.02	0.53 (0.32-0.87)	0.013
	6	1.75 (1.36-2.27)	<0.001	0.56 (0.40-0.78)	<0.001
	5	2.29 (1.87-2.80)	<0.001	0.73 (0.54-0.97)	0.029
	4	2.25 (1.83-2.76)	<0.001	0.71 (0.53-0.94)	0.018
	3	2.89 (2.31-3.61)	<0.001	0.87 (0.65-1.17)	0.36
	0-2	3.31 (2.52-4.36)	<0.001	1 (reference)	

Abbreviations: HR, hazard ratio.

[a]Subdistribution HRs and 95% CIs were calculated using Fine and Gray proportional hazards models adjusting for age, sex, education, ethnicity, Townsend index, morbidity count, body mass index, medication for hypertension and cholesterol, *APOE* ε4 carrier status, and cognitive performance at baseline.

[b]Among participants with diabetes, models were additionally adjusted for HbA$_{1c}$ level (<53 or ≥53 mmol/mol [7.0%]), diabetes duration (<5, 5-9, or ≥10 years), and diabetes medication use (oral antidiabetic drugs only, insulin use, or neither).

eTable 10. Risk of incident dementia according to diabetes and healthy lifestyle score by *APOE* ε4 carrier status.

		APOE ε4 non-carriers (n=121 159)		*APOE* ε4 carriers (n=46 787)		*P* values for
No diabetes	**Healthy lifestyle score**	**HR (95% CI)**	***P* value**	**HR (95% CI)**	***P* value**	**interaction**
	7	1 (reference)		1 (reference)		<0.001
	6	1.31 (1.05-1.64)	0.016	1.19 (0.99-1.44)	0.061	
	5	1.43 (1.15-1.77)	0.001	1.26 (1.05-1.51)	0.013	
	4	1.61 (1.29-2.00)	<0.001	1.37 (1.14-1.65)	<0.001	
	3	1.80 (1.42-2.28)	<0.001	1.48 (1.20-1.82)	<0.001	
	0-2	2.35 (1.79-3.10)	<0.001	1.92 (1.48-2.49)	<0.001	
Diabetes	**Healthy lifestyle score**					
	7	2.01 (1.10-3.68)	0.023	1.49 (0.76-2.93)	0.25	
	6	2.06 (1.43-2.96)	<0.001	1.67 (1.16-2.41)	0.006	
	5	2.64 (1.97-3.55)	<0.001	2.19 (1.66-2.88)	<0.001	
	4	2.95 (2.21-3.94)	<0.001	1.94 (1.45-2.61)	<0.001	
	3	3.74 (2.73-5.12)	<0.001	2.74 (1.97-3.80)	<0.001	
	0-2	5.21 (3.64-7.46)	<0.001	2.83 (1.84-4.35)	<0.001	

Abbreviations: HR, hazard ratio.

Results were adjusted for age, sex, education, ethnicity, Townsend index, morbidity count, body mass index, medication for hypertension and cholesterol, and cognitive performance at baseline. Individuals without diabetes plus a healthy lifestyle score of 7 were used as the reference category.

eTable 11. Risk of incident dementia according to the number of traditional or emerging healthy lifestyle factors by diabetes.

	No diabetes			Diabetes		
	No. of cases/ person-years	HR (95% CI)[a]	*P* value	No. of cases/ person-years	HR (95% CI)[b]	*P* value
Number of traditional healthy lifestyle factors[c]						
0-1	590/247 997	1 (reference)		143/27 824	1 (reference)	
2	1229/598 248	0.87 (0.79-0.96)	0.005	255/52 480	0.93 (0.76-1.14)	0.49
3	1322/680 690	0.84 (0.76-0.92)	<0.001	179/47 578	0.76 (0.61-0.95)	0.016
4	576/320 785	0.77 (0.68-0.86)	<0.001	57/17 127	0.70 (0.51-0.95)	0.023
Per 1 number increment		0.92 (0.89-0.95)	<0.001		0.88 (0.81-0.96)	0.003
Number of emerging healthy lifestyle factors[d]						
0-1	649/232 375	1 (reference)		176/28 744	1 (reference)	
2	1619/753 305	0.82 (0.75-0.90)	<0.001	283/65 603	0.77 (0.63-0.93)	0.006
3	1449/862 040	0.69 (0.63-0.76)	<0.001	175/50 661	0.65 (0.52-0.81)	<0.001
Per 1 number increment		0.84 (0.80-0.87)	<0.001		0.84 (0.76-0.93)	<0.001

Abbreviations: HR, hazard ratio.

[a]Adjusted for age, sex, education, ethnicity, Townsend index, morbidity count, body mass index, medication for hypertension and cholesterol, *APOE ε*4 carrier status, and cognitive performance at baseline. Traditional and emerging lifestyle factors were mutually adjusted.

[b]Among people with diabetes, models were additionally adjusted for HbA_{1c} level (<53 or ≥53 mmol/mol [7.0%]), diabetes duration (<5, 5-9, or ≥10 years), and diabetes medication use (oral antidiabetic drugs only, insulin use, or neither).

[c]Traditional healthy lifestyle factors include no current smoking, moderate alcohol consumption, regular physical activity, and healthy diet.

[d]Emerging healthy lifestyle factors include adequate sleep duration, less sedentary behavior, and frequent social contact.

eTable 12. Risk of incident dementia according to diabetes and lifestyle category[a].

	No. of cases/ total No.	Incidence rate per 1000 person-years	HR (95% CI)[b]	P value
No diabetes				
Favorable lifestyle	1057/52 038	1.69	1 (reference)	
Intermediate lifestyle	1990/81 305	2.05	1.18 (1.09-1.27)	<0.001
Unfavorable lifestyle	670/21 834	2.65	1.47 (1.33-1.62)	<0.001
Diabetes				
Favorable lifestyle	101/2814	3.09	1.54 (1.25-1.90)	<0.001
Intermediate lifestyle	338/6974	4.23	2.03 (1.78-2.31)	<0.001
Unfavorable lifestyle	195/2981	6.01	2.93 (2.49-3.44)	<0.001

Abbreviations: HR, hazard ratio.

[a]Participants were classified into three lifestyle categories according to healthy lifestyle score: favorable lifestyle (score 6-7), intermediate lifestyle (score 4-5), and unfavorable lifestyle (score 0-3).

[b]Results were adjusted for age, sex, education, ethnicity, Townsend index, morbidity count, body mass index, medication for hypertension and cholesterol, *APOE* ε4 carrier status, and cognitive performance at baseline. Individuals without diabetes plus a favorable lifestyle were used as the reference category. *P* value for interaction between diabetes and lifestyle category was 0.032.

eTable 13. Risk of incident dementia according to healthy lifestyle score among participants with diagnosed diabetes (n=11 419).

	Healthy lifestyle score					
	0-2	**3**	**4**	**5**	**6**	**7**
No. of cases/total No.	67/860	114/1789	150/3004	166/3232	74/1957	19/577
Incidence rate per 1000 person-years	7.42	5.78	4.42	4.45	3.26	2.81
HR (95% CI)[a]	1 (reference)	0.79 (0.58-1.07)	0.61 (0.46-0.82)	0.64 (0.48-0.86)	0.48 (0.34-0.67)	0.43 (0.26-0.73)
P value		0.12	0.001	0.003	<0.001	0.002
10-year absolute risk[b], % (95% CI)	5.58 (4.18-7.26)	4.03 (3.18-5.01)	3.40 (2.79-4.09)	2.88 (2.34-3.50)	2.40 (1.79-3.15)	1.73 (0.89-3.07)
Number needed to treat[c]		65	46	37	32	26

Abbreviations: HR, hazard ratio

[a]Adjusted for age, sex, education, ethnicity, Townsend index, morbidity count, body mass index, medication for hypertension and cholesterol, *APOE* ε4 carrier status, and cognitive performance at baseline. Among patients with diabetes, models were additionally adjusted for HbA_{1c} level (<53 or ≥53 mmol/mol [7.0%]), diabetes duration (<5, 5-9, or ≥10 years), and diabetes medication use (oral antidiabetic drugs only, insulin use, or neither).

[b]Calculated as the cumulative incidence accounting for competing risk of death.

[c]Refers to the number needed to adhere to a specified number of healthy lifestyle factors to prevent one dementia case over 10 years.

eTable 14. Population attributable fractions of lifestyle factors for incident dementia among participants with diabetes (n=12 769)[a].
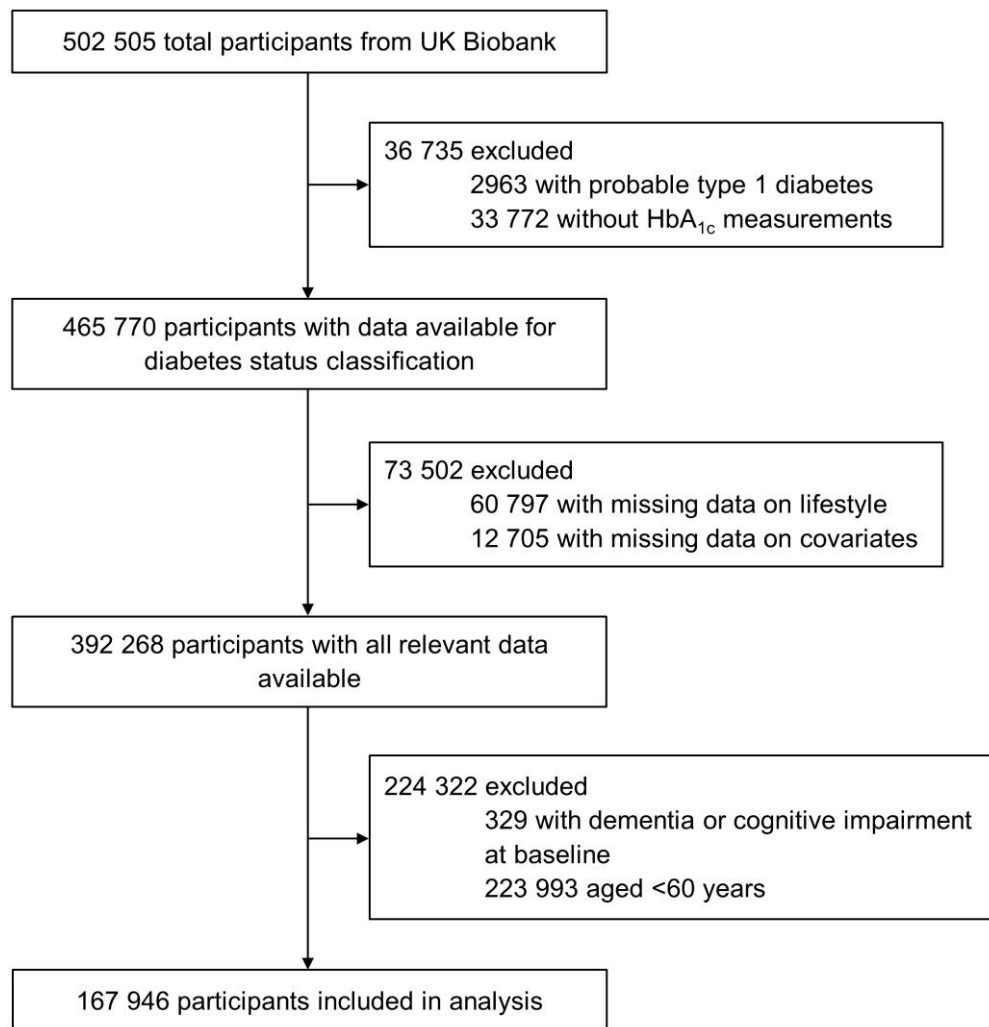
	No. of participants (%)	No. of cases (%)	PAF, % (95% CI)[b]
No current smoking	11 607 (90.9)	574 (4.9)	0.8 (-1.6, 3.2)
Moderate alcohol consumption	6197 (48.5)	264 (4.3)	12.4 (3.0, 21.6)
Regular physical activity	6017 (47.1)	279 (4.6)	7.1 (-2.1, 16.2)
Healthy diet	5987 (46.9)	288 (4.8)	1.9 (-6.8, 10.6)
Adequate sleep duration	9116 (71.4)	421 (4.6)	6.3 (0, 12.6)
Less sedentary behavior	6584 (51.6)	285 (4.3)	7.3 (-2.6, 17.0)
Frequent social contact	11 243 (88.0)	541 (4.8)	2.8 (-1.4, 6.9)
All 7 healthy lifestyle factors	639 (5.0)	21 (3.3)	32.5 (4.8, 55.5)

Abbreviations: HR, hazard ratio; PAF, population attributable fraction.

[a]PAF is percentage of dementia cases that would theoretically not have occurred if all people with diabetes had been adhering to a healthy lifestyle. The models were adjusted for age, sex, education, ethnicity, Townsend index, morbidity count, body mass index, medication for hypertension and cholesterol, *APOE ε4* carrier status, cognitive performance at baseline, HbA_{1c} level (<53 or ≥53 mmol/mol [7.0%]), diabetes duration (<5, 5-9, or ≥10 years), and diabetes medication use (oral antidiabetic drugs only, insulin use, or neither). Individual lifestyle factors were mutually adjusted.
[b]Compared with all other participants not in this category.

eFigure 1. Flowchart for the study sample from the UK Biobank.

502 505 total participants from UK Biobank

→ 36 735 excluded
    2963 with probable type 1 diabetes
    33 772 without HbA_{1c} measurements

465 770 participants with data available for diabetes status classification

→ 73 502 excluded
    60 797 with missing data on lifestyle
    12 705 with missing data on covariates

392 268 participants with all relevant data available

→ 224 322 excluded
    329 with dementia or cognitive impairment at baseline
    223 993 aged <60 years

167 946 participants included in analysis

eFigure 2. Dose-response relationships between healthy lifestyle score and incidence of dementia among participants with no diabetes (A) and diabetes (B).
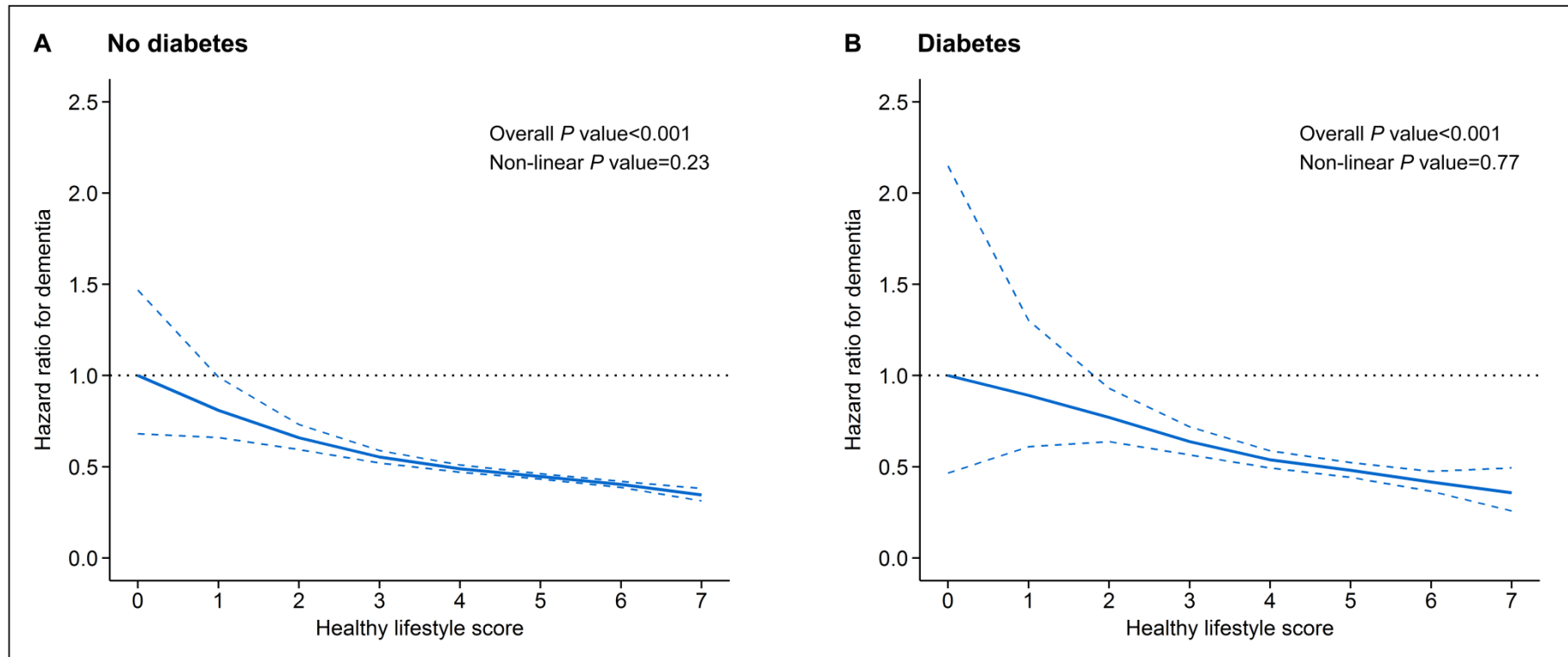
Solid lines indicate hazard ratios and dashed lines represent 95% CIs using penalized splines fitted in Cox proportional hazard models. Results were adjusted for age, sex, education, ethnicity, Townsend index, morbidity count, body mass index, medication for hypertension and cholesterol, *APOE* ε4 carrier status, and cognitive performance at baseline. Among participants with diabetes, results were additionally adjusted for HbA$_{1c}$ level (<53 or ≥53 mmol/mol [7.0%]), diabetes duration (<5, 5-9, or ≥10 years), and diabetes medication use (oral antidiabetic drugs only, insulin use, or neither). People with a healthy lifestyle score of 0 were used as the reference group.

eFigure 3. Cumulative incidence of dementia according to lifestyle category among participants with no diabetes (A) and diabetes (B).
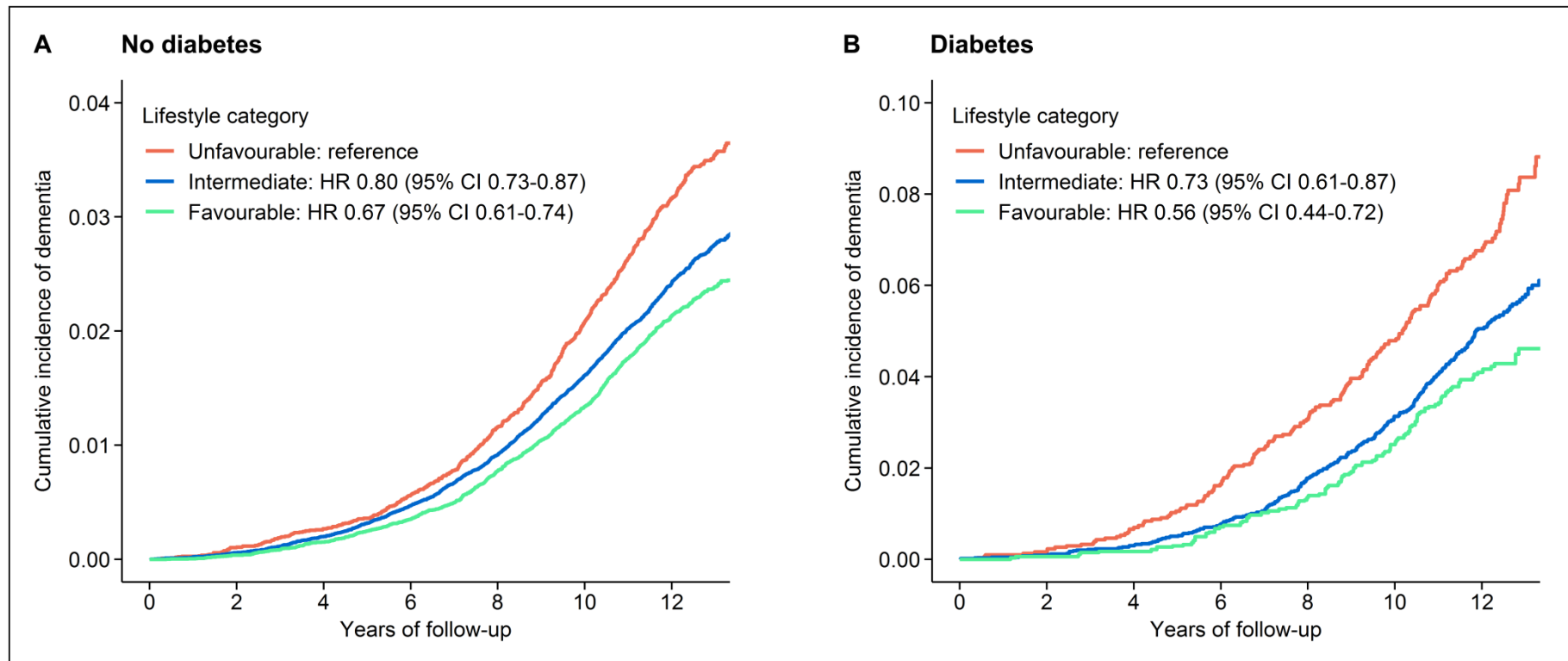
Participants were classified into three lifestyle categories according to healthy lifestyle score: favorable lifestyle (score 6-7), intermediate lifestyle (score 4-5), and unfavorable lifestyle (score 0-3). Cox proportional hazards models were adjusted for age, sex, education, ethnicity, Townsend index, morbidity count, body mass index, medication for hypertension and cholesterol, *APOE* ε4 carrier status, and cognitive performance at baseline. Among participants with diabetes, models were additionally adjusted for HbA$_{1c}$ level (<53 or ≥53 mmol/mol [7.0%]), diabetes duration (<5, 5-9, or ≥10 years), and diabetes medication use (oral antidiabetic drugs only, insulin use, or neither).