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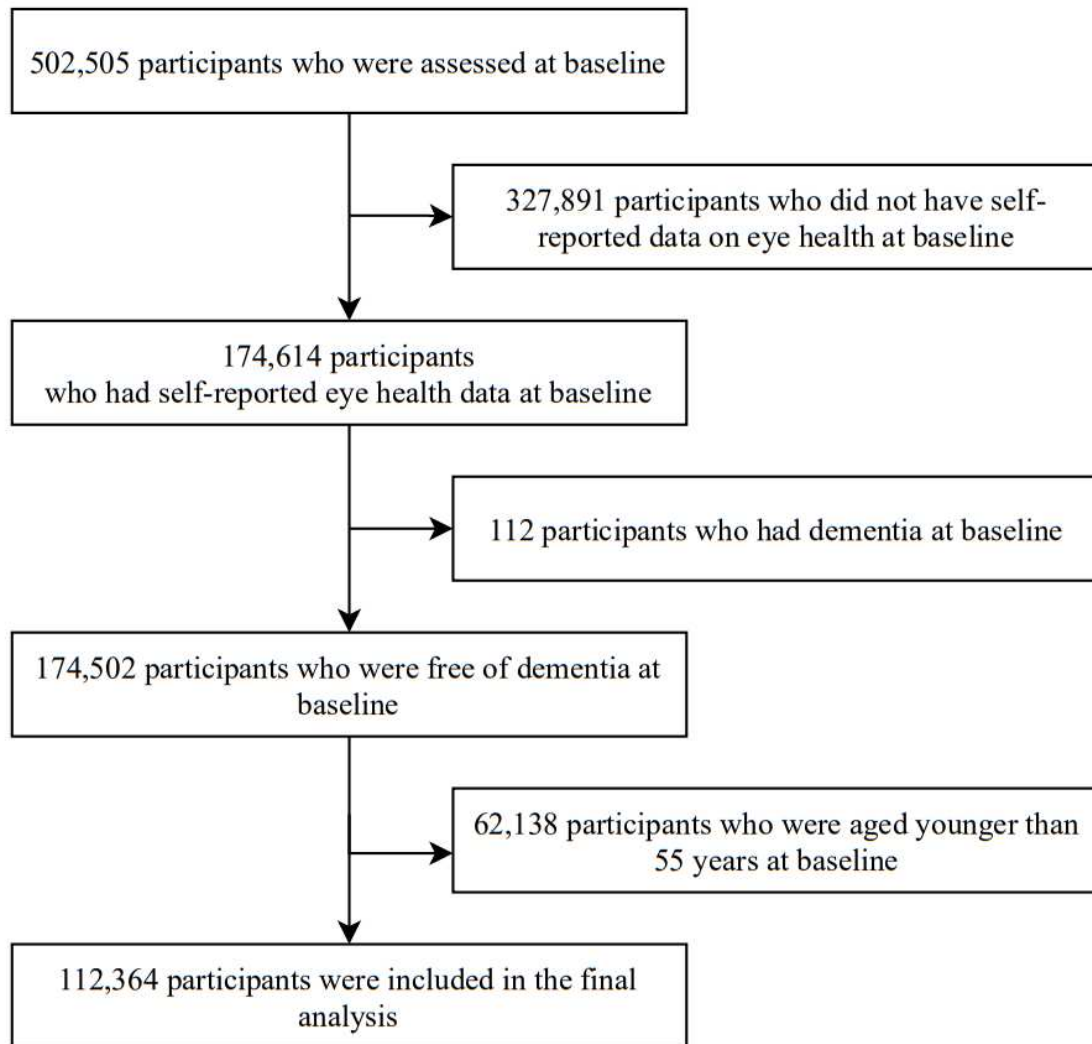


Figure e-1. Flowchart for participant selection from the UK Biobank cohort

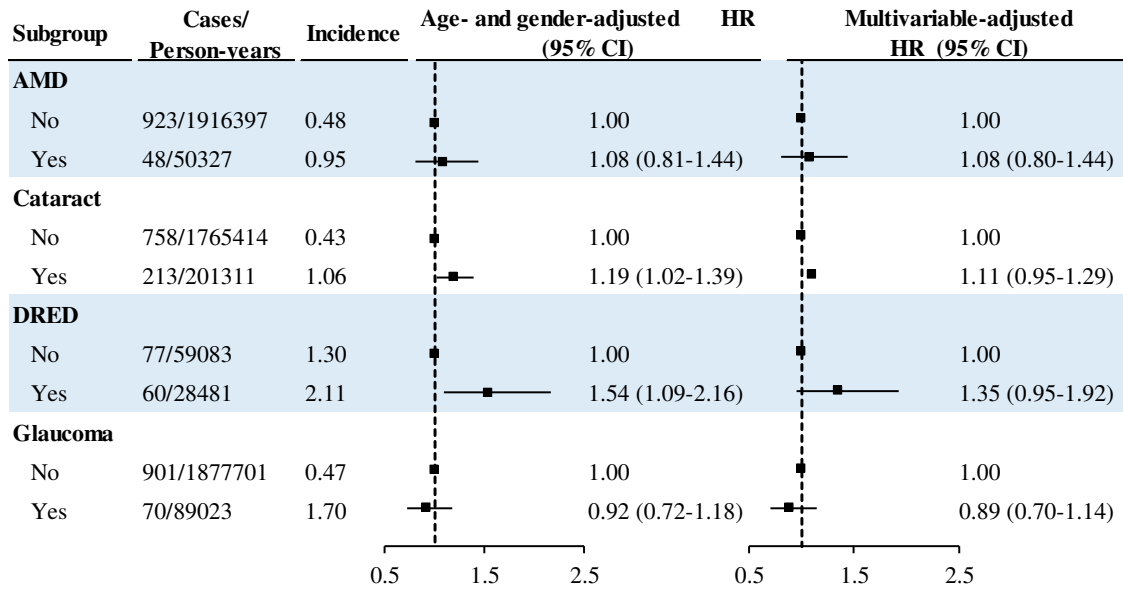


Figure e-2. The risk for Alzheimer's disease associated with ophthalmic conditions

Incidence of Alzheimer's disease represents cases per 1000 person-years. HR (95% CI) for incident Alzheimer's disease associated with ophthalmic conditions was estimated using Cox proportional regression models adjusted for age, gender, education, income, cooked vegetables intake, raw vegetables intake, fresh fruits intake, dried fruits intake, smoking, alcohol consumption, physical activity, BMI, cholesterol, and glucose at baseline. The association between DRED and Alzheimer's disease was conducted among diabetic patients. CI, confidence interval; HR, hazard ratio.

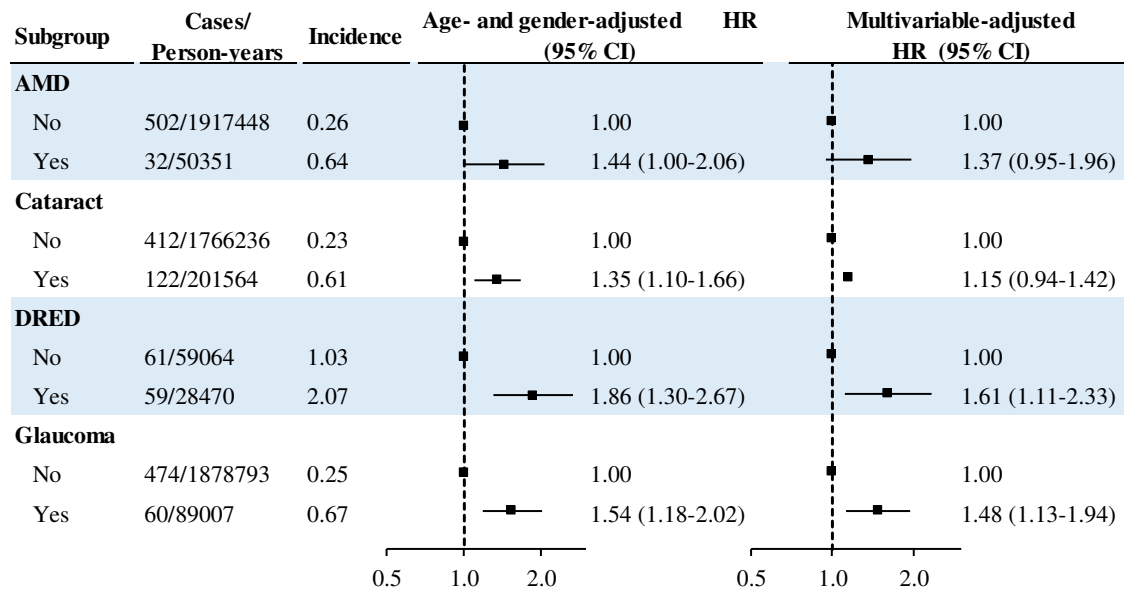


Figure e-3. The risk for vascular dementia associated with ophthalmic conditions

Incidence of vascular dementia represents cases per 1000 person-years. HR (95% CI) for incident vascular dementia associated with ophthalmic conditions was estimated using Cox proportional regression models adjusted for age, gender, education, income, cooked vegetables intake, raw vegetables intake, fresh fruits intake, dried fruits intake, smoking, alcohol consumption, physical activity, BMI, cholesterol, and glucose at baseline. The association between DRED and vascular dementia was conducted among diabetic patients. CI, confidence interval; HR, hazard ratio.

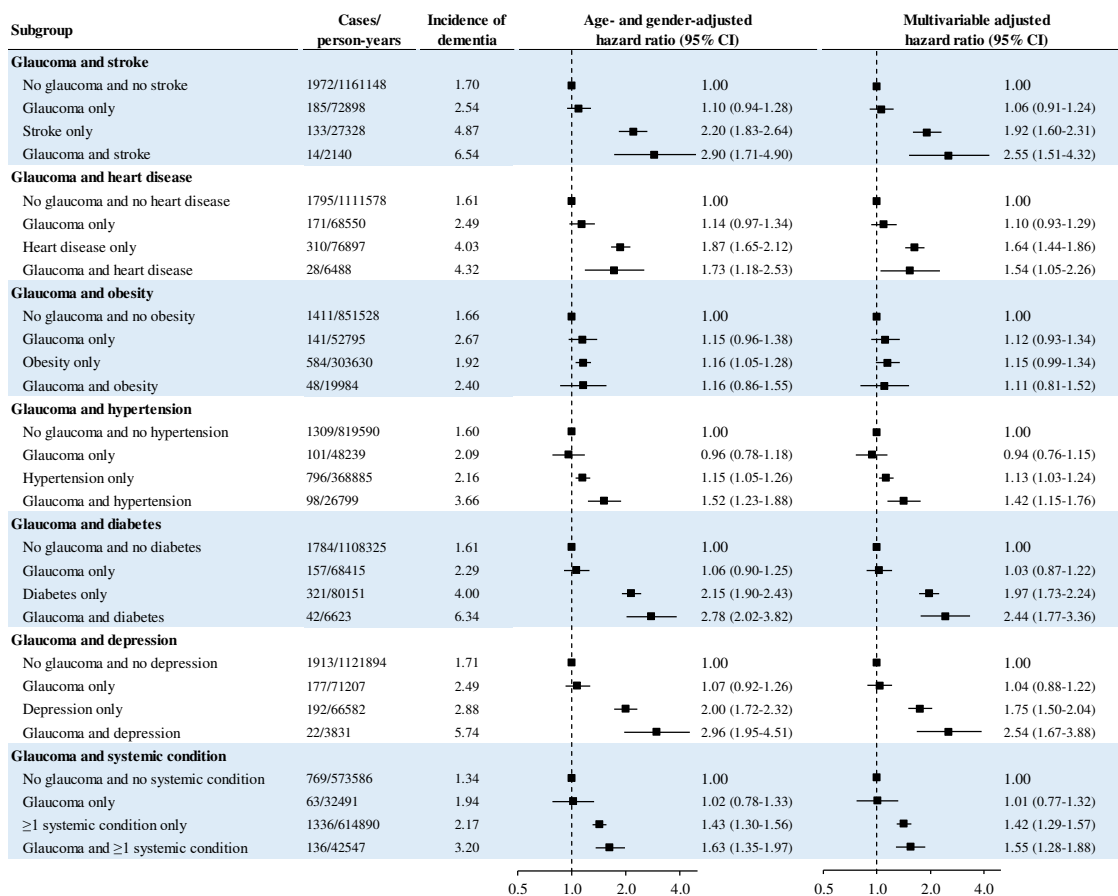


Figure e-4. The risk for incident all-cause dementia associated with glaucoma and systemic conditions

Incidence of all-cause dementia represents cases per 1000 person-years. Hazard ratio (95% CI) for incident all-cause dementia associated with glaucoma and systemic conditions was estimated using Cox proportional regression models. Multivariable analysis was adjusted for age, gender, education, income, cooked vegetables intake, raw vegetables intake, fresh fruits intake, dried fruits intake, smoking, alcohol consumption, physical activity, BMI, cholesterol, and glucose at baseline. Central squares of each horizontal line represent the hazard ratio for each subgroup. Horizontal lines indicate the range of the 95% CI and the vertical dash lines indicate the hazard ratio of 1.0. CI, confidence interval.

Exposure	Mediator	HR (95% CI) before adjustment for mediator	HR (95% CI) after adjustment for mediator	Percentage of total effect explained by mediator (95% CI)	P value for mediation
Cataract at baseline	Hypertension	1.14 (1.03-1.26)	1.13 (1.02-1.25)	7.1 (2.7-17.0)	<0.0001
Cataract at baseline	Diabetes	1.11 (1.00-1.23)	1.10 (0.99-1.22)	9.2 (2.9-25.4)	<0.0001
Cataract at baseline	Stroke	1.14 (1.03-1.26)	1.11 (1.00-1.22)	22.4 (8.0-48.9)	<0.0001
Cataract at baseline	Heart disease	1.13 (1.02-1.25)	1.12 (1.01-1.24)	9.1 (3.3-22.5)	<0.0001
Cataract at baseline	Depression	1.14 (1.03-1.26)	1.12 (1.01-1.24)	12.0 (4.5-28.4)	0.0001
Cataract at baseline	Chronic conditions combined ^a	1.11 (1.01-1.26)	1.03 (0.93-1.14)	65.4 (5.3-98.5)	<0.0001
DRED at baseline	Hypertension	2.34 (1.99-2.74)	2.30 (1.96-2.70)	1.9 (1.0-3.3)	<0.0001
DRED at baseline	Stroke	2.32 (1.98-2.73)	2.15 (1.82-2.52)	9.4 (6.0-14.5)	<0.0001
DRED at baseline	Heart disease	2.29 (1.95-2.68)	2.19 (1.86-2.56)	5.5 (3.7- 8.1)	<0.0001
DRED at baseline	Depression	2.35 (2.01-2.76)	2.29 (1.95-2.69)	3.3 (1.7- 6.5)	0.0011
DRED at baseline	Chronic conditions combined ^b	1.66 (1.37-2.02)	1.52 (1.24-1.85)	18.0 (9.4-31.5)	<0.0001

Figure e-5. Mediation analysis of the association between ophthalmic conditions and incident all-cause dementia by newly developed systemic conditions

HR (95% CI) for incident all-cause dementia associated with glaucoma and systemic conditions was estimated using Cox proportional regression models adjusted for age, gender, education, income, cooked vegetables intake, raw vegetables intake, fresh fruits intake, dried fruits intake, smoking, alcohol consumption, physical activity, BMI, cholesterol, and glucose at baseline. The corresponding systemic condition at baseline for the mediator was additionally adjusted for. Central squares of each horizontal line represent the mean percentage of total effect mediated by newly developed conditions during follow-up (before the onset of dementia). The horizontal line indicates the range of the 95% CI and the vertical dash line indicates the percentage of 0.0. CI, confidence interval; DRED, diabetes-related eye disease; HR, hazard ratio.

*The potential mediation effect of those systemic conditions as significant mediators combined was computed for the association between cataract and incident all-cause dementia.

†The potential mediation effect of those systemic conditions as significant mediators combined was computed for the association between DRED and incident all-cause dementia.

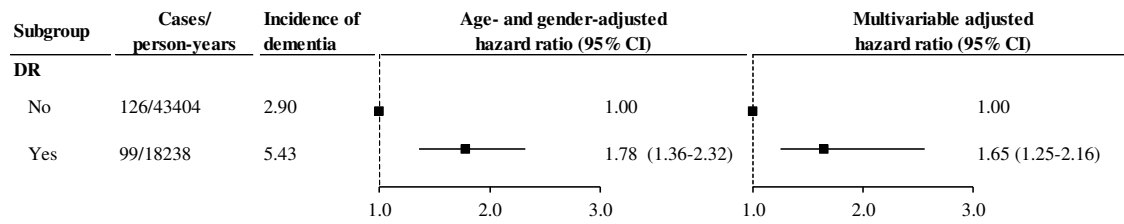


Figure e-6. Risk for incident all-cause dementia associated with diabetic retinopathy in participants with diabetes

Incidence of all-cause dementia represents cases per 1000 person-years. Hazard ratio (95% CI) for incident all-cause dementia associated with diabetic retinopathy was estimated using Cox proportional regression models adjusted for age, gender, education, income, cooked vegetables intake, raw vegetables intake, fresh fruits intake, dried fruits intake, smoking, alcohol consumption, physical activity, BMI, cholesterol, glucose, and duration of diabetes at baseline. Central squares of each horizontal line represent the hazard ratios for each subgroup. Horizontal lines indicate the ranges of the 95% CIs and the vertical dash lines indicate the hazard ratio of 1.0. CI, confidence interval; DRED, diabetes-related eye disease.

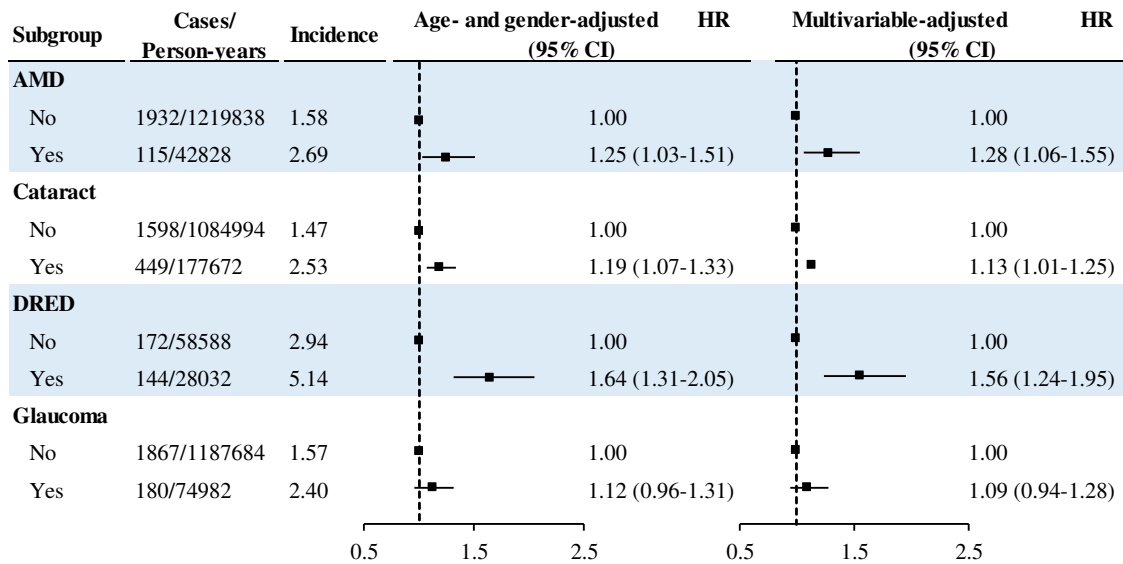


Figure e-7. Risk for incident all-cause dementia associated with ophthalmic conditions by excluding those who developed dementia in the first five years of follow-up

Incidence of all-cause dementia represents cases per 1000 person-years. HR (95% CI) for incident all-cause dementia associated with ophthalmic conditions was estimated using Cox proportional regression models adjusted for age, gender, education, income, cooked vegetables intake, raw vegetables intake, fresh fruits intake, dried fruits intake, smoking, alcohol consumption, physical activity, BMI, cholesterol, and glucose at baseline. Central squares of each horizontal line represent the hazard ratios for each subgroup. Horizontal lines indicate the ranges of the 95% CIs and the vertical dash lines indicate the hazard ratio of 1.0. AMD, age-related macular degeneration; CI, confidence interval; DRED, diabetes-related eye disease.

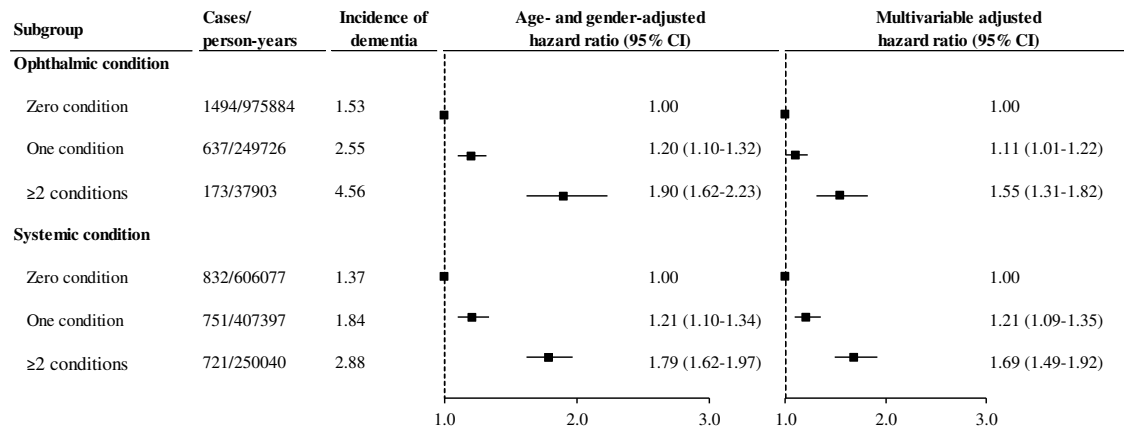


Figure e-8. Risk for incident all-cause dementia associated with the number of ophthalmic and systemic conditions

Incidence of all-cause dementia represents cases per 1000 person-years. Hazard ratio (95% CI) for incident all-cause dementia associated with the number of ophthalmic and systemic conditions was estimated using Cox proportional regression models adjusted for age, gender, education, income, cooked vegetables intake, raw vegetables intake, fresh fruits intake, dried fruits intake, smoking, alcohol consumption, physical activity, BMI, cholesterol, and glucose at baseline. Central squares of each horizontal line represent the hazard ratios for each subgroup. Horizontal lines indicate the ranges of the 95% CIs and the vertical dash lines indicate the hazard ratio of 1.0. CI, confidence interval.

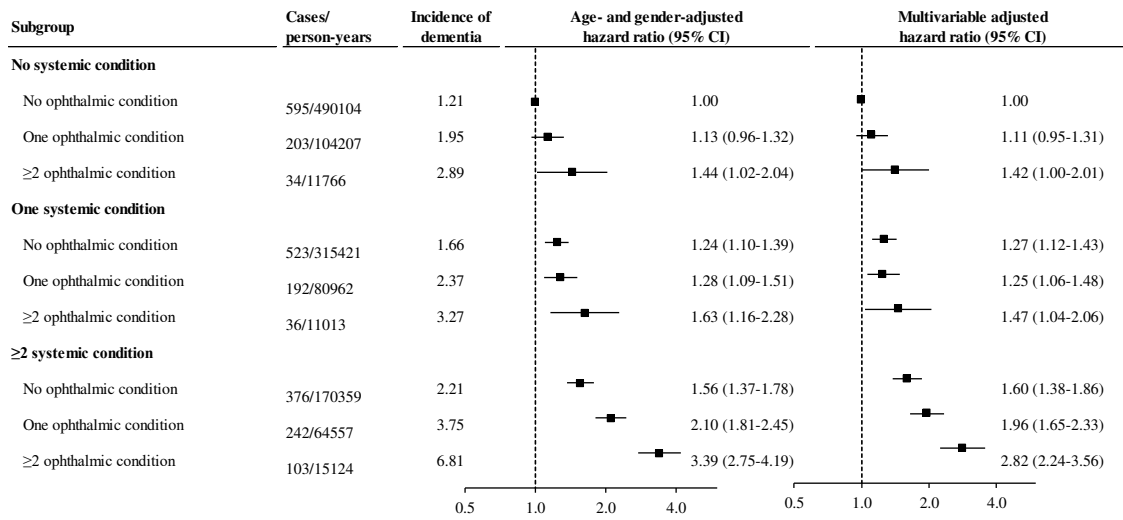


Figure e-9. Risk for incident all-cause dementia according to ophthalmic condition within each systemic condition category

Incidence of all-cause dementia represents cases per 1000 person-years. Hazard ratio (95% CI) for incident all-cause dementia associated with the number of ophthalmic within each systemic condition category was estimated using Cox proportional regression models adjusted for age, gender, education, income, cooked vegetables intake, raw vegetables intake, fresh fruits intake, dried fruits intake, smoking, alcohol consumption, physical activity, BMI, cholesterol, and glucose at baseline. Central squares of each horizontal line represent the hazard ratio for each subgroup. Horizontal lines indicate the ranges of the 95% CIs and the vertical dash lines indicate the hazard ratio of 1.0. CI, confidence interval.

Table e-1. Codes for international classification disease and self-reported fields for systemic conditions

	ICD-9	ICD-10	Self-reported fields
Heart disease	410, 412, 414, 4273	I21-25, I48, Z951, Z955	1074, 1075, 1076
Stroke	3361, 36231, 36232, 430, 431, 4329, 43301, 43311, 43321, 43331, 43381, 43391, 434, 436	I60, I61, I629, I63, I64, I678, I690, I693, G951, H341, H342, S066	1081
Hypertension	401-405	I10-I13, I15, O10	1065
Diabetes	250	E10-E14	1223
Depression	2961, 3004, 3119	F32-F34, F38, F39	1286

Table e-2. Codes for international classification disease and self-reported fields for dementia

ICD-9	ICD-10	Self- reported fields
331.0, 290.4, 331.1,	F00, F00.0, F00.1, F00.2, F00.9,	1263
290.2, 290.3, 291.2,	G30, G30.0, G30.1, G30.8, G30.9,	
294.1, 331.2, 331.5	F01, F01.0, F01.1, F01.2, F01.3, F01.8, F01.9, I67.3, F02.0, G31.0, A81.0, F02, F02.1, F02.2, F02.3, F02.4, F02.8, F03, F05.1, F10.6, G31.1, G31.8	

Table e-3. Baseline characteristics in participants with and without incident dementia

	Incident dementia		P-value*
	No	Yes	
Age (years)	62.31 ± 4.05	65.06 ± 3.42	<0.0001
Gender			<0.0001
Women	59625 (54.2)	1099 (47.7)	
Men	50435 (45.8)	1205 (52.3)	
APOE4			
No	81509 (74.1)	1198 (52.0)	
Yes	24997 (22.7)	1009 (43.8)	
Missing	3554 (3.2)	97 (4.2)	
Education			<0.0001
College/university degree	33108 (30.1)	489 (21.2)	
Upper secondary	10927 (9.9)	195 (8.5)	
Final stage of secondary education	22174 (20.1)	396 (17.2)	
Lower secondary	3430 (3.1)	42 (1.8)	
First stage of secondary education	7557 (6.9)	160 (6.9)	
Vocational qualifications	7285 (6.6)	146 (6.3)	
Others	1701 (1.5)	69 (3.0)	
Missing	23878 (21.7)	807 (35.0)	
Household income			<0.0001
<18,000	26899 (24.4)	833 (36.2)	
18,000-30,999	26823 (24.4)	494 (21.4)	

31,000-51,999	20725 (18.8)	269 (11.7)	
52,000-100,000	13209 (12.0)	99 (4.3)	
>100,000	3425 (3.1)	29 (1.3)	
Unknown	5666 (5.1)	232 (10.1)	
Not answered	13313 (12.1)	348 (15.1)	
Physical activity (MET-h/week)	2652.17 ± 2362.13	2594.90 ± 2515.59	0.25
Sleep duration (hours)	7.11 ± 1.37	7.12 ± 1.87	0.73
Cooked vegetables (tablespoons/day)	2.67 ± 2.58	2.62 ± 3.06	0.38
Raw vegetables (tablespoons/day)	1.68 ± 3.36	1.75 ± 3.82	0.32
Fresh fruits (pieces/day)	2.00 ± 2.63	2.20 ± 2.89	0.0021
Dried fruits (pieces/day)	0.17 ± 3.46	0.48 ± 3.48	<0.0001
Alcohol consumption			<0.0001
Never	5607 (5.1)	174 (7.6)	
Previous	4608 (4.2)	192 (8.3)	
Current	99666 (90.6)	1925 (83.6)	
Missing	179 (0.2)	13 (0.6)	
Smoking			0.11
Never	100524 (91.3)	2073 (90.0)	
Former	7031 (6.4)	186 (8.1)	
Current	2405 (2.2)	39 (1.7)	
Missing	100 (0.1)	6 (0.3)	
BMI (kg/m ²)	27.65 ± 4.68	27.85 ± 4.90	0.0412
Cholesterol (mmol/L)	5.70 ± 1.16	5.40 ± 1.28	<0.0001

Glucose (mmol/L)	5.25 ± 1.22	5.54 ± 1.84	<0.0001
Diabetes	7343 (6.7)	363 (15.8)	<0.0001
Stroke	2451 (2.2)	147 (6.4)	<0.0001
Heart disease	7032 (6.4)	338 (14.7)	<0.0001
Hypertension	34204 (31.1)	894 (38.8)	<0.0001
Depression	6029 (5.5)	214 (9.3)	<0.0001

Data are mean (SD) or N (%).

*Chi-square test was used to analyze the difference of categorical variables and T-test was used to test the difference of continuous variables between participants with and without incident dementia.

Table e-4. Baseline characteristics in participants with and without self-reported eye health data

	Self-reported eye health data		P-value
	Yes	No	
Age (years)	57.19 ± 8.08	56.18 ± 8.08	<0.0001
Gender			0.79
Women	95018 (54.4)	178364 (54.4)	
Men	79553 (45.6)	149569 (45.6)	
Education			0.77
College/university degree	57618 (33.0)	103545 (31.6)	
Upper secondary	19213 (11.0)	36110 (11.0)	
Final stage of secondary education	35751 (20.5)	69446 (21.2)	
Lower secondary	9188 (5.3)	17699 (5.4)	
First stage of secondary education	11333 (6.5)	21394 (6.5)	
Vocational qualifications	9333 (5.3)	16471 (5.0)	
Others	2755 (1.6)	7378 (2.2)	
Missing	29380 (16.8)	55891 (17.0)	
Household income			<0.0001
<18,000	36593 (21.0)	60605 (18.5)	
18,000-30,999	37704 (21.6)	70473 (21.5)	
31,000-51,999	36573 (21.0)	74199 (22.6)	
52,000-100,000	28391 (16.3)	57875 (17.6)	
>100,000	8263 (4.7)	14666 (4.5)	

Unknown	8286 (4.7)	13018 (4.0)	
Not answered	18761 (10.7)	37098 (11.3)	
Physical activity (MET-h/week)	2641.90 ± 2419.43	2655.17 ± 2432.30	0.0651
Sleep duration (hours)	7.07 ± 1.38	7.09 ± 1.36	<0.0001
Cooked vegetables (tablespoons/day)	2.51 ± 2.75	2.43 ± 2.58	<0.0001
Raw vegetables (tablespoons/day)	1.67 ± 3.45	1.63 ± 3.31	0.0004
Fresh fruits (pieces/day)	1.86 ± 2.75	1.89 ± 2.65	0.0021
Dried fruits (pieces/day)	0.03 ± 3.48	-0.01 ± 3.35	<0.0001
Alcohol consumption			<0.0001
Never	9405 (5.4)	12980 (4.0)	
Previous	7188 (4.1)	10916 (3.3)	
Current	157649 (90.3)	302713 (92.3)	
Missing	329 (0.2)	1325 (0.4)	
Smoking			0.13
Never	156044 (89.4)	292163 (89.1)	
Former	13466 (7.7)	25778 (7.9)	
Current	4857 (2.8)	8877 (2.7)	
Missing	204 (0.1)	1116 (0.3)	
BMI (kg/m ²)	27.56 ± 4.84	27.37 ± 4.68	<0.0001
Cholesterol (mmol/L)	5.66 ± 1.11	5.71 ± 1.10	<0.0001
Glucose (mmol/L)	5.19 ± 1.21	5.09 ± 1.11	<0.0001
Diabetes	9918 (5.7)	11805 (3.6)	<0.0001
Stroke	3191 (1.8)	4117 (1.3)	<0.0001

Heart disease	8341 (4.8)	13312 (4.1)	<0.0001
Hypertension	45035 (25.8)	76159 (23.2)	<0.0001
Depression	10672 (6.1)	17534 (5.3)	<0.0001

Data are mean (SD) or N (%).

*Chi-square test was used to analyze the difference of categorical variables and T-test was used to test the difference of continuous variables between participants with and without self-reported eye health data.