

Supplementary Material

Association between retinal nerve fibre layer thickness and incident dementia in the European Prospective Investigation into Cancer in Norfolk cohort

Supplementary Table 1. Regression Results with GDx-VCC Derived Mean RNFL Thickness Stratified as a Continuous Variable and Incident All-Cause Dementia as Outcome of Interest

	HR	95% CI	p
Model 1 ¹	0.98	0.96-0.99	0.04
Model 2 ²	0.99	0.98-1.02	0.87
Model 3 ³	0.99	0.97-1.02	0.76

Hazard ratio (HR) for all-cause dementia per quartile increase in RNFL thickness.

¹Model adjusted for clustering between eyes of the same patient and the typical scan score

²Model adjusted for clustering between eyes of the same patient, the typical scan score, age, and sex

³Model adjusted for all covariates, including clustering between eyes of the same patient, the typical scan score, age, sex, body mass index, employment status at time of 3rd health examination, highest education level completed, smoking status, amount of alcohol consumed, and axial length.

95% CI, 95% confidence interval; GDx-VCC, Glaucoma detection with variable corneal compensation; RNFL, retinal nerve fiber layer. p<0.05 in bold.

Supplementary Table 2. Regression Results with HRT II Derived Mean RNFL Thickness Stratified as a Continuous Variable and Incident All-Cause Dementia as Outcome of Interest

	HR	95% CI	p
Model 1 ¹	0.26	0.07-0.98	0.04
Model 2 ²	1.48	0.39-4.49	0.56
Model 3 ³	1.43	0.30-6.78	0.65

Hazard ratio (HR) for all-cause dementia per quartile increase in RNFL thickness.

¹Model adjusted for clustering between eyes of the same patient

²Model adjusted for clustering between eyes of the same patient, age, and sex

³Model adjusted for all covariates, including clustering between eyes of the same patient, age, sex, body mass index, employment status at time of 3rd health examination, highest education level completed, smoking status, amount of alcohol consumed, and axial length.

95% CI, 95% confidence interval; HRT II, Heidelberg Retinal Tomography II; RNFL, retinal nerve fiber layer. p<0.05 in bold.

Supplementary Table 3. Descriptive characteristics of all included eyes stratified by GDx-VCC derived RNFL measurements.

	Quartile 1	Quartile 2	Quartile 3	Quartile 4	p
Total Eyes, n (%)	2735 (100)	2732 (100)	2739 (100)	2743 (100)	
Age, mean (SD)	68.9 (7.7)	67.3 (7.6)	66.9 (7.3)	67.1 (7.5)	<0.0001
Sex, n (%)					
Female	1505 (55)	1529 (60.0)	1582 (57.8)	1582 (57.7)	0.11
BMI, mean (SD)	26.8 (4.2)	26.7 (4.4)	26.7 (4.4)	26.8 (5.3)	0.72
Family History of Dementia ¹ , No. yes (%)	397 (14.5)	368 (13.4)	362 (13.2)	387 (14.1)	0.49
Social Class ² , No. (%)					0.004
Professional	152 (5.6)	163 (6.0)	165 (6.1)	165 (6.0)	
Managerial/technical	982 (36.2)	998 (36.8)	1033 (38.0)	1098 (40.2)	
Skilled, non-manual	757 (27.9)	748 (27.6)	725 (26.7)	724 (26.5)	
Skilled, manual	420 (15.5)	379 (14.0)	346 (12.7)	322 (11.8)	
Semi-skilled	328 (12.1)	338 (12.5)	352 (13.0)	360 (13.2)	
Nonskilled	75 (2.8)	88 (3.2)	96 (3.5)	64 (2.3)	
Education Level					
Degree	465 (17.0)	487 (17.8)	559 (20.4)	515 (18.8)	0.006
Education to Age 18	1260 (46.1)	1224 (44.8)	1201 (43.8)	1255 (45.8)	
Education to Age 16	306 (11.2)	317 (11.6)	317 (11.6)	353 (12.9)	
Education less than age of 16	704 (25.7)	704 (25.8)	662 (24.2)	620 (22.6)	
Alcohol Intake, No. (%)					
No intake	793 (29.0)	788 (28.8)	748 (27.3)	815 (29.7)	0.82
>0 to <7 units/week	1012 (37.0)	992 (36.3)	1021 (37.3)	992 (36.2)	
>/= 7 to <14 units/week	555 (20.3)	535 (19.6)	562 (20.5)	531 (19.4)	
>/=14 to <21 units/week	214 (7.8)	232 (8.5)	228 (8.3)	228 (8.3)	
>/= 21 units/week	161 (5.9)	185 (6.8)	180 (6.6)	177 (6.5)	
Smoking Status					
Never	1375 (50.3)	1346 (49.3)	1396 (51.0)	1396 (50.9)	0.57
Ever	1360 (49.7)	1386 (50.7)	1343 (49.0)	1347 (49.1)	
Employment Status ³ , No. yes (%)	713 (26.1)	851 (31.1)	883 (32.2)	845 (30.8)	<0.0001
Axial Length, mm; mean (SD)	23.4 (0.9)	23.4 (1.0)	23.5 (1.0)	23.8 (1.3)	<0.0001
Number of All-Cause Dementia Cases, n (%)	173 (7.1)	131 (4.7)	101 (3.4)	129 (4.7)	<0.0001

¹First-degree relatives;²Derived from participant self-reported own and partner's last occupation based on the Registrar General's occupation-based classification scheme³Employed with paid job at time of 3rd health examination;

SD, standard deviation; BMI, body mass index; p<0.05 in bold.

Supplementary Table 4. Descriptive characteristics of all included eyes stratified by HRT II derived RNFL measurements.

	Quartile 1	Quartile 2	Quartile 3	Quartile 4	p
Total Eyes, n (%)	2443 (100)	2746 (100)	3013 (100)	2747 (100)	
Age, mean (SD)	69.7 (7.6)	67.7 (7.3)	67.1 (7.2)	65.9 (7.5)	<0.0001
Sex, n (%)					
Female	1263 (51.7)	1528 (55.6)	1751 (58.1)	1656 (60.3)	<0.0001
BMI, mean (SD)	26.7 (4.3)	26.8 (4.3)	26.7 (4.2)	26.8 (4.5)	0.58
Family History of Dementia ¹ , No. yes (%)	354 (14.5)	363 (13.2)	416 (15.3)	381 (13.9)	
Social Class ² , No. (%)					
Professional	166 (6.8)	139 (5.1)	169 (5.7)	171 (6.3)	0.0001
Managerial/technical	917 (37.7)	1035 (37.9)	1113 (37.4)	1046 (38.3)	
Skilled, non-manual	617 (25.4)	701 (25.7)	868 (29.2)	758 (27.8)	
Skilled, manual	375 (15.4)	404 (14.8)	358 (12.0)	330 (12.1)	
Semi-skilled	282 (11.6)	357 (13.1)	383 (12.9)	356 (13.0)	
Nonskilled	75 (3.1)	94 (3.4)	86 (2.9)	68 (2.5)	
Education Level					
Degree	436 (17.8)	467 (17.0)	548 (18.2)	575 (20.9)	<0.0001
A level	1114 (46.0)	1263 (46.0)	1370 (45.5)	1193 (43.4)	
O level	263 (10.8)	298 (10.9)	351 (11.6)	381 (13.9)	
No qualifications	630 (25.9)	718 (26.1)	744 (24.7)	598 (21.8)	
Alcohol Intake, No. (%)					
No intake	723 (29.6)	808 (29.4)	832 (27.6)	781 (28.4)	0.16
>0 to <7 units/week	861 (35.2)	1032 (38.6)	1121 (37.2)	1003 (36.5)	
>= 7 to <14 units/week	509 (20.8)	497 (18.1)	614 (20.4)	563 (20.5)	
>=14 to <21 units/week	204 (8.4)	242 (8.8)	249 (8.3)	207 (7.5)	
>= 21 units/week	146 (6.0)	167 (6.1)	197 (6.5)	193 (7.0)	
Smoking Status					
Never	1234 (50.5)	1356 (49.4)	1546 (51.3)	1377 (50.1)	0.53
Ever	1209 (49.5)	1390 (50.6)	1467 (48.7)	1370 (49.9)	
Employment Status ³ , No. yes (%)	580 (23.7)	799 (29.1)	930 (30.9)	983 (35.8)	<0.0001
Axial Length, mm; mean (SD)	23.7 (1.2)	23.5 (1.0)	23.4 (1.1)	23.4 (1.1)	<0.0001
Number of All-Cause Dementia Cases	140 (5.7)	129 (4.7)	143 (4.7)	122 (4.4)	0.15

¹First-degree relatives;²Derived from participant self-reported own and partner's last occupation based on the Registrar General's occupation based classification scheme;³Employed with paid job at time of 3rd health examination;

SD, standard deviation; BMI, body mass index; p<0.05 in bold.

Supplementary Table 5. Descriptive characteristics of glaucoma, age-related macular degeneration, and diabetic retinopathy by dementia status

	All	Incident Dementia		p
		Yes	No	
Glaucoma Status, n eyes (%)				0.23
No glaucoma	5669 (91.1)	283 (88.4)	5386 (91.3)	
Glaucoma suspect	400 (6.4)	23 (7.2)	377 (6.4)	
Glaucoma	153 (2.5)	14 (4.4)	139 (2.4)	
Age-related Macular Degeneration, n eyes (%)	656 (18.6)	50 (35.5)	606 (17.9)	<0.001
Diabetic Retinopathy, n eyes (%)	129 (1.2)	7 (1.3)	122 (1.2)	<0.001