

Supplemental Files – eTables

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eTable 1. Event Proportions and Incidence Rates per 1,000 Person-Years Over the Study Period, by Number of Midlife Vascular Risk Factors

	Overall (N = 12,409)	0 Risk Factors (N = 5,217)	1 Risk Factor (N = 5,154)	2 Risk Factors (N = 1,808)	3 Risk Factors (N = 176)
Dementia					
Event proportion No. of Events/Total at baseline	24.2% (3,008/12,409)	23.8% (1,254/5,271)	25.3% (1,306/5,154)	22.7% (410/1,808)	21.6% (38/176)
Incidence Rate (95% CI)	9.7 (9.3, 10.0)	8.8 (8.3, 9.3)	10.2 (9.7, 10.8)	11.1 (10.1, 12.2)	12.5 (9.1, 17.1)
Dementia-free death					
Event proportions No. of Events/Total at baseline	42.2% (5,238/12,409)	28.6% (1,508/5,271)	46.7% (2,409/5,154)	65.9% (1,192/1,808)	73.3% (129/176)
Incidence Rate (95% CI)	16.8 (16.4, 17.3)	10.5 (10.0, 11.1)	18.8 (18.1, 19.6)	32.2 (30.5, 34.1)	42.3 (35.6, 50.3)
Dementia or Dementia-free death					
Event proportions No. of Events/Total at baseline	66.5% (8,246/12,409)	52.4% (2,762/5,271)	72.1% (3,715/5,154)	88.6% (1,602/1,808)	94.9% (167/176)
Incidence Rate (95% CI)	26.5 (25.9, 27.1)	19.3 (18.6, 20.0)	29.0 (28.1, 30.0)	43.3 (41.3, 45.5)	54.8 (47.1, 63.7)
Death Following dementia					
Event proportions No. of Events/Total at baseline	78.3% (2,354/3,008)	70.8% (888/1,254)	81.5% (1,064/1,306)	89.8% (368/410)	89.5% (34/38)
Incidence Rate (95% CI)	264.7 (254.2, 275.6)	237.9 (222.8, 254.1)	276.5 (260.3, 293.6)	304.0 (274.5, 336.7)	333.7 (238.5, 467.1)

Abbreviations: CI, confidence interval.

eTable 2. Cumulative Incidence of Dementia and Dementia-Free Mortality from Age 55 to Specified Ages, by Number of Midlife Vascular Risk Factors

	Overall (N = 12,409)	0 Risk Factors (N = 5,217)	1 Risk Factor (N = 5,154)	2 Risk Factors (N = 1,808)	3 Risk Factors (N = 176)
Cumulative incidence of dementia, % (95% CI)					
Age 65	0 (0, 0)	0 (0, 0)	0 (0, 1)	1 (0, 1)	1 (0, 4)
Age 75	4 (3, 4)	3 (2, 3)	4 (3, 5)	6 (5, 7)	10 (6, 15)
Age 85	19 (19, 20)	18 (17, 20)	20 (19, 21)	20 (18, 22)	18 (13, 24)
Age 90	30 (29, 31)	32 (30, 34)	30 (29, 32)	24 (22, 27)	23 (17, 30)
Age 95	37 (36, 38)	42 (40, 44)	36 (34, 38)	27 (25, 29)	23 (17, 30)
Cumulative incidence of dementia-free mortality, % (95% CI)					
Age 65	5 (5, 5)	2 (2, 3)	5 (4, 6)	11 (10, 12)	18 (12, 24)
Age 75	19 (18, 20)	10 (9, 10)	20 (19, 21)	40 (38, 42)	53 (46, 60)
Age 85	38 (37, 39)	24 (23, 25)	41 (40, 43)	63 (60, 65)	73 (65, 79)
Age 90	48 (47, 49)	35 (33, 37)	52 (50, 53)	69 (67, 72)	74 (67, 80)
Age 95	55 (54, 57)	44 (42, 47)	59 (57, 61)	72 (69, 74)	74 (67, 80)

Abbreviations: CI, confidence interval.

Note: All values represent cumulative incidence from age 55 to the specified age.

eTable 3. Cumulative Incidence of Dementia by Age 95, Dementia-Free Survival Years and Post-Dementia Survival Years, From Different Index Ages, by Number of Midlife Vascular Risk Factors

	Index Age, 55	Index Age, 65	Index Age, 75	Index Age, 85
0 risk factors				
No. alive and dementia free ^a	5,271	5,136	4,628	1,839
Cumulative incidence of dementia, % (95% CI)	42 (40, 44)	43 (41, 45)	45 (42, 48)	41 (38, 45)
Dementia-free survival, y (95% CI) ^b	30.1 (29.9, 30.4)	20.8 (20.5, 21.0)	12.4 (12.2, 12.6)	5.9 (5.7, 6.1)
Post-dementia survival, y (95% CI) ^c	4.1 (3.8, 4.4)	4.1 (3.9, 4.4)	4.1 (3.8, 4.4)	3.1 (2.8, 3.5)
1 risk factor				
No. alive and dementia free ^a	5,154	4,880	3,926	1,369
Cumulative incidence of dementia, % (95% CI)	36 (34, 38)	37 (36, 39)	42 (40, 44)	41 (37, 44)
Dementia-free survival, y (95% CI) ^b	26.3 (26.1, 26.6)	17.4 (17.2, 17.7)	10.3 (10.1, 10.5)	5.1 (4.9, 5.3)
Post-dementia survival, y (95% CI) ^c	3.6 (3.4, 3.9)	3.6 (3.4, 3.8)	3.4 (3.2, 3.7)	2.6 (2.4, 2.9)
2 risk factors				
No. alive and dementia free ^a	1,808	1,599	975	226
Cumulative incidence of dementia, % (95% CI)	27 (25, 29)	30 (27, 33)	39 (35, 43)	39 (30, 49)
Dementia-free survival, y (95% CI) ^b	21.0 (20.5, 21.4)	12.9 (12.5, 13.2)	7.7 (7.4, 8.1)	4.2 (3.8, 4.7)
Post-dementia survival, y (95% CI) ^c	3.3 (3.0, 3.7)	3.3 (2.9, 3.7)	2.8 (2.5, 3.1)	2.0 (1.6, 2.5)
3 risk factors				
No. alive and dementia free ^a	176	143	65	13
Cumulative incidence of dementia, % (95% CI)	23 (17, 30)	27 (20, 35)	37 (25, 49)	55 (23, 78)
Dementia-free survival, y (95% CI) ^b	17.5 (16.3, 18.7)	10.1 (9.1, 11.2)	6.0 (4.9, 7.1)	3.0 (2.0, 4.0)
Post-dementia survival, y (95% CI) ^c	3.0 (2.0, 4.1)	3.1 (2.0, 4.2)	3.4 (1.8, 5.0)	1.0 (0.4, 1.7)

Abbreviations: y, year; CI, confidence interval.

^aNo. alive and dementia-free indicates individuals alive and dementia-free at the index age.

^bDementia-free survival years were calculated from index ages through age 95.

^cPost-dementia survival years were calculated from index ages through age 95.

eTable 4. Interaction Tests for Vascular Risk Burden by Subgroups

Subgroup	Dementia	Death without dementia
× Sex	0.020	0.086
× Race	0.077	0.014
× <i>APOE-ε4</i> Alleles	0.418	0.110

Note: P-values are from Wald tests for multiplicative interaction terms (number of vascular risk factor × subgroup) in cause-specific Cox proportional hazards models. Separate models were fit for each outcome, adjusting for sex, race, education, physical activity, body mass index (BMI), prevalent stroke, and *APOE-ε4* genotype as applicable.

eTable 5. Model-Based Estimates of Dementia-Free Survival Years, Cumulative Incidence of Dementia and Post-Dementia Survival Years by Age 95, by Number of Midlife Vascular Risk Factors and Stratified by Sex, Race and *APOE-ε4* Status

	0 Risk Factors (N = 5,271)	1 Risk Factor (N = 5,154)	2 Risk Factors (N = 1,808)	3 Risk Factors (N = 176)
Overall				
Dementia-free survival, y	29.9	26.3	21.5	18.2
Cumulative incidence of dementia, %	37.1	37.7	34.6	33.6
Post-dementia survival, y	4.2	3.6	3.3	3.1
Men				
Dementia-free survival, y	28.7	24.8	20.3	17
Cumulative incidence of dementia, %	34.5	33.1	26.8	41.2
Post-dementia survival, y	3.7	3.2	3.3	2.6
Women				
Dementia-free survival, y	30.8	27.5	22.4	19.2
Cumulative incidence of dementia, %	39.2	41.6	41	27.4
Post-dementia survival, y	4.5	3.9	3.3	3.6
White				
Dementia-free survival, y	30.3	26.7	21.8	20.1
Cumulative incidence of dementia, %	37	36.9	30.4	35.3
Post-dementia survival, y	3.9	3.2	3	3
Black				
Dementia-free survival, y	28	25.3	21	16.5
Cumulative incidence of dementia, %	41.5	39.7	37.8	30.7
Post-dementia survival, y	5.4	4.7	3.6	3.1
<i>APOE-ε4</i> non-carrier (0 alleles)				
Dementia-free survival, y	30.6	26.9	21.7	17.9
Cumulative incidence of dementia, %	33.6	35.4	31.3	29.3
Post-dementia survival, y	4.3	3.6	3.3	2.5
<i>APOE-ε4</i> carrier (1 or 2 alleles)				
Dementia-free survival, y	28.2	25	21.1	19
Cumulative incidence of dementia, %	44.9	43.4	41	43.6
Post-dementia survival, y	4.1	3.7	3.3	3.9

Note: Estimates are derived from cause-specific Cox proportional hazards models, adjusting for sex, race, education, physical activity, body mass index (BMI), prevalent stroke, and *APOE-ε4* genotype. Dementia-free survival years and post-dementia survival years are restricted mean times between ages 55 and 95. Cumulative incidence of dementia by age 95 accounts for competing mortality and is presented as a percentage (multiplied by 100).