

	Crude					Model 1					Model 2				
	event/total	HR	95%-CI	p-value		event/total	HR	95%-CI	p-value		event/total	HR	95%-CI	p-value	
Apathy	577/3492	1.35	1.24	1.46	<0.001	577/3492	1.33	1.23	1.45	<0.001	566/3409	1.21	1.11	1.32	<0.001
Isolated Apathy	423/2839	1.35	1.22	1.51	<0.001	423/2839	1.34	1.20	1.49	<0.001	415/2771	1.23	1.10	1.37	<0.001
Depression	577/3492	1.15	1.11	1.20	<0.001	577/3492	1.16	1.12	1.21	<0.001	566/3409	1.10	1.05	1.15	<0.001
Isolated Depression	406/2802	1.18	1.09	1.27	<0.001	406/2802	1.18	1.10	1.28	<0.001	397/2741	1.14	1.05	1.23	0.002

Table e-1. Association between symptoms and mortality. Crude model, model 1: adjusted for age and gender, model 2: additionally adjusted for activities of daily living (AMC linear disability scale), MMSE score at visit 2, history cardiovascular disease and history of stroke.

	Crude					Model 1					Model 2				
	event/total	HR	95%-CI	p-value		event/total	HR	95%-CI	p-value		event/total	HR	95%-CI	p-value	
Apathy	736/3425	1.31	1.22	1.41	<0.001	736/3425	1.29	1.20	1.39	<0.001	719/3343	1.19	1.1	1.29	<0.001
Isolated apathy	546/2788	1.31	1.19	1.44	<0.001	546/2788	1.28	1.16	1.41	<0.001	534/2720	1.20	1.08	1.33	<0.001
Depression	736/3425	1.14	1.10	1.18	<0.001	736/3425	1.14	1.10	1.18	<0.001	719/3343	1.09	1.05	1.14	<0.001
Isolated depression	535/2754	1.18	1.10	1.26	<0.001	535/2754	1.18	1.10	1.26	<0.001	521/2693	1.13	1.05	1.21	0.001

Table e-2. Association between symptoms and dementia or mortality. Crude model, model 1: adjusted for age and gender, model 2: additionally adjusted for activities of daily living (AMC linear disability scale), MMSE score at visit 2, history cardiovascular disease and history of stroke.

		Crude				Model 1				Model 2			
		events/total	HR	95%-CI	p-value	events/total	HR	95%-CI	p-value	events/total	HR	95%-CI	p-value
Apathy ordinal	0 (ref)	91/1792	1.00			91/1792	1.00			89/1756	1.00		
	1	84/938	1.80	1.34 2.43	<0.001	84/938	1.76	1.31 2.37	<0.001	81/918	1.7	1.26 2.3	0.001
	2	36/460	1.66	1.13 2.44	0.01	36/460	1.52	1.03 2.23	0.04	35/449	1.42	0.95 2.12	0.09
	3	20/202	2.04	1.26 3.32	0.004	20/202	1.84	1.13 2.99	0.01	19/195	1.74	1.03 2.94	0.04
Isolated apathy ordinal	0 (ref)	83/1639	1.00			83/1639	1.00			81/1605	1.00		
	1	64/767	1.67	1.21 2.32	0.002	64/767	1.63	1.18 2.26	0.003	62/749	1.56	1.11 2.17	0.01
	2	22/288	1.59	0.99 2.55	0.053	22/288	1.44	0.90 2.31	0.13	22/280	1.44	0.89 2.34	0.14
	3	5/67	1.44	0.58 3.55	0.43	5/67	1.26	0.51 3.11	0.62	5/63	1.28	0.51 3.24	0.60

Table e-3. Association between apathy symptoms at baseline as ordinal predictor and incident dementia. Crude model, model 1: adjusted for age and gender, model 2: additionally adjusted for activities of daily living (AMC linear disability scale), MMSE score, history cardiovascular disease and history of stroke.

		Crude				Model 1				Model 2			
		n	Beta	95%-CI	p-value	n	Beta	95%-CI	p-value	n	Beta	95%-CI	p-value
Apathy ordinal	0 ref	1519/2803	0.00			1519/2803	0.00			1490/2745	0.00		
	1	770/2803	-0.17	-0.29 -0.05	0.007	770/2803	-0.15	-0.28 -0.03	0.01	756/2745	-0.12	-0.24 0.00	0.06
	2	356/2803	-0.33	-0.49 -0.16	<0.001	356/2803	-0.30	-0.46 -0.13	<0.001	345/2745	-0.22	-0.39 -0.04	<0.001
	3	158/2803	-0.50	-0.74 -0.27	<0.001	158/2803	-0.47	-0.70 -0.23	<0.001	154/2745	-0.29	-0.54 -0.04	0.02
Isolated apathy ordinal	0 ref	1394/2313	0.00			1394/2313	0.00			1367/2263	0.00		
	1	635/2313	-0.18	-0.30 -0.05	0.005	635/2313	-0.16	-0.29 -0.04	0.01	622/2263	-0.13	-0.26 -0.01	0.04
	2	228/2313	-0.33	-0.49 -0.16	<0.001	228/2313	-0.30	-0.46 -0.13	<0.001	220/2263	-0.22	-0.39 -0.05	<0.001
	3	56/2313	-0.45	-0.69 -0.21	<0.001	56/2313	-0.41	-0.65 -0.18	<0.001	54/2263	-0.24	-0.49 0.01	0.06

Table e-4. Association between apathy symptoms at baseline as ordinal predictor and adjusted mean change in MMSE score during study compared to baseline. Crude model, model 1: adjusted for age and gender, model 2: additionally adjusted for activities of daily living (AMC linear disability scale), history cardiovascular disease and history of stroke. Beta: Adjusted Mean Difference,

		Crude				Model 1				Model 2			
		events/total	HR	95%-CI	p-value	events/total	HR	95%-CI	p-value	events/total	HR	95%-CI	p-value
Apathy ordinal	0 (ref)	232/1845	1.00			232/1845	1.00			226/1806	1.00		
	1	174/957	1.46	1.2 1.78	<0.001	174/957	1.42	1.17 1.73	<0.001	171/935	1.33	1.09 1.63	0.005
	2	115/476	2.03	1.62 2.53	<0.001	115/476	2.00	1.59 2.50	<0.001	113/461	1.66	1.31 2.10	<0.001
	3	56/214	2.19	1.64 2.94	<0.001	56/214	2.14	1.6 2.87	<0.001	56/207	1.55	1.14 2.12	0.005
Isolated apathy ordinal	0 (ref)	302/1807	1.00			302/1807	1.00			294/1768	1.00		
	1	137/781	1.48	1.19 1.84	<0.001	137/781	1.43	1.15 1.78	0.001	134/763	1.33	1.06 1.66	0.013
	2	68/295	2.03	1.54 2.68	<0.001	68/295	2.00	1.52 2.64	<0.001	68/286	1.72	1.29 2.28	<0.001
	3	17/75	1.93	1.18 3.17	0.009	17/75	1.83	1.11 3.00	0.02	17/71	1.37	0.82 2.28	0.23

Table e-5. Association between apathy symptoms at baseline as ordinal predictor and mortality. Crude model, model 1: adjusted for age and gender, model 2: additionally adjusted for activities of daily living (AMC linear disability scale), MMSE score at visit 2, history cardiovascular disease and history of stroke.

		Crude				Model 1				Model 2			
		events/total	HR	95%-CI	p-value	events/total	HR	95%-CI	p-value	events/total	HR	95%-CI	p-value
Apathy ordinal	0 (ref)	201/1688	1.00			201/1688	1.00			196/1651	1.00		
	1	233/947	1.51	1.27 1.79	<0.001	233/947	1.48	1.25 1.76	<0.001	227/925	1.4	1.18 1.67	<0.001
	2	133/463	1.84	1.50 2.25	<0.001	133/463	1.77	1.44 2.17	<0.001	131/449	1.54	1.24 1.90	<0.001
	3	68/208	2.09	1.61 2.72	<0.001	68/208	2.00	1.54 2.61	<0.001	67/201	1.53	1.15 2.03	0.003
Isolated apathy ordinal	0 (ref)	266/1654	1.00			266/1654	1.00			259/1617	1.00		
	1	180/773	1.47	1.22 1.78	<0.001	180/773	1.44	1.19 1.74	<0.001	175/755	1.35	1.12 1.64	0.002
	2	81/290	1.85	1.44 2.37	<0.001	81/290	1.77	1.38 2.27	<0.001	81/281	1.58	1.22 2.04	<0.001
	3	19/71	1.70	1.07 2.72	0.03	19/71	1.60	1.00 2.55	0.049	19/67	1.28	0.79 2.07	0.309

Table e-6. Association between apathy symptoms at baseline as ordinal predictor and dementia or mortality. Crude model, model 1: adjusted for age and gender, model 2: additionally adjusted for activities of daily living (AMC linear disability scale), MMSE score at visit 2, history cardiovascular disease and history of stroke.

	Crude					Model 1					Model 2				
	event/total	HR	95%-CI	p-value		event/total	HR	95%-CI	p-value		event/total	HR	95%-CI	p-value	
Apathy	115/955	1.17	0.98	1.4	0.09	115/955	1.14	0.95	1.37	0.15	113/941	1.18	0.97	1.44	0.09
Isolated Apathy	80/712	1.11	0.86	1.44	0.42	80/712	1.08	0.84	1.41	0.54	78/700	1.17	0.88	1.55	0.29
Depression	115/955	1.07	0.99	1.17	0.11	115/955	1.07	0.98	1.16	0.15	113/941	1.08	0.98	1.18	0.13
Isolated Depression	85/713	1.16	0.99	1.36	0.06	85/713	1.15	0.98	1.35	0.08	83/702	1.13	0.96	1.34	0.14

Table e-7. Association between symptoms at baseline and incident dementia in participants with a baseline MMSE score <28. Crude model, model 1: adjusted for age and gender, model 2: additionally adjusted for activities of daily living (AMC linear disability scale), MMSE score at visit 2, history cardiovascular disease and history of stroke.

	Crude					Model 1					Model 2				
	event/total	HR	95%-CI	p-value		event/total	HR	95%-CI	p-value		event/total	HR	95%-CI	p-value	
Apathy	116/2450	1.32	1.10	1.59	0.003	116/2450	1.26	1.04	1.51	0.02	111/2389	1.21	0.99	1.48	0.07
Isolated apathy	94/2061	1.35	1.07	1.70	0.01	94/2061	1.27	1.01	1.61	0.04	92/2008	1.23	0.97	1.58	0.09
Depression	116/2450	1.10	0.98	1.22	0.09	116/2450	1.09	0.98	1.22	0.12	111/2389	1.05	0.93	1.19	0.46
Isolated depression	90/2021	1.07	0.88	1.30	0.53	90/2021	1.07	0.88	1.30	0.52	87/1976	1.01	0.82	1.25	0.92

Table e-8. Association between symptoms at baseline and incident dementia in participants with a baseline MMSE score ≥28. Model 1: adjusted for MMSE score at visit 2, model 2: additionally adjusted for age and gender, model 2: additionally adjusted for activities of daily living (AMC linear disability scale), history cardiovascular disease and history of stroke. Beta: Adjusted Mean Difference,

	Crude					Model 1					Model 2				
< 3.89 years, mean 2.5, SD 0.93	events/total	HR	95%-CI	p-value		events/total	HR	95%-CI	p-value		events/total	HR	95%-CI	p-value	
Apathy symptoms	77/3281	1.43	1.16	1.78	0.001	77/3281	1.37	1.11	1.70	0.004	74/3204	1.32	1.04	1.68	0.02
Isolated apathy symptoms	56/2678	1.43	1.07	1.90	0.02	56/2678	1.36	1.02	1.82	0.03	55/2614	1.38	1.02	1.88	0.04
Depressive symptoms	77/3276	1.15	1.04	1.28	0.007	77/3276	1.14	1.03	1.27	0.01	74/3199	1.07	0.95	1.22	0.28
Isolated depressive symptoms	55/2622	1.20	0.98	1.46	0.08	55/2622	1.19	0.97	1.45	0.09	53/2567	1.08	0.87	1.35	0.49
3.89-5.77 years, mean 4.9, SD 0.6:															
Apathy symptoms	78/3049	1.17	0.93	1.47	0.19	78/3049	1.14	0.9	1.44	0.28	77/2978	1.10	0.86	1.41	0.44
Isolated apathy symptoms	59/2516	1.04	0.75	1.44	0.83	59/2516	1.01	0.73	1.40	0.96	58/2456	0.99	0.70	1.4	0.96
Depressive symptoms	78/3044	1.13	1.01	1.26	0.04	78/3044	1.12	1.00	1.26	0.045	77/2973	1.05	0.92	1.2	0.48
Isolated depressive symptoms	61/2486	1.22	1.01	1.46	0.04	61/2486	1.22	1.02	1.47	0.03	60/2433	1.12	0.92	1.37	0.26
> 5.77 years, mean 6.8, SD 0.6															
Apathy symptoms	77/2794	1.25	1.00	1.56	0.05	77/2794	1.2	0.95	1.50	0.12	73/2727	1.30	1.01	1.67	0.04
Isolated apathy symptoms	60/2324	1.31	0.98	1.74	0.07	60/2324	1.23	0.92	1.64	0.16	57/2267	1.28	0.93	1.75	0.13
Depressive symptoms	77/2789	1.07	0.94	1.21	0.31	77/2789	1.06	0.94	1.21	0.35	73/2722	1.06	0.93	1.22	0.37
Isolated depressive symptoms	60/2293	1.05	0.82	1.34	0.70	60/2293	1.05	0.82	1.34	0.70	57/2244	1.01	0.78	1.32	0.91

Table e-9. Association between predictors in tertiles of time to dementia. Crude model, model 1: adjusted for age and gender, model 2: additionally adjusted for activities of daily living (AMC linear disability scale), MMSE score at visit 2, history cardiovascular disease and history of stroke.

Apathy symptoms	Crude					Model 1					Model 2				
	event/total	HR	95%-CI	p-value		event/total	HR	95%-CI	p-value		event/total	HR	95%-CI	p-value	
Stable low (reference)	104/1982	1.00				104/1982	1.00				101/1943	1.00			
Decrease >1	5/81	1.13	0.46 2.78	0.79		5/81	1.06	0.43 2.6	0.90		5/78	1.02	0.41 2.51	0.97	
Stable moderate	68/762	1.79	1.31 2.42	<0.001		68/762	1.73	1.28 2.35	<0.001		65/740	1.58	1.16 2.17	<0.001	
Increase >1	11/114	1.85	0.99 3.44	0.05		11/114	1.77	0.95 3.29	0.07		11/112	1.53	0.82 2.86	0.18	
Stable high	44/465	2.07	1.45 2.94	<0.001		44/465	1.86	1.31 2.66	<0.001		42/451	1.75	1.19 2.56	<0.001	

Table e-10. Association between apathy stability categories and incident dementia. Crude model, model 1: adjusted for age and gender, model 2: additionally adjusted for activities of daily living (AMC linear disability scale), MMSE score at visit 2, history cardiovascular disease and history of stroke.

Depressive symptoms	Crude					Model 1					Model 2				
	n	HR	95%-CI	p-value		n	Beta	95%-CI	p-value		n	Beta	95%-CI	p-value	
Stable low (reference)	100/2110	1.00				100/2110	1.00				97/2062	1.00			
Decrease >1	7/88	1.50	0.70 3.23	0.30		7/88	1.52	0.71 3.27	0.28		7/88	1.32	0.61 2.85	0.49	
Stable moderate	65/618	2.40	1.75 3.28	<0.001		65/618	2.37	1.73 3.24	<0.001		63/602	2.17	1.58 2.98	<0.001	
Increase >1	14/122	2.38	1.36 4.16	<0.001		14/122	2.37	1.36 4.15	<0.001		13/121	2.27	1.27 4.06	0.01	
Stable high	46/458	2.37	1.67 3.36	<0.001		46/458	2.27	1.6 3.22	<0.001		44/443	1.77	1.21 2.58	<0.001	

Table e-11. Association between depression stability categories and incident dementia. Crude model, model 1: adjusted for age and gender, model 2: additionally adjusted for activities of daily living (AMC linear disability scale), MMSE score at visit 2, history cardiovascular disease and history of stroke.

		Crude					Model 1					Model 2				
		events/total	HR	95%-CI	p-value		events/total	HR	95%-CI	p-value		events/total	HR	95%-CI	p-value	
Apathy		232/3425	1.28	1.12	1.45	<0.001	232/3425	1.23	1.08	1.40	0.002	224/3343	1.21	1.06	1.4	0.007
Isolated Apathy		189/2914	1.27	1.08	1.49	0.004	189/2914	1.22	1.04	1.44	0.02	184/2845	1.22	1.03	1.46	0.02
Depression		231/3406	1.06	0.97	1.15	0.19	231/3406	1.05	0.97	1.14	0.26	223/3324	0.99	0.91	1.09	0.91
Isolated Depression		176/2725	1.03	0.88	1.20	0.73	176/2725	1.03	0.88	1.20	0.75	170/2666	0.94	0.79	1.11	0.46
Isolated apathy ordinal	0 (ref)	86/1689	1.00				86/1689	1.00				83/1653	1.00			
	1	73/807	1.82	1.33	2.48	<0.001	73/807	1.77	1.30	2.42	<0.001	71/789	1.73	1.26	2.38	0.001
	2	24/311	1.60	1.01	2.51	0.04	24/311	1.47	0.93	2.32	0.10	24/302	1.46	0.92	2.32	0.11
	3	6/82	1.42	0.62	3.25	0.41	6/82	1.29	0.56	2.95	0.55	6/78	1.34	0.57	3.15	0.50
GDS question 10		231/3406	3.03	2.32	3.96	<0.001	231/3406	3.00	2.30	3.93	<0.001	223/3324	2.63	1.99	3.47	<0.001

Table e-12. Association of apathy symptoms with GDS question 10 referring to subjective memory complaints removed: Apathy symptoms according to the GDS-3A, depressive symptoms according to the GDS-12D minus GDS question 10: “Do you feel you have more problems with your memory than most people?”. Isolated apathy defined according to GDS-12D with GDS question 10 removed. Unless indicated as “ordinal”, the number of symptoms were analyzed as continuous predictor. “Ordinal” indicates the number of symptoms were analyzed as separate categories, compared to no symptoms as reference category. “GDS question 10” depicts the individual association between GDS question 10 and dementia incidence. Crude model, model 1: adjusted for age and gender, model 2: additionally adjusted for activities of daily living (AMC linear disability scale), MMSE score at visit 3, endorsement of GDS question 10, history cardiovascular disease and history of stroke.