

Supplementary table 1. All-cause mortality and dose-response of cholinesterase inhibitor use

Whole cohort analysis		Diabetes & Dementia	Diabetes-free & Dementia
Fully adjusted models (Model 1)		HR (95% CI)	HR (95% CI)
ChEI	Non-user	1.41 (1.24-1.62)†	1.46 (1.38-1.55)†
	Low-dose	Reference	Reference
	High-dose	0.98 (0.82-1.17)	0.99 (0.91-1.06)
Donepezil	Non-user	1.29 (1.07-1.57)*	1.45 (1.33-1.58)†
	Low-dose	Reference	Reference
	High-dose	0.97 (0.75-1.24)	0.99 (0.89-1.11)
Rivastigmine	Non-user	1.35 (0.99-1.82)	1.15 (1.02-1.29)*
	Low-dose	Reference	Reference
	High-dose	1.36 (0.93-2.01)	0.88 (0.75-1.04)
Galantamine	Non-user	1.50 (1.21-1.86)†	1.42 (1.30-1.55)†
	Low-dose	Reference	Reference
	High-dose	1.07 (0.76-1.50)	1.16 (1.02-1.33)*

PS-matched cohorts		Diabetes & Dementia	Diabetes-free & Dementia
		HR (95% CI)	HR (95% CI)
ChEI	Non-user	1.29 (1.12-1.47)†	1.28 (1.21-1.36)†
	Low-dose	Reference	Reference
	High-dose	0.84 (0.63-1.12)	1.17 (1.04 -1.32)†
Donepezil	Non-user	1.15 (1.01-1.32)*	1.19 (1.12 -1.25)†
	Low-dose	Reference	Reference
	High-dose	0.74 (0.51-1.07)	1.07 (0.94-1.22)
Rivastigmine	Non-user	1.13 (0.90-1.44)	1.03 (0.94-1.13)
	Low-dose	Reference	Reference
	High-dose	1.34 (0.99-1.82)	1.26 (1.11-1.44)†
Galantamine	Non-user	1.30 (1.03-1.54)*	1.09 (1.01-1.18)*
	Low-dose	Reference	Reference
	High-dose	1.09 (0.74-1.62)	1.09 (0.95-1.25)

ChEI, cholinesterase inhibitors;

Dosage groups were obtained by splitting on the 50th percentile of prescribed daily doses received during all yearly intervals for respective exposure cohorts;

Model 1 was adjusted for age at dementia diagnosis, gender, dementia type, cohabitation, Mini-Mental State Examination score, Charlson comorbidity index, antipsychotics, hypnotics/sedatives, cardiovascular and antithrombotic medication; Model 1 for the analysis in Diabetes & Dementia patients was additionally adjusted for the use of antidiabetic medication and diabetes duration;

PS-matched analysis of ChEI is adjusted for age and MMSE in the Diabetes-Free cohort, and age and dementia type in the Diabetes cohort due to residual differences in the matched cohorts; *p-value <0.05; †p-value <0.001

Supplementary table 2. Balance statistics in propensity-score matched cohorts by donepezil use

	Diabetes & Dementia		p	SMD
	Donepezil + (1,246 users)	Donepezil – (1,246 non-users)		
Age	78.5 (6.7)	78.9 (7.4)	0.21	-0.05

Male sex		531 (42.6%)	535 (42.9 %)	0.87	-0.01
Dementia	AD	777 (62.4%)	749 (60.1%)	0.25	-0.05
	Mixed	469 (37.6%)	497 (39.9%)		
Cohabitation	Living alone	530 (42.5%)	536 (43.0%)	0.01	-0.04
	Living with an adult	669 (53.7%)	632 (50.7%)		
	At nursing home	47 (3.8%)	78 (6.3%)		
MMSE score		22 (6)	22 (7)	0.59	0.06
Charlson comorbidity index		2 (2)	2 (2)	0.29	-0.05
Antidiabetic medication		1,056 (84.8%)	1,033 (82.9%)	0.23	0.05
Cardiovascular medication		1,151 (92.4%)	1,152 (92.5%)	0.94	-0.01
Antithrombotic medication		825 (66.2%)	860 (69.0%)	0.13	-0.06
Antipsychotics		37 (3.0%)	31 (2.5%)	0.46	0.03
Hypnotics/Sedatives		302 (24.2%)	325 (26.1%)	0.29	-0.04
Diabetes duration		5.8 (8)	6.6 (7.5)	0.04	0.03

Diabetes-free & Dementia

	Donepezil + (7,942 users)	Donepezil – (7,942 non-users)	p	SMD	
Age	79.0 (7.3)	79.0 (8.4)	0.53	-0.01	
Male sex	2,751 (34.6%)	2,820 (35.5%)	0.25	-0.02	
Dementia	AD	5,590 (70.4%)	0.27	-0.02	
	Mixed	2,352 (29.6%)			2,416 (30.4%)
Cohabitation	Living alone	3,554 (44.7%)	<0.001	-0.03	
	Living with an adult	4,102 (51.6%)			3,988 (50.2%)
	At nursing home	286 (3.6%)			408 (5.1%)
MMSE score	22 (6)	22 (7)	<0.001	0.09	
Charlson comorbidity index	1 (1)	1 (2)	0.02	-0.03	
Cardiovascular medication	5,310 (66.9%)	5,343 (67.3%)	0.58	-0.01	
Antithrombotic medication	3,510 (44.2%)	3,551 (44.7%)	0.51	-0.01	
Antipsychotics	255 (3.2%)	238 (3.0%)	0.44	0.01	
Hypnotics/Sedatives	2,005 (25.2%)	2,031 (25.6%)	0.64	-0.01	

AD, Alzheimer's disease; Mixed, mixed-pathology dementia; MMSE, Mini-Mental State Examination; ChEI,

cholinesterase inhibitors; SMD, standardized mean differences;

Age is described as mean (SD); MMSE score, diabetes duration (in years) and Charlson index are described as median (IQR); Other variables are described as number of patients (%);

Supplementary table 3. Balance statistics in propensity-score matched cohorts by rivastigmine use

		Diabetes & Dementia		p	SMD
		Rivastigmine + (478 users)	Rivastigmine – (478 non-users)		
Age		77.1 (6.9)	77.5 (6.8)	0.36	-0.06
Male sex		227 (47.5%)	239 (50.0%)	0.44	-0.05
Dementia	AD	271 (56.7%)	277 (57.9%)	0.70	0.03
	Mixed	207 (43.3%)	201 (42.1%)		
Cohabitation	Living alone	175 (36.6%)	177 (37.0%)	0.07	-0.05
	Living with an adult	287 (60.0%)	270 (56.5%)		
	At nursing home	16 (3.3%)	31 (6.5%)		
MMSE score		22 (5)	23 (5)	0.88	-0.01
Charlson comorbidity index		2 (2)	2 (2)	0.87	0.03
Antidiabetic medication		387 (81.0%)	385 (80.5%)	0.87	0.01
Cardiovascular medication		441 (92.3%)	442 (92.5%)	0.90	-0.01
Antithrombotic medication		336 (70.3%)	329 (68.8%)	0.62	0.03
Antipsychotics		21 (4.4%)	21 (4.4%)	1.00	<0.01
Hypnotics/Sedatives		113 (23.6%)	99 (20.7%)	0.28	0.07
Diabetes duration		5.5 (6.7)	5.6 (6.8)	0.92	0.01

Diabetes-free & Dementia

	Rivastigmine + (3,363 users)	Rivastigmine – (3,363 non-users)	p	SMD	
Age	76.7 (7.9)	77.0 (8.3)	0.11	-0.04	
Male sex	1,274 (37.9%)	1,283 (38.2%)	0.82	-0.01	
Dementia	AD	2,259 (67.2%)	2,294 (68.2)	0.36	0.02
	Mixed	1,104 (32.8%)	1,069 (31.8%)		
Cohabitation	Living alone	1,124 (33.4%)	1,211 (36.0%)	<0.001	-0.02
	Living with an adult	2,125 (63.2%)	1,924 (57.2%)		
	At nursing home	114 (3.4%)	228 (6.8%)		
MMSE score	23 (7)	23 (5)	0.82	-0.01	
Charlson comorbidity index	1 (1)	1 (1)	0.78	-0.01	
Cardiovascular medication	2,204 (65.5%)	2,223 (66.1%)	0.63	-0.01	
Antithrombotic medication	1,428 (42.5%)	1,444 (42.9%)	0.69	-0.01	
Antipsychotics	156 (4.6%)	180 (5.4%)	0.18	-0.03	
Hypnotics/Sedatives	850 (25.3%)	862 (25.6%)	0.74	-0.01	

AD, Alzheimer's disease; Mixed, mixed-pathology dementia; MMSE, Mini-Mental State Examination; ChEI, cholinesterase inhibitors; SMD, standardized mean differences;

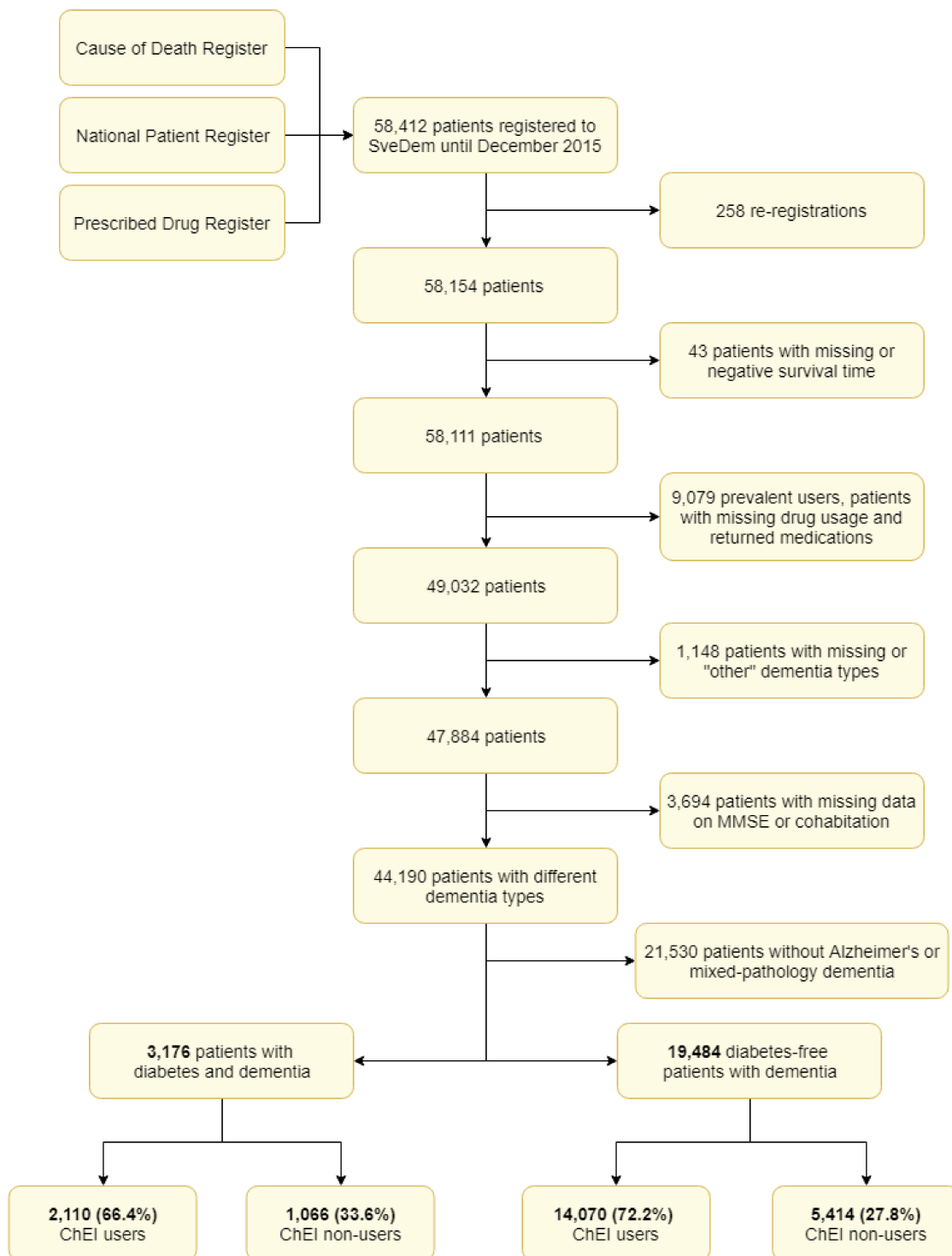
Age is described as mean (SD); MMSE score, diabetes duration (in years) and Charlson index are described as median (IQR); Other variables are described as number of patients (%);

Supplementary table 4. Balance statistics for propensity-score matched cohorts by galantamine use

		Diabetes & Dementia			
		Galantamine + (516 users)	Galantamine – (516 non-users)	p	SMD
Age		77.3 (6.9)	77.2 (7.2)	0.90	0.01
Male sex		229 (44.4%)	222 (43.0%)	0.66	0.03
Dementia	AD	258 (50.0%)	250 (48.4%)	0.62	-0.03
	Mixed	258 (50.0%)	266 (51.6%)		
Cohabitation	Living alone	213 (41.3%)	221 (42.8%)	0.21	-0.01
	Living with an adult	287 (55.6%)	269 (52.1%)		
	At nursing home	16 (3.1%)	26 (5.0%)		
MMSE score		23 (6)	22 (6)	0.45	0.03
Charlson comorbidity index		2 (2)	2 (1)	0.68	-0.02
Antidiabetic medication		431 (83.5%)	438 (84.9%)	0.55	-0.04
Cardiovascular medication		472 (91.5%)	477 (92.4%)	0.57	-0.03
Antithrombotic medication		355 (68.8%)	351 (68.0%)	0.79	0.02
Antipsychotics		21 (4.1%)	23 (4.5%)	0.76	-0.02
Hypnotics/Sedatives		132 (25.6%)	137 (26.6%)	0.72	-0.02
Diabetes duration		5.4 (7.5)	5.7 (7.5)	0.65	0.03
		Diabetes-free & Dementia			
		Galantamine + (4,157 users)	Galantamine – (4,157 non-users)	p	SMD
Age		76.6 (8.2)	76.7 (8.3)	0.54	-0.01
Male sex		1,428 (34.4%)	1,447 (34.8%)	0.66	-0.01
Dementia	AD	2,747 (66.1%)	2,750 (66.2%)	0.95	0.01
	Mixed	1,410 (33.9%)	1,407 (33.8%)		
Cohabitation	Living alone	1,738 (41.8%)	1,778 (42.8%)	0.01	<0.01
	Living with an adult	2,313 (55.6%)	2,232 (53.7%)		
	At nursing home	106 (2.5%)	147 (3.5%)		
MMSE score		23 (6)	23 (6)	0.22	0.01
Charlson comorbidity index		1 (1)	1 (1)	0.05	-0.02
Cardiovascular medication		2,647 (63.7%)	2,674 (64.3%)	0.54	-0.01
Antithrombotic medication		1,703 (41.0%)	1,743 (41.9%)	0.37	-0.02
Antipsychotics		169 (4.1%)	168 (4.0%)	0.96	0.01
Hypnotics/Sedatives		1,008 (24.2%)	999 (24.0%)	0.82	0.01

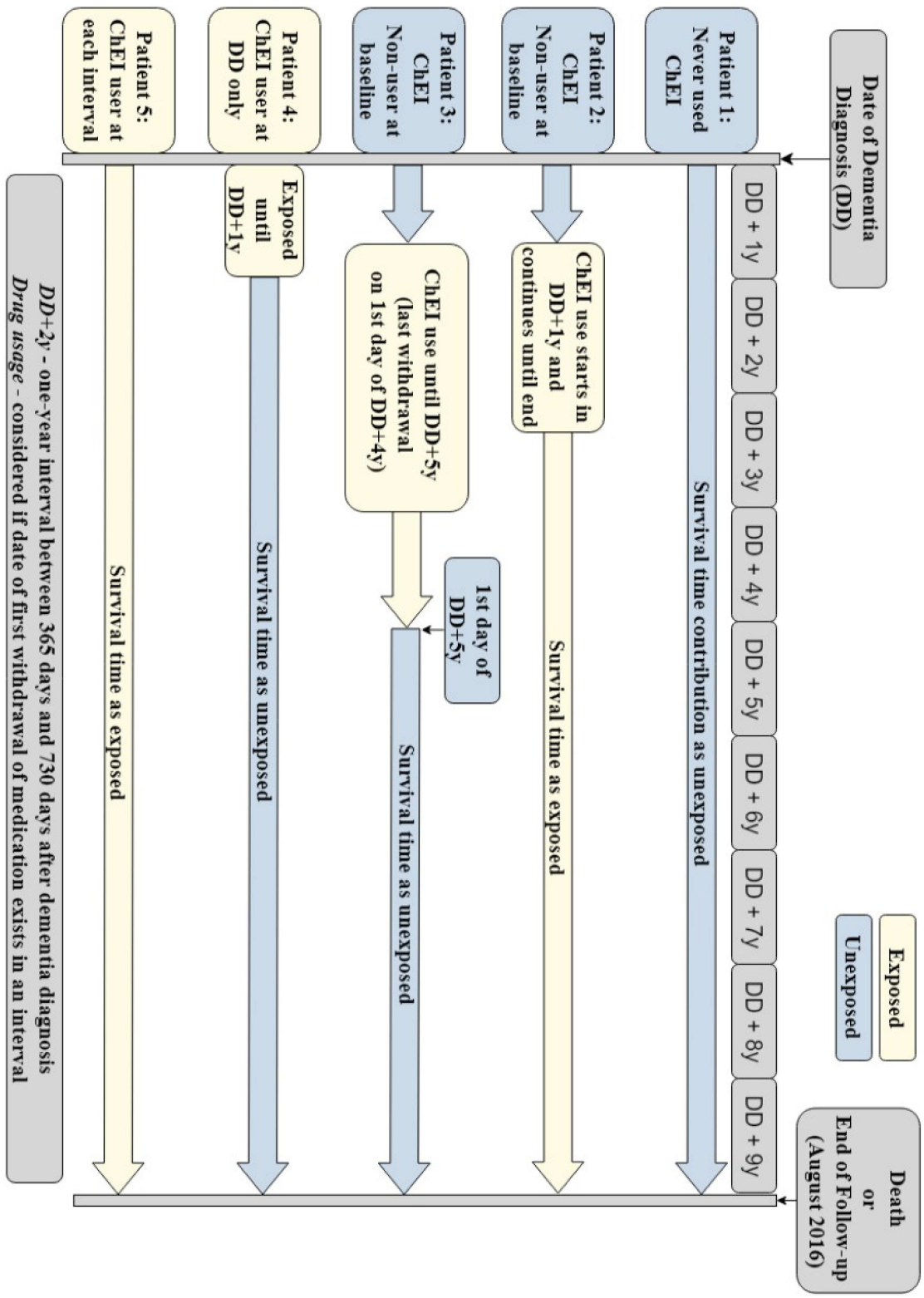
AD, Alzheimer's disease; Mixed, mixed-pathology dementia; MMSE, Mini-Mental State Examination; ChEI, cholinesterase inhibitors; SMD, standardized mean differences;
Age is described as mean (SD); MMSE score, diabetes duration (in years) and Charlson index are described as median (IQR); Other variables are described as number of patients (%);

Supplementary figure 1. Study sample selection



ChEI, cholinesterase inhibitors;

Supplementary figure 2. Assignment of exposure times for the whole-cohort analysis



ChEI, cholinesterase inhibitors;