

Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

eTable 1. ICD-10-AM codes for identification of comorbidities.

Comorbidity	ICD-10-AM
Anxiety	F40, F41
Arthritis	M00, M05, M06, M076, M13, M15-M19, M77.2
Alcohol use disorder	F10
Cancer	C00-C99
Cardiovascular disease	I00-I99
Cerebrovascular disease	I60-I69
Chronic kidney disease	N00-19, N25-N28, N39.1, N39.2, D59.3, B52.0, E85.3, Q60-Q63, T82.4, T86.1, Z49.0, Z94.0, Z99.2, U87.1
COPD/ asthma	J40-J46
Delirium	F05
Dementia	F00-F03, F10.7, F13.7, F18.7, F05.1, G30
Depression or other affective disorders	F32-F39
Diabetes mellitus	E10, E11, E13, E14, O24
Epilepsy/seizures	G40, R56
Fall	W00-W19
Gastroesophageal reflux disease	K21
Osteoporosis	M80-M82
Peptic ulcer disease	K25-K27
Previous vertebral fracture	M484, S12, S220, S320, M8008
Visual disturbances and blindness	H53, H54

Abbreviation: ICD-10-AM, International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification

eTable 2. Characteristics of patients included and matched future-case controls for subgroup analyses for patients with low frailty risk (Hospital Frailty Risk Score [HFRS]<5), high frailty risk (HFRS≥5), without chronic kidney disease (CKD) and with CKD.

Subgroup	Low frailty risk			High frailty risk			Without CKD			With CKD		
	Cases	Controls	SMD	Cases	Controls	SMD	Cases	Controls	SMD	Cases	Controls	SMD
Total, n	1451	6953		1168	5502		1822	8814		793	3688	
Age, n (%)			0.098			0.114			0.063			0.146
50-59	62 (4.3)	178 (2.6)		38 (3.3)	92 (1.7)		85 (4.7)	305 (3.5)		13 (1.6)	23 (0.6)	
60-69	170 (11.7)	776 (11.2)		106 (9.1)	435 (7.9)		205 (11.3)	968 (11.0)		70 (8.8)	226 (6.1)	
70-79	369 (25.4)	1777 (25.6)		298 (25.5)	1401 (25.5)		483 (26.5)	2343 (26.6)		186 (23.5)	857 (23.2)	
80-84	281 (19.4)	1391 (20.0)		254 (21.7)	1262 (22.9)		348 (19.1)	1724 (19.6)		187 (23.6)	927 (25.1)	
85+	569 (39.2)	2831 (40.7)		472 (40.4)	2312 (42.0)		701 (38.5)	3474 (39.4)		337 (42.5)	1655 (44.9)	
Sex, n (%)			0.035			0.031			0.025			0.022
Males	369 (25.4)	1662 (23.9)		376 (32.2)	1692 (30.8)		450 (24.7)	2082 (23.6)		289 (36.4)	1305 (35.4)	
Females	1082 (74.6)	5291 (76.1)		792 (67.8)	3810 (69.2)		1372 (75.3)	6732 (76.4)		504 (63.6)	2383 (64.6)	
HFRS, n (%)			0.018			0.010			0.030			0.040
<5	518 (35.7)	2542 (36.6)		943 (80.7)	4420 (80.3)		1235 (67.8)	6097 (69.2)		211 (26.6)	1047 (28.4)	
≥5	933 (64.3)	4411 (63.4)		225 (19.3)	1082 (19.7)		587 (32.2)	2717 (30.8)		582 (73.4)	2641 (71.6)	
Comorbidities, n (%)												
Anxiety	55 (3.8)	248 (3.6)	0.012	149 (12.8)	657 (11.9)	0.025	112 (6.1)	462 (5.2)	0.039	91 (11.5)	432 (11.7)	0.007
Arthritis		1215 (17.5)			1391 (25.3)							
Alcohol use disorder	249 (17.2)	79 (1.1)	0.008	288 (24.7)	281 (5.1)	0.014	350 (19.2)	1725 (19.6)	0.009	187 (23.6)	861 (23.3)	0.006
Cancer	27 (1.9)	1087 (15.6)	0.060	69 (5.9)	1468 (26.7)	0.035	58 (3.2)	245 (2.8)	0.024	38 (4.8)	163 (4.4)	0.018
Cardiovascular disease	223 (15.4)	3456 (49.7)	0.007	286 (24.5)	4642 (84.4)	0.050	326 (17.9)	1566 (17.8)	0.003	178 (22.4)	859 (23.3)	0.020
Cerebrovascular disease	679 (46.8)	445 (6.4)	0.058	987 (84.5)	842 (15.3)	0.004	977 (53.6)	4719 (53.5)	0.002	684 (86.3)	3215 (87.2)	0.027
Chronic kidney disease	87 (6.0)	1188 (17.1)	0.017	182 (15.6)	2908 (52.9)	0.008	145 (8.0)	725 (8.2)	0.010	123 (15.5)	518 (14.0)	0.041
COPD/ asthma	214 (14.7)	1098 (20.0)	0.064	588 (50.3)	1604 (29.2)	0.050	(100.0)	(100.0)	<0.001	(100.0)	(100.0)	<0.001
Delirium	122 (8.4)	595 (8.6)	0.005	250 (21.4)	468 (8.5)	0.036	185 (10.2)	783 (8.9)	0.043	183 (23.1)	881 (23.9)	0.019
Dementia	78 (5.4)	407 (5.9)	0.021	343 (29.4)	1098 (20.0)	0.005	185 (10.2)	920 (10.4)	0.009	234 (29.5)	1021 (27.7)	0.040
	25 (1.7)	109 (1.6)	0.012	91 (7.8)	1604 (29.2)	0.026	57 (3.1)	293 (3.3)	0.011	58 (7.3)	287 (7.8)	0.018

Depression or other affective disorders	38 (2.6)	159 (2.3)	0.021	133 (11.4)	633 (11.5)	0.004	89 (4.9)	418 (4.7)	0.007	83 (10.5)	381 (10.3)	0.004
		1355			1952							
Diabetes mellitus	284 (19.6)	(19.5)	0.002	412 (35.3)	(35.5)	0.004	318 (17.5)	1605 (18.2)	0.020	374 (47.2)	1680 (45.6)	0.032
Epilepsy/seizures	23 (1.6)	82 (1.2)	0.035	50 (4.3)	225 (4.1)	0.010	40 (2.2)	179 (2.0)	0.011	33 (4.2)	143 (3.9)	0.014
		1152			3056							
Fall	250 (17.2)	(16.6)	0.018	621 (53.2)	(55.5)	0.048	514 (28.2)	2435 (27.6)	0.013	357 (45.0)	1751 (47.5)	0.049
Gastroesophageal reflux disease	106 (7.3)	536 (7.7)	0.015	152 (13.0)	618 (11.2)	0.055	162 (8.9)	790 (9.0)	0.003	94 (11.9)	413 (11.2)	0.021
		1536			2184							
Osteoporosis	312 (21.5)	(22.1)	0.014	455 (39.0)	(39.7)	0.015	481 (26.4)	2426 (27.5)	0.025	283 (35.7)	1235 (33.5)	0.046
Peptic ulcer disease	34 (2.3)	158 (2.3)	0.005	64 (5.5)	279 (5.1)	0.018	44 (2.4)	199 (2.3)	0.010	52 (6.6)	185 (5.0)	0.066
Previous vertebral fracture	31 (2.1)	134 (1.9)	0.015	123 (10.5)	731 (13.3)	0.085	88 (4.8)	422 (4.8)	0.002	67 (8.4)	377 (10.2)	0.061
Visual disturbances and blindness	28 (1.9)	136 (2.0)	0.002	60 (5.1)	272 (4.9)	0.009	49 (2.7)	241 (2.7)	0.003	37 (4.7)	182 (4.9)	0.013

Abbreviations: COPD, chronic obstructive pulmonary disease; SMD, standardized mean difference

eTable 3. Characteristics of patients included and matched future-case controls for sensitivity analyses with exposure assessment period (index and reference periods) of 60 days and washout periods of 90, 120, 150, and 180 days.

Washout period	90 days			120 days			150 days			180 days		
	Cases	Controls	SMD	Cases	Controls	SMD	Cases	Controls	SMD	Cases	Controls	SMD
Total, n	2630	12846		2632	12844		2630	12852		2615	12786	
Age, n (%)			0.04			0.039			0.04			0.041
50-59	110 (4.2)	442 (3.4)		111 (4.2)	448 (3.5)		112 (4.3)	451 (3.5)		113 (4.3)	453 (3.5)	
60-69	278 (10.6)	1350 (10.5)		282 (10.7)	1359 (10.6)		282 (10.7)	1365 (10.6)		280 (10.7)	1369 (10.7)	
70-79	669 (25.4)	3257 (25.4)		663 (25.2)	3226 (25.1)		653 (24.8)	3190 (24.8)		657 (25.1)	3208 (25.1)	
80-84	533 (20.3)	2646 (20.6)		539 (20.5)	2672 (20.8)		535 (20.3)	2652 (20.6)		535 (20.5)	2652 (20.7)	
85+	1040 (39.5)	5151 (40.1)		1037 (39.4)	5139 (40.0)		1048 (39.8)	5194 (40.4)		1030 (39.4)	5104 (39.9)	
Sex, n (%)			0.019			0.021			0.018			0.017
Males		3571 (27.8)			3609 (28.1)			3626 (28.2)			3615 (28.3)	
Females	754 (28.7)	9275 (72.2)		764 (29.0)	9235 (71.9)		764 (29.0)	9226 (71.8)		760 (29.1)	9171 (71.7)	
HFRS, n (%)			0.001			0.005			0.031			0.020
<5	1447 (55.0)	7062 (55.0)		1183 (54.7)	7062 (55.0)		1433 (54.5)	7198 (56.0)		1434 (54.4)	7085 (55.4)	
≥5	1183 (45.0)	5784 (45.0)		1191 (45.3)	5782 (45.0)	0.005	1197 (45.5)	5654 (44.0)	0.031	1192 (45.6)	5701 (44.6)	0.020
Comorbidities, n (%)												
Anxiety	210 (8.0)	977 (7.6)	0.014	209 (7.9)	1040 (8.1)	0.006	212 (8.1)	1033 (8.0)	0.001	206 (7.9)	997 (7.8)	0.003
Arthritis		2717 (21.2)			2686 (20.9)			2718 (21.1)			2646 (20.7)	
Alcohol use disorder	538 (20.5)	476 (3.7)	0.017	546 (20.7)	439 (3.4)	0.004	544 (20.7)	456 (3.5)	0.011	542 (20.7)	458 (3.6)	0.019
Cancer	100 (3.8)	2541 (19.8)	0.005	102 (3.9)	2502 (19.5)	0.024	103 (3.9)	2633 (20.5)	0.019	103 (3.9)	2560 (20.0)	0.018
Cardiovascular disease	506 (19.2)	8365 (65.1)	0.014	514 (19.5)	8338 (64.9)	0.001	507 (19.3)	8302 (64.6)	0.030	505 (19.3)	8297 (64.9)	0.011
Cerebrovascular disease	1679 (63.8)	1393 (10.8)	0.027	1686 (64.1)	1376 (10.7)	0.018	1688 (64.2)	1334 (10.4)	0.009	1683 (64.4)	1290 (10.1)	0.017
Chronic kidney disease	276 (10.5)	4170 (32.5)	0.011	275 (10.4)	4203 (32.7)	0.009	276 (10.5)	4153 (32.3)	0.004	277 (10.6)	4199 (32.8)	0.038
COPD/ asthma	806 (30.6)	1795 (14.0)	0.039	816 (31.0)	1848 (14.4)	0.037	820 (31.2)	1815 (14.1)	0.024	813 (31.1)	1872 (14.6)	0.003
Delirium	375 (14.3)	2116 (16.5)	0.008	378 (14.4)	2176 (16.9)	0.001	383 (14.6)	2104 (16.4)	0.013	380 (14.5)	2119 (16.6)	0.003
	421 (16.0)		0.013	422 (16.0)		0.024	426 (16.2)		0.005	426 (16.3)		0.008

Dementia	109 (4.1)	599 (4.7)	0.025	111 (4.2)	675 (5.3)	0.049	114 (4.3)	595 (4.6)	0.014	112 (4.3)	611 (4.8)	0.024
Depression or other affective disorders	176 (6.7)	874 (6.8)	0.004	175 (6.6)	897 (7.0)	0.013	177 (6.7)	902 (7.0)	0.011	179 (6.8)	874 (6.8)	<0.001
Diabetes mellitus	698 (26.5)	3425 (26.7)	0.003	695 (26.4)	3495 (27.2)	0.018	700 (26.6)	3419 (26.6)	<0.001	704 (26.9)	3534 (27.6)	0.016
Epilepsy/seizures	78 (3.0)	312 (2.4)	0.033	77 (2.9)	356 (2.8)	0.009	76 (2.9)	357 (2.8)	0.007	74 (2.8)	329 (2.6)	0.016
Fall	877 (33.3)	4385 (34.1)	0.017	878 (33.4)	4418 (34.4)	0.022	884 (33.6)	4392 (34.2)	0.012	887 (33.9)	4444 (34.8)	0.018
Gastroesophageal reflux disease	261 (9.9)	1231 (9.6)	0.012	261 (9.9)	1191 (9.3)	0.022	262 (10.0)	1253 (9.7)	0.007	260 (9.9)	1213 (9.5)	0.015
Osteoporosis	778 (29.6)	3753 (29.2)	0.008	780 (29.6)	3747 (29.2)	0.010	776 (29.5)	3878 (30.2)	0.015	773 (29.6)	3803 (29.7)	0.004
Peptic ulcer disease	99 (3.8)	451 (3.5)	0.014	99 (3.8)	452 (3.5)	0.013	98 (3.7)	419 (3.3)	0.025	98 (3.7)	444 (3.5)	0.015
Previous vertebral fracture	158 (6.0)	894 (7.0)	0.039	161 (6.1)	872 (6.8)	0.027	164 (6.2)	859 (6.7)	0.018	164 (6.3)	928 (7.3)	0.039
Visual disturbances and blindness	89 (3.4)	464 (3.6)	0.012	90 (3.4)	411 (3.2)	0.012	90 (3.4)	451 (3.5)	0.005	90 (3.4)	418 (3.3)	0.010

Abbreviations: COPD, chronic obstructive pulmonary disease; SMD, standardized mean difference

eTable 4. Characteristics of patients included and matched future-case controls for sensitivity analyses with exposure assessment period (index and reference periods) of 30 days and washout periods of 30, 60, and 90 days.

Washout period	30 days			60 days			90 days		
	Cases	Controls	SMD	Cases	Controls	SMD	Cases	Controls	SMD
Total, n	2660	12980		2643	12909		2649	12930	
Age, n (%)			0.043			0.04			0.039
50-59	113 (4.2)	446 (3.4)		114 (4.3)	457 (3.5)		108 (4.1)	434 (3.4)	
60-69	291 (10.9)	1413 (10.9)		285 (10.8)	1379 (10.7)		289 (10.9)	1399 (10.8)	
70-79	674 (25.3)	3283 (25.3)		666 (25.2)	3264 (25.3)		671 (25.3)	3262 (25.2)	
80-84	535 (20.1)	2652 (20.4)		534 (20.2)	2647 (20.5)		530 (20.0)	2629 (20.3)	
85+	1047 (39.4)	5186 (40.0)		1044 (39.5)	5162 (40.0)		1051 (39.7)	5206 (40.3)	
Sex, n (%)			0.02			0.018			0.019
Males	769 (28.9)	3636 (28.0)		763 (28.9)	3623 (28.1)		764 (28.8)	3621 (28.0)	
Females	1891 (71.1)	9344 (72.0)		1880 (71.1)	9286 (71.9)		1885 (71.2)	9309 (72.0)	
HFRS, n (%)			0.022			0.01			0.021
<5	1470 (55.3)	7031 (54.2)		1459 (55.2)	7190 (55.7)		1451 (54.8)	7216 (55.8)	
≥5	1190 (44.7)	5949 (45.8)	0.022	1184 (44.8)	5719 (44.3)	0.01	1198 (45.2)	5714 (44.2)	0.021
Comorbidities, n (%)									
Anxiety	210 (7.9)	1013 (7.8)	0.003	209 (7.9)	1034 (8.0)	0.004	205 (7.7)	961 (7.4)	0.012
Arthritis	530 (19.9)	2631 (20.3)	0.009	538 (20.4)	2685 (20.8)	0.011	542 (20.5)	2721 (21.0)	0.014
Alcohol use disorder	105 (3.9)	464 (3.6)	0.020	103 (3.9)	474 (3.7)	0.012	103 (3.9)	461 (3.6)	0.017
Cancer	514 (19.3)	2577 (19.9)	0.013	506 (19.1)	2523 (19.5)	0.010	510 (19.3)	2594 (20.1)	0.020
Cardiovascular disease	1700 (63.9)	8490 (65.4)	0.031	1683 (63.7)	8388 (65.0)	0.027	1687 (63.7)	8315 (64.3)	0.013
Cerebrovascular disease	276 (10.4)	1372 (10.6)	0.006	274 (10.4)	1312 (10.2)	0.007	279 (10.5)	1284 (9.9)	0.020
Chronic kidney disease	815 (30.6)	4342 (33.5)	0.060	805 (30.5)	4254 (33.0)	0.054	816 (30.8)	4177 (32.3)	0.032
COPD/ asthma	380 (14.3)	1931 (14.9)	0.017	372 (14.1)	1892 (14.7)	0.017	370 (14.0)	1821 (14.1)	0.003
Delirium	424 (15.9)	2168 (16.7)	0.021	424 (16.0)	2120 (16.4)	0.010	427 (16.1)	2142 (16.6)	0.012
Dementia	111 (4.2)	635 (4.9)	0.035	114 (4.3)	645 (5.0)	0.032	116 (4.4)	611 (4.7)	0.017
Depression or other affective disorders	176 (6.6)	862 (6.6)	0.001	172 (6.5)	857 (6.6)	0.005	173 (6.5)	836 (6.5)	0.003
Diabetes mellitus	700 (26.3)	3483 (26.8)	0.012	700 (26.5)	3555 (27.5)	0.024	705 (26.6)	3501 (27.1)	0.010
Epilepsy/seizures	80 (3.0)	356 (2.7)	0.016	76 (2.9)	326 (2.5)	0.022	79 (3.0)	327 (2.5)	0.028
Fall	882 (33.2)	4472 (34.5)	0.027	880 (33.3)	4358 (33.8)	0.010	884 (33.4)	4344 (33.6)	0.005
Gastroesophageal reflux disease	265 (10.0)	1255 (9.7)	0.010	260 (9.8)	1250 (9.7)	0.005	262 (9.9)	1245 (9.6)	0.009
Osteoporosis	771 (29.0)	3821 (29.4)	0.010	769 (29.1)	3738 (29.0)	0.003	777 (29.3)	3779 (29.2)	0.002
Peptic ulcer disease	103 (3.9)	457 (3.5)	0.019	100 (3.8)	416 (3.2)	0.031	100 (3.8)	415 (3.2)	0.031
Previous vertebral fracture	166 (6.2)	918 (7.1)	0.033	164 (6.2)	863 (6.7)	0.020	156 (5.9)	856 (6.6)	0.030
Visual disturbances and blindness	97 (3.6)	448 (3.5)	0.011	95 (3.6)	417 (3.2)	0.020	96 (3.6)	464 (3.6)	0.002

Abbreviations: COPD, chronic obstructive pulmonary disease; SMD, standardized mean difference

eTable 5. Characteristics of patients included and matched future-case controls for sensitivity analyses with exposure assessment period (index and reference periods) of 30 days and washout periods of 120, 150, and 180 days.

Washout period	120 days			150 days			180 days		
	Cases	Controls	SMD	Cases	Controls	SMD	Cases	Controls	SMD
Total, n	2652	12959		2639	12901		2613	12774	
Age, n (%)			0.04			0.041			0.038
50-59	107 (4.1)	429 (3.4)		108 (4.1)	431 (3.4)		109 (4.2)	441 (3.4)	
60-69	281 (10.8)	1375 (10.8)		285 (10.9)	1380 (10.8)		286 (10.9)	1384 (10.8)	
70-79	662 (25.4)	3226 (25.3)		668 (25.5)	3251 (25.4)		657 (25.1)	3205 (25.0)	
80-84	524 (20.1)	2607 (20.4)		530 (20.2)	2627 (20.5)		532 (20.3)	2637 (20.6)	
85+	1037 (39.7)	5136 (40.2)		1030 (39.3)	5106 (39.9)		1037 (39.6)	5139 (40.1)	
Sex, n (%)			0.017			0.020			0.018
Males	746 (28.6)	3550 (27.8)		755 (28.8)	3573 (27.9)		757 (28.9)	3593 (28.1)	
Females	1865 (71.4)	9223 (72.2)		1866 (71.2)	9222 (72.1)		1864 (71.1)	9213 (71.9)	
HFRS, n (%)			0.016			0.008			0.019
<5	1448 (55.5)	7186 (56.3)		1141 (55.0)	7085 (55.4)		1437 (54.8)	7139 (55.7)	
≥5	1163 (44.5)	5587 (43.7)		1180 (45.0)	5710 (44.6)		1184 (45.2)	5667 (44.3)	
Comorbidities, n (%)									
Anxiety	205 (7.9)	934 (7.3)	0.020	203 (7.7)	970 (7.6)	0.006	206 (7.9)	1008 (7.9)	<0.001
Arthritis	536 (20.5)	2696 (21.1)	0.014	534 (20.4)	2687 (21.0)	0.015	536 (20.5)	2664 (20.8)	0.009
Alcohol use disorder	99 (3.8)	420 (3.3)	0.027	101 (3.9)	442 (3.5)	0.021	101 (3.9)	425 (3.3)	0.029
Cancer	499 (19.1)	2539 (19.9)	0.019	508 (19.4)	2591 (20.3)	0.022	506 (19.3)	2543 (19.9)	0.014
Cardiovascular disease	1659 (63.5)	8178 (64.0)	0.010	1675 (63.9)	8274 (64.7)	0.016	1674 (63.9)	8250 (64.4)	0.012
Cerebrovascular disease	273 (10.5)	1262 (9.9)	0.019	276 (10.5)	1363 (10.7)	0.004	278 (10.6)	1296 (10.1)	0.016
Chronic kidney disease	798 (30.6)	4093 (32.0)	0.032	805 (30.7)	4164 (32.5)	0.039	817 (31.2)	4028 (31.5)	0.006
COPD/ asthma	367 (14.1)	1842 (14.4)	0.010	368 (14.0)	1789 (14.0)	0.002	370 (14.1)	1828 (14.3)	0.005
Delirium	416 (15.9)	2050 (16.0)	0.003	413 (15.8)	2066 (16.1)	0.011	423 (16.1)	2085 (16.3)	0.004
Dementia	110 (4.2)	599 (4.7)	0.023	108 (4.1)	580 (4.5)	0.020	114 (4.3)	603 (4.7)	0.017
Depression or other affective disorders	171 (6.5)	839 (6.6)	0.001	171 (6.5)	847 (6.6)	0.004	177 (6.8)	871 (6.8)	0.002
Diabetes mellitus	690 (26.4)	3388 (26.5)	0.002	689 (26.3)	3479 (27.2)	0.020	695 (26.5)	3397 (26.5)	<0.001
Epilepsy/seizures	74 (2.8)	315 (2.5)	0.023	77 (2.9)	327 (2.6)	0.023	77 (2.9)	332 (2.6)	0.021
Fall	865 (33.1)	4283 (33.5)	0.009	868 (33.1)	4368 (34.1)	0.022	873 (33.3)	4320 (33.7)	0.009
Gastroesophageal reflux disease	258 (9.9)	1233 (9.7)	0.008	262 (10.0)	1202 (9.4)	0.020	262 (10.0)	1224 (9.6)	0.015
Osteoporosis	763 (29.2)	3772 (29.5)	0.007	776 (29.6)	3831 (29.9)	0.007	775 (29.6)	3779 (29.5)	0.001
Peptic ulcer disease	101 (3.9)	442 (3.5)	0.022	99 (3.8)	438 (3.4)	0.019	99 (3.8)	423 (3.3)	0.026
Previous vertebral fracture	151 (5.8)	903 (7.1)	0.052	161 (6.1)	887 (6.9)	0.032	161 (6.1)	871 (6.8)	0.027
Visual disturbances and blindness	91 (3.5)	426 (3.3)	0.008	94 (3.6)	452 (3.5)	0.003	92 (3.5)	465 (3.6)	0.007

Abbreviations: COPD, chronic obstructive pulmonary disease; SMD, standardized mean difference

eTable 6. Characteristics of patients included and matched future-case controls for sensitivity analyses with exposure assessment period (index and reference periods) of 90 days and washout periods of 90, 120, 150, and 180 days.

Washout period	90 days			120 days			150 days			180 days		
	Cases	Controls	SMD	Cases	Controls	SMD	Cases	Controls	SMD	Cases	Controls	SMD
Total, n	2652	12959		2639	12901		2613	12774		2578	12609	
Age, n (%)			0.039			0.038			0.038			0.034
50-59	113 (4.3)	457 (3.5)		112 (4.2)	454 (3.5)		111 (4.2)	451 (3.5)		109 (4.2)	452 (3.6)	
60-69	288 (10.9)	1394 (10.8)		285 (10.8)	1382 (10.7)		286 (10.9)	1387 (10.9)		282 (10.9)	1367 (10.8)	
70-79	656 (24.7)	3202 (24.7)		655 (24.8)	3199 (24.8)		646 (24.7)	3155 (24.7)		639 (24.8)	3119 (24.7)	
80-84	540 (20.4)	2677 (20.7)		541 (20.5)	2682 (20.8)		540 (20.7)	2677 (21.0)		533 (20.7)	2642 (21.0)	
85+	1055 (39.8)	5229 (40.4)		1046 (39.6)	5184 (40.2)		1030 (39.4)	5104 (40.0)		1015 (39.4)	5029 (39.9)	
Sex, n (%)			0.018			0.018			0.017			0.017
Males	765 (28.8)	3631 (28.0)		761 (28.8)	3615 (28.0)		759 (29.0)	3610 (28.3)		749 (29.1)	3564 (28.3)	
Females	1887 (71.2)	9328 (72.0)		1878 (71.2)	9286 (72.0)		1854 (71.0)	9164 (71.7)		1829 (70.9)	9045 (71.7)	
HFRS, n (%)			0.009			0.001			0.019			0.026
<5	1436 (54.1)	7067 (54.6)		1426 (54.0)	6964 (54.0)		1410 (54.0)	7017 (54.9)		1392 (54.0)	6970 (55.3)	
≥5	1216 (45.9)	5883 (45.4)		1213 (46.0)	5937 (46.0)		1203 (46.0)	5757 (45.1)		1186 (46.0)	5639 (44.7)	
Comorbidities, n (%)												
Anxiety	212 (8.0)	1004 (7.7)	0.009	211 (8.0)	990 (7.7)	0.012	203 (7.8)	995 (7.8)	0.001	199 (7.7)	975 (7.7)	0.001
Arthritis	553 (20.9)	2747 (21.2)	0.008	554 (21.0)	2664 (20.6)	0.008	544 (20.8)	2702 (21.2)	0.008	538 (20.9)	2709 (21.5)	0.015
Alcohol use disorder	102 (3.8)	465 (3.6)	0.014	103 (3.9)	452 (3.5)	0.021	102 (3.9)	463 (3.6)	0.015	98 (3.8)	433 (3.4)	0.020
Cancer	519 (19.6)	2627 (20.3)	0.018	517 (19.6)	2581 (20.0)	0.010	513 (19.6)	2533 (19.8)	0.005	504 (19.6)	2492 (19.8)	0.005
Cardiovascular disease	1705 (64.3)	8459 (65.3)	0.021	1696 (64.3)	8400 (65.1)	0.018	1681 (64.3)	8256 (64.6)	0.006	1655 (64.2)	8123 (64.4)	0.005
Cerebrovascular disease	273 (10.3)	1332 (10.3)	0.001	273 (10.3)	1343 (10.4)	0.002	273 (10.4)	1324 (10.4)	0.003	270 (10.5)	1251 (9.9)	0.018
Chronic kidney disease	827 (31.2)	4228 (32.6)	0.031	824 (31.2)	4317 (33.5)	0.048	822 (31.5)	4152 (32.5)	0.022	812 (31.5)	4191 (33.2)	0.037
COPD/ asthma	382 (14.4)	1862 (14.4)	0.001	385 (14.6)	1874 (14.5)	0.002	382 (14.6)	1840 (14.4)	0.006	375 (14.5)	1789 (14.2)	0.010
Delirium	424 (16.0)	2166 (16.7)	0.020	421 (16.0)	2209 (17.1)	0.031	418 (16.0)	2142 (16.8)	0.021	414 (16.1)	2090 (16.6)	0.014
Dementia	113 (4.3)	614 (4.7)	0.023	113 (4.3)	635 (4.9)	0.031	113 (4.3)	597 (4.7)	0.017	115 (4.5)	575 (4.6)	0.005
Depression or other affective disorders	178 (6.7)	930 (7.2)	0.018	182 (6.9)	916 (7.1)	0.008	176 (6.7)	949 (7.4)	0.027	178 (6.9)	906 (7.2)	0.011
Diabetes mellitus	707 (26.7)	3513 (27.1)	0.010	711 (26.9)	3591 (27.8)	0.020	710 (27.2)	3421 (26.8)	0.009	705 (27.3)	3465 (27.5)	0.003
Epilepsy/seizures	77 (2.9)	357 (2.8)	0.009	76 (2.9)	375 (2.9)	0.002	74 (2.8)	340 (2.7)	0.010	76 (2.9)	329 (2.6)	0.021
Fall	895 (33.7)	4431 (34.2)	0.009	898 (34.0)	4538 (35.2)	0.024	887 (33.9)	4411 (34.5)	0.012	866 (33.6)	4250 (33.7)	0.002
Gastroesophageal reflux disease	264 (10.0)	1226 (9.5)	0.017	263 (10.0)	1198 (9.3)	0.023	259 (9.9)	1235 (9.7)	0.008	256 (9.9)	1261 (10.0)	0.002
Osteoporosis	788 (29.7)	3853 (29.7)	<0.001	785 (29.7)	3882 (30.1)	0.008	779 (29.8)	3790 (29.7)	0.003	762 (29.6)	3747 (29.7)	0.003
Peptic ulcer disease	101 (3.8)	431 (3.3)	0.026	99 (3.8)	417 (3.2)	0.028	97 (3.7)	425 (3.3)	0.021	95 (3.7)	430 (3.4)	0.015

Previous vertebral fracture	169 (6.4)	954 (7.4)	0.039	169 (6.4)	922 (7.1)	0.030	168 (6.4)	888 (7.0)	0.021	163 (6.3)	881 (7.0)	0.027
Visual disturbances and blindness	91 (3.4)	466 (3.6)	0.009	93 (3.5)	473 (3.7)	0.008	92 (3.5)	446 (3.5)	0.002	93 (3.6)	436 (3.5)	0.008

Abbreviations: COPD, chronic obstructive pulmonary disease; SMD, standardized mean difference

eTable 7. Results of case-case-time-control analyses for sensitivity analyses.

Exposure assessment period	60 days			30 days			90 days		
	Index period only	Reference period only	Odds ratio (95% CI)	Index period only	Reference period only	Odds ratio (95% CI)	Index period only	Reference period only	Odds ratio (95% CI)
Washout period: 30 days									
Case crossover				362	197	1.88 [1.58-2.24]			
Control crossover				880	686	1.32 [1.20-1.45]			
Case-case-time-control				N.A.	N.A.	1.42 [1.17-1.74]			
Adjusted case-case-time-control ^a				N.A.	N.A.	1.40 [1.15-1.71]			
Washout period: 60 days									
Case crossover				416	232	1.79 [1.53-2.11]	467	235	1.99 [1.70-2.32]
Control crossover				1010	860	1.17 [1.07-1.29]	1472	1089	1.35 [1.25-1.46]
Case-case-time-control				N.A.	N.A.	1.53 [1.27-1.84]	N.A.	N.A.	1.47 [1.23-1.75]
Adjusted case-case-time-control ^a				N.A.	N.A.	1.50 [1.24-1.80]	N.A.	N.A.	1.43 [1.20-1.70]
Washout period: 90 days									
Case crossover	459	224	2.05 [1.75-2.40]	426	227	1.88 [1.60-2.20]	508	261	1.95 [1.68-2.26]
Control crossover	1496	1076	1.39 [1.29-1.50]	1255	1005	1.25 [1.15-1.36]	1805	1386	1.30 [1.21-1.40]
Case-case-time-control	N.A.	N.A.	1.47 [1.23-1.76]	N.A.	N.A.	1.50 [1.25-1.80]	N.A.	N.A.	1.49 [1.27-1.76]
Adjusted case-case-time-control ^a	N.A.	N.A.	1.42 [1.19-1.70]	N.A.	N.A.	1.46 [1.22-1.75]	N.A.	N.A.	1.45 [1.23-1.72]
Washout period: 120 days									
Case crossover	485	238	2.04 [1.75-2.38]	484	228	2.12 [1.81-2.48]	540	263	2.05 [1.77-2.38]
Control crossover	1697	1305	1.30 [1.21-1.40]	1402	976	1.44 [1.32-1.56]	2109	1326	1.59 [1.48-1.70]
Case-case-time-control	N.A.	N.A.	1.57 [1.32-1.86]	N.A.	N.A.	1.48 [1.24-1.76]	N.A.	N.A.	1.29 [1.10-1.52]
Adjusted case-case-time-control ^a	N.A.	N.A.	1.53 [1.28-1.81]	N.A.	N.A.	1.44 [1.21-1.72]	N.A.	N.A.	1.26 [1.06-1.48]
Washout period: 150 days									
Case crossover	522	258	2.02 [1.74-2.35]	494	239	2.07 [1.77-2.41]	556	268	2.07 [1.79-2.4]
Control crossover	1895	1413	1.34 [1.25-1.44]	1679	1213	1.38 [1.29-1.49]	2341	1626	1.44 [1.35-1.53]
Case-case-time-control	N.A.	N.A.	1.51 [1.28-1.78]	N.A.	N.A.	1.49 [1.26-1.77]	N.A.	N.A.	1.44 [1.23-1.69]
Adjusted case-case-time-control ^a	N.A.	N.A.	1.46 [1.24-1.73]	N.A.	N.A.	1.43 [1.21-1.70]	N.A.	N.A.	1.40 [1.19-1.64]
Washout period: 180 days									
Case crossover	549	258	2.13 [1.84-2.47]	514	243	2.12 [1.82-2.46]	580	267	2.17 [1.88-2.51]
Control crossover	2160	1431	1.51 [1.41-1.61]	1738	1320	1.32 [1.23-1.41]	2296	1565	1.47 [1.38-1.56]
Case-case-time-control	N.A.	N.A.	1.41 [1.20-1.66]	N.A.	N.A.	1.61 [1.36-1.90]	N.A.	N.A.	1.48 [1.26-1.74]
Adjusted case-case-time-control ^a	N.A.	N.A.	1.37 [1.16-1.61]	N.A.	N.A.	1.57 [1.32-1.86]	N.A.	N.A.	1.45 [1.23-1.70]

Abbreviations: CI, confidence interval; CKD, chronic kidney disease; HFRS, Hospital Frailty Risk Score. ^aAdjusted for time-vary exposure to antidepressants, antipsychotics, benzodiazepines and opioids.