Supplementary material

Selected characteristics of the 49 included articles according to 32 IP indicators

First author (Country, Data source) (Quality assessment)	Study design	Outcomes	Sample size	Age: mean age ± SD (years)	Gender: % of women	Follow-up: mean (years)	Estimates (95% CIs)	Notes
Anticholinergics (no 1)								
Huang et al [25] (China, Longitudinal Health Insurance database of the National Health Insurance Research Database) (NOS 8/9)	Retrospective cohort study Population: elder people aged > 65 Exposure: Potentially inappropriate anticholinergics vs no-potentially inappropriate one (the Anticholinergic Risk Scale was the criterion)	(1) Emergency visit (2) Hospitalization (3) Constipation (4) Delirium (5) Cardiac arrhythmia (6) Cognitive impairment	54,888 vs 17,668	73.98 ± 6.51 vs 74.26 ± 7.01	56.83 vs 51.32	90.55 vs 144.64 (days)	**(1) 1.85 (1.76–1.95)** **(2) 1.07 (1.01–1.13)** **(3) 1.87 (1.72–2.03)** **(4) 1.51 (1.18–1.93)** **(5) 1.16 (1.05–1.28)** (6) 1.29 (0.89-1.88)	Number of events: (1) 13398 vs 2154 (2) 9177 vs 2111 (3) 4985 vs 757 (4) 456 vs 78 (5) 2272 vs 503 (6) 185 vs. 34
In cardiovascular patients (no 2)								
Uusvaara et al [50] (Finland, ad hoc data of previous RCT) (NOS 6/9)	Prospective cohort study Population: home-dwelling individuals aged 75-90 years with diagnosis of CardioV disease Exposure: patients users of anticholinergic drugs vs nonusers	(1) Hospitalization (2) Mortality	295 vs 105	80.7 ± 4.8 vs 78.4 ± 4.6	66 vs 63	3.3	**(1) 2.08 (1.23–3.51)** (2) 1.57 (0.78-3.15)	Mortality: 20.7% vs 9.5% Number of events: (1) 242 vs 88 (2) 61 vs 10
Antidepressants (no 3)								
Blanchette et al [12] (USA, Medicare Current	Historical pooled cohort Population: community	Acute MI	1,814 vs 10,856 (1,052 SSRI; 762 others)	NA	66.5 and 68.4 vs 56.5	2	For SSRI: **1.85 (1.13–3.00)** For other antidepressants	

Beneficiary Survey) (NOS 8/9)	residents who are ≥ 65 years Exposure: users of antidepressant (SSRIs or other) vs nonusers						1.01 (0.52-1.96)	
Coupland et al [15] (UK, supplying data to the QResearch primary care database) (NOS 8/9)	Cohort study Population: patients with a diagnosis of depression and between the ages of 65 and 100 years Exposure: antidepressants users (TCA, SSRI, others) vs nonusers	(1) All-cause mortality (2) Attempted suicide/self-harm (3) MI (4) Stroke/transient ischaemic attack (5) Falls (6) Fractures (7) Upper gatrointestinal bleeding (8) Epilepsy/seizures (9) Road traffic accidents (10) ADRs (11) Hyponatraemia	54,038 vs 6,708 (TCA 21,043; SSRI 29,763; others 3,060)	75 ± 7.6	66.7	1	For TCA: **(1) 1.16 (1.10–1.22)** **(2) 1.70 (1.28–2.25)** (3)1.09 (0.96 – 1.23) (4) 1.02 (0.93-1.11) **(5) 1.30 (1.23–1.38)** **(6) 1.26 (1.16–1.37)** **(7) 1.29 (1.10–1.51)** (8) 1.02 (0.76-1.38) (9) 0.86 (0.64-1.15) (10) 1.06 (0.86-1.29) (11) 1.05 (0.87-1.27) For SSRI: **(1) 1.54 (1.48–1.59)** **(2) 2.16 (1.71–2.71)** **(3) 1.15 (1.04–1.27)** **(4) 1.17 (1.10–1.26)** **(5) 1.66 (1.58–1.73)** **(6) 1.58 (1.48–1.68)** **(7) 1.22 (1.07–1.40)** **(8) 1.83 (1.49–2.26)** (9) 0.89 (0.70-1.13) (10) 1.16 (0.98-1.37) **(11) 1.52 (1.33–1.75)** For Others: **(1) 1.66 (1.56–1.77)** **(2) 5.16 (3.90–6.83)** (3)1.04 (0.85-1.27) **(4) 1.37 (1.22–1.55)** **(5) 1.39 (1.28–1.52)** **(6) 1.64 (1.46–1.84)** **(7) 1.37 (1.08–1.74)** **(8) 2.24 (1.60–3.15)** (9) 0.67 (0.39-1.14)	Number of events: (1) Non users: 8,210 TCA: 2,337 SSRIs: 5,782 Others: 1,268 (2) Non users: 150 TCA: 89 SSRIs: 178 Others: 79 (3) Non users: 1,264 TCA: 362 SSRIs: 614 Others: 110 (4) Non users: 2,811 TCA: 791 SSRIs: 1,384 Others: 317 (5) Non users: 5,208 TCA: 1,704 SSRIs: 3,575 Others: 631 (6) Non users: 2,507 TCA: 809 SSRIs: 1,597 Others: 341 (7) Non users: 671 TCA: 229 SSRIs: 365 Others: 79 (8)

							(10) 0.95 (0.68-1.34) (11) 1.28 (0.98-1.67)	Non users: 223 TCA: 58 SSRIs: 177 Others: 39 (9) Non users: 252 TCA: 56 SSRIs: 96 Others: 15 (10) Non users: 417 TCA: 139 SSRIs: 231 Others: 37 (11) Non users: 503 TCA: 155 SSRIs: 383 Others: 62
Zivin et al [57] (USA, Veterans Health Administration data) (NOS 7/9)	Cohort study Population: patients with a diagnosis of depression and at least one citalopram or sertraline prescription Exposure: users of citalopram vs users of sertraline	(1) Ventricular arrhythmia (2) All-cause mortality (3) Cardiac mortality (4) Non-cardiac mortality	618,450 vs 365,898 (patients 70-79 years: 71,187 vs 46,585; patients ≥ 80 years: 54,557 vs 33,487)	56.9 ± 15.2	9.6 vs 9.9	NA	Among patients aged 70–79 years, for citalopram: **(1) 5.52 (3.97–7.66)** **(2) 5.99 (5.30–6.77)** **(3) 28.60 (18.58–44.03)** **(4) 4.16 (3.66–4.73)** For sertraline: **(1) 2.99 (2.13–4.21);** **(2) 8.22 (6.89–9.82);** **(3) 23.06 (14.27–37.25);** **(4) 5.98 (4.94–7.24)** Among patients aged ≥80 years, for citalopram: **(1) 4.59 (3.28–6.41);** **(2) 9.96 (8.81–11.25);** **(3) 54.63 (35.50–84.05);** **(4) 6.38 (5.62–7.26)** for sertraline: **(1) 2.75 (1.94–3.90);**	

							(2) 13.57 (11.36–16.20); **(3) 41.81 (25.88–67.54);** **(4) 9.33 (7.71–11.3)**	
In CAD patients (no 4)								
Wu et al [55] (Taiwan, National Health Insurance Research database) (Quality Assessment 8/9)	Case-crossover study Population: patients with a hospitalization for a primary diagnosis of CerebroV event Exposure: users of antipsychotics	Hospitalization for CerebroV events	24,214 (16,258 aged ≥ 65 years)	68.6 ± 12.0	48.30	7-28 (days)	Among patients aged 65–75 years: **1.48 (1.30–1.68);** Among patients aged ≥75 years: **1.56 (1.37–1.78)**	
Antidiabetics (no 5)								
Margolis et al [37] (UK, The Health Information Network THIN Data) (NOS 7/9)	Retrospective cohort study Population: patients with at least two records for diabetes and at least 40 years old Exposure: users of insulin or sulfonylureas or biguadine or meglitinide or thiazolidinediones or rosiglitazone or pioglitazone vs nonusers	Serious atherosclerotic vascular disease of the heart	63,579 (15,514 patients aged 70-80 years; 6,930 patients aged >80 years)	Aged between 40-50 years: 8,522; between 50-60: 14,235; between 60-70: 18,378; between 70 and 80: 15,514; >80: 6,930	45.9%	8.7 ± 7.5	Among subjects aged 70–80 years: **3.3 (3.0–3.7)** Among subjects aged >80 years: **2.8 (2.5–3.2)**	
Vanasse et al [51] (Canada, Québec's provincial hospital discharge register and Québec's provincial demographic database)	Nested case-control study Population: diabetic patients aged ≥ 65 years Exposure: users of rosiglitazone	(1) All cause death (2) CV death (3) Hospitalization for acute MI (4) Hospitalization for congestive HF (5) Hospitalization for stroke	18,335 vs 370,866 4,455 vs 89,037 4,274 vs 85,480 4,274 vs 85,480 4,711 vs 94,209	(1)77.8 ± 7.5 vs 76.9 ± 6.9 (2)78.2 ± 7.3 vs 77.3 ±6.8 (3)76.5 ± 6.9 vs 75.1 ± 6.5 (4)75.6± 6.9 vs 75.1 ± 6.5 (5)75.7 ± 6.7 vs 72.2 ±6.2	(1) 49.5 (2) 49.6 (3) 48.5 (4) 52.4 (5) 49.6	2	**(1) 0.87 (0.76– 0.99)** (2) 0.88 (0.69-1.12) **(3) 1.41 (1.21–1.65)** **(4) 1.94 (1.71–2.19)** **(**5)1.14 (0.97-1.34)	Number of events: 18,553 4,454 4,274 6,307 4,711

(NOS 6/9)								
Winkelmayer et al [54] (USA, New Jersey Pharmaceutical Assistance for the Aged and Disabled program and the Pennsylvania Pharmaceutical Assistance Contract for Elderly program) (NOS 6/9)	Inception cohort study Population: people > 65 years with state-sponsored prescription drug benefits who had diabetes mellitus Exposure: patients initiated treatment with rosiglitazone vs pioglitazone	(1) All-cause mortality (2) MI (3) Stroke (4) Hospitalization for congestive HF	14,101 vs 14,260	76.3	73.6 vs 74	Median (mean): 215 (369) vs 217 (380) (days)	**(1) 1.15 (1.05–1.26)** (2) 1.08 (0.93-1.25) (3) 1.07 (0.93-1.23) **(4) 1.13 (1.01–1.26)**	Events rates per 1000 person-year: (1) 69.2 vs. 59.7 (2) 26.5 vs. 24.7 (3) 28.3 vs. 26.5 (4) 46.0 vs. 42.0
In end-stage renal disease or disabled patients (no 6)								
Graham et al [22] **(**USA, Medicare) (NOS 7/9)	Retrospective cohort study Population: patients aged ≥ 65 years who have end-stage renal disease or are disabled Exposure: new users of rosiglitazone vs new users of pioglitazone	(1) Acute MI (2) stroke (3) HF (4) All-cause mortality (5) Composite end point of acute MI, stroke, HF or death	67,593 vs 159,978	74.4	60.8% vs 59.5%	Median: 105 (days)	(1) 1.06 (0.96-1.18) **(2) 1.27 (1.12–1.45)** **(3) 1.25 (1.16–1.34)** **(4) 1.14 (1.05–1.24)** **(5) 1.18 (1.12–1.23)**	Attributable risk per 100 person-years: (1) 0.15 (-0.03 to 0.33) (2) 0.32 (0.17-0.47) (3) 0.94 (0.68-1.20) (4) 0.45 (0.22-0.67) **(5) 1.68 (1.27-2.08)**
Antipsychotics (no 7)								
Franchi et al [17] (Italy, Drug Administration database of the Lombardy Region) (NOS 6/9)	Retrospective case-control study Population: community-dwelling elderly patients aged between 65 and 94 years Exposure: patients who were given at least two consecutive boxes	Hospital discharge diagnosis of CerebroV events	3,855 vs 15,420 (13,805 patients aged ≥75 years)	Range: 65-94	53.9%	NA	Considering prescriptions of at least 2 boxes of drugs: For any antipsychotic vs non users: 1.09 (0.8-1.3); For typical vs non users: 1.3 (0.9-1.9); For atypical vs non users: 0.9 (0.7-1.2)	

	of antipsychotics (any, typical, atypical)						Considering prescriptions of at least 19 boxes of drugs: For any antipsychotic vs non users: 1.3 (0.86 – 2.03) For typical antipsychotics vs non users: **2.4 (1.08–5.5)** For atypical vs non users: 0.93 (0.53 – 1.62)	
Gisev et al [21] (Finland, Finnish National Prescription Register and the Special Reimbursement Register) (NOS 8/9)	Retrospective cohort study Population: community-dwelling older adults (≥ 65 years) Exposure: users of antipsychotics vs nonusers	Mortality	139 vs 2,085	76.7 ± 7.4 vs 74.1 ± 6.8	70.5 vs 57.9	9	**2.07 (1.73–2.47)**	
Pratt et al [42] (Australia, Australian Government Department of Veterans' Affairs administrative claims dataset**)** (Quality Assessment 8/8)	Self-controlled case series Population: elderly users of antipsychotics aged ≥ 65 years Exposure: users of antipsychotic vs nonusers	Hospitalization for stroke after (1) 1 week (2) 2-4 weeks (3) 5-8 weeks and (4) 8 or more weeks of treatment	514 typical, 564 atypical vs 9,560	≥ 65 years	NA	NA	For typical antipsychotics: **(1) 2.25 (1.32–3.83)** (2) 0.61 (0.33-1.13) **(3) 1.62 (1.14–2.32)** (4) 0.82 (0.61-1.11) For atypical antipsychotics: (1) 1.46 (0.83-2.56) (2) 0.94 (0.62-1.43) (3) 1.14 (0.80-1.64) (4) 0.86 (0.69-1.08)	Number of events: For typical antipsychotics: (1)8 (2) 6 (3) 19 (4) 40 For atypical antipsychotics: (1) 7 (2) 13 (3) 18 (4) 79
Setoguchi et al [48] (USA, General practice database) (NOS 6/9)	Cohort study Population: British Columbia residents aged ≥ 65 years who were new users of antipsychotics	(1) Overall non-cancer death (2) CardioV death (3) Out-of-hospital CardioV death (4) Infection (including pneumonia)	24,359 vs 12,882	80.3 vs 79.88	64.8 vs 60.3	180 (days)	For typical antipsychotics: **(1) 1.27 (1.18–1.37)** **(2) 1.23 (1.10–1.36)** **(3) 1.36 (1.19–1.56)** (4)1.21 (0.95-1.53) **(5) 1.71 (1.35–2.17)**	

	Exposure: new users of atypical antipsychotics agents vs users of conventional agents	(5) Respiratory disorders (excluding pneumonia) (6) Nervous system disorders (7) Mental disorders (8) Others disorders					**(6) 1.42 (1.01–1.86)** (7) 1.02 (0.74-1.39) **(8) 1.27 (1.07–1.51)**	
Vasilyeva et al [52] (Canada, Manitoba Population Health Research Data Repository) (NOS 7/9)	Retrospective cohort study Population: residents in Manitoba aged ≥ 65 years treated with antipsychotics for the first time Exposure: users of first or second generation antipsychotics	(1) CerebroV events (2) MI (3) Cardiac arrhythmia (4) Congestive HF (5) Mortality	4,655 vs 7,779	77.90 ± 7.98 vs 82.62 ± 7.80	57.22 vs 62.50	1	For atypical antipsychotics: (1) 1.14 (0.96-1.34) **(2) 1.61 (1.02-2.54)** (3) 0.86 (0.34-2.23) (4)1.13 (0.90-1.41) (5)0.68 (0.58-0.81)	Events: (1) 197 vs 809 (2) 26 vs 125 (3) 7 vs 21 (4) 118 vs 406 (5) 205 vs. 646
In dementia patients (no 8)								
Chan et al [14] (Japan, ad hoc data) (NOS 6/9)	Retrospective cohort study Population: patients with vascular and mixed dementia or Alzheimer disease aged ≥ 65 years Exposure: users of typical and atypical antipsychotic vs nonusers	CerebroV events	72 atypical, 654 typical vs 363 non-user	Atypical 79.93 ± 6.05, typical 81.48 ± 6.71 vs. non-user 80.47 ± 7.05	Atypical 69.4, typical 66.2, nonuser 63.9	NA	For atypical antipsychotics:1.04 (0.35–3.07); For typical antipsychotics: 0.96 (0.58–1.59)	Events rate per 1000 person years: atypical 49.6; typical 32.7; nonuser 44.6
Liperoti et al [33] (USA, Systematic Assessment of Geriatric drug use via Epidemiology database) (NOS 6/9)	Retrospective cohort study Population: nursing homes residents with dementia, aged ≥ 65 years, who	All cause-mortality	6,524 vs 3,205	83.5 vs 84.5	71.8 vs 72	6 (months)	For typical antipsychotics: **1.26 (1.13–1.42)**	Death rate: 44.6 per 100 person-years

	were new users of antipsychotics Exposure: users of conventional antipsychotics vs users of atypical ones							
Pariente et al [39] (Canada, Public prescription drug and medical services coverage programs databases) (NOS 7/9)	Retrospective cohort study Population: community-dwelling elderly (≥ 65 years) patients with dementia, who were new users of cholinesterase inhibitors Exposure: incident antipsychotic users vs antipsychotic nonusers	MI after (1) 30 days (2) 60 days (3) 90 days and (4) 365 days of treatment	10,969 vs 10,969 (17,532 patients aged ≥75 years)	Aged between 66-74: 2,443 vs 1,963; between 75-79: 3,029 vs 2,832; between 80-84: 2,991 vs 3,217; ≥ 85 years: 2,506 vs 2,957	66.0 vs. 65.7	1	**(1)2.19 (1.11–4.32)** (2)1.62 (0.99-2.65) (3)1.36 (0.89-2.08) (4)1.15 (0.89-1.47)	Number of MI cases:138 vs 126
Aspirin + clopidogrel + enoxaparin in NSTE-ACS patients (no 9)								
Heer et al [24] (Germany, Acute Coronary Syndromes Registry) (NOS 5/9)	Observational retrospective multicenter study Population: patients with NSTE-ACSs Exposure: users of aspirin + clopidogrel + enoxaparin vs users of aspirin + UFH	(1) Hospital mortality (2) Non-fatal reinfarction (3) Congestive HF (4) Stroke (5) CABG (6) MACE (7) All bleeding (8) Major bleeding	2,956 (128 vs 760 patients aged ≥75 years)	Median: 67.4 (range 59.8-75.6) vs 69.1 (range 60.6-76.7)	33.8 vs 36.8	NA	Overall: **(1) 0.35 (0.18-0.69)** **(2) 0.16 (0.06-0.44)** **(3) 0.58 (0.35-0.97)** (4) 0.53 (0.12-2.29) (5) 0.67 (0.45-1.01) **(6) 0.25 (0.14-0.44)** **(7) 2.61 (1.30-5.23)** (8) 1.72 (0.54-5.44) Among subjects aged ≥75 years: **(6) 0.44 (0.20 – 0.96)** (7) 1.4 (0.46-4.3) (8) 1.68 (0.28-10.24)	Number of events: (1)9 vs 130 (2) 4 vs 121 (3) 17 vs 144 (4) 2 vs 19 (5) 28 vs 212 (6) 13 vs 251 (7) 17 vs 16 (8) 5 vs 7
Atorvastatin + ezetimibe + OAC in AF patients no 10)								

Enajat et al [16] **(**The Netherlands, ad hoc data) (Jadad 4/5)	Randomized double-blind clinical trial Population: patients aged between 69 and 85 years with chronic or paroxysmal AF with blood cholesterol levels between 4.5 and 7.0 mmol/L Exposure: users of OAC + atorvastatin 40 mg/day + ezetimibe 10 mg/day vs users of OAC + Placebo (target INR of 2.5-3.5)	Major and minor bleeding; intracerebral bleeding; change in median total cholesterol level and low-density lipoprotein cholesterol level	14 vs 17	In acenocumarol group: 74.8 ± 4.1 vs 73.5 ± 4.3 In phenprocoumon group: 72.7 ± 2.5 vs 75.0 ± 2.0	7% vs. 18%	1	In the treatment group: 1 Minor bleeding in the treatment group; 3 Increasing in liver enzymes; 1 Myalgia	Compared with 6-months pre-intervention period, the mean daily dose ± standard error was 4.4 ± 1.5% lower in the treatment group (p=0.003)
Benzodiazepines + benzodiazepines-related drugs (no 11)								
Gisev et al [20] (Finland, Finnish National Prescription Regiter) (NOS 8/9)	Population-based retrospective cohort study Population: community-dwelling people aged ≥ 65 years Exposure: users of benzodiazepine + benzodiazepine-related drugs (zoplicone and zolpidem) vs nonusers	Mortality	325 vs 1,520				No association	
Bisphosphonates in fracture patients (no 12)								
Abrahamsen et al [10] (Denmark,	Register-based restricted cohort study	(1) Probable AF (2) Hospital-treated AF (3) Ischemic stroke (4) MI	14,302 vs 28,731	74.3 ± 8.8	89.1%	2.7	Overall: **(1) 1.18 (1.08-1.29)** **(2) 1.13 (1.01-1.26)** (3) 1.06 (0.74-1.52)	Overall rates per 1000 person years: 20.6 vs 16.5 13.7 vs 11.2

National Hospital Discharge Register and National Prescription Database**)** (NOS 9/9)	Population: fractures patients Exposure: new users of bisphosphonates vs nonusers						(4) 1.06 (0.92-1.22) Among subjects aged >75 years: **(1) 1.20 (1.07–1.34)** **(2) 1.17 (1.02–1.34)** (3) 1.16 (0.70–1.92) (4) 1.00 (0.84–1.20)	1.3 vs 1.1 8.3 vs 7.1
in women with CKD (no 13)								
Hartle et al [23] (USA, EpicCare, Geisinger Medical Center's electronic health records) (NOS 8/9)	Retrospective cohort study Population: women aged 18-88 years who were enrolled for primary care at any Geisinger facility and with baseline CKD Exposure: users of bisphosphonates vs nonusers	(1) Death (2) Composite major CardioV events	3,234 vs 6,370 (5100 patients aged ≥73 years)	74.2 ± 8.0 vs 71.2 ± 10.7	100%	3.9	Overall: **(1) 0.78 (0.67-0.91)** (2) 1.14 (0.94-1.39) For subjects aged ≥73 years: **(1) 0.78 (0.66 – 0.93)** (2) 1.04 (0.84-1.30)	Overall rates per 1000 person years: (1) 26.8 vs 30.3 (2) 20.0 vs 20.4
CCBs + CYP3A4 inhibitors in hypertensive patients (no 14)								
Yoshida et al [56] (Japan, Administrative database) (NOS 6/9)	Nested case-control study Population: hypertensive patients treated with CCBs Exposure: users of CCB + CYP3A4 inhibitor or CCB + other drugs (non CYP3A4 inhibitor) vs users of CCBs alone	ADRs	17,430 (Patients >70 years old 30 vs 160)	Aged <30 years: 18 vs 63; between 31 and 40: 99 vs 297; between 41 and 50: 175 vs 593; between 51 and 60: 198 vs 823; between 61 and 70: 120 vs 624; >70: 30 vs 160	63.6 vs. 52.2	12 (weeks)	For patients aged >70 years: 0.52 (0.20–1.34)	
CCBs in hypertensive patients (no 15)								
Jung et al [27] (Korea, Health Insurance Review	Observational case-crossover study	(1) Stroke (total risk) (2) Ischemic stroke (3) Haemorrhagic stroke	373/16,069 (5,546 patients aged 70-74 years)	68.3 ± 2.1	53.3	1 year	**(1) 2.56 (1.96–3.37)** **(2) 2.56 (1.89–3.47)** **(3) 5.16 (2.29–11.66)** **(4) 3.60 (1.34–9.66)**	Number of events (of whom among exposed patients): (1) 16,060 (373)

and Assessment Service database) (Quality Assessment 7/8)	Population: elderly patients aged ≥ 65 years with at least one diagnosis of hypertension and at least one prescription of CCBs Exposure: users of nifedipine vs users of other CCBs	(4) Intracranial haemorrhage (5)Subarachnoid Haemorrhage					**(5) 14.10 (1.84–108.25)**	(2) 12,961 (299) (3) 2,686 (67) (4) 1,970 (40) (5) 530 (18)
Cholinesterase inhibitors in dementia patients (no 16)								
Gill et al [19] (Canada, Ontario administrative healthcare databases) (NOS 689)	Population-based cohort study Population: community-dwelling patients aged ≥ 66 years with a prior diagnosis of dementia Exposure: users of cholinesterase inhibitors vs nonusers	(1) Hospital visits for syncope (2) Hospital visits for bradycardia (3) Permanent pacemaker insertion (4) Hospitalization for hip fracture	19,803 vs 61,499	80.4 ± 6.3 vs 80.4 ± 7.4	62.5 vs 61.2	2	**(1) 1.76 (1.57–1.98)** **(2) 1.69 (1.32–2.15)** **(3) 1.49 (1.12–2.00)** **(4) 1.18 (1.04–1.34)**	Number of events: (1) 428 vs 944 (2) 95 vs 224 (3) 64 vs 166 (4) 306 vs 1,008 Event rate, events per 1000 person-years: (1) 31.5 vs 18.6 (2) 6.9 vs 4.4 (3) 4.7 vs 3.3 (4) 22.4 vs 19.8
Clopidogrel + PPIs (no 17)								
Juurlink et al [28] (Canada, Ontario Public Drug Program) (NOS 7/9)	Nested case-control study Population: subjects ≥ 66 years with a prescription of clopidogrel within 3 days after hospital discharge following treatment for acute MI Exposure: users PPIs	(1) Recurrent MI < 90 days (2) Death < 90 days (3) Recurrent MI < 1 year (4) Death <1 year	734 vs 2,057	Median: 77 (range 72-83)	47.7 vs 44.9	5	**(1)1.27 (1.03–1.57)** (2) 0.82 (0.57-1.18) **(3) 1.23 (1.01–1.49)** (4) 0.89 (0.67-1.18)	Number of current users among cases: (1) 194/734 (2) 71/323 (3) 240/982 (4) 116/531 among controls: (1) 424/2,057 (2) 188/916 (3) 497/2,626 (4) 269/1,407

Mahabaleshwarkar et al [36] (USA, Medicare) (NOS 6/9)	Nested case-control study Population: subjects ≥ 65 years who had initiated clopidogrel therapy and with no gap of 30 days or more between clopidogrel prescription fills Exposure: users of PPIs	(1) Major CardioV events or all-cause mortality (composite) (2) Acute MI (3) Stroke (4) CABG (5) PCI (6) All-cause mortality (7) Any major CardioV events	9,908 vs 9,908	79.0 ± 7.7 vs 78.9 ± 7.5	60.5 vs 66.2	2	**(1) 1.26 (1.18–1.34)** (2) 0.85 (0.59-1.23) (3) 1.05 (0.86-1.28) (4) 0.82 (0.54-1.26) (5) 1.11 (0.94-1.31) **(6) 1.40 (1.29–1.53)** (7) 1.06 (0.95-1.18)	
Rassen et al [43] (USA, Provincial health care system funded by the British Columbia government , Pharmaceutical Assistance Contract for the Elderly in Pennsylvania and Pharmaceutical Assistance to the Aged and Disabled in New Jersey) (NOS 7/9)	Cohort study Population: subjects that underwent PCI or hospitalized for ACS and were new users of clopidogrel Exposure: concurrent users of PPIs vs nonusers	(1) MI hospitalization or death; (2) MI hospitalization; (3) All-cause death; (4) Revascularization	Cohort 1: 1,353 vs 9,038 Cohort 2: 1,352 vs 2,824 Cohort 3: 1,291 vs 2,707	Cohort 1: 75.7 ± 6.7 vs 74.3 ± 6.4 Cohort 2: 78.7 ± 6.6 vs 78.3 ± 6.7 Cohort 3: 78.4 ± 6.9 vs 77.7 ± 6.9	Cohort 1: 46.1 vs. 36% Cohort 2: 78.4% vs. 73.3% Cohort 3: 69.1% vs. 63.6%	3 (months)	(1)1.22 (0.99–1.51) (2) 1.22 (0.95–1.57) (3) 1.20 (0.84–1.70) (4) 0.97 (0.79–1.21)	Number of events (1) cohort 1: 73 vs 272 cohort 2: 46 vs 63 cohort 3: 37 vs 71 (2) cohort 1: 62 vs 240 cohort 2: 22 vs 29 cohort 3: 18 vs 33 (3) cohort 1: 15 vs 45 cohort 2: 25 vs 38 cohort 3: 21 vs41 (4) Cohort 1: 43 vs 179 cohort 2: 41 vs 112 cohort 3: 52 vs 158 Incidence rate per 100 person-year: (1) 47.9-48.3-33.2; (2) 40.6-23.1-16.2; (3) 9.5-25.8-18.8; (4) 27.9-43.1-48.2
Rossini et al [44] (Italy, Administrative database) (NOS 7/9)	Observational study Population: patients that underwent PCI	MACE; bleeding; death; any stent thrombosis	1,158 vs 170	64 ± 11 vs 63 ± 11	24.4 vs 18.8	1	For patients aged >75 years: 1.61 (0.35–7.37)	

	and drug-eluting stents implantation treated with aspirin and clopidogrel Exposure: concurrent users of PPIs vs nonusers							
Donepezil + clarithromycin (no 18)								
Hutson et al [26] (Canada, Ontario Provincial healthcare database) (NOS 6/9)	Nested case-control study Population: residents aged ≥66 years and users of antibacterial agents for respiratory tract infections Exposure: recent users of antibacterial agents	Hospitalization for CardioV events	59 vs 295	81.69 ± 6.14 vs 82.39 ± 5.98	49.2	8	For clarithromycin: 0.67 (0.28-1.63); for cefurozime: 2.07 (0.76-5.68); for levofloxacin or moxifloxacin: 1.01 (0.48-2.16)	
LABA and LAA in COPD patients (no 19)								
Gershon et al [18] (Canada, Ontario health care database) (NOS 6/9)	Nested case-control study Population: individuals aged ≥ 66 with COPD Exposure: new users of inhaled LABAs or LAAs	(1) Hospitalization or emergency department visit for acute coronary syndrome (2) HF (3) Cardiac arrhythmia (4) Ischemic stroke	26,628 vs 26,628	79.0 ± 7.1 vs 78.9 ± 7.1	48.1	5	For LAAs: **(1) 1.30 (1.04–1.62)** **(2) 1.31 (1.08–1.60)** (3) 1.26 (0.91-1.75) **(4) 0.68 (0.50–0.91)** For LABAs: **(1) 1.43 (1.08–1.89)** **(2) 1.42 (1.10–1.83)** (3) 1.17 (0.74-1.83) (4) 1.17 (0.78-1.74)	For LABAs vs LAAs: (1)1.10 (0.78- 1.56) (2) 1.08 (0.79 - 1.47) (3) 0.93 (0.54 – 1.59) **(4) 1.73 (1.06 – 2.83)**
New ACE inhibitors in AF patients (no 20)								
Mujib et al [38] (USA, Organized Program to Initiate Lifesaving Treatment in Hospitalized	Cohort study Population: patients aged ≥ 65 years with HF and preserved ejection fraction ≥40%	(1) Composite outcome (all-cause mortality or HF hospitalization) (2) all-cause mortality (3) HF hospitalization	After propensity score matching: 1,337 vs 1,337	81 ± 8	64 vs 63	6; Median 2.4 (range: 0.7 – 4.5)	**(1) 0.91 (0.84 – 0.99)** (2) 0.96 (0.88-1.05) (3) 0.93 (0.83-1.05) (4) 0.97 (0.89-1.05)	Number of events: (1) 1,076 vs 1,112 (2) 930 vs 951 (3) 558 vs 564 (4) 1,165 vs 1,155

Patients With Heart Failure) (NOS 7/9)	Exposure: users of ACE inhibitors vs nonusers	(4) all-cause hospitalization						
NSAIDs (no 21)								
Abraham et al [9] (USA, Veterans Affairs -Pharmacy Benefits Management) (NOS 8/9)	Retrospective cohort study Population: veterans > 65years prescribed an NSAID at any Veterans Affairs facility Exposure: users of NSAIDs, NSAIDs + PPIs, coxib, coxib + PPIs, PPIs vs NSAIDs nonusers	All-cause mortality following (1) Upper GI events (2) MI (3) CerebroV events	474,495	73.0 ± 5.5	2.1	3	**(1) 3.3 (2.8–3.4)** **(2) 10.3 (9.2–11.6)** **(3) 12.4 (10.9–14.3)**	Rate of events pre 1000 person-years: (1) 5.5 (CI 5.4-5.6); (2) 17.7 (CI 17.5-17.9); (3) 21.8 (CI 21.6-22.0)
Caughey et al [13] (Australia, Administrative database) (NOS 7/9)	Retrospective cohort study Population: Australian veterans with incident dispensing of an NSAIDs Exposure: users of NSAIDs	(1) All stroke (2) Ischaemic stroke (3) Haemorrhagic stroke	162,065	76.0 ± 7.9	40	1	**(1) 1.88 (1.70–2.08)** **(2) 1.90 (1.65–2.18)** **(3) 2.19 (1.74–2.77)**	Absolute risk of stroke for 1000 person-years: 7.1
Roumie et al [45] (USA, Tennesee Medicaid program) (NOS 7/9)	Retrospective Observational Study Population: non-institutionalized person aged 35-94 years who did not have evidence of any non-cardiovascular serious medical illness prior to cohort entry	Hospitalization for acute MI, stroke, or death from coronary heart disease	NSAIDs users with history of CardioV disease: – Colecoxib 1,882 – Rofecoxib 1,354 – Valdecoxib 394 – Ibuprofen 6,236	NSAIDs users with history of CardioV: -Colecoxib 56.8 ± 14.6 -Rofecoxib 53.6 ± 14.2 -Valdecoxib 55.7 ± 15.3 -Ibuprofen 51.4 ± 13.5 -Naproxen 51.5 ± 13.2	NSAIDs users with history of CardioV: -Colecoxib 62.75 -Rofecoxib 56.06 -Valdecoxib 63.45 -Ibuprofen 58.88 -Naproxen 58.23	Patients with past history of CardioV: 397,977 person-years; Patients without past history of CardioV: 1,566,678 (person-years)	In patients aged ≥ 65 years and among subjects with CardioV history, for colecoxib: 0.98 (0.85 – 1.14) for rofecoxib: 1.14 (0.96- 1.34) for valdecoxib: 1.10 (0.84 – 1.45) for ibuprofen: 1.06 (0.88 – 1.27) for naproxen:0.89 (0.75 – 1.06)	Number of cardiovascular events/person-years: NSAIDs users with history of CardioV: -Colecoxib 199/7,665 -Rofecoxib 210/6,293 -Valdecoxib 53/2,423 -Ibuprofen 79/3,741 -Naproxen

	Exposure: users of NSAIDs vs nonusers, with CardioV or not		– Naproxen 7,249 – Indomethacin 1,361 – Diclofenac 496 NSAIDs non–users with history of CardioV disease: 60,784 NSAIDs users without history of CardioV disease: – Colecoxib 7,117 – Rofecoxib 6,840 – Valdecoxib 1,742 – Ibuprofen 44,261 – Naproxen 48,103 – Indomethacin 6,730 – Diclofenac 3,420 NSAIDs non–users without history of CardioV disease: 380,434	-Indomethacin 52.2 ± 12.9 -Diclofenac 51.6 ± 13.4 -NSAIDs non-users with history of CVD: 55.1 ± 14.4 NSAIDs users without history of CardioV: -Colecoxib 49.4 ± 14 -Rofecoxib 45.4 ± 12.6 -Valdecoxib 47.8 ± 14.3 -Ibuprofen 42.6 ± 11.3 -Naproxen 43.4 ± 11.4 -Indomethacin 45.2 ± 12.3 -Diclofenac 43.3 ± 11.2 NSAIDs non-users without history of CVD: 44.6 ± 12.7	-Indomethacin 46.88 -Diclofenac 58.27 NSAIDs non-users with history of CVD: 51.34 NSAIDs users without history of CardioV: -Colecoxib 68.6 -Rofecoxib 64.8 -Valdecoxib 69.9 -Ibuprofen 69.7 -Naproxen 68.2 -Indomethacin 54.7 -Diclofenac 66.0 NSAIDs non-users without history of CVD: 61.5		for diclofenac: 1.09 (0.69 – 1.71) for indomethacin: 0.92 (0.61 – 1.37) In patients aged ≥ 65 years and among subjects without CardioV history, for colecoxib: 1.15 (0.98 – 1.33) for rofecoxib: 1.26 (1.05–1.51) for valdecoxib: 1.40 (1.05–1.87) for ibuprofen: 0.98 (0.83 – 1.17) for naproxen: 0.92 (0.72 – 1.08) for diclofenac: 1.20 (0.79 – 1.83) for indomethacin: 1.57 (1.15–2.14)	130/5,798 -Indomethacin 24/953 -Diclofenac 30/1,499 NSAIDs non-users with history of CardioV: 5,885/207,965 NSAIDs users without history of CardioV: -Colecoxib 189/18,081 -Rofecoxib 186/16,537 -Valdecoxib 68/4,770 -Ibuprofen 116/16,327 -Naproxen 162/22,739 -Indomethacin 35/2,987 -Diclofenac 26/4,728 NSAIDs non-users without history of CardioV: 6,796/860,356

OACs (no 22)								
Poli et al [41] (Italy, Elderly Patients followed by Italian Centres for Anticoagulation study) (NOS 5/9)	Multicenter prospective observational study Population: old patients who started vitamin K antagonist treatment after 80 years of age for thromboprophylaxis of AF or venous thromboembolism Exposure: users vitamin K antagonist	Major bleedings	4,093	84 (range 80-102)	57	2.35 (SD ± 2.1)	NA	Number of events: 179 major bleedings; rate per 100 patient-years: 1.87; rate per 100 patient-years (<85 years): 1.71; rate per 100 patient-years (≥85 years): 2.22
In CAD patients (no 23)								
Ruiz Ortiz et al [46] **(**Spain, Administrative database) (NOS 7/9)	Observational study Population: patients aged ≥80 years with non-valvular AF treated Exposure: users of OAC vs nonusers	(1) Embolic events (2) Severe bleeding (3) All embolic and hemorrhagic events (4) All-cause death	164 vs105 (196 patients aged 80-84 years; 57 patients aged 85-89 years; 16 patients aged ≥90 years)	83 ± 3 vs 84 ± 4	65 vs 72	2.8 (SD ± 1.9)	**(1) 0.17 (0.07 – 0.41)** (2) 2.66 (0.76-9.32) **(3) 0.46 (0.25– 0.83)** **(4) 0.52 (0.31 – 0.88)**	Number of events: 7 vs 20 14 vs 3 21 vs 23 32 vs 28
Tanaka et al [49] **(**Japan, Administrative database) (NOS 2/9)	Retrospective case-control study Population: patients treated with antithrombotic drugs Exposure: users of OACs	GI injuries, including gastric ulcers, duodenal ulcers, and hemorrhagic injuries	172 vs. 3,099 (39 vs 156 patients aged 60-69 years; 102 vs 408 patients aged ≥70 years)	70.0 ± 14.0 vs 66.2 ± 18.0	43 vs 45	NA	Among patients aged 50-59 years, for low–dose aspirin: 1.73 (0.52 – 6.16) for clopidogrel: 2.56 (0.61 – 10.64) for warfarin: 2.10 (0.34 – 11.76) for NSAIDs: 6.42 (2.04 – 22.62) Among patients aged 60–69 years, for low–dose aspirin: 1.29 (0.56 – 2.96) for clopidogrel:	

							4.41 (1.56 – 12.43) for warfarin: 1.80 (0.74 – 4.26) for NSAIDs: **4.01 (1.83 – 8.86)** Among patients aged ≥70 years, for low–dose aspirin: **1.91 (1.17–3.16)** for clopidogrel: **3.07 (1.62–5.77)** for warfarin: **2.45 (1.35–4.43)** for NSAIDs: **4.26 (2.65–6.93)**	
Olmesartan medoxomil in hypertensive patients (no 24)								
Saito et al [47] (Japan, ad hoc database) (NOS 2/9)	Prospective cohort study Population: olmesartan-naïve hypertensive patients aged ≥65 years Exposure: olmesartan alone, in combination with drugs, or by switching from other antihypertensive medications	Blood pressure; Clinical laboratory tests; ADRs	550 (280 young-old patients 65-74 years; 270 older-old patients ≥75 years)	74.8 (range 65-95)	Young-old 65-74: SDH 58.6%; ISH 72.1% Older-old ≥75: SDH 74.3%; ISH 72.7%	6 (months)	No association	N (%) patients with ADRs: Young-old 65-74: SDH = 8 (5.67); ISH = 4 (2.84) Older-old ≥75: SDH = 6 (5.45); ISH = 9 (5.56)
Opioids (no 25)								
Li et al [32] (UK, General Practice Research Database) (NOS 6/9)	Nested case-control study Population: non-cancer pain patients who had a record for at least one opioid prescription Exposure: users of opioids	MI	11,693 vs 44,897	61.8 ± 11.2 vs 61.6 ± 11.2	31.1 vs. 31.3	NA	Among patients aged 71–80 years old, for male: **1.46 (1.23–1.75)** for female: **1.34 (1.12–1.61)**	Among patients aged 61-70 years, for male: 1.08 (0.92-1.26); for female: 1.20 (0.97-1.47)

Postmenopausal hormones (no 26)								
Løkkegaard et al [34] (Denmark, Danish Sex Hormone Register Study) (NOS 8/9)	Retrospective cohort study Population: healthy Danish women aged 51-69 years Exposure: users of hormone therapy vs nonusers	MI	Patients aged 65-69 years: – Previous use 27,338; – Current use 75,473	NA	100	7	For patients aged 65–69 years: -for past use **0.77 (0.60–0.99)** -for current use 0.92 (0.80-1.06)	Number of events: -previous use: 64 - current use: 211 Rate for 1000 women-year: -previous use: 2.34 -current use: 2.80
Statins + clopidogrel in PCI patients (no 27)								
Blagojevic et al [11] **(**Canada, Health Insurance databases of Quebec) (NOS 6/9)	Population-based cohort study Population: PCI patients aged ≥66 years and receiving their first post discharge clopidogrel prescription within 5 days of the hospital discharge date Exposure: users of clopidogrel + non-CYP3A4-metabolized statins, or clopidogrel + CYP3A4-metabolized statins vs clopidogrel and no statins	Death; MI; unstable angina; hospitalization with repeat revascularization; CerebroV events	8,417 vs 2,074	74.1 ± 5.7	40.1	90 (days)	HRs compared to non-CYP3A4-metabolized statins: -for CYP3A4 1.16 (0.91–1.47) - for no statin 1.22 (0.93–1.59)	Number of events: 76 for non-CYP3A4-matabolized statins, 316 for CYP3A4-metabolized statins, 231 for no statin
Statins + macrolides (no 28)								
Patel et al [40] (Canada, Ontario Drug Benefit database, Canadian Institute for health Information	Population-based cohort study Population: continuous statin users > 65 years with macrolide	(1) Hospitalization for rhabdomyolysis (2) hospitalization for acute kidney injury (3) hospitalization for hyperkalemia	75,858 vs 68,478	74 ± 6	52.9 vs. 53.0	30 (days)	**(1) 2.17 (1.03 - 4.52)** **(2) 1.83 (1.52 - 2.19)** (3) 1.32 (0.89 – 1.94) **(4) 1.57 (1.37 - 1.82)**	Absolute risk differences: (1) 0.02 (0.01 - 0.03) (2) 0.20 (0.14- 0.26) (3) 0.02 (0.01 - 0.05) (4) 0.25 (0.17 - 0.33) Number of events:

Discharge Abstract database, Ontario Health Insurance Plan database, and Registered persons database of Ontario) (NOS 7/9)	antibiotic co-prescription Exposure: users of statin + clarithromycin or erythromycin vs users of statin + azithromycin	(4) all-cause mortality						(1) 24 vs 10 (2) 347 vs 176 (3)61 vs 42 (4)529 vs 306
Statins								
In CAD patients (no 29)								
Kulik et al [29] (USA, Medicare, Pennsylvania Pharmaceutical Assistance Contract for the Elderly program, and the New Jersey Pharmaceutical Assistance to the Aged and Disabled program) (NOS 7/9)	Observational population-based study Population: patients ≥ 65 years old who had been hospitalized for acute MI or coronary revascularization Exposure: users of statins vs nonusers	New-onset AF	8,450 vs 20,638	76.6 ± 6.4 vs 78.8 ± 7.1	74.1 vs 72.2	3.8 (SD ± 3)	Adjusted HR in the entire cohort: **0.90 (0.85–0.96)** In CABG cohort: 0.96 (0.83 – 1.10) In PCI cohort: **0.89 (0.82–0.96)** In MI cohort: **0.84 (0.76–0.92)**	
Macchia et al [35] (Italy, Administrative database) (NOS 7/9)	Observational retrospective cohort study Population: patients discharged alive with a first diagnosis of MI treated with statins Exposure: users of statins + n–3 PUFA vs users of statins	(1) All-cause death (2) Death or MI (3) Death or AF (4) Death or congestive HF (5) Death or stroke	4,302 vs 7,230 (4,812 patients aged ≥70 years)	63.8 ± 10.7 vs. 68.5 ± 10.4	24.6 vs. 33.3	4	**(1) 0.59 (0.52–0.66)** (2) 0.94 (0.96 – 1.02) **(3) 0.78 (0.71–0.86)** **(4) 0.81 (0.74–0.88)** **(5) 0.66 (0.59–0.74)** In paired–matched cohort: **(1) 0.63 (0.56–0.72)** (2) 0.95 (0.87 – 1.03) **(3) 0.82 (0.75–0.90)** **(4) 0.86 (0.79–0.95)** **(5) 0.65 (0.58 – 0.73)**	Number of events in paired-matched populations: 340 vs 539 804 vs 848 660 vs 805 684 vs 792 456 vs 662
In COPD patients (no 30)								

Lawes et al [31] (New Zeland, Administrative database) (NOS 7/9)	Retrospective cohort study Population: patients with 50-80 years discharged from hospital with a first admission of COPD Exposure: users of statins vs nonusers	All-cause mortality	596 vs 1,091; (patients aged 70-79: 354 vs 593)	70.6	41.6 vs 51.5	4	**2.22 (1.60 - 3.07)**	
In women (no 31)								
LaCroix et al [30] (USA, Women's Health Initiative Observational Study) (NOS 4/9)	Prospective Study Population: women aged 65-79 years who did not have frailty at baseline Exposure: users of statin vs nonusers	Intermediate frailty; Frail	2,122 vs 23,256	51.6% aged between 65-69; 48.4% aged between 70-79	100	3	ORs compared to nonusers: -for intermediate frailty women 0.99 (0.88-1.11) -for frail women 1.00 (0.85-1.16)	
Warfarin + potentially interacting drugs (no 32)								
Vitry et al [53] (Australia, Australian Department of Veterans' Affairs administrative claims database) (NOS 6/9)	Retrospective cohort study Population: veterans aged ≥ 65 years who were new users of warfarin Exposure: users of Warfarin + potentially interacting drugs vs users of warfarin	Bleeding-related hospitalization	17,661	81.8 ± 4.4	36.2	4	Overall incidence rate: **4.1 (3.7-4.6) per 100 person-year**; RRs compared to treatment with warfarin only: -Low-dose aspirin 1.44 (1.00-2.07); -NSAIDs 1.19 (0.90-1.59); -Colecoxib 1.07 (0.69-1.68) -Clopidogrel **2.23 (1.48-3.36)**; -Clopidogrel + aspirin **3.44 (1.28-9.23)**; -NSAIDs + aspirin 1.01 (0.40-2.53); -Clopidogrel + NSAIDs	Number of events for each drug; incidence rate for 100 person-year for each drug

							2.5 (0.88-7.10); -Tramadol 2.37 (0.93-6.01); -SSRIs 2.17 (0.81-5.78); -Amiodarone **3.33 (1.38-8.00)**; -Antibiotics **2.34 (1.55-3.54)**; -Macrolides **3.07 (1.37-6.90);** -Trimethoprim or cotrimoxazole **5.08 (2.00-12.88);** -Thyroid hormones 1.66 (0.66-4.16)	

ACE: Angiotensin-Converting-Enzyme; ACS: Acute Coronary Syndromes; ADR: Adverse Drug Reaction; AF: Atrial Fibrillation; CardioV: CardioVascular; CABG: Coronary Artery Bypass Graft; CAD: Coronary Artery Disease; CCB: Calcium Channel Blocker; CerebroV: CerebroVascular; CKD: Chronic Kidney Disease; COPD: Chronic Obstructive Pulmonary Disease; CYP3A4: Cytochrome P450 3A4 ; GI: GastroIntestinal; HF: Heart Failure; HR: Hazard Ratio; INR: International Normalized Ratio; LAA: Long-Acting Anticholinergic; LABA: Long-Acting Beta-Agonist; MACE: Major Adverse Cardiac Events; MI: Myocardial Infraction; NOS: Newcastle Ottawa Scale; NSAID: NonSteroidal Anti-Inflammatory Drug; NSTE: Non-ST segment Elevation; OAC: Oral AntiCoagulant; OR: Odds Ratio; PCI: Percutaneous Coronary Intervention; PPI: Proton Pump Inhibitor; PUFA: PolyUnsaturated Fatty Acid; RR: Relative Risk; TCA: TriCyclic Antidepressants; UFH: UnFractionated Heparin; SSRI: Selective Serotonin Reuptake Inhibitor