

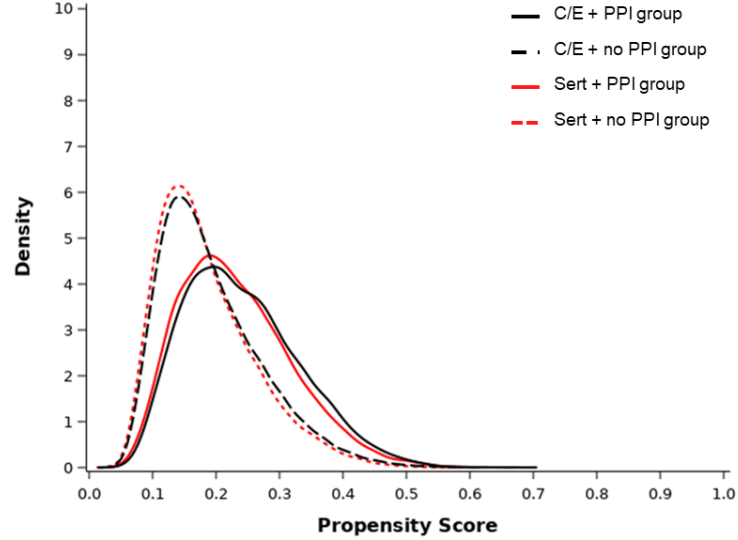
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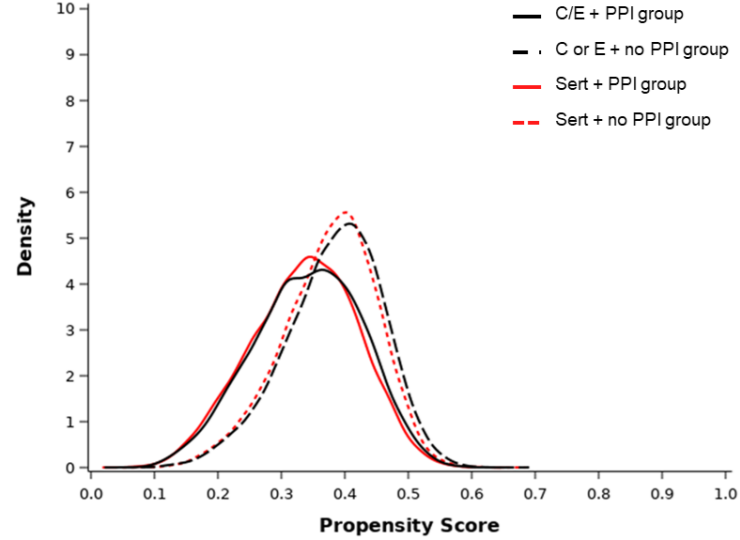
SUPPLEMENTAL FIGURES

Figure S1. Propensity score distributions

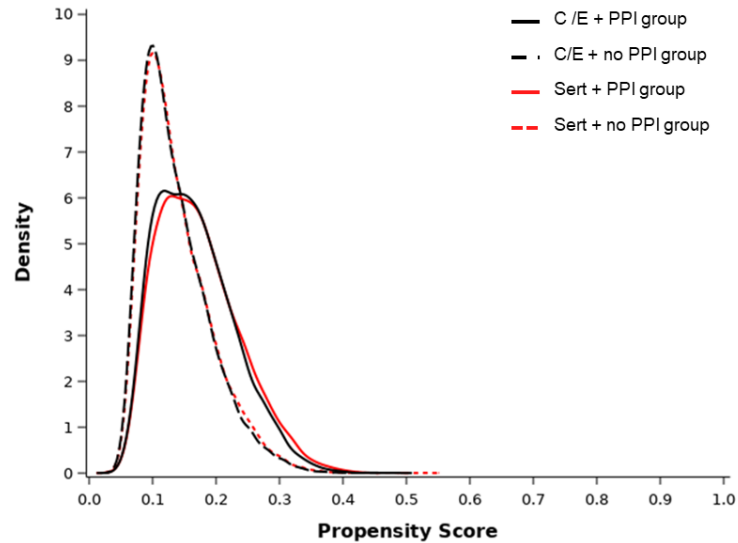
Panel A. Citalopram/escitalopram + PPI propensity score distribution



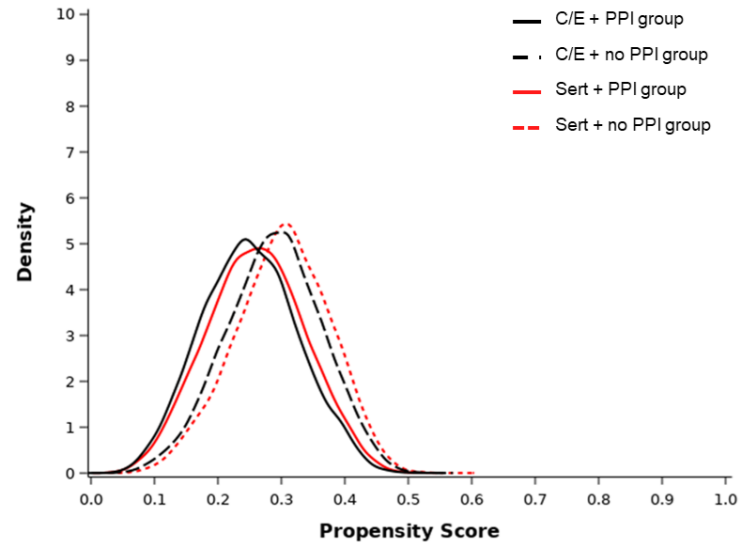
Panel B. Citalopram/escitalopram + no PPI propensity score distribution



Panel C. Sertraline + PPI propensity score distribution



Panel D. Sertraline + no PPI propensity score distribution



Each panel shows the distribution for one of the four estimated propensity scores across each of the exposure groups.

Abbreviations: C/E, citalopram or escitalopram; PPI, proton pump inhibitor; Sert, sertraline.

SUPPLEMENTAL TABLES

Table S1. Outcome definitions

Primary outcome	
Outcome	Specification
Sudden cardiac death	Death with a cardiac arrhythmia or cardiac arrest death code (28, 29) listed as the <i>primary</i> cause of death on the End Stage Renal Disease Death Notification Form.
Secondary outcomes	
Outcome	Specification
Composite outcome of sudden cardiac death <i>or</i> hospitalized ventricular arrhythmia	<p>Death with a cardiac arrhythmia or cardiac arrest death code (28, 29) listed as the <i>primary</i> cause of death on the End Stage Renal Disease Death Notification Form.</p> <p style="text-align: center;"><i>OR</i></p> <p>An inpatient hospitalization for a ventricular arrhythmia based on the <i>primary</i> ICD-9/ICD-10 discharge diagnosis code.</p> <ul style="list-style-type: none"> ○ ICD-9 codes^a: 427.1, 427.4 ○ ICD-10 codes^b: I47.2, I49.0
Cardiovascular mortality	Death with a cardiovascular cause of death code (23, 25, 26, 27, 28, 29, 30, 31, 32, 35, 36) listed as the <i>primary</i> cause of death on the End Stage Renal Disease Death Notification Form.
Negative control outcome	
Outcome	Specification
Death due to a cause other than sudden cardiac death (i.e., <i>non-sudden cardiac death</i>)	Death with a non-sudden cardiac death code (all codes except 28 and 29) the <i>primary</i> cause of death on the End Stage Renal Disease Death Notification Form.

^a Specified four-digit ICD-9 diagnosis codes listed included all existing includes all existing 5th digit codes.

^b Specified four-digit ICD-10 diagnosis codes listed include all existing 5th, 6th, and 7th digit codes.

Abbreviations: ICD-9, International Classification of Diseases, 9th Revision; ICD-10, International Classification of Diseases, 10th Revision.

Table S2. Diagnosis and procedure codes used to identify covariates

Comorbid conditions	
Comorbidity	Diagnosis ^a or procedure codes ^b
Anxiety	<ul style="list-style-type: none"> ○ ICD-9 codes: 300.0, 309.21, 309.24, 309.28 ○ ICD-10 codes: F41, F43.22, F43.23, F93.0
Depression	<ul style="list-style-type: none"> ○ ICD-9 codes: 296.2, 296.3, 296.5, 296.6, 296.82, 300.4, 309.0, 309.1, 309.28, 311 ○ ICD-10 codes: F31.30–F31.32, F31.4–F31.6, F31.75–F31.78, F32.0–F32.5, F32.89, F32.9, F33.0–F33.9, F34.1, F43.21, F43.23
Other psychiatric conditions	<ul style="list-style-type: none"> ○ ICD-9 codes: 296.0, 296.4–296.8, 297, 301, 295 ○ ICD-10 codes: F22, F23, F24, F21, F30, F31, F32.89, F34.0, F34.1, F60, F68.10, F68.12, F68.13, F69, F20, F25
Dementia	<ul style="list-style-type: none"> ○ ICD-9 diagnosis codes: 331.0–331.2, 331.7, 331.82, 290.0–290.4, 294.0–294.2, 797 ○ ICD-10 diagnosis codes: F01.5, F02.8, F03.9, F04, F05, G13.2, G13.8, G30, G31.0–G31.2, G31.83, G91.4, G94, R41.81, R54
Insomnia	<ul style="list-style-type: none"> ○ ICD-9 codes: 307.41, 307.42, 327.0, 780.51, 780.52 ○ ICD-10 codes: F51.0, G47.00, G47.0
Gastroesophageal reflux disease	<ul style="list-style-type: none"> ○ ICD-9 code: 530.81 ○ ICD-10 code: K21
Peptic ulcer	<ul style="list-style-type: none"> ○ ICD-9 code: 533 ○ ICD-10 code: K27
Other type of ulcer	<ul style="list-style-type: none"> ○ ICD-9 codes: 530.2, 531, 532, 534 ○ ICD-10 codes: K22.1, K25, K26, K28
Gastrointestinal bleed	<ul style="list-style-type: none"> ○ ICD-9 diagnosis codes: 531.0, 531.2, 531.4, 531.6, 532.0, 532.2, 532.4, 532.6, 533.0, 533.2, 533.4, 533.6, 534.0, 534.2, 534.4, 534.6, 562.02, 562.03, 562.12, 562.13, 569.3, 569.85, 578.0, 578.1, 578.9 ○ ICD-10 diagnosis codes: : K25.0, K25.2, K25.4, K25.6, K26.0, K26.2, K26.4, K26.6, K27.0, K27.2, K27.4, K27.6, K28.0, K28.2, K28.4, K28.6, K55.21, K57.01, K57.11, K57.13, K57.21, K57.31, K57.33, K57.41, K57.51, K57.53, K57.81, K57.91, K57.93, K62.5, K92.0, K92.1, K92.2
Arrhythmia	<ul style="list-style-type: none"> ○ ICD-9 diagnosis codes: 427 ○ ICD-10 diagnosis codes: I46–I49
Conduction disorder	<ul style="list-style-type: none"> ○ ICD-9 diagnosis codes: 426 ○ ICD-10 diagnosis codes: I44–I45
Dyslipidemia	<ul style="list-style-type: none"> ○ ICD-9 diagnosis codes: 272.0–272.2, 272.4 ○ ICD-10 diagnosis codes: E78.0, E78.1, E78.2, E78.4, E78.5
Heart failure	<ul style="list-style-type: none"> ○ ICD-9 diagnosis codes: 398.91, 402.x1, 404.x1, 404.x3, 428 ○ ICD-10 diagnosis codes: I09.81, I11.0, I13.0, I50

Hypertension	<ul style="list-style-type: none"> ○ ICD-9 diagnosis codes: 401–405 ○ ICD-10 diagnosis codes: I10–I16
Ischemic heart disease	<ul style="list-style-type: none"> ○ ICD-9 diagnosis codes: 410–414 ○ ICD-10 diagnosis codes: I20–I25
Peripheral arterial disease	<ul style="list-style-type: none"> ○ ICD-9 diagnosis codes: 250.7, 440.2–440.9, 443.1, 443.22, 443.81, 443.89, 443.9, 444.22, 444.81, 445.02 ○ ICD-10 diagnosis codes: E10.5, E11.5, E13.5, I70.2–I70.9, I73.1, I73.89, I73.9, I74.3–I74.5, I75.02, I77.72, I79.1, I79.8
Stroke	<ul style="list-style-type: none"> ○ ICD-9 diagnosis codes: 430–438 ○ ICD-10 diagnosis codes: G45–G46, I60–I69
Valvular disease	<ul style="list-style-type: none"> ○ ICD-9 diagnosis codes: 394–397, 424.0–424.3 ○ ICD-10 diagnosis codes: I05–I08, I09.1, I34–I37
Cardiac pacemaker	<ul style="list-style-type: none"> ○ ICD-9 diagnosis codes: V45.01 ○ ICD-10 diagnosis codes: Z95.0
Electrocardiogram	<ul style="list-style-type: none"> ○ CPT procedure codes: 93000, 93005, 93010, 93040, 93041, 93042
Cardiac surgery or procedure	<ul style="list-style-type: none"> ○ ICD-9 procedure codes: 35, 36, 37 ○ ICD-10 procedure code: 02
Asthma or chronic obstructive pulmonary disease	<ul style="list-style-type: none"> ○ ICD-9 diagnosis codes: 491–494, 496 ○ ICD-10 diagnosis codes: J41–J45, J47
Cancer	<ul style="list-style-type: none"> ○ ICD-9 diagnosis codes: 140–209 ○ ICD-10 diagnosis codes: C00–C96, C7A
Diabetes	<ul style="list-style-type: none"> ○ ICD-9 diagnosis codes: 250 ○ ICD-10 diagnosis codes: E10, E11, E13
Hypothyroidism	<ul style="list-style-type: none"> ○ ICD-9 diagnosis codes: 243, 244 ○ ICD-10 diagnosis codes: E00, E01.8, E02, E03.0–E03.3, E03.8, E03.9, E89.0
Liver disease	<ul style="list-style-type: none"> ○ ICD-9 code: 571 ○ ICD-10 codes: K70–K76
Sleep apnea	<ul style="list-style-type: none"> ○ ICD-9 codes: 327.2, 780.51, 780.53, 780.57 ○ ICD-10 code: G47.3
Alcohol use or dependence	<ul style="list-style-type: none"> ○ ICD-9 codes: 303, 305.0 ○ ICD-10 codes: F10.10, F10.11, F10.120, F10.129, F10.20, F10.21, F10.220, F10.229
Drug use or dependence	<ul style="list-style-type: none"> ○ ICD-9 codes: 304, 305.2–305.9 ○ ICD-10 codes: F11.10, F11.11, F11.120, F11.129, F11.20–F11.25, F11.28, F11.29, F11.90, F12.10, F12.11, F12.20–F12.25, F12.28, F12.29, F13.10, F13.11, F13.120, F13.20–

F13.29, F13.90, F14.10, F14.11, F14.120, F14.20–F14.25, F14.28, F14.29, F14.90, F15.10, F15.11, F15.120, F15.20–F15.25, F15.28, F15.29, F15.90, F16.10, F16.11, F16.120, F16.20–F16.25, F16.28, F16.29, F16.90, F18.10, F18.11, F18.120, F18.20–F18.25, F18.27, F18.28, F18.29, F18.90, F19.10, F19.11, F19.120, F19.20–F19.29, F19.90, F55

Tobacco use

- ICD-9 code: 305.1
- ICD-10 codes: F17.200, F17.201, F17.210, F17.211, F17.220, F17.221, F17.290, F17.291

History of non-compliance

- ICD-9 codes: V15.81, V45.12
- ICD-10 codes: Z91.1

Frailty indicators^c

Frailty indicator

Diagnosis^a or procedure codes^b

Abnormal gait

- ICD-9 code: 781.2
- ICD-10 codes: R26.0, R26.1, R26.81, R26.89, R26.9

Abnormal loss of weight or underweight

- ICD-9 codes: 783.21, 783.22
- ICD-10 codes: R63.4, R63.6

Cachexia

- ICD-9 code: 799.4
- ICD-10 code: R64

Debility

- ICD-9 code: 799.3
- ICD-10 code: R53.81

Difficulty walking

- ICD-9 code: 719.7
- ICD-10 code: R26.2

Failure to thrive

- ICD-9 code: 783.7
- ICD-10 code: R62.7

Fall history

- ICD-9 code: V15.88
- ICD-10 code: Z91.81

Malaise or fatigue

- ICD-9 code: 780.7
- ICD-10 codes: G93.3, R53

Muscular wasting or disease atrophy

- ICD-9 code: 728.2
- ICD-10 codes: M62.50–M62.59

Muscle weakness

- ICD-9 code: 728.87
- ICD-10 codes: M62.81

Pressure ulcer

- ICD-9 codes: 707.0, 707.2
- ICD-10 codes: L89.000–L89.004, L89.009, L89.010–L89.014, L89.019, L89.020–L89.024, L89.029, L89.100–L89.104, L89.109, L89.110–L89.114, L89.119, L89.120–L89.124, L89.129, L89.130–L89.134, L89.139, L89.140–L89.144, L89.149, L89.150–L89.154, L89.159, L89.200–L89.204, L89.209, L89.210–L89.214, L89.219, L89.220–L89.224, L89.229, L89.300–L89.304, L89.309, L89.310–L89.314, L89.319, L89.320–L89.324, L89.329, L89.40–L89.45, L89.500–L89.504, L89.509, L89.510–L89.514, L89.519, L89.520–

L89.520, L89.529, L89.600–L89.604, L89.609, L89.610–L89.614, L89.619, L89.620–L89.624, L89.629, L89.810–L89.814, L89.819, L89.890–L89.894, L89.899, L89.90–L89.95

Senility

- ICD-9 code: 797
- ICD-10 codes: R41.81, R54

Using durable medical equipment (cane, walker, bath equipment, or commode)

- HCPCS codes: E0100, E0105, E0130, E0135, E0140, E0141, E0143, E0144, E0147–E0149, E0160–E0171

Using nursing or personal healthcare services

- HCPCS codes: T1000–T1005, T1019–T1022, T1030, T1031

Healthcare encounters for mental health services

Encounter

Diagnosis^a or procedure codes^b

Psychotherapy

- CPT codes: 90785, 90804–90819, 90821–90824, 90826–90829, 90832–90834, 90836–90844, 90846–90847, 90849, 90853, 90855, 90857, 90863

Mental health hospitalization

- ICD-9 codes: 290–316
- ICD-10 codes: F01–F69, F80–99

^a Specified three-digit ICD-9 diagnosis codes included all existing 4th and 5th digit diagnosis codes, and specified four-digit ICD-9 diagnosis codes included all existing 5th digit diagnosis codes. Specified three-digit ICD-10 diagnosis codes included all existing 4th, 5th, 6th, and 7th digit diagnosis codes; specified four-digit ICD-10 diagnosis codes included all existing 5th, 6th, and 7th digit diagnosis codes; specified five-digit ICD-10 diagnosis codes included all existing 6th and 7th digit diagnosis codes; and specified six-digit ICD-10 diagnosis codes include all existing 7th digit codes.

^b Specified two-digit ICD-9 procedure codes include all existing 3rd and 4th digit procedure codes. Specified two-digit ICD-10 procedure codes include all specified 3rd, 4th, 5th, 6th, and 7th digit procedure codes.

^c A total of 14 validated frailty indicators associated with mortality were considered. Frailty indicators included: abnormal gait, abnormal loss of weight or underweight, cachexia, debility, difficulty walking, failure to thrive, fall history, malaise or fatigue, muscular wasting or disease atrophy, muscle weakness, pressure ulcers, senility, using durable medical equipment (cane, walker, bath equipment, or commode), and using nursing or healthcare services.

Abbreviations: CPT, Current Procedural Terminology; HCPCS, Healthcare Common Procedure Coding System, ICD-9, International Classification of Diseases, 9th Revision; ICD-10, International Classification of Diseases, 10th Revision.

Table S3. Lists of relevant medications

QT-prolonging medications with known torsade de pointes risk^{a,b}
Aclarubicin, amiodarone, anagrelide, arsenic trioxide, astemizole, azithromycin, bepridil, cesium chloride, chloroquine, chlorpromazine, chlorprothixene, cilostazol, ciprofloxacin, cisapride, clarithromycin, cocaine, disopyramide, dofetilide, domperidone, donepezil, dronedarone, droperidol, erythromycin, flecainide, fluconazole, gatifloxacin, grepafloxacin, halofantrine, haloperidol, hydroquinidine, hydroxychloroquine, ibogaine, ibutilide, levomepromazine, levomethadyl, levosulpiride, mesoridazine, methadone, , nifekalant, ondansetron, oxaliplatin, papaverine, pentamidine, pimozide, probucol, procainamide, propofol, quinidine, roxithromycin, sevoflurane, sotalol, sparfloxacin, sulpiride, sultopride, terfenadine, terlipressin, terodiline, thioridazine, vandetanib
QT-prolonging medications with possible torsade de pointes risk^{a,c}
Abarelix, alfuzosin, alimemazine, apalutamide, apomorphine, aripiprazole, artemether/lumefantrine, artenimol/piperaquine, asenapine, atomoxetine, bedaquiline, bendamustine, benperidol, betrixaban, bortezomib, bosutinib, buprenorphine, cabozantinib, capecitabine, carbetocin, ceritinib, clofazimine, clotiapine, clozapine, cobimetinib, crizotinib, cyamemazine, dabrafenib, dasatinib, degarelix, delamanid, desipramine, deutetrabenazine, dexmedetomidine, dextromethorphan/quinidine, dolasetron, efavirenz, eliglustat, encorafenib, epirubicin, eribulin, ezogabine, felbamate, fingolimod, fluorouracil, flupentixol, gemifloxacin, gilteritinib, glasdegib, granisetron, hydrocodone ER, iloperidone, imipramine, inotuzumab, isradipine, ivosidenib, ketanserin, lacidipine, lapatinib, lenvatinib leuprolide, lithium, lofexidine, lopinavir/ritonavir, lumateperone, lurasidone , maprotiline, melperone, memantine, mianserin, midostaurin, mifepristone, mirabegron, mirtazapine, moexipril/hydrochlorothiazide, necitumumab, nifedipine, nilotinib, norfloxacin, nortriptyline, nusinersen, ofloxacin, osilodrostat, osimertinib, oxytocin, paliperidone, palonosetron, panobinostat, pasireotide, pazopanib, perflutren, perphenazine, pilsicainide, pimavanserin, pipamperone, pitolisant, pretomanid, primaquine, promethazine, prothipendyl, ribociclib, rilpivirine, romidepsin, rucaparib, saquinavir, selpercatinib, sertindole, siponimod, sorafenib, sunitinib, tacrolimus, tamoxifen, tazemetostat, telavancin, telithromycin, tetrabenazine, tiapride, tipiracil/trifluridine, tizanidine, tolterodine, toremifene, tramadol, trimipramine, tropisetron, valbenazine, vardenafil, vemurafenib, venlafaxine, vorinostat, zotepine, zuclopenthixol
QT-prolonging medications with conditional torsade de pointes risk^{a,d}
Abiraterone, amantadine, amisulpride, amitriptyline, amphotericin B, amsacrine, atazanavir, bendroflumethiazide, bendrofluazide, chloral hydrate, cimetidine, clomipramine, diphenhydramine, doxepin, eperisone, famotidine, furosemide, galantamine, garenoxacin, hydrochlorothiazide, hydroxyzine, indapamide, itraconazole, ivabradine, ketoconazole, loperamide, metoclopramide, metolazone, metronidazole, nelfinavir, olanzapine, paroxetine, piperacillin/tazobactam, posaconazole, propafenone, quetiapine, quinine, ranolazine, risperidone, solifenacin, telaprevir, toremifene, trazodone, voriconazole, ziprasidone
Alpha blockers
Alfuzosin, doxazosin, prazosin, silodosin, terazosin
Angiotensin-converting enzyme inhibitors
Benazepril, captopril, enalapril, fosinopril, lisinopril, moexipril, perindopril, quinapril, ramipril, trandolapril
Angiotensin receptor blocker
Azilsartan, candesartan, eprosartan, irbesartan, losartan, olmesartan, telmisartan, valsartan
Beta blockers
Acebutolol, atenolol, betaxolol, bisoprolol, carteolol, carvedilol, esmolol, labetalol, metoprolol, nadolol, nebivolol, oxprenolol, penbutolol, pindolol, propranolol, sotalol, timolol
Calcium channel blockers
Amlodipine, clevidipine, diltiazem, felodipine, isradipine, levamlodipine, nifedipine, nimodipine, nisoldipine, verapamil
Central alpha agonists
Clonidine, methyl dopa, guanabenz, guanfacine
Diuretics

Bumetanide, ethacrynic acid, furosemide, torsemide, bendroflumethiazide, chlorothiazide, hydrochlorothiazide, methyclothiazide, polythiazide, chlorthalidone, indapamide, metolazone, amiloride, triamterene, spironolactone, eplerenone, acetazolamide
Vasodilators
Hydralazine, minoxidil
Anticoagulants
Warfarin, apixaban, betrixaban, dabigatran, edoxaban, rivaroxaban
Antiplatelet agents
Cliostazol, clopidogrel, dipyridamole, prasugrel, ticagrelor, ticlopidine, trifusal, vorapaxar
Statin
Atorvastatin, fluvastatin, lovastatin, mevastatin, pitavastatin, pravastatin, rosuvastatin, simvastatin
Non-statin cholesterol medication
Niacin, cholestyramine, colestipol, colesevelam, bezafibrate, ciprofibrate, clofibrate, gemfibrozil, fenofibrate, clinofibrate, ezetimibe
Antiarrhythmics (class I and III)
Quinidine, disopyramide, procainamide, lidocaine, mexiletine, propafenone, flecainide, ranolazine, amiodarone, dronedarone, dofetilide, ibutilide, sotalol, pinacidil
Digoxin
Digoxin
Long-acting nitrate
Nitroglycerin, isosorbide dinitrate, isosorbide mononitrate
Midodrine
Midodrine
Cytochrome P450 inhibitors (<i>other than PPIs</i>)^e
Amiodarone, amprenavir, aprepitant, atazanavir, chloramphenicol, clarithromycin, conivaptan, cyclosporine, darunavir, dasatinib, delavirdine, diltiazem, erythromycin, fluconazole, fosamprenavir, imatinib, indinavir, isoniazid, itraconazole, ketoconazole, lapatinib, miconazole, nefazodone, nelfinavir, posaconazole, ritonavir, quinupristin, saquinavir, tamoxifen, telithromycin, troleandomycin, verapamil, voriconazole
Cytochrome P450 3A4 inhibitors^e
Chloramphenicol, cimetidine, clopidogrel, delavirdine, efavirenz, felbamate, fluconazole, indomethacin, isoniazid, ketoconazole, luliconazole, moclobemide, modafinil, oritavancin, oxcarbazepine, probenecid, rucaparib, ticlopidine, topiramate, voriconazole

^a The CredibleMeds website (<https://crediblemeds.org>) is a reliable online clinical resource with up-to-date information about medications that can cause QT-prolongation and/or torsade de pointes. CredibleMeds classifies QT-prolonging medications as having a known, possible, or conditional TdP risk. Lists of QT-prolonging medications were obtained website on March 1, 2021.

^b CredibleMeds defines medications with known torsade de pointes risk as drugs that prolong the QT-interval *and* are clearly associated with a known risk of torsade de pointes, even when taken as recommended.

^c CredibleMeds defines medications with possible torsade de pointes risk as drugs that can cause QT-prolongation *but* currently lack evidence for a risk of torsade de pointes when taken as recommended.

^d CredibleMeds defines medications with conditional torsade de pointes risk as drugs that are associated with torsade de pointes only under certain conditions (e.g., excessive dose, when taken with interacting drugs) *or* drugs that create conditions that facilitate or induce torsade de pointes (e.g., cause an electrolyte disturbance that induces torsade de pointes).

^e Lists of cytochrome P450 inhibitors were obtained from the Pharmacy Times website (<https://www.pharmacytimes.com>) and Flockhart Table website (<https://drug-interactions.medicine.iu.edu/MainTable.aspx>) on March 1, 2021.

Table S4. Baseline characteristics of the SSRI-PPI exposure groups *before* inverse probability of treatment weighting

Characteristic	Citalopram/escitalopram		Sertraline		Max std diff ^a
	PPI n = 14,983	No PPI n = 26,503	PPI n = 10,779	No PPI n = 20,294	
Year of SSRI new-use					
2007	1,543 (10%)	2,539 (10%)	975 (9%)	1,819 (9%)	0.05
2008	1,613 (11%)	2,627 (10%)	919 (9%)	1,689 (8%)	0.08
2009	1,602 (11%)	2,566 (10%)	1,015 (9%)	1,684 (8%)	0.08
2010	1,525 (10%)	2,697 (10%)	889 (8%)	1,699 (8%)	0.07
2011	1,381 (9%)	2,721 (10%)	929 (9%)	1,631 (8%)	0.08
2012	1,319 (9%)	2,350 (9%)	927 (9%)	1,741 (9%)	0.01
2013	1,336 (9%)	2,227 (8%)	965 (9%)	1,872 (9%)	0.03
2014	1,300 (9%)	2,275 (9%)	1,018 (9%)	1,909 (9%)	0.03
2015	1,185 (8%)	2,201 (8%)	1,031 (10%)	1,991 (10%)	0.07
2016	1,147 (8%)	2,171 (8%)	1,049 (10%)	2,116 (10%)	0.10
2017	1,032 (7%)	2,129 (8%)	1,062 (10%)	2,143 (11%)	0.13
SSRI new-use before the 2011 FDA warning^b	7,209 (48%)	12,227 (46%)	4,398 (41%)	7,956 (39%)	0.18
Age (years)	61 ± 15	60 ± 16	61.5(14.58)	59.9(15.55)	0.11
Female	8,361 (56%)	13,683 (52%)	5,892 (55%)	10,222 (50%)	0.11
Race					
Black	5,320 (36%)	9,814 (37%)	3,633 (34%)	7,280 (36%)	0.07
White	9,068 (61%)	15,615 (59%)	6,602 (61%)	11,984 (59%)	0.05
Other	595 (4%)	1,074 (4%)	544 (5%)	1,030 (5%)	0.05
Hispanic	2,528 (17%)	4,247 (16%)	2,029 (19%)	3,812 (19%)	0.07
Medicare Part D low income subsidy	11,559 (77%)	18,607 (70%)	7,946 (74%)	13,782 (68%)	0.21
Cause of dialysis-dependent kidney failure					
Diabetes	7,811 (52%)	13,097 (49%)	5,682 (53%)	10,057 (50%)	0.07
Glomerular disease	1,518 (10%)	2,755 (10%)	1,058 (10%)	2,147 (11%)	0.03
Hypertension	3,709 (25%)	6,933 (26%)	2,641 (25%)	5,291 (26%)	0.04
Other	1,945 (13%)	3,718 (14%)	1,398 (13%)	2,799 (14%)	0.03
History of a prior kidney transplant	963 (6%)	1,675 (6%)	678 (6%)	1,343 (7%)	0.01
Dialysis vintage					
< 1.0 year	2,443 (16%)	4,591 (17%)	1,648 (15%)	3,397 (17%)	0.06
1.0 – 1.9 years	2,697 (18%)	5,129 (19%)	1,903 (18%)	3,861 (19%)	0.04
2.0 – 2.9 years	2,265 (15%)	3,915 (15%)	1,644 (15%)	2,982 (15%)	0.02

≥ 3.0 years	7,578 (51%)	12,868 (49%)	5,584 (52%)	10,054 (50%)	0.07
Anxiety	3,635 (24%)	5,717 (22%)	2,644 (25%)	4,299 (21%)	0.08
Depression	5,657 (38%)	9,557 (36%)	3,831 (36%)	6,775 (33%)	0.09
Other psychiatric conditions	853 (6%)	1,385 (5%)	530 (5%)	964 (5%)	0.04
Dementia	1,730 (12%)	2,976 (11%)	1,128 (10%)	1,992 (10%)	0.06
Insomnia	1,298 (9%)	2,091 (8%)	1,007 (9%)	1,666 (8%)	0.05
GERD	6,432 (43%)	6,711 (25%)	4,719 (44%)	4,964 (24%)	0.42
Peptic ulcer	396 (3%)	379 (1%)	274 (3%)	267 (1%)	0.10
Other type of ulcer	802 (5%)	639 (2%)	525 (5%)	399 (2%)	0.18
GI bleed	2,383 (16%)	2,510 (9%)	1,663 (15%)	1,734 (9%)	0.23
Arrhythmia	5,288 (35%)	7,918 (30%)	3,809 (35%)	6,070 (30%)	0.12
Conduction disorder	1,497 (10%)	2,339 (9%)	1,178 (11%)	1,997 (10%)	0.07
Dyslipidemia	8,565 (57%)	14,161 (53%)	6,484 (60%)	11,069 (55%)	0.14
Heart failure	7,884 (53%)	12,335 (47%)	5,663 (53%)	9,327 (46%)	0.13
Hypertension	14,068 (94%)	24,068 (91%)	10,074 (93%)	18,337 (90%)	0.13
Ischemic heart disease	8,110 (54%)	12,531 (47%)	5,811 (54%)	9,498 (47%)	0.15
Peripheral artery disease	6,026 (40%)	9,562 (36%)	4,302 (40%)	7,014 (35%)	0.12
Stroke	4,395 (29%)	6,898 (26%)	3,005 (28%)	4,956 (24%)	0.11
Valvular disease	3,501 (23%)	5,540 (21%)	2,666 (25%)	4,223 (21%)	0.09
Cardiac pacemaker	807 (5%)	1,222 (5%)	588 (5%)	912 (4%)	0.04
ECG during the last 30 days of baseline	4,859 (32%)	7,633 (29%)	3,531 (33%)	5,695 (28%)	0.10
Cardiac surgery during the last 30 days of baseline	158 (1%)	269 (1%)	114 (1%)	193 (1%)	0.01
Asthma or COPD	5,352 (36%)	7,660 (29%)	3,826 (35%)	5,726 (28%)	0.16
Cancer	1,475 (10%)	2,384 (9%)	1,020 (9%)	1,793 (9%)	0.04
Diabetes	11,007 (73%)	18,270 (69%)	7,919 (73%)	14,003 (69%)	0.10
Hypothyroidism	3,241 (22%)	4,826 (18%)	2,343 (22%)	3,670 (18%)	0.09
Liver disease	1,049 (7%)	1,558 (6%)	834 (8%)	1,306 (6%)	0.07
Sleep apnea	1,993 (13%)	2,991 (11%)	1,568 (15%)	2,395 (12%)	0.10
Alcohol use or dependence	404 (3%)	635 (2%)	273 (3%)	427 (2%)	0.04
Drug Abuse or dependence	787 (5%)	1,567 (6%)	577 (5%)	1,090 (5%)	0.03
Tobacco use	2,246 (15%)	3,886 (15%)	1,606 (15%)	2,947 (15%)	0.01
History of non-compliance	1,809 (12%)	3,492 (13%)	1,407 (13%)	2,814 (14%)	0.05
# of frailty indicators					
0	5,544 (37%)	11,724 (44%)	4,245 (39%)	9,535 (47%)	0.20
1	3,416 (23%)	5,537 (21%)	2,404 (22%)	4,254 (21%)	0.05
2	2,159 (14%)	3,438 (13%)	1,545 (14%)	2,479 (12%)	0.07

3	1,628 (11%)	2,410 (9%)	1,054 (10%)	1,675 (8%)	0.09
4	1,074 (7%)	1,663 (6%)	713 (7%)	1,114 (5%)	0.07
5	669 (4%)	971 (4%)	476 (4%)	673 (3%)	0.06
6	285 (2%)	474 (2%)	218 (2%)	336 (2%)	0.03
≥ 7	208 (1%)	286 (1%)	124 (1%)	228 (1%)	0.03
Abnormal gait	2,751 (18%)	4,396 (17%)	1,911 (18%)	3,169 (16%)	0.07
Abnormal loss of weight or underweight	586 (4%)	840 (3%)	437 (4%)	649 (3%)	0.05
Cachexia	234 (2%)	329 (1%)	157 (1%)	242 (1%)	0.03
Debility	1,949 (13%)	2,975 (11%)	1,320 (12%)	2,118 (10%)	0.08
Difficulty walking	2,390 (16%)	3,685 (14%)	1,656 (15%)	2,525 (12%)	0.10
Failure to thrive	500 (3%)	668 (3%)	290 (3%)	433 (2%)	0.07
Fall history	1,035 (7%)	1,694 (6%)	758 (7%)	1,283 (6%)	0.03
Malaise and fatigue	5,622 (38%)	8,817 (33%)	3,952 (37%)	6,514 (32%)	0.11
Muscular wasting and disease atrophy	782 (5%)	1,245 (5%)	494 (5%)	792 (4%)	0.06
Muscle weakness	3,948 (26%)	6,053 (23%)	2,721 (25%)	4,205 (21%)	0.13
Pressure ulcer	2,303 (15%)	3,239 (12%)	1,446 (13%)	2,272 (11%)	0.12
Senility	112 (1%)	177 (1%)	79 (1%)	164 (1%)	0.02
Using durable medical equipment (e.g., cane, walker)	1,290 (9%)	1,985 (7%)	888 (8%)	1,407 (7%)	0.06
Using nursing or healthcare services	< 11 (0%)	< 11 (0%)	< 11 (0%)	< 11 (0%)	< 0.00
Alpha blocker	442 (3%)	649 (2%)	329 (3%)	576 (3%)	0.04
ACE inhibitor	2,852 (19%)	4,305 (16%)	2,008 (19%)	3,278 (16%)	0.08
ARB	1,734 (12%)	2,372 (9%)	1,249 (12%)	1,890 (9%)	0.09
Beta blocker	6,469 (43%)	9,269 (35%)	4,689 (44%)	7,329 (36%)	0.18
Calcium channel blocker	4,658 (31%)	7,327 (28%)	3,475 (32%)	5,741 (28%)	0.10
Central alpha agonist	1,966 (13%)	3,080 (12%)	1,384 (13%)	2,324 (11%)	0.05
Diuretic	1,651 (11%)	2,354 (9%)	1,235 (11%)	1,945 (10%)	0.09
Vasodilator	1,824 (12%)	2,801 (11%)	1,415 (13%)	2,217 (11%)	0.08
Anticoagulant	1,276 (9%)	1,836 (7%)	967 (9%)	1,421 (7%)	0.08
Antiplatelet	2,054 (14%)	2,782 (10%)	1,470 (14%)	2,171 (11%)	0.10
Statin	4,665 (31%)	5,994 (23%)	3,625 (34%)	4,903 (24%)	0.25
Non-statin cholesterol med	747 (5%)	805 (3%)	466 (4%)	596 (3%)	0.11
Antiarrhythmic	584 (4%)	756 (3%)	496 (5%)	599 (3%)	0.09
Digoxin	258 (2%)	370 (1%)	179 (2%)	252 (1%)	0.04
Long-acting nitrate	1,240 (8%)	1,468 (6%)	927 (9%)	1,188 (6%)	0.12
Midodrine	559 (4%)	602 (2%)	445 (4%)	597 (3%)	0.11

≥ 1 CYP 3A4 inhibitor	1,278 (9%)	1,728 (7%)	919 (9%)	1,311 (6%)	0.08
≥ 1 other CYP 2C19 inhibitor	2,174 (15%)	2,913 (11%)	1,537 (14%)	2,266 (11%)	0.11
≥ 1 med with any TdP risk^c	6,314 (42%)	8,726 (33%)	4,489 (42%)	6,613 (33%)	0.20
≥ 1 med with known TdP risk^c	1,770 (12%)	2,381 (9%)	1,317 (12%)	1,804 (9%)	0.11
≥ 1 med with possible TdP risk^c	1,893 (13%)	2,388 (9%)	1,267 (12%)	1,665 (8%)	0.15
≥ 1 med with conditional TdP risk^c	4,272 (29%)	5,855 (22%)	2,994 (28%)	4,447 (22%)	0.15
Number of baseline hospital admissions					
0 admissions	4,859 (32%)	10,237 (39%)	3,721 (35%)	8,522 (42%)	0.20
1 – 2 admissions	5,794 (39%)	10,096 (38%)	4,199 (39%)	7,582 (37%)	0.03
3 – 4 admissions	2,794 (19%)	4,075 (15%)	1,863 (17%)	2,826 (14%)	0.13
≥ 5 admissions	1,536 (10%)	2,095 (8%)	996 (9%)	1,364 (7%)	0.13
Hospitalized in the last 30 days of baseline	5,198 (35%)	7,781 (29%)	3,477 (32%)	5,479 (27%)	0.17
Number of baseline ED visits					
0 ED visits	3,227 (22%)	7,090 (27%)	2,476 (23%)	5,814 (29%)	0.17
1 – 2 ED visits	5,406 (36%)	9,624 (36%)	3,856 (36%)	7,417 (37%)	0.02
3 – 4 ED visits	3,111 (21%)	5,021 (19%)	2,211 (21%)	3,645 (18%)	0.07
≥ 5 ED visits	3,239 (22%)	4,768 (18%)	2,236 (21%)	3,418 (17%)	0.12
ED visit in the last 30 days of baseline	5,616 (37%)	8,829 (33%)	3,957 (37%)	6,567 (32%)	0.11
SNF admission during baseline	4,061 (27%)	6,351 (24%)	2,500 (23%)	3,899 (19%)	0.19
Mental health hospitalization during baseline	72 (0%)	160 (1%)	66 (1%)	129 (1%)	0.02
Outpatient visit with a psychiatrist during baseline	466 (3%)	793 (3%)	235 (2%)	446 (2%)	0.06
Psychotherapy during baseline	1,651 (11%)	2,666 (10%)	995 (9%)	1,617 (8%)	0.10

Values are given as number (%) for categorical variables and as mean ± standard deviation for continuous variables. All covariates were measured during the 180-day baseline period. The weighted cohort is the pseudo-population generated by inverse probability of treatment weighting.

^a The standardized differences displayed in the table are the maximum absolute standardized differences observed across all exposure group pairs. A standardized difference > 0.10 represents meaningful imbalance between groups.

^b The FDA issued a Drug Safety Communication on August 28, 2011, warning that abnormal heart rhythms have been associated with high doses of citalopram.

^c The CredibleMeds website (<https://crediblemeds.org>) is a reliable online clinical resource with up-to-date information about medications that can cause QT-prolongation and/or torsades de pointes. CredibleMeds classifies QT-prolonging medications as having a known, possible, or conditional TdP risk. Lists of medications falling into each category are provided in Table S3. Medications classified as having any level of TdP risk are those falling into any of the three CredibleMeds categories.

Abbreviations: ACE, angiotensin converting enzyme; ARB, angiotensin receptor blocker; COPD, chronic obstructive pulmonary disease; CYP, cytochrome P450; ECG, electrocardiogram; ED, emergency department; FDA, Food and Drug Administration; GERD, gastroesophageal reflux disease; GI, gastrointestinal; med, medication; PPI, proton pump inhibitor; SNF, skilled nursing facility; SSRI, selective serotonin reuptake inhibitor; TdP, Torsades de Pointes

Table S5. Baseline characteristics of the SSRI-PPI exposure groups after inverse probability of treatment weighting

Characteristic	Citalopram/escitalopram		Sertraline		Max std diff ^a
	PPI n = 14,860	No PPI n = 26,581	PPI n = 10,726	No PPI n = 20,341	
Year of SSRI new-use					
2007	1,406 (9%)	2,524 (9%)	1,029 (10%)	1,909 (9%)	0.01
2008	1,387 (9%)	2,488 (9%)	1,017 (9%)	1,916 (9%)	0.01
2009	1,414 (10%)	2,528 (10%)	1,038 (10%)	1,925 (9%)	0.01
2010	1,401 (9%)	2,500 (9%)	1,022 (10%)	1,886 (9%)	0.01
2011	1,378 (9%)	2,467 (9%)	997 (9%)	1,866 (9%)	< 0.01
2012	1,310 (9%)	2,304 (9%)	927 (9%)	1,792 (9%)	0.01
2013	1,302 (9%)	2,357 (9%)	953 (9%)	1,795 (9%)	< 0.01
2014	1,320 (9%)	2,363 (9%)	948 (9%)	1,826 (9%)	0.01
2015	1,320 (9%)	2,357 (9%)	920 (9%)	1,802 (9%)	0.01
2016	1,339 (9%)	2,363 (9%)	944 (9%)	1,837 (9%)	0.01
2017	1,283 (9%)	2,329 (9%)	930 (9%)	1,787 (9%)	0.01
SSRI new-use before the 2011 FDA warning^b	6,513 (44%)	11,658 (44%)	4,758 (44%)	8,864 (44%)	0.02
Age (years)	61 ± 15	61 ± 15	61 ± 15	61 ± 15	0.01
Female	7,872 (53%)	13,989 (53%)	5,646 (53%)	10,709 (53%)	0.01
Race					< 0.01
Black	5,303 (36%)	9,528 (36%)	3,872 (36%)	7,304 (36%)	0.01
White	8,884 (60%)	15,867 (60%)	6,375 (59%)	12,119 (60%)	0.01
Other	673 (5%)	1,185 (4%)	479 (4%)	917 (5%)	< 0.01
Hispanic	2,609 (18%)	4,648 (17%)	1,861 (17%)	3,537 (17%)	0.01
Medicare Part D low income subsidy	10,659 (72%)	19,025 (72%)	7,693 (72%)	14,556 (72%)	< 0.01
Cause of dialysis-dependent kidney failure					
Diabetes	7,530 (51%)	13,453 (51%)	5,457 (51%)	10,296 (51%)	0.01
Hypertension	3,809 (26%)	6,794 (26%)	2,713 (25%)	5,204 (26%)	0.01
Glomerular disease	1,523 (10%)	2,721 (10%)	1,097 (10%)	2,089 (10%)	< 0.01
Other	1,998 (13%)	3,613 (14%)	1,458 (14%)	2,752 (14%)	< 0.01
History of a prior kidney transplant	957 (6%)	1,714 (6%)	691 (6%)	1,291 (6%)	< 0.01
Dialysis vintage					< 0.01
< 1.0 year	2,461 (17%)	4,405 (17%)	1,788 (17%)	3,374 (17%)	< 0.01
1.0 – 1.9 years	2,769 (19%)	4,974 (19%)	1,976 (18%)	3,796 (19%)	0.01
2.0 – 2.9 years	2,193 (15%)	3,965 (15%)	1,603 (15%)	3,005 (15%)	0.01

≥ 3.0 years	7,437 (50%)	13,237 (50%)	5,358 (50%)	10,165 (50%)	< 0.01
Anxiety	3,359 (23%)	6,003 (23%)	2,411 (22%)	4,547 (22%)	0.01
Depression	5,310 (36%)	9,484 (36%)	3,818 (36%)	7,237 (36%)	< 0.01
Other psychiatric conditions	765 (5%)	1,353 (5%)	549 (5%)	1,044 (5%)	< 0.01
Dementia	1,662 (11%)	2,915 (11%)	1,190 (11%)	2,208 (11%)	0.01
Insomnia	1,251 (8%)	2,237 (8%)	905 (8%)	1,716 (8%)	< 0.01
GERD	4,797 (32%)	8,413 (32%)	3,400 (32%)	6,488 (32%)	0.01
Peptic ulcer	281 (2%)	506 (2%)	205 (2%)	371 (2%)	0.01
Other type of ulcer	513 (3%)	925 (3%)	361 (3%)	678 (3%)	0.01
GI bleed	1,768 (12%)	3,139 (12%)	1,270 (12%)	2,360 (12%)	0.01
Arrhythmia	4,799 (32%)	8,509 (32%)	3,492 (33%)	6,538 (32%)	0.01
Conduction disorder	1,456 (10%)	2,580 (10%)	1,038 (10%)	1,979 (10%)	< 0.01
Dyslipidemia	8,293 (56%)	14,795 (56%)	5,990 (56%)	11,325 (56%)	< 0.01
Heart failure	7,278 (49%)	12,968 (49%)	5,314 (50%)	9,930 (49%)	0.02
Hypertension	13,668 (92%)	24,399 (92%)	9,858 (92%)	18,676 (92%)	0.01
Ischemic heart disease	7,422 (50%)	13,249 (50%)	5,392 (50%)	10,151 (50%)	0.01
Peripheral artery disease	5,597 (38%)	9,917 (37%)	4,005 (37%)	7,624 (37%)	0.01
Stroke	4,015 (27%)	7,139 (27%)	2,920 (27%)	5,422 (27%)	0.01
Valvular disease	3,284 (22%)	5,842 (22%)	2,374 (22%)	4,492 (22%)	< 0.01
Cardiac pacemaker	738 (5%)	1,306 (5%)	531 (5%)	1,004 (5%)	< 0.01
ECG during the last 30 days of baseline	4,450 (30%)	7,984 (30%)	3,258 (30%)	6,096 (30%)	0.01
Cardiac surgery during the last 30 days of baseline	155 (1%)	264 (1%)	107 (1%)	214 (1%)	0.01
Asthma or COPD	4,647 (31%)	8,292 (31%)	3,411 (32%)	6,391 (31%)	0.01
Cancer	1,366 (9%)	2,459 (9%)	1,003 (9%)	1,867 (9%)	0.01
Diabetes	10,509 (71%)	18,815 (71%)	7,626 (71%)	14,361 (71%)	0.01
Hypothyroidism	2,934 (20%)	5,177 (19%)	2,119 (20%)	3,974 (20%)	0.01
Liver disease	1,006 (7%)	1,751 (7%)	709 (7%)	1,368 (7%)	0.01
Sleep apnea	1,827 (12%)	3,272 (12%)	1,324 (12%)	2,516 (12%)	< 0.01
Alcohol use or dependence	356 (2%)	641 (2%)	254 (2%)	479 (2%)	< 0.01
Drug abuse or dependence	825 (6%)	1,469 (6%)	596 (6%)	1,136 (6%)	< 0.01
Tobacco use	2,169 (15%)	3,916 (15%)	1,592 (15%)	2,997 (15%)	0.01
History of non-compliance	1,935 (13%)	3,481 (13%)	1,422 (13%)	2,677 (13%)	0.01
Number of frailty indicators					
0	6,268 (42%)	11,281 (42%)	4,504 (42%)	8,663 (43%)	0.01
1	3,198 (22%)	5,681 (21%)	2,309 (22%)	4,377 (22%)	< 0.01
2	1,942 (13%)	3,546 (13%)	1,461 (14%)	2,703 (13%)	0.02

3	1,422 (10%)	2,508 (9%)	997 (9%)	1,886 (9%)	0.01
4	972 (7%)	1,719 (6%)	699 (7%)	1,301 (6%)	0.01
5	597 (4%)	1,034 (4%)	427 (4%)	790 (4%)	0.01
6	281 (2%)	495 (2%)	208 (2%)	376 (2%)	0.01
≥ 7	180 (1%)	316 (1%)	120 (1%)	245 (1%)	0.01
Abnormal gait	2,553 (17%)	4,516 (17%)	1,829 (17%)	3,450 (17%)	0.01
Abnormal loss of weight or underweight	534 (4%)	935 (4%)	384 (4%)	726 (4%)	< 0.01
Cachexia	204 (1%)	360 (1%)	149 (1%)	271 (1%)	0.01
Debility	1,771 (12%)	3,126 (12%)	1,268 (12%)	2,367 (12%)	0.01
Difficulty walking	2,156 (15%)	3,813 (14%)	1,538 (14%)	2,902 (14%)	0.01
Failure to thrive	399 (3%)	709 (3%)	281 (3%)	530 (3%)	0.01
Fall history	987 (7%)	1,757 (7%)	720 (7%)	1,339 (7%)	0.01
Malaise and fatigue	5,153 (35%)	9,174 (35%)	3,734 (35%)	6,997 (34%)	0.01
Muscular wasting and disease atrophy	721 (5%)	1,246 (5%)	495 (5%)	959 (5%)	0.01
Muscle weakness	3,514 (24%)	6,285 (24%)	2,555 (24%)	4,749 (23%)	0.01
Pressure ulcer	1,972 (13%)	3,472 (13%)	1,405 (13%)	2,633 (13%)	0.01
Senility	112 (1%)	198 (1%)	81 (1%)	149 (1%)	< 0.01
Using durable medical equipment (e.g., cane, walker)	1,159 (8%)	2,060 (8%)	857 (8%)	1,588 (8%)	0.01
Using nursing or healthcare services	< 11 (0%)	< 11 (0%)	< 11 (0%)	< 11 (0%)	< 0.00
Alpha blocker	414 (3%)	738 (3%)	294 (3%)	560 (3%)	< 0.01
ACE inhibitor	2,547 (17%)	4,550 (17%)	1,833 (17%)	3,475 (17%)	< 0.01
ARB	1,485 (10%)	2,640 (10%)	1,063 (10%)	2,031 (10%)	< 0.01
Beta blocker	5,731 (39%)	10,160 (38%)	4,089 (38%)	7,819 (38%)	0.01
Calcium channel blocker	4,355 (29%)	7,746 (29%)	3,114 (29%)	5,947 (29%)	0.01
Central alpha agonist	1,809 (12%)	3,212 (12%)	1,285 (12%)	2,453 (12%)	0.01
Diuretic	1,475 (10%)	2,623 (10%)	1,066 (10%)	2,035 (10%)	0.01
Vasodilator	1,706 (11%)	3,028 (11%)	1,208 (11%)	2,321 (11%)	0.01
Anticoagulant	1,139 (8%)	2,026 (8%)	834 (8%)	1,537 (8%)	0.01
Antiplatelet	1,759 (12%)	3,118 (12%)	1,255 (12%)	2,400 (12%)	< 0.01
Statin	3,981 (27%)	7,014 (26%)	2,847 (27%)	5,443 (27%)	0.01
Non-statin cholesterol med	542 (4%)	950 (4%)	389 (4%)	748 (4%)	0.01
Antiarrhythmic	507 (3%)	890 (3%)	368 (3%)	700 (3%)	0.01
Digoxin	221 (1%)	396 (1%)	164 (2%)	295 (1%)	0.01
Long-acting nitrate	991 (7%)	1,770 (7%)	725 (7%)	1,365 (7%)	< 0.01
Midodrine	449 (3%)	813 (3%)	331 (3%)	616 (3%)	< 0.01

≥ 1 CYP 3A4 inhibitor	1,068 (7%)	1,919 (7%)	786 (7%)	1,487 (7%)	0.01
≥ 1 other CYP 2C19 inhibitor	1,846 (12%)	3,279 (12%)	1,319 (12%)	2,505 (12%)	< 0.01
≥ 1 med with any TdP risk	5,417 (36%)	9,620 (36%)	3,916 (37%)	7,345 (36%)	0.01
≥ 1 med with known TdP risk	1,513 (10%)	2,694 (10%)	1,095 (10%)	2,048 (10%)	< 0.01
≥ 1 med with possible TdP risk	1,495 (10%)	2,671 (10%)	1,081 (10%)	2,016 (10%)	0.01
≥ 1 med with conditional TdP risk	3,664 (25%)	6,452 (24%)	2,630 (25%)	4,970 (24%)	0.01
Number of baseline hospital admissions					
0 admissions	5,530 (37%)	9,956 (37%)	3,982 (37%)	7,636 (38%)	0.01
1 – 2 admissions	5,647 (38%)	10,078 (38%)	4,027 (38%)	7,740 (38%)	0.01
3 – 4 admissions	2,416 (16%)	4,298 (16%)	1,781 (17%)	3,285 (16%)	0.01
≥ 5 admissions	1,267 (9%)	2,249 (8%)	936 (9%)	1,680 (8%)	0.02
Hospitalized in the last 30 days of baseline	4,565 (31%)	8,102 (30%)	3,287 (31%)	6,167 (30%)	0.01
Number of baseline ED visits					
0 ED visits	3,758 (25%)	6,788 (26%)	2,725 (25%)	5,188 (26%)	0.01
1 – 2 ED visits	5,378 (36%)	9,605 (36%)	3,848 (36%)	7,382 (36%)	0.01
3 – 4 ED visits	2,873 (19%)	5,109 (19%)	2,058 (19%)	3,907 (19%)	< 0.01
≥ 5 ED visits	2,850 (19%)	5,078 (19%)	2,094 (20%)	3,863 (19%)	0.01
ED visit in the last 30 days of baseline	5,131 (35%)	9,143 (34%)	3,711 (35%)	7,004 (34%)	< 0.01
SNF admission during baseline	3,557 (24%)	6,281 (24%)	2,597 (24%)	4,763 (23%)	0.02
Mental health hospitalization during baseline	91 (1%)	155 (1%)	55 (1%)	117 (1%)	0.01
Outpatient visit with a psychiatrist during baseline	392 (3%)	704 (3%)	284 (3%)	536 (3%)	< 0.01
Psychotherapy during baseline	1,461 (10%)	2,578 (10%)	1,037 (10%)	1,938 (10%)	0.01

Values are given as number (%) for categorical variables and as mean ± standard deviation for continuous variables. All covariates were measured during the 180-day baseline period. The weighted cohort is the pseudo-population generated by inverse probability of treatment weighting.

^a The standardized differences displayed in the table are the maximum absolute standardized differences observed across all exposure group pairs. A standardized difference > 0.10 represents meaningful imbalance between groups.

^b The FDA issued a Drug Safety Communication on August 28, 2011, warning that abnormal heart rhythms have been associated with high doses of citalopram.

^c The CredibleMeds website (<https://crediblemeds.org>) is a reliable online clinical resource with up-to-date information about medications that can cause QT-prolongation and/or torsades de pointes. CredibleMeds classifies QT-prolonging medications as having a known, possible, or conditional TdP risk. Lists of medications falling into each category are provided in Table S3. Medications classified as having any level of TdP risk are those falling into any of the 3 CredibleMeds categories.

Abbreviations: ACE, angiotensin converting enzyme; ARB, angiotensin receptor blocker; COPD, chronic obstructive pulmonary disease; CYP, cytochrome P450; ECG, electrocardiogram; ED, emergency department; FDA, Food and Drug Administration; GERD, gastroesophageal reflux disease; GI, gastrointestinal; med, medication; PPI, proton pump inhibitor; SNF, skilled nursing facility; SSRI, selective serotonin reuptake inhibitor; TdP, Torsades de Pointes

Table S6. Association between SSRI-PPI exposure group and the 1-year risk of sudden cardiac death

Sudden cardiac death – primary outcome					
Exposure group	n	No. of events	Rate per 1,000 p-y	Crude HR (95% CI)	Weighted HR (95% CI)
Sert + no PPI	20,294	280	62.9	1.00 (ref.)	1.00 (ref.)
Sert + PPI	10,779	177	78.0	1.24 (1.03, 1.50)	1.03 (0.85, 1.26)
Cital/escit + no PPI	26,503	448	78.6	1.25 (1.07, 1.45)	1.22 (1.06, 1.41)
Cital/escit + PPI	14,983	292	95.3	1.50 (1.27, 1.77)	1.31 (1.11, 1.54)

An on-treatment analytic approach was used in all analyses. Fine and Gray proportional subdistribution hazards models were used to estimate hazard ratios and Inverse probability of treatment weighting was used for confounding control.

Abbreviations: CI, confidence interval; cital/escital, citalopram or escitalopram; HR hazard ratio; No., number PPI, proton pump inhibitor; p-y, person-years; ref., referent; sert, sertraline

Table S7. Association between SSRI–PPI exposure group and the 1-year risk of sudden cardiac death considering citalopram and escitalopram separately

Considering citalopram separately					
Exposure group	n	No. of events	Rate per 1,000 p-y	Crude HR (95% CI)	Weighted HR (95% CI)
Sert + no PPI	20,294	280	62.9	1.00 (ref.)	1.00 (ref.)
Sert + PPI	10,779	177	78.0	1.24 (1.03, 1.50)	1.03 (0.85, 1.26)
Cital + no PPI	13,620	235	77.7	1.24 (1.04, 1.47)	1.20 (1.02, 1.44)
Cital + PPI	7,433	138	88.0	1.40 (1.14, 1.71)	1.28 (1.03, 1.58)
Considering escitalopram separately					
Exposure group	n	No. of events	Rate per 1,000 p-y	Crude HR (95% CI)	Weighted HR (95% CI)
Sert + no PPI	20,294	280	62.9	1.00 (ref.)	1.00 (ref.)
Sert + PPI	10,779	177	78.0	1.24 (1.03, 1.50)	1.04 (0.86, 1.27)
Escit + no PPI	11,418	213	79.5	1.25 (1.05, 1.50)	1.23 (1.03, 1.46)
Escit + PPI	6,464	154	102.9	1.61 (1.32, 1.96)	1.36 (1.11, 1.66)

An on-treatment analytic approach was used in all analyses. Fine and Gray proportional subdistribution hazards models were used to estimate hazard ratios and Inverse probability of treatment weighting was used for confounding control.

Abbreviations: CI, confidence interval; cital, citalopram; escital, escitalopram; HR hazard ratio; No., number PPI, proton pump inhibitor; p-y, person-years; ref., referent; sert, sertraline

Table S8. Results from sensitivity analyses

Sensitivity analysis using a zero day grace period to define SSRI and PPI discontinuation					
Exposure group	n	No. of events	Rate per 1,000 p-y	Crude HR (95% CI)	Weighted HR (95% CI)
Sert + no PPI	20,294	218	65.2	1.00 (ref.)	1.00 (ref.)
Sert + PPI	10,779	127	86.9	1.32 (1.05, 1.64)	1.10 (0.85, 1.40)
Cital/escit + no PPI	26,503	327	76.0	1.16 (0.98, 1.38)	1.15 (0.97, 1.36)
Cital/escit + PPI	14,983	189	93.9	1.42 (1.16, 1.72)	1.21 (1.00, 1.48)
Sensitivity analysis excluding patients on other CYP 2C19 inhibitors					
Exposure group	n	No. of events	Rate per 1,000 p-y	Crude HR (95% CI)	Weighted HR (95% CI)
Sert + no PPI	18,028	247	63.0	1.00 (ref.)	1.00 (ref.)
Sert + PPI	9,242	146	75.4	1.08 (0.96, 1.22)	0.98 (0.80, 1.21)
Cital/escit + no PPI	23,590	391	78.5	1.05 (0.95, 1.15)	1.20 (1.03, 1.40)
Cital/escit + PPI	12,809	245	94.8	1.22 (1.10, 1.36)	1.28 (1.07, 1.53)
Sensitivity analysis restricted to patients with the Medicare Part D low income subsidy					
Exposure group	n	No. of events	Rate per 1,000 p-y	Crude HR (95% CI)	Weighted HR (95% CI)
Sert + no PPI	13,782	170	56.1	1.00 (ref.)	1.00 (ref.)
Sert + PPI	7,946	125	74.3	1.33 (1.06, 1.67)	1.09 (0.84, 1.46)
Cital/escit + no PPI	18,607	319	79.9	1.42 (1.18, 1.71)	1.35 (1.13, 1.63)
Cital/escit + PPI	11,559	224	93.1	1.64 (1.35, 2.01)	1.41 (1.15, 1.71)
Sensitivity analysis only considering PPI users taking an PPI for >30 days					
Exposure group	n	No. of events	Rate per 1,000 p-y	Crude HR (95% CI)	Weighted HR (95% CI)
Sert + no PPI	20,294	280	62.9	1.00 (ref.)	1.00 (ref.)
Sert + PPI	6,398	99	66.7	1.09 (0.87, 1.37)	1.04 (0.82, 1.32)
Cital/escit + no PPI	26,503	448	78.6	1.25 (1.07, 1.45)	1.22 (1.05, 1.41)
Cital/escit + PPI	8,588	153	79.9	1.29 (1.06, 1.57)	1.31 (1.08, 1.60)
Sensitivity analysis only considering PPI users taking an PPI for ≤ 30 days					
Exposure group	n	No. of events	Rate per 1,000 p-y	Crude HR (95% CI)	Weighted HR (95% CI)
Sert + no PPI	20,294	280	62.9	1.00 (ref.)	1.00 (ref.)
Sert + PPI	4,381	78	99.3	1.51 (1.17, 1.93)	1.03 (0.75, 1.31)
Cital/escit + no PPI	26,503	448	78.6	1.25 (1.07, 1.44)	1.21 (1.04, 1.40)
Cital/escit + PPI	6,395	139	121.0	1.82 (1.49, 2.23)	1.30 (1.04, 1.64)

An on-treatment analytic approach was used in all analyses. Fine and Gray proportional subdistribution hazards models were used to estimate hazard ratios and inverse probability of treatment weighting was used for confounding control.

Abbreviations: CI, confidence interval; cital/escital, citalopram or escitalopram; CYP, cytochrome P450; HR hazard ratio; No., number PPI, proton pump inhibitor; p-y, person-years; ref., referent; sert, sertraline; SSRI, selective serotonin reuptake inhibitor.

Table S9. Association between SSRI-PPI exposure group and the 1-year risk of the negative control outcome

Death due to a cause other than sudden cardiac death – negative control outcome					
Exposure group	n	No. of events	Rate per 1,000 p-y	Crude HR (95% CI)	Weighted HR (95% CI)
Sert + no PPI	20,294	883	198.2	1.00 (ref.)	1.00 (ref.)
Sert + PPI	10,779	465	205.0	1.04 (0.93, 1.16)	1.00 (0.89, 1.11)
Cital/escit + no PPI	26,503	1,166	204.5	1.03 (0.94, 1.12)	0.97 (0.89, 1.06)
Cital/escit + PPI	14,983	711	232.0	1.16 (1.05, 1.28)	1.01 (0.91, 1.12)

An on-treatment analytic approach was used in all analyses. Fine and Gray proportional subdistribution hazards models were used to estimate hazard ratios and inverse probability of treatment weighting was used for confounding control.

Abbreviations: CI, confidence interval; cital/escital, citalopram or escitalopram; HR hazard ratio; No., number; PPI, proton pump inhibitor; p-y, person-years; ref., referent; sert, sertraline.