# SUPPLEMENTAL MATERIAL

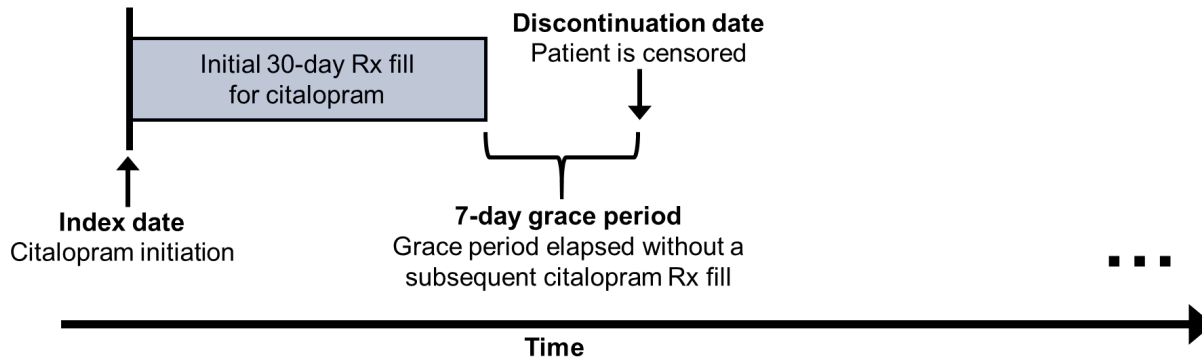**TABLE OF CONTENTS**

# SUPPLEMENTAL FIGURES

## Supplemental Figure 1. Illustration of SSRI discontinuation and switching events

### Panel A. SSRI discontinuation

**Discontinuation date**
Patient is censored

Initial 30-day Rx fill
for citalopram

**Index date**
Citalopram initiation

**7-day grace period**
Grace period elapsed without a
subsequent citalopram Rx fill

**Time**

### Panel B. SSRI switching

Initial 30-day Rx fill
for citalopram

2nd 30-day Rx fill
for citalopram

**Index date**
Citalopram initiation

New 30-day Rx fill
for sertraline

**Switch Date**
Patient is censored

**Time**
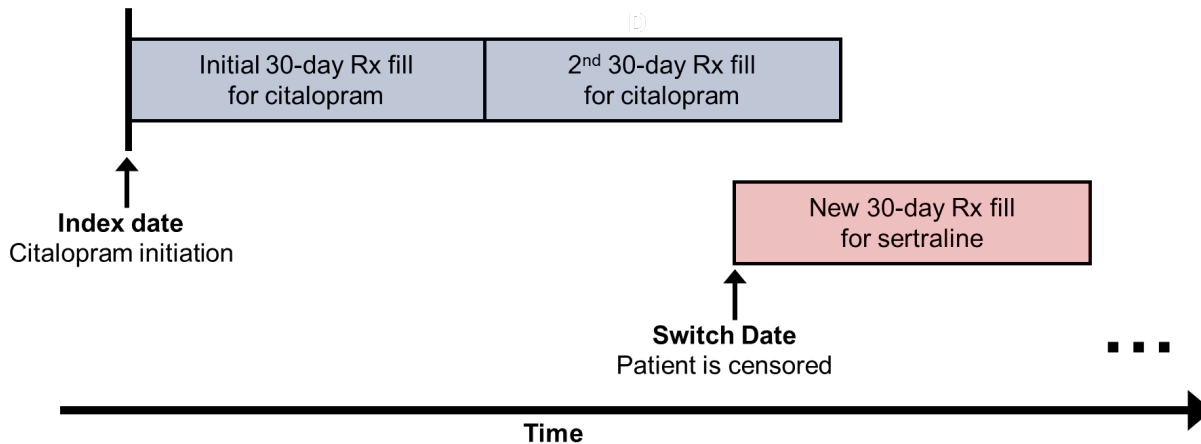
Patients were censored during study follow-up if they discontinued index SSRI therapy or if they switched from their index SSRI to a different generic product (i.e. from citalopram to sertraline). We defined the SSRI discontinuation date as the date when the index SSRI was exhausted for greater than 7-days (i.e. grace period) without a subsequent dispensing of the same SSRI (Panel A). We defined the SSRI switch date as the date of the first prescription fill for a non-index SSRI during follow-up (Panel B). Patients were only "at risk" for a switching event during times of continuous index medication use (i.e. prior to the end of the 7 day grace period).

Abbreviations: Rx, prescription; SSRI, selective serotonin reuptake inhibitor.

**Supplemental Figure 2. Propensity score distribution of patients treated with higher and lower QT-prolonging-potential SSRIs**
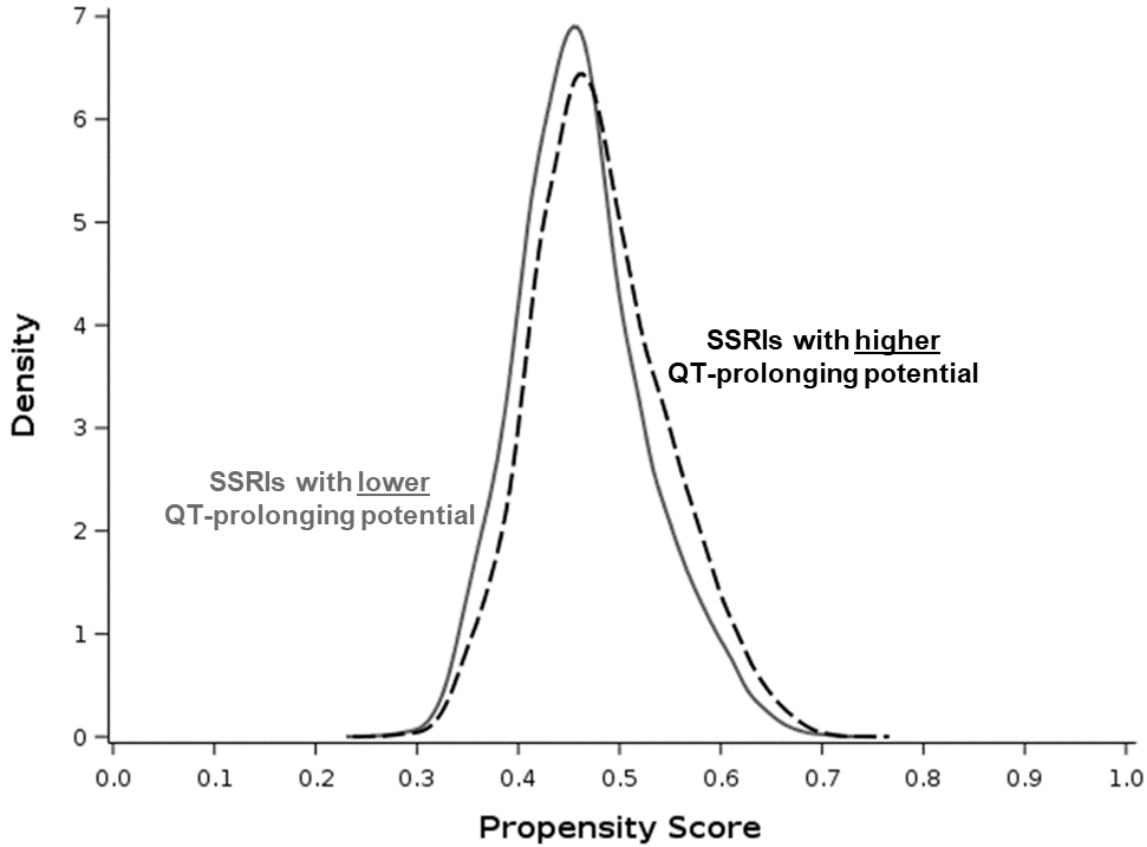


The black dashed line is the propensity score distribution for initiators of SSRIs with higher QT-prolonging potential SSRIs. The gray solid line represents the propensity score distribution for initiators of lower QT-prolonging-potential SSRIs. Higher QT-prolonging-potential SSRIs include citalopram and escitalopram. Lower QT-prolonging-potential SSRIs include fluoxetine, fluvoxamine, paroxetine, and sertraline.

Abbreviations: SSRI, selective serotonin reuptake inhibitor.

**SUPPLEMENTAL TABLES**

**Supplemental Table 1. Outcome definitions**

| Primary study outcome | |
|---|---|
| **Outcome** | **Specification** |
| Sudden cardiac death[27] | Death with a cardiac arrhythmia or cardiac arrest cause of death code (28, 29) listed as the <u>primary</u> cause on the ESRD Death Notification Form. |

| Alternative study outcomes considered in sensitivity analyses | |
|---|---|
| **Outcome** | **Specification** |
| Composite outcome of sudden cardiac death <u>*or*</u> hospitalized ventricular arrythmia | Death with a cardiac arrhythmia or cardiac arrest cause of death code (28, 29) listed as the <u>primary</u> cause on the ESRD Death Notification Form.<br><br>*or*<br><br>An inpatient hospitalization[a] for ventricular arrythmia (ICD-9 codes 427.1 or 427.4 in the primary position). |
| Cardiovascular mortality[27] | Death with any cardiovascular cause death code[b] (23, 25, 26, 27, 28, 29, 30, 31, 32, 35 or 36) listed as the <u>primary</u> cause on the ESRD Death Notification Form. |

| Alternative study outcomes considered in sensitivity analyses | |
|---|---|
| **Outcome** | **Specification** |
| Non-sudden cardiac death | Death with a non-sudden cardiac death code (all codes except 28 and 29) listed as the <u>primary</u> cause on the ESRD Death Notification Form. |

[a] Inpatient hospitalizations were identified using Medicare Part A claims (i.e. institutional claims). Specified four-digit ICD-9 diagnosis codes included all existing 5th digit diagnosis codes.

[b] The cardiovascular cause of death codes include the following clinical conditions: acute myocardial infarction, pericarditis (including cardiac tamponade), atherosclerotic heart disease, cardiomyopathy, cardiac arrhythmia, cardiac arrest (cause unknown), valvular heart disease, pulmonary edema due to exogenous fluid, congestive heart failure, pulmonary embolus, and cerebrovascular accident (including intracranial hemorrhage).

<u>Abbreviations:</u> ESRD, end-stage renal disease; ICD-9, International Classification of Diseases, Ninth Revision.

**Supplemental Table 2. ICD-9 diagnosis, ICD-9 procedure and CPT procedure codes used to identify relevant baseline covariates**

| Baseline comorbidities | |
|---|---|
| **Comorbid condition** | **ICD-9 diagnosis code(s)[a]** |
| Depression | 296.2, 296.3, 296.5, 300.4, 309.0, 309.1, 309.28, 311 |
| Anxiety | 300.0 |
| Bipolar disorder | 296.0, 296.4–296.8 |
| Schizophrenia | 295 |
| Delusional disorders | 297 |
| Personality disorders | 301 |
| Dementia | 331.0-331.2, 331.7, 290.0-290.4, 294.0-294.2, 294.8, 797 |
| Arrythmia | 427 |
| Conduction disorder | 426 |
| Dyslipidemia | 272.0–272.2, 272.4 |
| Heart failure | 398.91, 402.x1, 404.x1, 404.x3, 428 |
| Hypertension | 401–405 |
| Ischemic heart disease | 410–414 |
| Peripheral arterial disease | 249.9, 250.7, 440.2, 440.3, 440.4, 440.8, 440.9, 443.1, 443.22, 443.81, 443.89, 443.9, 444.22, 444.81, 445.02 |
| Stroke | 430–438 |
| Valvular disease | 394–397 |
| Cancer | 140–209 |
| COPD or asthma | 491–494, 496 |
| Chronic liver disease | 571 |
| Diabetes | 250 |
| Diabetic neuropathy | 250.6 |
| GI bleed | 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 |
| Hypothyroidism | 243, 244 |
| History of alcohol abuse | 303, 305.0 |
| History of cocaine abuse | 304.2, 305.6 |
| Tobacco use | 305.1 |
| History of non-compliance | V15.81, V45.12 |
| Cardiac pacemaker | V45.01 |

| Baseline procedures | |
|---|---|
| **Procedure** | **ICD-9 procedure code(s)[b] or CPT procedure code(s)** |
| Cardiac surgery | *ICD-9 procedure codes*: 35, 36, 37 |
| Electrocardiogram | *CPT procedure codes*: 93000, 93005, 93010, 93040, 93041, 93042 |
| Psychotherapy | *CPT procedure codes*: 90785, 90804–90819, 90821–90824, 90826–90829, 90832–90834, 90836–90844, 90846–90847, 90849, 90853, 90855, 90857, 90863 |

[a] Specified three-digit ICD-9 diagnosis code categories included all existing 4th and 5th digit diagnosis codes and specified four-digit ICD-9 diagnosis code categories included all existing 5th digit diagnosis codes.

[b] Specified two-digit ICD-9 procedure code categories included all existing 3rd and 4th digit procedure codes.

Abbreviations: COPD, chronic obstructive pulmonary disease; CPT, Current Procedural Terminology; GI, gastrointestinal; ICD-9, International Classification of Diseases, Ninth Revision.

**Supplemental Table 3. List of non-SSRI QT prolonging medications**

| Known risk of torsades de pointes[a] |
|---|
| Amiodarone, anagrelide, arsenic trioxide, astemizole, azithromycin, bepridil, chloroquine chlorpromazine, cilostazol, ciprofloxacin, clarithromycin, cocaine, disopyramide, dofetilide, donepezil, dronedarone, droperidol, erythromycin, flecainide, fluconazole, gatifloxacin, grepafloxacin, haloperidol, ibutilide, levofloxacin, levomethadyl, mesoridazine, methadone, moxifloxacin, ondansetron, oxaliplatin, papaverine, pentamidine, pimozide, probucol, procainamide, propofol, quinidine, sevoflurane, sotalol, sparfloxacin, terfenadine, thioridazine and vandetanib |

| Conditional risk of torsades de pointes[b] |
|---|
| Amantadine, amitriptyline, amphotericin B, atazanavir, chloral hydrate, cimetidine, diphenhydramine, doxepin, esomeprazole, famotidine, furosemide, galantamine, hydrochlorothiazide, hydroxychloroquine, hydroxyzine, indapamide, itraconazole, ivabradine, ketoconazole, lansoprazole, loperamide, metoclopramide, metolazone, metronidazole, nelfinavir, olanzapine, omeprazole, pantoprazole, piperacillin/tazobactam, posaconazole, propafenone, quetiapine, quinine sulfate, ranolazine, solifenacin, telaprevir, torsemide, trazodone, voriconazole and ziprasidone |

| Possible risk of torsades de pointes[c] |
|---|
| Alfuzosin, apomorphine, aripiprazole, asenapine, atomoxetine, bedaquiline, bendamustine, betrixaban, bortezomib, bosutinib, buprenorphine, cabozantinib, capecitabine, ceritinib, clomipramine, clozapine, crizotinib, dabrafenib, dasatinib, degarelix, delamanid, desipramine, deutetrabenazine, dexmedetomidine, dolasetron, efavirenz, eliglustat, epirubicin, eribulin, ezogabine, retigabine, felbamate, fingolimod, fluorouracil, gemifloxacin, granisetron, hydrocodone (extended release formulations), iloperidone, imipramine, melipramine, inotuzumab, isradipine, lapatinib, lenvatinib, leuprolide, lithium, lopinavir/ritonavir, maprotiline, memantine, midostaurin, mifepristone, mirabegron, mirtazapine, moexipril/hctz, necitumumab, nicardipine, nilotinib, norfloxacin, nortriptyline, nusinersen, ofloxacin, osimertinib, oxytocin, paliperidone, palonosetron, panobinostat, pasireotide, pazopanib, perflutren, perphenazine, pimavanserin, primaquine, promethazine, ribociclib, rilpivirine, risperidone, romidepsin, saquinavir, sorafenib, sunitinib, tacrolimus, tamoxifen, telavancin, telithromycin, tetrabenazine, tipiracil/trifluridine, tizanidine, tolterodine, toremifene, tramadol, trimipramine, valbenazine, vardenafil, vemurafenib, venlafaxine, vorinostat |

Medication lists were obtained from the CredibleMeds® website (www.Crediblemeds.org) on September 27, 2018.

[a] According to the CredibleMeds® website, medications with a known risk of torsades de pointes are defined as drugs that prolong the QT interval _and_ are clearly associated with a known risk of torsades de pointes, even when taken as recommended.[26]

[b] According to the CredibleMeds® website, medications with a conditional risk of torsades de pointes are defined as drugs are associated with torsades de pointes only under certain conditions (e.g. excessive dose, in patients with conditions such as hypokalemia, or when taken with interacting drugs) _or_ medications that create conditions that facilitate or induce torsades de pointes (e.g. cause an electrolyte disturbance that induces torsades de pointes).[26]

[c] According to the CredibleMeds® website, medications with a possible risk of torsades de pointes are defined as drugs that can cause QT prolongation _but_ currently lack evidence for a risk of torsades de pointes when taken as recommended.[26]

**Supplemental Table 4. HCPCS codes used to identify QT prolonging medications not billable to Medicare Part D**

| Known risk of Torsades de pointes[a] | |
|---|---|
| **Medication** | **HCPCS code(s)** |
| Arsenic trioxide | J9017 |
| Droperidol | J1790, J1810 |
| Ibutilide | J1742 |
| Oxaliplatin | J9263 |
| Papaverine | J2440 |
| Pentamidine | J2545, J7676 |
| Procainamide | J2690 |
| Propofol | J2704 |
| **Conditional risk of Torsades de pointes[b]** | |
| **Medication** | **HCPCS code(s)** |
| Amphotericin B | J0285, J0287, J0288, J0289 |
| Piperacillin/tazobactam | J2543 |
| **Possible risk of Torsades de pointes[c]** | |
| **Medication** | **HCPCS code(s)** |
| Bendamustine | J9033, J9034 |
| Bortezomib | J9041 |
| Degarelix | J9155 |
| Epirubicin | J9178 |
| Eribulin | J9179 |
| Fluorouracil | J9190 |
| Inotuzumab | FDA approved after the study period |
| Leuprolide | J1950, J9217, J9218, J9219 |
| Necitumumab | J9295 |
| Nusinersen | J2326 |
| Oxytocin | J2590 |
| Palonosetron | J2469, J8655 |
| Pasireotide | J2502 |
| Perflutren | Q9957 |
| Romidepsin | J9315 |
| Telavancin | J3095 |

HCPCS codes used to identify QT prolonging medications not billable to Medicare Part D were identified in Medicare Part A and B claims (i.e. institutional and physician/supplier claims).

[a] According to the CredibleMeds® website, medications with a known risk of torsades de pointes are defined as drugs that prolong the QT interval _and_ are clearly associated with a known risk of torsades de pointes, even when taken as recommended.[26]

[b] According to the CredibleMeds® website, medications with a conditional risk of torsades de pointes are defined as drugs are associated with torsades de pointes only under certain conditions (e.g. excessive dose, in patients with conditions such as hypokalemia, or when taken with interacting drugs) or medications that create conditions that facilitate or induce torsades de pointes (e.g. cause an electrolyte disturbance that induces torsades de pointes).[26]

[c] According to the CredibleMeds® website, medications with a possible risk of torsades de pointes are defined as drugs that can cause QT prolongation but currently lack evidence for a risk of torsades de pointes when taken as recommended.[26]

Abbreviations: FDA, Food and Drug Administration; HCPCS, Healthcare Common Procedure Coding System.

**Supplemental Table 5. List of cytochrome P450 inhibitors**

| Inhibitors of cytochrome P450 1A2 |
|---|
| Amiodarone, cimetidine, ciprofloxacin, efavirenz, interferon alpha, methoxsalen, ticlopidine |

| Inhibitors of cytochrome P450 3A4 |
|---|
| Amiodarone, aprepitant, buprenorphine, chloramphenicol, cimetidine, ciprofloxacin, clarithromycin, delavirdine, diethyldithiocarbamate, diltiazem, erythromycin, fluconazole, gestodene, imatinib, indinavir, itraconazole, ketoconazole, mifepristone, nefazodone, nelfinavir, norfloxacin, ritonavir, saquinavir, telaprevir, telithromycin, verapamil, voriconazole |

| Inhibitors of cytochrome P450 2C9 |
|---|
| Amiodarone, efavirenz, fenofibrate, fluconazole, fluvastatin, isoniazid, lovastatin, metronidazole, phenylbutazone, probenecid, sulfamethoxazole, sulfaphenazole, teniposide, voriconazole, zafirlukast |

| Inhibitors of cytochrome P450 2C19 |
|---|
| Chloramphenicol, cimetidine, esomeprazole, felbamate, indomethacin, isoniazid, ketoconazole, lansoprazole, modafinil, omeprazole, oral contraceptives, oxcarbazepine, pantoprazole, probenecid, ticlopidine, topiramate, voriconazole |

| Inhibitors of cytochrome P450 2D6 |
|---|
| Amiodarone, bupropion**,** celecoxib, chlorpheniramine, chlorpromazine, cimetidine, cinacalcet, clemastine, clomipramine, diphenhydramine, doxepin, doxorubicin, duloxetine, haloperidol, hydroxyzine, methadone, metoclopramide, midodrine, moclobemide, perphenazine, promethazine, quinidine, ranitidine, ritonavir, terbinafine, ticlopidine, tripelennamine |

List of medications that can inhibit the metabolism of SSRIs via cytochrome P450  isoenzyme interactions were obtained from the Flockhart Table™ website (https://drug-interactions.medicine.iu.edu/Main-Table.aspx) on September 27, 2018.[29] Citalopram and escitalopram are major substrates of cytochrome P450 3A4 and 2C19. Fluoxetine is a major substrate of cytochrome P450 2C9 and 2D6. Fluvoxamine is a major substrate of cytochrome P450 1A2 and 2D6. Paroxetine is a major substrate of cytochrome P450 2D6.

Abbreviations: SSRI, selective serotonin reuptake inhibitor.

**Supplemental Table 6. Full list of baseline characteristics among study patients initiating a higher and lower QT-prolonging-potential SSRI**

| Characteristic | Unweighted | | | Weighted | | |
|---|---|---|---|---|---|---|
| | SSRI with *higher* QT-prolonging potential n = 30,932 | SSRI with *lower* QT-prolonging potential n = 34,722 | Std diff[a] (%) | SSRI with *higher* QT-prolonging potential n = 30,927 | SSRI with *lower* QT-prolonging potential n = 34,730 | Std diff[a] (%) |
| **Age (years)** | 67.6 ± 17.2 | 66.5 ± 17.2 | 6.2 | 67.0 ± 17.2 | 67.0 ± 17.21 | 0.0 |
| **Female** | 16,512 (53.4%) | 18,121 (52.2%) | 2.3 | 16,316 (52.8%) | 18,324 (52.8%) | 0.0 |
| **Race** | | | | | | |
| Black | 11,339 (36.7%) | 11,959 (34.4%) | 6.3 | 10,967 (35.5%) | 12,320 (35.5%) | 0.0 |
| White | 18,434 (59.6%) | 21,005 (60.5%) | 1.5 | 18,589 (60.1%) | 20,870 (60.1%) | 0.0 |
| Other | 1,159 (3.7%) | 1,758 (5.1%) | 33.5 | 1,371 (4.4%) | 1,540 (4.4%) | 0.0 |
| **Hispanic** | 5,233 (16.9%) | 7,346 (21.2%) | 22.7 | 5,933 (19.2%) | 6,654 (19.2%) | 0.1 |
| **Year index SSRI was filled** | | | | | | |
| 2007 | 3,961 (12.8%) | 4,751 (13.7%) | 6.9 | 4,086 (13.2%) | 4,594 (13.2%) | 0.1 |
| 2008 | 4,095 (13.2%) | 4,388 (12.6%) | 4.8 | 3,977 (12.9%) | 4,468 (12.9%) | 0.0 |
| 2009 | 4,061 (13.1%) | 4,343 (12.5%) | 5.0 | 3,948 (12.8%) | 4,435 (12.8%) | 0.1 |
| 2010 | 4,139 (13.4%) | 4,161 (12.0%) | 11.5 | 3,907 (12.6%) | 4,386 (12.6%) | 0.0 |
| 2011 | 4,034 (13.0%) | 4,061 (11.7%) | 11.3 | 3,814 (12.3%) | 4,287 (12.3%) | 0.1 |
| 2012 | 3,611 (11.7%) | 4,152 (12.0%) | 2.5 | 3,670 (11.9%) | 4,118 (11.9%) | 0.1 |
| 2013 | 3,507 (11.3%) | 4,398 (12.7%) | 11.5 | 3,738 (12.1%) | 4,194 (12.1%) | 0.1 |
| 2014 | 3,524 (11.4%) | 4,468 (12.9%) | 12.7 | 3,787 (12.2%) | 4,246 (12.2%) | 0.2 |
| **Low-dose index SSRI[b]** | 27,935 (90.3%) | 31,560 (90.9%) | 0.6 | 28,011 (90.6%) | 31,456 (90.6%) | 0.0 |
| **Cause of ESRD** | | | | | | |
| Diabetes | 15,563 (50.3%) | 17,416 (50.2%) | 0.3 | 15,542 (50.3%) | 17,458 (50.3%) | 0.0 |
| Hypertension | 7,941 (25.7%) | 8,760 (25.2%) | 1.8 | 7,848 (25.4%) | 8,813 (25.4%) | 0.0 |
| Glomerular disease | 3,359 (10.9%) | 3,934 (11.3%) | 4.4 | 3,442 (11.1%) | 3,864 (11.1%) | 0.1 |
| Other | 4,069 (13.2%) | 4,612 (13.3%) | 1.0 | 4,095 (13.2%) | 4,596 (13.2%) | 0.1 |
| **Dialysis vintage** | | | | | | |
| 0.7 – 0.9 years | 5,467 (17.7%) | 5,903 (17.0%) | 4.0 | 5,364 (17.3%) | 6,023 (17.3%) | 0.0 |
| 1.0 – 1.9 years | 5,965 (19.3%) | 6,622 (19.1%) | 1.1 | 5,933 (19.2%) | 6,661 (19.2%) | 0.0 |
| 2.0 – 2.9 years | 4,631 (15.0%) | 5,136 (14.8%) | 1.3 | 4,594 (14.9%) | 5,162 (14.9%) | 0.1 |
| ≥ 3 years | 14,869 (48.1%) | 17,061 (49.1%) | 2.2 | 15,035 (48.6%) | 16,883 (48.6%) | 0.0 |
| **History of a failed kidney transplant** | 2,029 (6.6%) | 2,377 (6.8%) | 4.6 | 2,083 (6.7%) | 2,336 (6.7%) | 0.1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Medicare Part D low income subsidy | 24,601 (79.5%) | 27,694 (79.8%) | 0.3 | 24,620 (79.6%) | 27,653 (79.6%) | 0.0 |
| Depression | 10,960 (35.4%) | 10,851 (31.3%) | 12.7 | 10,298 (33.3%) | 11,567 (33.3%) | 0.0 |
| Anxiety | 5,590 (18.1%) | 6,046 (17.4%) | 3.8 | 5,492 (17.8%) | 6,169 (17.8%) | 0.0 |
| Bipolar disorder | 810 (2.6%) | 741 (2.1%) | 26.6 | 734 (2.4%) | 825 (2.4%) | 0.2 |
| Other mental health disorders[c] | 872 (2.8%) | 794 (2.3%) | 26.5 | 786 (2.5%) | 884 (2.5%) | 0.2 |
| Dementia | 3,978 (12.9%) | 3,174 (9.1%) | 34.9 | 3,380 (10.9%) | 3,800 (10.9%) | 0.1 |
| Arrythmia | 9,616 (31.1%) | 10,135 (29.2%) | 6.4 | 9,327 (30.2%) | 10,471 (30.1%) | 0.0 |
| Conduction disorder | 2,434 (7.9%) | 2,659 (7.7%) | 2.9 | 2,403 (7.8%) | 2,699 (7.8%) | 0.0 |
| Dyslipidemia | 15,756 (50.9%) | 17,566 (50.6%) | 0.7 | 15,723 (50.8%) | 17,652 (50.8%) | 0.0 |
| Heart failure | 14,937 (48.3%) | 15,884 (45.7%) | 5.5 | 14,536 (47.0%) | 16,321 (47.0%) | 0.0 |
| Hypertension | 28,289 (91.5%) | 31,297 (90.1%) | 1.5 | 28,073 (90.8%) | 31,522 (90.8%) | 0.0 |
| Ischemic heart disease | 15,171 (49.0%) | 16,216 (46.7%) | 4.9 | 14,810 (47.9%) | 16,624 (47.9%) | 0.0 |
| Peripheral arterial disease | 11,332 (36.6%) | 11,737 (33.8%) | 8.2 | 10,878 (35.2%) | 12,216 (35.2%) | 0.0 |
| Stroke | 8,225 (26.6%) | 8,033 (23.1%) | 14.2 | 7,668 (24.8%) | 8,615 (24.8%) | 0.0 |
| Valvular disease | 2,112 (6.8%) | 2,165 (6.2%) | 9.8 | 2,023 (6.5%) | 2,273 (6.5%) | 0.1 |
| Cancer | 2,671 (8.6%) | 2,763 (8.0%) | 8.7 | 2,564 (8.3%) | 2,881 (8.3%) | 0.1 |
| COPD or asthma | 9,384 (30.3%) | 9,980 (28.7%) | 5.5 | 9,134 (29.5%) | 10,255 (29.5%) | 0.0 |
| Chronic liver disease | 1,385 (4.5%) | 1,577 (4.5%) | 1.6 | 1,400 (4.5%) | 1,570 (4.5%) | 0.1 |
| Diabetes | 21,520 (69.6%) | 23,690 (68.2%) | 2.0 | 21,305 (68.9%) | 23,927 (68.9%) | 0.0 |
| Diabetic neuropathy | 7,718 (25.0%) | 8,352 (24.1%) | 3.7 | 7,584 (24.5%) | 8,523 (24.5%) | 0.1 |
| GI bleed | 3,586 (11.6%) | 3,582 (10.3%) | 12.2 | 3,378 (10.9%) | 3,793 (10.9%) | 0.0 |
| Hypothyroidism | 5,567 (18.0%) | 5,960 (17.2%) | 4.9 | 5,440 (17.6%) | 6,110 (17.6%) | 0.0 |
| History of alcohol abuse | 785 (2.5%) | 795 (2.3%) | 13.4 | 745 (2.4%) | 835 (2.4%) | 0.2 |
| History of cocaine abuse | 529 (1.7%) | 554 (1.6%) | 11.0 | 510 (1.6%) | 572 (1.6%) | 0.0 |
| Tobacco use | 4,327 (14.0%) | 4,829 (13.9%) | 0.6 | 4,321 (14.0%) | 4,857 (14.0%) | 0.1 |
| History of non-compliance | 3,501 (11.3%) | 4,072 (11.7%) | 3.7 | 3,575 (11.6%) | 4,013 (11.6%) | 0.0 |
| Had a cardiac pacemaker | 1,431 (4.6%) | 1,463 (4.2%) | 10.6 | 1,361 (4.4%) | 1,529 (4.4%) | 0.0 |
| Had cardiac surgery during the last 30 days of baseline | 588 (1.9%) | 614 (1.8%) | 10.7 | 565 (1.8%) | 635 (1.8%) | 0.1 |
| Had an ECG during the last 30 days of baseline | 9,908 (32.0%) | 10,796 (31.1%) | 3.0 | 9,777 (31.6%) | 10,974 (31.6%) | 0.1 |
| Alpha-blocker | 240 (0.8%) | 285 (0.8%) | 11.2 | 249 (0.8%) | 280 (0.8%) | 0.0 |

| | | | | | | |
|---|---|---|---|---|---|---|
| ACE inhibitor | 5,749 (18.6%) | 6,542 (18.8%) | 1.4 | 5,801 (18.8%) | 6,509 (18.7%) | 0.1 |
| ARB | 3,018 (9.8%) | 3,530 (10.2%) | 4.3 | 3,082 (10.0%) | 3,462 (10.0%) | 0.0 |
| Beta blocker | 11,442 (37.0%) | 13,114 (37.8%) | 2.1 | 11,562 (37.4%) | 12,981 (37.4%) | 0.0 |
| Calcium channel blocker | 8,768 (28.3%) | 10,385 (29.9%) | 5.5 | 9,031 (29.2%) | 10,141 (29.2%) | 0.0 |
| Central alpha agonist | 3,906 (12.6%) | 4,413 (12.7%) | 0.7 | 3,913 (12.7%) | 4,394 (12.7%) | 0.0 |
| Diuretic | 2,903 (9.4%) | 3,565 (10.3%) | 9.5 | 3,048 (9.9%) | 3,420 (9.8%) | 0.1 |
| Vasodilator | 3,292 (10.6%) | 3,837 (11.1%) | 3.9 | 3,364 (10.9%) | 3,779 (10.9%) | 0.0 |
| Anticoagulant | 2,279 (7.4%) | 2,450 (7.1%) | 4.7 | 2,233 (7.2%) | 2,506 (7.2%) | 0.1 |
| Antiplatelet agent | 3,520 (11.4%) | 3,980 (11.5%) | 0.8 | 3,530 (11.4%) | 3,964 (11.4%) | 0.0 |
| Digoxin | 515 (1.7%) | 596 (1.7%) | 4.8 | 529 (1.7%) | 592 (1.7%) | 0.5 |
| Nitrate | 1,987 (6.4%) | 2,299 (6.6%) | 3.3 | 2,016 (6.5%) | 2,264 (6.5%) | 0.0 |
| Statin | 7,492 (24.2%) | 8,885 (25.6%) | 5.6 | 7,721 (25.0%) | 8,671 (25.0%) | 0.0 |
| Other cholesterol medication[d] | 1,244 (4.0%) | 1,429 (4.1%) | 2.7 | 1,260 (4.1%) | 1,414 (4.1%) | 0.0 |
| Midodrine | 732 (2.4%) | 874 (2.5%) | 8.0 | 754 (2.4%) | 848 (2.4%) | 0.2 |
| Use of ≥ 1 medication with a known risk of TdP[e] | 2,919 (9.4%) | 3,210 (9.2%) | 2.2 | 2,891 (9.3%) | 3,244 (9.3%) | 0.1 |
| Use of ≥ 1 medication with a conditional risk of TdP[e] | 12,634 (40.8%) | 14,238 (41.0%) | 0.4 | 12,675 (41.0%) | 14,231 (41.0%) | 0.0 |
| Use of ≥ 1 medication with a possible risk of TdP[e] | 3,228 (10.4%) | 3,123 (9.0%) | 15.6 | 3,001 (9.7%) | 3,375 (9.7%) | 0.1 |
| Use of ≥ 1 CYP 1A2 inhibitor[f] | 1,154 (3.7%) | 1,290 (3.7%) | 0.5 | 1,155 (3.7%) | 1,296 (3.7%) | 0.1 |
| Use of ≥ 1 CYP 3A4 inhibitor[f] | 2,419 (7.8%) | 2,770 (8.0%) | 2.1 | 2,450 (7.9%) | 2,746 (7.9%) | 0.2 |
| Use of ≥ 1 CYP 2C9 inhibitor[f] | 2,074 (6.7%) | 2,385 (6.9%) | 2.6 | 2,104 (6.8%) | 2,360 (6.8%) | 0.1 |
| Use of ≥ 1 CYP 2C19 inhibitor[f] | 8,119 (26.2%) | 9,022 (26.0%) | 1.0 | 8,095 (26.2%) | 9,087 (26.2%) | 0.0 |
| Use of ≥ 1 CYP 2D6 inhibitor[f] | 8,777 (28.4%) | 9,999 (28.8%) | 1.5 | 8,845 (28.6%) | 9,931 (28.6%) | 0.0 |
| Hospitalized during the last 30 days of the baseline period | 8,701 (28.1%) | 8,749 (25.2%) | 11.2 | 8,248 (26.7%) | 9,264 (26.7%) | 0.0 |
| Number of hospital admissions during the baseline period | | | | | | |
| 0 | 11,219 (36.3%) | 14,063 (40.5%) | 11.2 | 11,890 (38.4%) | 13,354 (38.5%) | 0.0 |
| 1 – 2 | 13,223 (42.7%) | 14,199 (40.9%) | 4.5 | 12,916 (41.8%) | 14,499 (41.7%) | 0.0 |
| 3 – 4 | 4,704 (15.2%) | 4,651 (13.4%) | 13.1 | 4,421 (14.3%) | 4,965 (14.3%) | 0.0 |
| ≥ 5 | 1,786 (5.8%) | 1,809 (5.2%) | 11.3 | 1,700 (5.5%) | 1,911 (5.5%) | 0.1 |

| Number of ED visits during the baseline period | | | | | | |
|---|---|---|---|---|---|---|
| 0 | 7,621 (24.6%) | 9,625 (27.7%) | 12.0 | 8,113 (26.2%) | 9,114 (26.2%) | 0.0 |
| 1 – 2 | 11,966 (38.7%) | 13,336 (38.4%) | 0.7 | 11,918 (38.5%) | 13,379 (38.5%) | 0.0 |
| 3 – 4 | 6,135 (19.8%) | 6,436 (18.5%) | 6.9 | 5,924 (19.2%) | 6,651 (19.2%) | 0.0 |
| ≥ 5 | 5,210 (16.8%) | 5,325 (15.3%) | 9.7 | 4,973 (16.1%) | 5,585 (16.1%) | 0.0 |
| Had ≥ 1 psychotherapy visit during the baseline period | 3,314 (10.7%) | 2,738 (7.9%) | 31.8 | 2,859 (9.2%) | 3,211 (9.2%) | 0.0 |
| Had ≥ 1 skilled nursing facility admission during the baseline period | 7,947 (25.7%) | 6,566 (18.9%) | 30.7 | 6,853 (22.2%) | 7,701 (22.2%) | 0.1 |

Values are given as number (percent) for categorical variables and as mean ± standard deviation for continuous variables. Higher QT-prolonging-potential SSRIs included citalopram and escitalopram. Lower QT-prolonging-potential SSRIs included fluoxetine, fluvoxamine, paroxetine, and sertraline. All-covariates were measured during the 180-day baseline period prior to SSRI initiation. The weighted cohort is the pseudo-population generated by inverse probability of treatment weighting.

[a] A std diff > 10.0% represents meaningful imbalance between groups.[33]

[b] The definition of low-dose was based on the dosing recommendations found in each SSRI's package insert.[62-67] Low doses: citalopram ≤ 20 mg/day; escitalopram ≤ 10 mg/day; fluoxetine ≤ 20 mg per day; immediate release fluvoxamine ≤ 50 mg/day; controlled release fluvoxamine ≤ 100 mg/day; immediate release paroxetine ≤ 20 mg/day; controlled release paroxetine ≤ 25 mg/day; and sertraline 50 mg/day.

[c] Other mental health disorders included schizophrenia, delusional disorders, and personality disorders.

[d] Other cholesterol medications (i.e. non-statin cholesterol medications) included bile acid sequestrants, cholesterol absorption inhibitors, fibrates, and niacin.

[e] Lists medications with known, conditional, and possible risks of TdP are presented in Supplemental Table 3.

[f] Lists of medications that are relevant CYP 1A2, 3A4, 2C9, 2C19, and 2D6 inhibitors provided in Supplemental Table 4.

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; COPD, chronic obstructive pulmonary disease; CYP, cytochrome P450; ED, emergency department; ECG, electrocardiogram; ESRD, end-stage renal disease; GI, gastrointestinal; SSRI, selective serotonin reuptake inhibitor; std diff, standardized differences; TdP, torsades de pointes.

**Supplemental Table 7. Association between the initiation of a higher versus lower QT-prolonging-potential SSRI and the 1-year risk of fatal cardiac outcomes**

| SSRI | n | No. of events | Rate per 1,000 p-y | Unadjusted HR (95% CI) | Adjusted HR (95% CI) |
|---|---|---|---|---|---|
| **Sudden cardiac death – primary outcome** | | | | | |
| Lower QT-prolonging-potential | 34,722 | 601 | 68.5 | 1.00 (ref.) | 1.00 (ref.) |
| Higher QT-prolonging-potential | 30,932 | 702 | 89.3 | 1.30 (1.16, 1.45) | 1.18 (1.05, 1.31) |
| **Composite of sudden cardiac death or hospitalized ventricular arrythmia – alternative outcome** | | | | | |
| Lower QT-prolonging-potential | 34,722 | 635 | 72.4 | 1.00 (ref.) | 1.00 (ref.) |
| Higher QT-prolonging-potential | 30,932 | 742 | 94.5 | 1.30 (1.17, 1.44) | 1.18 (1.06, 1.31) |
| **Cardiovascular mortality – alternative outcome** | | | | | |
| Lower QT-prolonging-potential | 34,722 | 912 | 103.9 | 1.00 (ref.) | 1.00 (ref.) |
| Higher QT-prolonging-potential | 30,932 | 1,002 | 127.5 | 1.22 (1.12, 1.34) | 1.11 (1.02, 1.22) |

An on-treatment analytic approach was used in all analyses. Fine and Gray proportional subdistribution hazards models were used to estimate the association between the initiation of higher versus lower QT-prolonging-potential SSRIs and the 1-year risk of fatal cardiac outcomes. Higher QT-prolonging-potential SSRIs included citalopram and escitalopram. Lower QT-prolonging potential-SSRIs included fluoxetine, fluvoxamine, paroxetine, and sertraline. Adjusted analyses controlled for baseline covariates listed in Supplemental Table 6 using inverse probability of treatment weighting.

Abbreviations: CI, confidence interval; HR, hazard ratio; ref., referent; No., number; p-y, person-years; SSRI, selective serotonin reuptake inhibitor.

**Supplemental Table 8. Association between the initiation of a higher versus lower QT-prolonging-potential SSRI and the 1-year risk of sudden cardiac death within clinically relevant subgroups**

| | | | Age subgroups | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | **Age ≥ 65 years** | | | | | **Age < 65 years** | | | |
| **SSRI** | **n** | **No. of events** | **Rate per 1,000 p-y** | **Unadjusted HR (95% CI)** | **Adjusted HR (95% CI)** | **n** | **No. of events** | **Rate per 1,000 p-y** | **Unadjusted HR (95% CI)** | **Adjusted HR (95% CI)** |
| Lower QT-prolonging-potential | 19,631 | 446 | 85.0 | 1.00 (ref.) | 1.00 (ref.) | 15,091 | 161 | 43.9 | 1.00 (ref.) | 1.00 (ref.) |
| Higher QT-prolonging-potential | 18,259 | 541 | 110.1 | 1.29 (1.13, 1.46) | 1.19 (1.05, 1.35) | 12,673 | 155 | 54.7 | 1.24 (1.00, 1.56) | 1.13 (0.90, 1.41) |
| | | | Sex subgroups | | | | | | | |
| | | **Female** | | | | | **Male** | | | |
| **SSRI** | **n** | **No. of events** | **Rate per 1,000 p-y** | **Unadjusted HR (95% CI)** | **Adjusted HR (95% CI)** | **n** | **No. of events** | **Rate per 1,000 p-y** | **Unadjusted HR (95% CI)** | **Adjusted HR (95% CI)** |
| Lower QT-prolonging-potential | 18,121 | 280 | 61.6 | 1.00 (ref.) | 1.00 (ref.) | 16,601 | 321 | 75.9 | 1.00 (ref.) | 1.00 (ref.) |
| Higher QT-prolonging-potential | 16,512 | 356 | 85.7 | 1.38 (1.18, 1.62) | 1.23 (1.06, 1.44) | 14,420 | 346 | 93.4 | 1.23 (1.05, 1.43) | 1.12 (0.96, 1.31) |
| | | | Conduction disorder subgroups | | | | | | | |
| | | **(+) Conduction disorder** | | | | | **(-) Conduction disorder** | | | |
| **SSRI** | **n** | **No. of events** | **Rate per 1,000 p-y** | **Unadjusted HR (95% CI)** | **Adjusted HR (95% CI)** | **n** | **No. of events** | **Rate per 1,000 p-y** | **Unadjusted HR (95% CI)** | **Adjusted HR (95% CI)** |
| Lower QT-prolonging-potential | 2,659 | 54 | 84.4 | 1.00 (ref.) | 1.00 (ref.) | 32,063 | 547 | 67.2 | 1.00 (ref.) | 1.00 (ref.) |
| Higher QT-prolonging-potential | 2,434 | 83 | 138.5 | 1.64 (1.16, 2.30) | 1.47 (1.05, 2.06) | 28,498 | 619 | 85.3 | 1.26 (1.12, 1.42) | 1.14 (1.02, 1.28) |

| Heart failure subgroups | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **(+) Heart failure** | | | | | | **(-) Heart failure** | | | |
| SSRI | n | No. of events | Rate per 1,000 p-y | Unadjusted HR (95% CI) | Adjusted HR (95% CI) | n | No. of events | Rate per 1,000 p-y | Unadjusted HR (95% CI) | Adjusted HR (95% CI) |
| Lower QT-prolonging-potential | 15,884 | 413 | 105.6 | 1.00 (ref.) | 1.00 (ref.) | 18,838 | 188 | 38.7 | 1.00 (ref.) | 1.00 (ref.) |
| Higher QT-prolonging-potential | 14,937 | 484 | 131.8 | 1.24 (1.09, 1.42) | 1.16 (1.02, 1.32) | 15,995 | 218 | 52.1 | 1.34 (1.20, 1.63) | 1.21 (1.00, 1.48) |
| **Liver disease subgroups** | | | | | | | | | | |
| | **(+) Liver disease** | | | | | | **(-) Liver disease** | | | |
| SSRI | n | No. of events | Rate per 1,000 p-y | Unadjusted HR (95% CI) | Adjusted HR (95% CI) | n | No. of events | Rate per 1,000 p-y | Unadjusted HR (95% CI) | Adjusted HR (95% CI) |
| Lower QT-prolonging-potential | 1,577 | 31 | 87.8 | 1.00 (ref.) | 1.00 (ref.) | 33,145 | 570 | 67.7 | 1.00 (ref.) | 1.00 (ref.) |
| Higher QT-prolonging-potential | 1,385 | 35 | 115.5 | 1.32 (0.82, 2.13) | 1.20 (0.74, 1.95) | 29,547 | 667 | 88.3 | 1.30 (1.16, 1.45) | 1.17 (1.05, 1.31) |
| **Non-SSRI QT-prolonging medication subgroups** | | | | | | | | | | |
| | **Use of ≥ 1 non-SSRI QT-prolonging medication** | | | | | | **Use of zero non-SSRI QT-prolonging medications** | | | |
| SSRI | n | No. of events | Rate per 1,000 p-y | Unadjusted HR (95% CI) | Adjusted HR (95% CI) | n | No. of events | Rate per 1,000 p-y | Unadjusted HR (95% CI) | Adjusted HR (95% CI) |
| Lower QT-prolonging-potential | 16,478 | 286 | 62.7 | 1.00 (ref.) | 1.00 (ref.) | 18,244 | 315 | 74.8 | 1.00 (ref.) | 1.00 (ref.) |
| Higher QT-prolonging-potential | 14,774 | 356 | 86.9 | 1.38 (1.18, 1.61) | 1.29 (1.10, 1.50) | 16,158 | 346 | 92.0 | 1.22 (1.05, 1.43) | 1.08 (0.93, 1.26) |

An on-treatment analytic approach was used in all analyses. Fine and Gray proportional subdistribution hazards models were used to estimate the association between the initiation of a higher versus lower QT-prolonging-potential SSRI and the 1-year risk of sudden cardiac death within clinically relevant subgroups. Higher QT-prolonging-potential SSRIs included citalopram and escitalopram. Lower QT-prolonging-potential SSRIs included fluoxetine, fluvoxamine, paroxetine, and sertraline. Adjusted analyses controlled for baseline covariates listed in Supplemental Table 6 using inverse probability of treatment weighting.

Abbreviations: CI, confidence interval; HR, hazard ratio; ref., referent; No., number; p-y, person-years; SSRI, selective serotonin reuptake inhibitor.

**Supplemental Table 9. Association between the initiation of individual higher QT-prolonging-potential SSRIs versus lower QT-prolonging-potential SSRIs and the 1-year risk of sudden cardiac death**

| Citalopram versus SSRIs with lower QT prolonging potential | | | | | |
|---|---|---|---|---|---|
| **SSRI** | **n** | **No. of events** | **Rate per 1,000 p-y** | **Unadjusted HR (95% CI)** | **Adjusted HR (95% CI)** |
| Lower QT-prolonging-potential | 34,722 | 601 | 68.5 | 1.00 (ref.) | 1.00 (ref.) |
| Citalopram | 16,288 | 366 | 85.6 | 1.25 (1.10, 1.42) | 1.16 (1.02, 1.32) |
| **Escitalopram versus SSRIs with lower QT prolonging potential** | | | | | |
| **SSRI** | **n** | **No. of events** | **Rate per 1,000 p-y** | **Unadjusted HR (95% CI)** | **Adjusted HR (95% CI)** |
| Lower QT-prolonging-potential | 34,722 | 601 | 68.5 | 1.00 (ref.) | 1.00 (ref.) |
| Escitalopram | 14,644 | 336 | 93.8 | 1.36 (1.19, 1.55) | 1.21 (1.05, 1.38) |

An on-treatment analytic approach was used in all analyses. Fine and Gray proportional subdistribution hazards models were used to estimate: 1) the association between the initiation of citalopram versus lower QT-prolonging-potential SSRIs and the 1-year risk of sudden cardiac death, and 2) the association between the initiation of escitalopram versus lower QT-prolonging-potential SSRIs and the 1-year risk of sudden cardiac death. Higher QT-prolonging-potential SSRIs included citalopram and escitalopram. Lower QT-prolonging-potential SSRIs included fluoxetine, fluvoxamine, paroxetine, and sertraline. Adjusted analyses controlled for baseline covariates listed in Supplemental Table 6 using inverse probability of treatment weighting.

Abbreviations: CI, confidence interval; HR, hazard ratio; ref., referent; No., number; p-y, person-years; SSRI, selective serotonin reuptake inhibitor.

**Supplemental Table 10. Association between the initiation of a higher versus lower QT-prolonging-potential SSRI and the 1-year risk of the sudden cardiac death when longer grace periods were used to define SSRI discontinuation**

| SSRI | n | No. of events | Rate per 1,000 p-y | Unadjusted HR (95% CI) | Adjusted HR (95% CI) |
|---|---|---|---|---|---|
| **14-day grace period used to define discontinuation** | | | | | |
| Lower QT-prolonging-potential | 34,722 | 746 | 71.8 | 1.00 (ref.) | 1.00 (ref.) |
| Higher QT-prolonging-potential | 30,932 | 845 | 90.6 | 1.26 (1.14, 1.39) | 1.14 (1.03, 1.26) |
| **30-day grace period grace period used to define discontinuation** | | | | | |
| Lower QT-prolonging-potential | 34,722 | 966 | 73.9 | 1.00 (ref.) | 1.00 (ref.) |
| Higher QT-prolonging-potential | 30,932 | 1,083 | 92.6 | 1.25 (1.14, 1.36) | 1.14 (1.04, 1.24) |

An on-treatment analytic approach was used in all analyses. Fine and Gray proportional subdistribution hazards models were used to estimate the association between the initiation of a higher versus lower QT-prolonging-potential SSRI and the 1-year risk of sudden cardiac death. Higher QT-prolonging-potential SSRIs included citalopram and escitalopram. Lower QT-prolonging-potential SSRIs included fluoxetine, fluvoxamine, paroxetine, and sertraline. Adjusted analyses controlled for baseline covariates listed in Supplemental Table 6 using inverse probability of treatment weighting.

Abbreviations: CI, confidence interval; HR, hazard ratio; ref., referent; No., number; p-y, person-years; SSRI, selective serotonin reuptake inhibitor.

**Supplemental Table 11. Association between the initiation of a higher versus lower QT-prolonging-potential SSRI and the risk of sudden cardiac death considering all possible follow-up time**

| Sudden cardiac death – primary outcome | | | | | |
|---|---|---|---|---|---|
| SSRI | n | No. of events | Rate per 1,000 p-y | Unadjusted HR (95% CI) | Adjusted HR (95% CI) |
| Lower QT-prolonging-potential | 34,722 | 688 | 65.4 | 1.00 (ref.) | 1.00 (ref.) |
| Higher QT-prolonging-potential | 30,932 | 791 | 84.3 | 1.28 (1.15, 1.42) | 1.17 (1.05, 1.29) |

An on-treatment analytic approach was used in all analyses. Fine and Gray proportional subdistribution hazards models were used to estimate the association between the initiation of higher versus lower QT-prolonging-potential SSRIs and the 1-year risk of sudden cardiac death. Higher QT-prolonging-potential SSRIs included citalopram and escitalopram. Lower-QT-prolonging potential SSRIs included fluoxetine, fluvoxamine, paroxetine, and sertraline. Adjusted analyses controlled for baseline covariates listed in Supplemental Table 6 using inverse probability of treatment weighting.

Abbreviations: CI, confidence interval; HR, hazard ratio; ref., referent; No., number; p-y, person-years; SSRI, selective serotonin reuptake inhibitor.

**Supplemental Table 12. Association between the initiation of a higher versus lower QT-prolonging-potential SSRI and the 1-year risk of the sudden cardiac death using an intent-to-treat analytic approach**

| | | | | | |
|---|---|---|---|---|---|
| **Intention-to-treat analysis** | | | | | |
| **SSRI** | **n** | **No. of events** | **Rate per 1,000 p-y** | **Unadjusted HR (95% CI)** | **Adjusted HR (95% CI)** |
| Lower QT-prolonging-potential | 34,722 | 2,015 | 74.4 | 1.00 (ref.) | 1.00 (ref.) |
| Higher QT-prolonging-potential | 30,932 | 2,184 | 92.0 | 1.22 (1.15, 1.30) | 1.13 (1.07, 1.20) |

An intention-to-treat analytic approach was used in all analyses. Fine and Gray proportional subdistribution hazards models were used to estimate the association between the initiation of a higher versus lower QT prolonging potential SSRI and the 1-year risk of sudden cardiac death. Higher QT-prolonging-potential SSRIs included citalopram and escitalopram. Lower QT-prolonging-potential SSRIs included fluoxetine, fluvoxamine, paroxetine, and sertraline. Adjusted analyses controlled for baseline covariates listed in Supplemental Table 6 using inverse probability of treatment weighting.

Abbreviations: CI, confidence interval; HR, hazard ratio; ref., referent; No., number; p-y, person-years; SSRI, selective serotonin reuptake inhibitor.

**Supplemental Table 13. Association between the initiation of an SSRI with higher versus lower QT-prolonging potential and the 1-year risk of the negative control outcome**

| Non-sudden cardiac death – negative control outcome | | | | | |
|---|---|---|---|---|---|
| SSRI | n | No. of events | Rate per 1,000 p-y | Unadjusted HR (95% CI) | Adjusted HR (95% CI) |
| Lower QT-prolonging-potential | 34,722 | 1,519 | 173.1 | 1.00 (ref.) | 1.00 (ref.) |
| Higher QT-prolonging-potential | 30,932 | 1,552 | 197.5 | 1.14 (1.06, 1.22) | 1.01 (0.95, 1.09) |

An on-treatment analytic approach was used in all analyses. Fine and Gray proportional subdistribution hazards models were used to estimate the association between the initiation of a higher versus lower QT-prolonging-potential SSRI and the 1-year risk of the negative control outcome, non-sudden cardiac death. Higher QT-prolonging-potential SSRIs included citalopram and escitalopram. Lower QT-prolonging-potential SSRIs included fluoxetine, fluvoxamine, paroxetine, and sertraline. Adjusted analyses controlled for baseline covariates listed in Supplemental Table 6 using inverse probability of treatment weighting.

Abbreviations: CI, confidence interval; HR, hazard ratio; ref., referent; No., number; p-y, person-years; SSRI, selective serotonin reuptake inhibitor.