Increased Odds of Ventricular Arrhythmias Associated with Selective Serotonin Reuptake Inhibitor Use among the Pediatric and Young Adult Population: A Case–Control Study

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Objective To measure the association between selective serotonin reuptake inhibitor (SSRI) use and out-of-hospital ventricular arrhythmia among the pediatric and young adult population.

Study design Case–control study using US claims data from 2007 to 2018. Cases were subjects with at least 1 event between ages 2 and 24 years. Controls (matched 10:1 on index date, age, sex, and continuous enrollment) had no events during study period. Independent association between current SSRI use (prescription fill with continuous exposure ending on, or after, the index date) and incident out-of-hospital ventricular arrhythmia (hospitalization or emergency room encounter with primary diagnostic code for ventricular arrhythmia) was estimated using multivariable conditional logistic regression. Separate analyses were performed for pediatric (2-17 years of age) vs young adult (18-24 years of age) subjects and between citalopram/escitalopram vs other SSRIs.

Results During the study period, 237 eligible cases were identified with 2370 matched controls. Cases were more likely to have government insurance and have a mental health, cardiac, or other complex chronic condition. Thirteen cases (5%) and 15 controls (<1%) had current SSRI exposure. After adjustment for mental health and chronic conditions, there was an increased odds of current SSRI use among cases compared with controls (OR 5.11, 95% CI 1.22-21.37). No difference was observed between pediatric and young adult ages, nor between citalopram/escitalopram and other SSRIs.

Conclusions These findings demonstrate increased odds of out-of-hospital ventricular arrhythmia associated with SSRI use in the pediatric and young adult population, suggesting a need for heightened awareness and ongoing monitoring of this potential adverse effect. *(J Pediatr 2020;226:173-8)*.

Selective serotonin reuptake inhibitors (SSRIs) are the most commonly prescribed class of antidepressants in the pediatric population.[1,2] They are currently recommended as the first-line pharmacotherapy for treatment of adolescent and childhood depression as well as pediatric obsessive compulsive disorder.[3-6] However, among the 6 available SSRIs, only 4 medications have any pediatric indications, leading to considerable off-label use in adolescents and children.[7,8] Given the significant SSRI use and degree of off-label prescribing in the pediatric population, post-marketing safety studies of this class of medications are especially important.

Compared with other classes of antidepressants, SSRIs are generally believed to be relatively safe. However, both animal and clinical data suggest varying potential for cardiac arrhythmias with SSRI use. One putative mechanism is prolongation of the QT interval, through interference with the cardiac potassium channels encoded by the human ether-a-go-go–related gene. This interference increases the risk of a certain life-threatening ventricular arrhythmia (torsade de pointes). Limited animal data demonstrate all SSRIs have some ability to interact with the human ether-a-go-go–related gene channels.[9-16] Postmarketing clinical studies show variable associations between SSRI use and QT prolongation.[17-21] Citalopram, in particular, has been most consistently reported, leading to a Drug Safety Communication and subsequent label change by the US Food and Drug Administration.[22] However, QT prolongation alone is an intermediate outcome, and it is difficult to quantify the risk for progression to ventricular arrhythmia, the true outcome of interest.

Clinical studies examining the association between life-threatening ventricular arrhythmia and SSRI use have been primarily described in overdose situations or through spontaneous reporting systems.[23-29] The 2 major adult pharmacoepidemiology studies have conflicting results, which may be due to different study designs and definitions. The case–time–control study found an increased risk of out-of-hospital cardiac arrest associated with SSRI use.[28] The comparative safety study did not demonstrate increased risk, as compared with other antidepressants, but did not include an unexposed group.[29] One pediatric study demonstrated a differential risk between SSRIs but was also a comparative safety

SSRI Selective serotonin reuptake inhibitor

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study, without an unexposed group.[30] Therefore, the primary goal of this study was to estimate the risk of out-of-hospital ventricular arrhythmia associated with SSRIs use in the pediatric and young adult population.

Methods

The Colorado Multiple Institutional Review Board reviewed this study and deemed it as non-human subjects research.

Study Design and Data Source

To examine the association between SSRI use and ventricular arrhythmia, we performed a retrospective case–control study. The data source was a 10% randomly drawn sample from the commercially available IQVIA PharMetrics Health Plan Claims Database, containing longitudinal, integrated medical and pharmacy claims data from 75 US-based managed care plans. Accessed information included patient demographics (sex, year of birth, US Census Bureau region, insurance type), medical diagnoses and procedures (according to *International Classification of Diseases, Ninth and Tenth Revisions*, and Current Procedural Terminology, version 4 codes on paid medical claims), filled medications (generic name, quantity, and days supplied, as listed on paid pharmacy claims, date filled), and provider type. All data were de-identified by the database provider before release for research use. Eligible subjects had enrollment between January 2007 and September 2017.

Outcome Measurement, Case and Control Definitions, and Selection

The primary outcome of interest was out-of-hospital ventricular arrhythmia, defined as the presence of a ventricular arrhythmia diagnostic code (427.1x, 427.4x, I47.2, I47.0, I49.0) in the primary diagnosis position. Allowable diagnoses were restricted to the primary position to reduce the risk of capturing in-hospital ventricular arrhythmias.[31,32] Furthermore, to increase the likelihood of detecting an acute event requiring emergent care or hospitalization (rather than chronic condition requiring outpatient care), only encounters with a location in the emergency department or inpatient setting were included. Cases were identified by the presence of the outcome occurring between the ages of 2 and 24 years. The lower age bound was selected to reduce the risk of misclassification, given the rarity of SSRI exposure in children younger than 2 years. Although still uncommon in the preschool age range, subjects aged 2-5 years were included because of reports describing increasing rates of mental health diagnoses and exposure to psychotropic medications.[33-35] The first event meeting outcome criteria was defined as the "index" event, with an associated "index date." No other exclusion criteria were applied at this stage, to maximize capture of all available cases.

Controls were subjects who had never had an event during the study period and were matched on 4 criteria: (1) continuous health plan enrollment during the same month as the case index date; (2) age category, defined as early childhood (2-5 years), middle childhood (6-11 years), adolescence (12-17 years), and young adult (18-24 years); (3) sex; and (4) continuous health plan enrollment started on or before the continuous health plan enrollment start date of the case. Matching on index date was based on an incidence density sampling approach, to ensure similar observation time between cases and controls and opportunity for measurement.[36] Matched controls were selected randomly from the source population at a ratio of 10:1 controls per case. The random selection approach ensured they are selected without consideration of exposure and should reflect the underlying population exposure rate (accounting for the matching variables). The 10:1 ratio was selected to maximize statistical efficiency to detect a clinically meaningful difference, assuming a relatively low exposure rate and small number of cases.[37]

Primary Medication Exposure of Interest

The primary exposure of interest was the SSRI medication class (citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline). Exposure was defined by the presence of at least 1 prescription fill for any SSRI, as identified by a Medi-Span General Product Identifier code beginning with "5816" within 365 days before the index date. The continuous exposure period was calculated as days between the first prescription fill date and last prescription fill date + days supplied, allowing for a 14-day gap. Because the proposed mechanism for increased risk of ventricular arrhythmia and cardiac arrest requires presence of medication within the body, the main focus of exposure was proximate to the index date. Continuous exposure longer than 365 days was censored due to the risk of a "healthy user effect," ie, subjects with prolonged exposure may have lower risk allowing them to continue medication use.

SSRI exposure was categorized as current or recent based on the most recent continuous exposure period for each SSRI. Exposure periods ending on or later than the index date were classified as "current use." Recent use was classified as continuous exposure periods ending either (1) within 30 days before the index date, or (2) within 60 days before the index date (**Figure**). Each SSRI medication has a different half-life, with the longest half-life occurring with fluoxetine (between 5 and 7 days).[38] Given unknown individual pharmacokinetics, selecting 30-day and 60-day windows allows for likely sufficient lag time between "end of exposure" and complete elimination from the body. Finally, because there has been specific attention drawn to citalopram regarding a risk of QT prolongation and therefore, ventricular arrhythmia, the individual SSRIs will be categorized into citalopram or escitalopram exposure, and other SSRIs, to assess for differential risk associated with the outcome.

Statistical Analyses

Descriptive statistics were used to characterize the population of cases and controls. Comparative testing of demographic variables and other potential covariates was

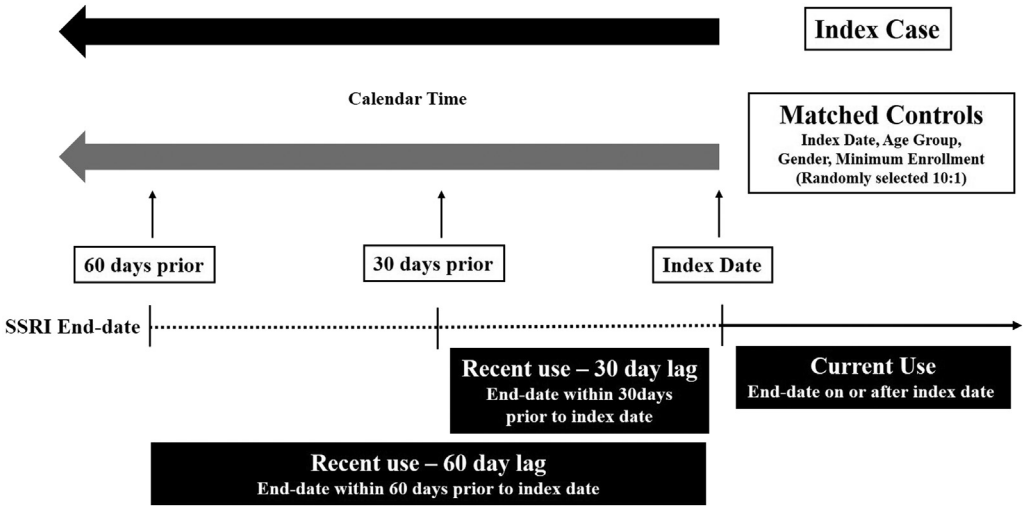

Figure. Illustration of SSRI use categorization based on exposure end-date.

performed using χ^2 analyses. To account for matching, conditional logistic regression was performed to estimate the association between exposure and outcome, presented as ORs with 95% CIs. The primary analysis focused upon the association between current SSRI exposure (vs noncurrent SSRI use) and the outcome. Unadjusted regression was initially performed, followed by multivariable regression to adjust for potential confounders. Candidate variables for inclusion in multivariable regression were: geographic region, insurance type, presence or absence of mental health diagnoses, presence or absence of other cardiac diagnoses, presence or absence of other non-cardiac complex chronic conditions, and exposure to medications categorized as known risk for QT prolongation or conditional risk for QT prolongation by the CredibleMeds, previously the federally funded Arizona Center for Education and Research on Therapeutics (**Tables I-IV**; available at www.jpeds.com).[39,40] Backwards elimination was performed to determine the final multivariable model. Inclusion was based on a significant change in the risk estimate when removed from the model (defined by ≥10%), and significant likelihood ratio test when comparing the nested model to fuller model. The only exception was the previous cardiac diagnoses, which was included a priori, based on high likelihood of confounding. Age, sex, and calendar time, as matching variables, were not included in the multivariable model. The final adjustment variables identified for the main model (current SSRI exposure) were used in all subsequent exploratory analyses and sensitivity analyses. Separate analyses were performed for cases that occurred in the pediatric age range (defined as 2-17 years) and cases that occurred during the young adult age range (18-24 years) to test the hypothesis of effect modification by age. Similarly, separate analyses were performed comparing citalopram/escitalopram exposure and other SSRI exposure to unexposed.

Prespecified Sensitivity Analyses

Separate sensitivity analyses were performed varying the definition of current exposure to allow for lag times of 30 days or 60 days. The lag times were selected based on the pharmacokinetics of SSRIs, with complete elimination expected by the end of 30 days for most people.

Results

During the study period, 8787 subjects had at least one out-of-hospital ventricular arrhythmia event. Among those subjects, 237 (2.7%) had an event occurring between the ages of 2 and 24 years and thus were identified as cases. The encounter location was inpatient for 196 cases (83%) and emergency department for 41 cases (17%). The matched controls were randomly sampled from the remaining 10 761 406 subjects without an event, resulting in 2370 control subjects.

As expected, due to matching, the age, sex, and year of index date were the same between cases and controls (**Table V**). The distribution of age and sex within the cases, however, did demonstrate more events occurring as a young adult (ages 18-24 years) than pediatric (ages 2-17 years) and slightly more male than female subjects. Furthermore, more events occurred during the first 5 years of the dataset than the second 5 years. When we compared cases and controls, there was some regional variation, with slightly more cases in the East region of the US and fewer in the Midwest and South regions. Cases were slightly more likely to have government-based insurance than controls. They were more likely to have a mental health diagnosis before the index date, including depression diagnosis. They also more frequently had both non-outcome cardiac diagnoses and other non-cardiac complex chronic conditions before the index date. No subject (case or control) had prescription fills for any of the medications associated with high- or conditional risk of QT prolongation. A small number of

Table V. Demographics of cases and controls

Demographics	Cases N = 237	Controls* N = 2370
Age at index date, y, n (%)		
2-5	12 (5%)	120 (5%)
6-11	26 (11%)	260 (11%)
12-17	65 (27%)	650 (27%)
18-24	134 (57%)	1340 (57%)
Male sex	131 (55%)	1310 (55%)
Index year		
2007-2012	154 (65%)	1540 (65%)
2013-2017	83 (35%)	830 (35%)
Region,† n (%)		
East	67 (28%)	430 (18%)
Midwest	57 (24%)	723 (31%)
South	68 (29%)	748 (32%)
West	45 (19%)	469 (19%)
Insurance type,† n (%)		
Private	154 (65%)	1706 (72%)
Public	60 (25%)	399 (17%)
Self-pay/unknown	23 (10%)	265 (11%)
Previous any mental health diagnosis,† n (%)	82 (35%)	260 (11%)
Previous depression diagnosis,† n (%)	31 (31%)	85 (4%)
Previous other cardiac diagnosis,† n (%)	183 (77%)	37 (2%)
Previous chronic complex condition,† n (%)	47 (20%)	28 (1%)
Other antidepressants (ever),† n (%)		
Bupropion	5 (2%)	17 (<1%)
SNRI	5 (2%)	12 (<1%)
Tricyclic/tetracyclic	4 (2%)	7 (<1%)

SNRI, serotonin-norepinephrine reuptake inhibitor.
*Matched on index month, sex, age category, and enrollment.
†$P < .05$ by χ^2 test.

both cases and controls had prescription fills for other non-SSRI antidepressants before the index date, but not concurrently with SSRI exposure.

Among the subjects, 28 had current exposure to 1 of the SSRIs; 13 were cases (5%) and 15 were controls (<1%) (**Table VI**). The most common SSRI exposure was sertraline, followed by fluoxetine. No subjects had current use of fluvoxamine, and there was no concurrent use of more than one SSRI. A small number of additional subjects had a recent exposure to SSRIs, with continuous use ending within 30 or 60 days, although the majority ended more than 60 days before the index date.

To test the main effect of current SSRI exposure, both unadjusted and adjusted conditional regression without any continuous enrollment requirements was performed. The final multivariable model adjusted for previous mental health diagnoses, previous non-event cardiac diagnoses, and previous non-cardiac complex chronic conditions. The unadjusted OR for the outcome associated with current SSRI was 9.88 (95% CI 4.48-21.80) (**Table VII**). After adjustment for other potential confounders, the odds associated with current SSRI remained elevated but with smaller effect size and wider CIs (aOR 5.11, 95% CI 1.22-21.37). Separate analyses for pediatric (age 2-17 years) and young adult (age 18-24 years) demonstrated elevated unadjusted ORs with overlapping CIs. However, once adjusted for other factors, although the odds remained increased, the CIs for both widened considerably to now include the null effect. Similarly, examining the association between citalopram or escitalopram current exposure and outcome, the unadjusted ORs were elevated with significant confidence bounds but with adjustment, the effect size was smaller with loss of statistical significance. However, other SSRIs, in combination, had significantly elevated unadjusted and adjusted odds ratios associated with the outcome.

In general, allowing a lag between the index date and the end of continuous exposure period did not significantly affect the risk estimate. The aOR for current plus either 30-day or 60-day lag times remained elevated and significant (**Table VIII**; available at www.jpeds.com).

Table VI. SSRI exposure between cases and controls

SSRI Exposure Categories	Cases N = 237	Controls* N = 2370
Any current SSRI use,† n (%)	13 (5%)	15 (0.63%)
Current citalopram use, n (%)	3 (1%)	1 (0.04%)
Current escitalopram use, n (%)	0 (0%)	4 (0.17%)
Current fluoxetine use, n (%)	4 (2%)	5 (0.21%)
Current fluvoxamine use, n (%)	0	0
Current paroxetine use, n (%)	1 (0.42%)	0
Current sertraline use, n (%)	5 (2%)	5 (0.21%)
Any recent SSRI use ending: n (%)		
Within 30 d of index date	2 (0.84%)	8 (0.34%)
Within 60 d of index date	0	2 (0.08%)

*Matched on index month, sex, age category, and enrollment.
†Censored at 365 days.

Discussion

In this case–control study, drawn from a large national dataset, we observed an increased odds of current SSRI use among cases with out-of-hospital ventricular arrhythmia compared with controls in the pediatric and young adult population. This effect was persistent, even after adjustment for important confounders, and with sensitivity analyses. We could not demonstrate differential effects by age (pediatric vs young adult), nor a heightened odds for citalopram/escitalopram users compared with other SSRIs.

The demonstrated SSRI effect is consistent with the observed effects on QT prolongation and adult studies of out-of-hospital cardiac arrest and SSRI use compared with unexposed.[17,26-28] The associated risk estimates were lower in those studies than observed in this study, albeit with overlapping CIs. The higher estimate may be due to difference in outcome measurement, differences in study design, and confounder adjustment or differential effects among children and young adults as compared with older adults. We chose to not include the cardiac arrest diagnostic codes, as commonly applied in adult studies, because of the high risk of misclassification with the high rate of non-cardiac causes of cardiac arrest in pediatrics.[31] Thus, the narrower definition might have impacted the estimate, although difficult to assess the directionality. Including hospitalizations may increase the potential for misclassifying in-hospital events as out-of-hospital events. However, we did restrict diagnoses to the

Table VII. Association between current SSRI and outcome

SSRI Exposure Categories	Unadjusted cOR (95% CI)	Adjusted cOR (95% CI)
Current SSRI (vs unexposed)	9.88 (4.48-21.80)	5.11 (1.22-21.37)
Current SSRI – pediatric age (2-17 y)	17.80 (3.21-98.52)	21.97 (0.50-961.42)
Current SSRI – young adult age (18-24 y)	8.29 (3.35-20.53)	3.61 (0.80-16.27)
Current citalopram or escitalopram	6.52 (1.54-27.51)	2.17 (0.17-27.25)
Current other SSRI	11.80 (4.62-30.16)	15.90 (3.04-82.98)

cOR, conditional Odds Ratio.

primary position only, based on previous data suggesting improved separation between out-of-hospital and in-hospital events. The compromise would be decreased case ascertainment through lost out-of-hospital events.[31,32] Furthermore, the considerably older age of most adult studies likely results in a very different baseline risk, thus, "diluting" any medication effect. Finally, the outcome was extremely rare (approximately 200 cases in more than 10 million subjects). Therefore, although we were able to capture all cases in this population, adjustment for potential confounders widened confidence intervals considerably.

Based on these results, there does not appear to be heightened odds associated with citalopram/escitalopram as compared with other SSRIs, a contrary finding to other studies of out-of-hospital cardiac arrest and QT prolongation.[17,18,21,23,24,30] There are several potential explanations for this apparent discrepancy. First, prolonged QT may confer a certain degree of risk but does not guarantee development of a life-threatening arrhythmia.[41] It may be that a certain threshold must be reached, or other modifying factors present, to progress to arrhythmia. This hypothesis would be supported by the case reports and series describing adverse cardiac effects of citalopram in overdose situations, and the US Food and Drug Administration adult crossover study demonstrating greater prolongation with higher doses.[22-24] Second, the effects may truly differ by age and younger people may be less susceptible to the electrophysiologic changes associated with citalopram/escitalopram. Although there is currently insufficient data to support this hypothesis, there have been historical examples of differential medication effects by age.[42,43] In addition, although the focus of attention has been QT prolongation, the outcome measure is not specific for torsade de pointes, and thus, the underlying mechanism may be different than QT prolongation. Finally, perhaps there is a true difference but the rarity of the event limited our ability to improve precision around estimates.

Several limitations of this study should be acknowledged. As an observational study, we are limited in our ability to establish causation in the measured associations. In addition, we used an administrative database, which allows for study of a very rare outcome. However, reliance on coding data risks misclassification of outcome, exposure, and adjustment variables. The degree and type of misclassification (ie, differential vs nondifferential), however, is uncertain and therefore, direction of impact is unknown. In addition, because of the rarity of the event, the ability to adjust for confounding and perform separate analyses assessing for effect modification with precision was limited, even with such a large underlying sample. Thus, although the lower confidence bounds remained elevated, the strength of the association could be considerably weaker or stronger than the OR would suggest. Similarly, we were unable to examine any potential dose-dependent effect with sufficient precision to draw meaningful conclusions.

The results suggest a need for heightened awareness and ongoing monitoring of this adverse effect of SSRIs in the pediatric and young adult population. Furthermore, clinicians should carefully consider this potential risk during shared decision-making, weighing against the known therapeutic benefits. The risk–benefit balance may differ between a child with no other health conditions and a single mental health condition and another child with multiple chronic health conditions on multiple medications. Additional studies should be performed to confirm these findings before any policy changes can be recommended, to avoid unintended secondary consequences as was observed with suicidality and antidepressants. Therefore, ongoing efforts to perform rigorous pediatric-focused pharmacoepidemiologic studies will ensure the safety of these medications. ■

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Table I. Diagnostic codes for mental health diagnoses

ICD-9 descriptions	ICD-9 codes	ICD-10 descriptions	ICD-10 codes
Depression			
Major depressive disorder, atypical depressive disorder	296.2x, 296.3; 296.82	Major Depressive Disorder	F32.x, F33.x
Dysthymic disorder	300.4	Dysthymic Disorder	F34.1
Adjustment disorder with mixed anxiety and depressed mood	309.28	Adjustment Disorder with mixed anxiety and depressed mood	F43.23
Depressive disorder, NEC	311		
Attention-deficit hyperactivity disorder			
Hyperkinetic syndrome of childhood	314	ADHD	F90
Anxiety disorders			
Anxiety, dissociative and somatoform disorders, *except* dysthymic condition	300* except 330.4	Anxiety, dissociative and somatoform disorders, except adjustment disorder with mixed anxiety and depressed mood	F40-F48
Other mood disorders			
Episodic mood disorders, except depressive diagnoses	296, except 296.2*, 296.3*	Mood [affective] disorders, except Dysthymia and Depression	F30-F39, except F32, F33, F34.1
Pervasive developmental disorders			
Pervasive developmental disorders	299	Pervasive Developmental Disorders	F84
Psychotic disorders			
Transient mental disorders due to conditions classified elsewhere, schizophrenic disorders, delusional disorders, other nonorganic psychoses	293*, 295*, 297*, 298*	Schizophrenia, schizotypal, delusional, and other non-mood psychotic disorders	F20-F29
Substance use disorders			
Alcohol dependence, drug dependence, nondependent abuse of drugs	303-305	Mental and behavioral disorders due to psychoactive substance use	F10-F19
Other mental health disorders			
All other MH diagnoses, not specified above	290-316, except 309.28 and 311	All other MH diagnoses, not specified above	F01-F69, F80-F99

ICD-9, *International Classification of Diseases, Ninth Revision*; *ICD-10*, *International Classification of Diseases, Tenth Revision*; *MH*, mental health; *NEC*, not elsewhere classified.

Table II. Diagnostic codes for other cardiac conditions

Descriptions	ICD-9 codes	ICD-10 codes
Other cardiac disorders		
Other arrhythmias	426.0-427.4 excluding 427.1, 427.4 427.6-427.9	I44, I45, I47, I48, I49.0, except I47.0, I47.2, I49.0 I49.1-I49.5, I49.8, I49.9, R00.1
Cardiomyopathy	425.0-425.4, 425.8, 429.1	I42, I43, I51.5
Heart and great vessel malformations	745.0-745.3, 745.60-745.69, 746, 747.1-747.49, 747.81, 747.89, Procedure Codes: 35.8, 35.81, 35.82, 35.83, 35.84	Q20, Q21.2-Q24, Q25.1-Q26, Q28.2, Q28.3, Q28.9 Procedure Codes: 02170ZP, 02170ZQ, 02170ZR, 02BK0ZZ, 02LR0ZT, 02LS0ZZ, 02LT0ZZ, 02NH0ZZ, 02RK0JZ, 02RL0JZ, 02RM0JZ, 02RP0JZ, 02RQ07Z, 02RQ0JZ, 02RR07Z, 02RR0JZ, 02SP0ZZ, 02SW0ZZ, 02U70JZ, 02UA0JZ, 02UA3JZ, 02UA4JZ, 02VR0ZT, 02WA0JZ
Endocardium diseases	424.0, 424.2, 424.3	I34.0, I34.8, I36.0, I36.8, I37.0, I37.8
Heart transplant	996.83,V42.1, V42.2, V43.2, Procedure Codes: 37.5, 37.51	T86.20-T86.22, Z94.1 Procedure Codes: 02YA0Z0, 02YA0Z1, 02YA0Z2
Other cardiovascular disorders	416.1, 416.8, 416.9, 428.0, 429.3, 428.83, 433.11, V45.81	I27.0, I27.1, I27.2, I27.81, I27.89, I27.9, I50.9, I51.7, I51.81, I63.139, I63.239, Z95.1

Table III. Diagnostic codes for noncardiac complex chronic conditions*

Descriptions	ICD-9 codes	ICD-10 codes
Neurologic and neuromuscular		
Brain and spinal cord malformations	740.0-742.9	Q00-Q07, G90.1
Mental retardation	318.0-318.2	F71-F73
CNS degeneration and diseases	330.0-330.9, 334, 335.0-335.9, 331.1, 331.11, 331.19, 331.4, 331.8, 331.89, 331.9, 333.2, 336.1, 336.8, 337.9, 759.5	E75.0, E75.1, E75.2, E75.4, F84.2, G11.1-G11.4, G11.8, G11.9, G12.0-G12.2, G12.8, G12.9, G31.01, G31.09, G31.8, G31.89, G32.89, G93.8, G93.9, G94, G91.1, G31.9, G25.3, G95.19, G95.89, G90.9, Q85.1
Infantile cerebral palsy	343.0-343.9	G80
Epilepsy	345.01, 345.11, 345.3, 345.41, 345.61, 345.71, 345.81, 345.91	G40.311, G40.301, G40.211, G40.219, G40.411, G40.419, G40.111, G40.119, G40.804, G40.911, G40.919
Other disorders of CNS	341.8, 342.90, 344.0, 344.81, 344.9, 348.1, 348.4, 780.03, 01.52, 01.53	G37.1, G37.2, G37.8, G81.90, G82.90, G82.50-G82.54, G83.5, G83.9, G93.1, G93.5, R40.3, 0016070, 0016071, 0016072, 0016073, 0016074, 0016075, 0016076, 0016077, 0016078, 001607B, 0016370, 0016371, 0016372, 0016373, 0016374, 0016375, 0016376, 0016377, 0016378, 001637B, 001U074, 001U076, 001U077, 001U079, 001U374, 001U376, 001U377, 001U379, 00B70ZZ, 00B73ZZ, 00B74ZZ, 00T70ZZ, 00T73ZZ, 00T74ZZ
Occlusion of cerebral arteries	434.01, 434.91	I63.30, I63.50
Muscular dystrophies and myopathies	359.0-359.3	G71, G72
Movement diseases	332.0, 332.1, 333.0, 333.2,33.4, 333.5, 333.7, 333.9	G10, G20, G21.0, G21.11, G21.19, G21.8, G23.0-G23.2, G23.8, G24.02, G24.8, G25.3-G25.5, G25.81-G25.83, G25.89, G25.9, G80.3
Devices	996.2, 996.63, V45.2, V53.01, V53.02, 02.2, 02.21, 02.22, 02.3, 02.31, 02.32, 02.33, 02.34, 02.35, 02.39, 02.4, 02.41, 02.42, 02.93, 03.7, 03.71, 03.72. 03.79, 03.93, 03.97, 04.92	T85.09XA, T85.190A, T85.192A, T85.199A, T85.79XA, Z98.2, Z45.41, Z45.42, 00160J0, 00160J1, 00160J2, 00160J3, 00160J4, 00160J5, 00160J6, 00160J7, 00160J8, 00160JB, 00160K0, 00160K1, 00160K2, 00160K3, 00160K4, 00160K5, 00160K6, 00160K7, 00160K8, 00160KB, 00163J0, 00163J1, 00163J2, 00163J3, 00163J4, 00163J5, 00163J6, 00163J7, 00163J8, 00163JB, 00163K0, 00163K1, 00163K2, 00163K3, 00163K4, 00163K5, 00163K6, 00163K7, 00163K8, 00163KB, 001U0J4, 001U0J6, 001U0J7, 001U0J9, 001U0K4, 001U0K6, 001U0K7, 001U0K9, 001U3J4, 001U3J6, 001U3J7, 001U3J9, 001U3K4, 001U3K6, 001U3K7, 001U3K9, 009600Z, 009630Z, 009640Z, 00H00MZ, 00H03MZ, 00H04MZ, 00H60MZ, 00H63MZ, 00H64MZ, 00HE0MZ, 00HE3MZ, 00HE4MZ, 00HU0MZ, 00HU3MZ, 00HU4MZ, 00HV0MZ, 00HV3MZ, 00HV4MZ, 00W60JZ, 00W63JZ, 00W64JZ, 00WU0JZ, 00WU3JZ, 00WU4JZ, 01HY0MZ, 01HY3MZ, 01HY4MZ, 0DH60MZ, 0DH63MZ, 0DH64MZ, 0W110J9, 0W110JB, 0W110JG, 0W110JJ, 3E1Q38X, 3E1Q38Z
Respiratory		
Respiratory malformations	748.0-748.9	Q30-Q34, P280
Chronic respiratory diseases	327.25, 416.2, 516.3, 516.31, 518.84, 770.4, V45.76	G47.35, I27.82, I43, J84.112, J96.20, Z90.2
Cystic fibrosis	277	E84
Other	30.3, 30.4, 32.4, 32.41, 32.49, 32.5, 32.50, 32.59	0B110Z4, 0B113Z4, 0B114Z4, 0BTC0ZZ, 0BTC4ZZ, 0BTD0ZZ, 0BTD4ZZ, 0BTF0ZZ, 0BTF4ZZ, 0BTG0ZZ, 0BTG4ZZ, 0BTJ0ZZ, 0BTJ4ZZ, 0BTK0ZZ, 0BTK4ZZ, 0BTL0ZZ, 0BTL4ZZ, 0BTM0ZZ, 0BTM4ZZ, 0CTS0ZZ, 0CTS4ZZ, 0CTS7ZZ, 0CTS8ZZ
Devices	519.0, V44.0, V55.0, V46.0, V46.1, 31.2, 31.21, 31.29, 31.41, 31.74, 33.21, 34.85, 96.55, 97.23	J95.00-J95.04, J95.09, Z43.0, Z93.0, Z99.0, J95.850, Z99.11, Z99.12, 0B110F4, 0B113F4, 0B114F4, 0B21XFZ, 0BHR0MZ, 0BHR3MZ, 0BHR4MZ, 0BHS0MZ, 0BHS3MZ, 0BHS4MZ, 0BW10FZ, 0BW13FZ, 0BW14FZ, 0JH604Z, 0JH634Z, 0JH804Z, 0JH834Z, 0WQ6XZ2, 3E1F78Z
Transplantation	996.84,V42.6, 33.5, 33.50, 33.51, 33.52, 33.6	T86.810, T86.811, T86.819, Z94.2, 0BYC0Z0, 0BYC0Z1, 0BYC0Z2, 0BYD0Z0, 0BYD0Z1, 0BYD0Z2, 0BYF0Z0, 0BYF0Z1, 0BYF0Z2, 0BYG0Z0, 0BYG0Z1, 0BYG0Z2, 0BYH0Z0, 0BYH0Z1, 0BYH0Z2, 0BYJ0Z0, 0BYJ0Z1, 0BYJ0Z2, 0BYK0Z0, 0BYK0Z1, 0BYK0Z2, 0BYL0Z0, 0BYL0Z1, 0BYL0Z2, 0BYM0Z0, 0BYM0Z1, 0BYM0Z2

(*continued*)

Table III. Continued

Descriptions	ICD-9 codes	ICD-10 codes
Renal and urologic		
Congenital anomalies	753.0-753.9	Q60-Q64
Chronic renal failure	585	N18
Other	V45.73, V45.74, 55.5, 55.51, 55.52, 55.53, 55.54, 56.4, 56.41, 56.42, 56.7, 56.71, 56.79, 57.7, 57.71, 57.79	Z90.5, Z90.6, 0T160Z8, 0T160ZA, 0T164Z8, 0T164ZA, 0T170Z8, 0T170ZA, 0T174Z8, 0T174ZA, 0T180Z8, 0T180ZA, 0T184Z8, 0T184ZA, 0TB60ZZ, 0TB63ZZ, 0TB64ZZ, 0TB67ZZ, 0TB68ZZ, 0TB70ZZ, 0TB73ZZ, 0TB74ZZ, 0TB77ZZ, 0TB78ZZ, 0TT00ZZ, 0TT04ZZ, 0TT10ZZ, 0TT14ZZ, 0TT20ZZ, 0TT24ZZ, 0TT60ZZ, 0TT64ZZ, 0TT67ZZ, 0TT68ZZ, 0TT70ZZ, 0TT74ZZ, 0TT77ZZ, 0TT78ZZ, 0TTB0ZZ, 0TTB4ZZ, 0TTB7ZZ, 0TTB8ZZ, 0TTD0ZZ, 0TTD4ZZ, 0TTD7ZZ, 0TTD8ZZ
Chronic bladder diseases	344.61, 596.4, 596.53, 596.54	G83.4, N31.2, N31.9
Devices	996.68, V44.5, V44.6, V45.1, V53.6, V55.5, V55.6, 38.95, 39.27, 39.42, 39.93, 39.94, 39.95, 54.98, 55.02, 55.03, 55.04, 55.12, 55.93, 55.94, 55.97, 56.5, 56.51, 56.52, 56.6, 56.61, 56.62, 56.72, 56.73, 56.74, 56.75, 57.2, 57.21, 57.22, 59.93, 59.94, 86.07, 96.45, 96.46, 96.47	T85.71XA, Z93.50-Z93.52, Z93.59, Z93.6, Z91.15, Z99.2, Z43.5, Z43.6, Z46.6, 031209D, 031209F, 03120AD, 03120AF, 03120JD, 03120JF, 03120KD, 03120KF, 03120ZD, 03120ZF, 031309D, 031309F, 03130AD, 03130AF, 03130JD, 03130JF, 03130KD, 03130KF, 03130ZD, 03130ZF, 031409D, 031409F, 03140AD, 03140AF, 03140JD, 03140JF, 03140KD, 03140KF, 03140ZD, 03140ZF, 031509D, 031509F, 03150AD, 03150AF, 03150JD, 03150JF, 03150KD, 03150KF, 03150ZD, 03150ZF, 031609D, 031609F, 03160AD, 03160AF, 03160JD, 03160JF, 03160KD, 03160KF, 03160ZD, 03160ZF, 031709D, 031709F, 03170AD, 03170AF, 03170JD, 03170JF, 03170KD, 03170KF, 03170ZD, 03170ZF, 031809D, 031809F, 03180AD, 03180AF, 03180JD, 03180JF, 03180KD, 03180KF, 03180ZD, 03180ZF, 031909F, 03190AF, 03190JF, 03190KF, 03190ZF, 031A09F, 031A0AF, 031A0JF, 031A0KF, 031A0ZF, 031B09F, 031B0AF, 031B0JF, 031B0KF, 031B0ZF, 031C09F, 031C0AF, 031C0JF, 031C0KF, 031C0ZF, 03WY0JZ, 03WY3JZ, 03WY4JZ, 03WYXJZ, 05HY33Z, 06HY33Z, 0JH60WZ, 0JH60XZ, 0JH63WZ, 0JH63XZ, 0JH80WZ, 0JH80XZ, 0JH83WZ, 0JH83XZ, 0JHD0WZ, 0JHD0XZ, 0JHD3WZ, 0JHD3XZ, 0JHF0WZ, 0JHF0XZ, 0JHF3WZ, 0JHF3XZ, 0JHL0WZ, 0JHL0XZ, 0JHL3WZ, 0JHL3XZ, 0JHM0WZ, 0JHM0XZ, 0JHM3WZ, 0JHM3XZ, 0T130ZB, 0T134ZB, 0T140ZB, 0T144ZB, 0T16079, 0T1607C, 0T1607D, 0T160J9, 0T160JC, 0T160JD, 0T160K9, 0T160KC, 0T160KD, 0T160Z9, 0T160ZC, 0T160ZD, 0T163JD, 0T16479, 0T1647C, 0T1647D, 0T164J9, 0T164JC, 0T164JD, 0T164K9, 0T164KC, 0T164KD, 0T164Z9, 0T164ZC, 0T164ZD, 0T17079, 0T1707C, 0T1707D, 0T170J9, 0T170JC, 0T170JD, 0T170K9, 0T170KC, 0T170KD, 0T170Z9, 0T170ZC, 0T170ZD, 0T173JD, 0T17479, 0T1747C, 0T1747D, 0T174J9, 0T174JC, 0T174JD, 0T174K9, 0T174KC, 0T174KD, 0T174Z9, 0T174ZC, 0T174ZD, 0T18079, 0T1807C, 0T1807D, 0T180J9, 0T180JC, 0T180JD, 0T180K9, 0T180KC, 0T180KD, 0T180Z9, 0T180ZC, 0T180ZD, 0T183JD, 0T18479, 0T1847C, 0T1847D, 0T184J9, 0T184JC, 0T184JD, 0T184K9, 0T184KC, 0T184KD, 0T184Z9, 0T184ZC, 0T184ZD, 0T1B0ZD, 0T1B4ZD, 0T25X0Z, 0T29X0Z, 0T29XYZ, 0T2BX0Z, 0T9000Z, 0T9030Z, 0T9040Z, 0T9070Z, 0T9080Z, 0T9100Z, 0T9130Z, 0T9140Z, 0T9170Z, 0T9180Z, 0T9370Z, 0T9380Z, 0T9470Z, 0T9480Z, 0TQ67ZZ, 0TQ77ZZ, 3E1K38Z, 3E1M39Z, 5A1D60Z
Transplantation	996.81,V42.0, 55.6, 55.61, 55.69	T86.10-T86.12, Z94.0, 0TY00Z0, 0TY00Z1, 0TY00Z2, 0TY10Z0, 0TY10Z1, 0TY10Z2
Gastrointestinal		
Congenital anomalies	750.3, 751.1-751.9	Q39.0-Q39.4, Q41-Q45
Chronic liver disease and cirrhosis	571.4-571.9	K73, K74, K75.4, K760-K763, K765, K768
Inflammatory bowel diseases	555.0-556.9	K50, K51

(*continued*)

Table III. Continued

Descriptions	ICD-9 codes	ICD-10 codes
Other	453.0, 557.1, 560.2, 564.7, V45.3, V45.72, V45.75, 25.3, 25.4, 42.42, 43.9, 43.91, 43.99, 45.63, 45.8, 45.81, 45.82, 45.83, 50.4, 52.6, 52.7, 54.71	I82.0, K55.1, K56.2, K59.3, Z98.0, Z90.3, Z90.49, 0CT70ZZ, 0CT7XZZ, 0D13079, 0D1307A, 0D1307B, 0D1607A, 0D160ZA, 0DT50ZZ, 0DT54ZZ, 0DT57ZZ, 0DT58ZZ, 0DT60ZZ, 0DT64ZZ, 0DT67ZZ, 0DT68ZZ, 0DT80ZZ, 0DT84ZZ, 0DT87ZZ, 0DT88ZZ, 0DT90ZZ, 0DT94ZZ, 0DT97ZZ, 0DT98ZZ, 0DTE0ZZ, 0DTE4ZZ, 0DTE7ZZ, 0DTE8ZZ, 0FT00ZZ, 0FT04ZZ, 0FTG0ZZ, 0FTG4ZZ
Devices	536.4, V44.1-V44.4, V53.50, V53.51, V53.59, V55.1-V55.4, 42.1, 42.10, 42.11, 42.81, 43.1, 43.11, 43.19, 44.12, 44.3, 44.32, 44.38, 44.39, 46.1, 46.13, 46.2, 46.22, 46.23, 46.3, 46.32, 46.4, 46.40, 46.41, 46.43, 96.24, 96.36, 97.02	K94.20, K94.22, K94.23, K94.29, Z93.1-Z93.4, Z43.1-Z43.4, Z46.51, Z46.59, 0D11074, 0D110J4, 0D110K4, 0D110Z4, 0D113J4, 0D11474, 0D114J4, 0D114K4, 0D114Z4, 0D15074, 0D150J4, 0D150K4, 0D150Z4, 0D153J4, 0D15474, 0D154J4, 0D154K4, 0D154Z4, 0D16074, 0D160J4, 0D160J9, 0D160JA, 0D160K4, 0D160K9, 0D160KA, 0D160Z4, 0D163J4, 0D16474, 0D164J4, 0D164J9, 0D164JA, 0D164K4, 0D164K9, 0D164KA, 0D164Z4, 0D16874, 0D168J4, 0D168J9, 0D168JA, 0D168K4, 0D168K9, 0D168KA, 0D168Z4, 0D1B0Z4, 0D1B4Z4, 0D1B8Z4, 0D1H0Z4, 0D1H4Z4, 0D1H8Z4, 0D1K0Z4, 0D1K4Z4, 0D1K8Z4, 0D1L0Z4, 0D1L4Z4, 0D1L8Z4, 0D1N0Z4, 0D1N4Z4, 0D1N8Z4, 0D20X0Z, 0D20XUZ, 0D20XYZ, 0D787ZZ, 0D7E7ZZ, 0DBB7ZZ, 0DH50DZ, 0DH50UZ, 0DH53DZ, 0DH53UZ, 0DH54DZ, 0DH54UZ, 0DH57DZ, 0DH57UZ, 0DH58DZ, 0DH58UZ, 0DH63UZ, 0DH64UZ, 0DHA3UZ, 0DHA4UZ, 0DHA8UZ, 0DN87ZZ, 0DNE7ZZ, 0DW04UZ, 0DW08UZ, 0WQFXZ2, 3E1G78Z, 3E1H78Z
Transplantation	996.82,996.86,996.87,V42.7, V42.83, V42.84, 46.97, 50.5, 50.51, 50.59, 52.8, 52.80, 52.82, 52.83, 52.84, 52.85, 52.86	T86.40-T86.42, T86.890, T86.891, T86.899, T86.850, T86.851, T86.859, Z94.4, Z94.82, Z94.83, 0DY80Z0, 0DY80Z1, 0DY80Z2, 0DYE0Z0, 0DYE0Z1, 0DYE0Z2, 0FY00Z0, 0FY00Z1, 0FY00Z2, 0FYG0Z0, 0FYG0Z1, 0FYG0Z2, 3E030U0, 3E030U1, 3E033U0, 3E033U1, 3E0J3U0, 3E0J3U1, 3E0J7U0, 3E0J7U1, 3E0J8U0, 3E0J8U1
Hematologic or immunologic		
Hereditary anemias	282.0-282.6	D55-D58
Aplastic anemias	284	D60-D61, D71
Hereditary immunodeficiency	279.0-279.9, 288.1, 288.2, 446.1	D80-D89, D72.0, M30.3, M35.9
Coagulation/hemorrhagic	286.0, 286.3, 287.32, 287.33, 287.39	D66, D68.2, D69.41, D69.42, D69.49
Leukopenia	288.01, 288.02	D70.0, D70.4
Hemophagocytic Syndromes	288.4	D76.1-D76.3
Sarcoidosis	135	D86.9
Acquired immunodeficiency	042-044	B20-B24
Polyarteritis nodosa and related conditions	446.0, 446.21, 446.4-446.7	M30.0, M31.0, M31.1, M31.30, M31.4, M31.6
Diffuse diseases of connective tissue	710.0, 710.1, 710.3	M32.10, M33.90, M34.0, M34.1, M34.9
Other	41.5	07TP0ZZ, 07TP4ZZ
Devices	N/A	N/A
Transplantation	41.00, 41.01, 41.02, 41.03, 41.04, 41.05, 41.06, 41.07, 41.08, 41.09, 41.94	07YP0Z0, 07YP0Z1, 07YP0Z2, 30230AZ, 30230G0, 30230G1, 30230X0, 30230X1, 30230Y0, 30230Y1, 30233AZ, 30233G0, 30233G1, 30233X0, 30233X1, 30233Y0, 30233Y1, 30240AZ, 30240G0, 30240G1, 30240X0, 30240X1, 30240Y0, 30240Y1, 30243AZ, 30243G0, 30243G1, 30243X0, 30243X1, 30243Y0, 30243Y1, 30250G0, 30250G1, 30250X0, 30250X1, 30250Y0, 30250Y1, 30253G0, 30253G1, 30253X0, 30253X1, 30253Y0, 30253Y1, 30260G0, 30260G1, 30260X0, 30260X1, 30260Y0, 30260Y1, 30263G0, 30263G1, 30263X0, 30263X1, 30263Y0, 30263Y1
Metabolic		
Amino acid metabolism	270.0-270.9	E70.0, E70.2, E70.3, E70.4, E70.8, E71.0-E71.5, E72.0-E72.4, E72.8, E72.9
Carbohydrate metabolism	271.0-271.9	E74.0-E74.4, E74.8, E74.9
Lipid metabolism	272.0-272.9	E75, E77.0, E77.1, E78.0-E78.4, E78.5-E78.9, E88.1, E88.8
Storage disorder	277.3, 277.5	E76.0-E76.3, E85
Other metabolic disorders	275.0-275.3, 277.2277.6, 277.8-277.9	277.4, E79.1, E79.8, E80.4-E80.7, E83.0, E83.1, E83.3, E83.4, D84.1, E88, H49.8

(*continued*)

Table III. Continued

Descriptions	ICD-9 codes	ICD-10 codes
Endocrine disorders	243, 253.2, 253.5, 253.6, 235.9, 255.0, 255.13, 255.2, 06.4, 06.52, 06.81, 07.3, 07.64, 07.65, 07.68, 07.69, 62.4, 62.41, 64.5, 65.5, 65.51, 65.53, 65.6, 65.61, 65.63, 68.4, 68.41, 68.49, 68.5, 68.51, 68.59, 68.6, 68.61, 68.69, 68.7, 68.71, 68.79	E00.9, E23.0, E23.2, E22.2, E23.3, E23.7, E24.0, E24.2, E24.3, E24.8, E24.9, E26.81, E25.0, E25.8, E25.9, 0GT00ZZ, 0GT04ZZ, 0GT40ZZ, 0GT44ZZ, 0GTK0ZZ, 0GTK4ZZ, 0GTR0ZZ, 0GTR4ZZ, 0UT20ZZ, 0UT24ZZ, 0UT27ZZ, 0UT28ZZ, 0UT2FZZ, 0UT40ZZ, 0UT44ZZ, 0UT47ZZ, 0UT48ZZ, 0UT70ZZ, 0UT74ZZ, 0UT90ZZ, 0UT94ZZ, 0UT97ZZ, 0UT98ZZ, 0UT9FZZ, 0UTC0ZZ, 0UTC7ZZ, 0UTC8ZZ, 0VTC0ZZ, 0VTC4ZZ, 0W4M070, 0W4M0J0, 0W4M0K0, 0W4M0Z0, 0W4N071, 0W4N0J1, 0W4N0K1, 0W4N0Z1
Devices	V45.85, V53.91, 86.06	Z46.81, Z96.41, 0JH60VZ, 0JH63VZ, 0JH70VZ, 0JH73VZ, 0JH80VZ, 0JH83VZ, 0JHD0VZ, 0JHD3VZ, 0JHF0VZ, 0JHF3VZ, 0JHG0VZ, 0JHG3VZ, 0JHH0VZ, 0JHH3VZ, 0JHL0VZ, 0JHL3VZ, 0JHM0VZ, 0JHM3VZ, 0JHN0VZ, 0JHN3VZ, 0JHP0VZ, 0JHP3VZ, 0JHT0VZ, 0JHT3VZ
Other congenital or genetic defect		
Chromosomal anomalies	758.0-758.9	Q90.9, Q91.3, Q91.4, Q91.7, Q92.8, Q93, Q95.0, Q96.9, Q97, Q98, Q99.8, Q99.9
Bone and join anomalies	259.4, 737.3, 756.0-756.5	E34.3, M41.0, M41.2, M41.30, M41.8, M41.9, M43.30, M96.5, Q72.2, Q75.0, Q75.2, Q75.9, Q76.0-Q76.2, Q76.4-Q76.7, Q77, Q78.0-Q78.4, Q78.8, Q78.9
Diaphragm and abdominal wall	553.3, 756.6, 756.7	K44.9, Q79.0-Q79.5, Q79.9, Q79.59
Other congenital anomalies	757.39, 759.7-759.9	Q81, Q87.1-Q87.3, Q87.40, Q87.81, Q87.89, Q89.7, Q89.9, Q99.2
Malignancy		
Neoplasms	140-209, 230-239, 00.10, 99.25	C00-C96, D01-D09, D3A.0, D37-D49, Q85.0, 3E00X05, 3E01305, 3E02305, 3E03005, 3E03305, 3E04005, 3E04305, 3E05005, 3E05305, 3E06005, 3E06305, 3E0A305, 3E0F305, 3E0F705, 3E0F805, 3E0G305, 3E0G705, 3E0G805, 3E0H305, 3E0H705, 3E0H805, 3E0J305, 3E0J705, 3E0J805, 3E0K305, 3E0K705, 3E0K805, 3E0L305, 3E0L705, 3E0M305, 3E0M705, 3E0N305, 3E0N705, 3E0N805, 3E0P305, 3E0P705, 3E0P805, 3E0Q305, 3E0Q705, 3E0R305, 3E0S305, 3E0V305, 3E0W305, 3E0Y305, 3E0Y705
Transplantation	996.85,V42.81, V42.82	T86.00-T86.02, T86.09, Z94.81, Z94.84
Prematurity and neonatal		
Fetal malnutrition	764.01, 764.02, 764.11, 764.12, 764.21, 764.22, 764.91, 764.92	P05.01, P05.11, P05.02, P05.12, P05.2, P05.9
Extreme immaturity	765.01, 765.02, 765.11, 765.12, 765.21-765.23	P07.01, P07.02, P07.21-P07.25
Cerebral hemorrhage at birth	767	P10.0, P10.1, P10.4, P52.4, P52.8
Spinal cord injury at birth	767.4	P11.5
Birth asphyxia	768.5, 768.9	P21.0, P21.9, P84
Respiratory diseases	770.2, 770.7	P25.0-P25.3, P25.8, P27.0, P27.1, P27.8
Hypoxic–ischemic encephalopathy	768.7	P91.6
Other	771.0, 771.1, 772.13, 772.14, 773.3, 773.4, 774.7, 776.5, 777.53, 778.0, 779.7	P35.0, P35.1, P25.21, P25.22, P56.0, P57.0, P57.8, P61.3, P61.4, P77.3, P83.2, P91.2
Other, not classified elsewhere		

(*continued*)

Table III. Continued

Descriptions	ICD-9 codes	ICD-10 codes
Devices	996.4, 996.66, 996.67, 996.9, V46.2 81.00, 81.01, 81.02, 81.03, 81.04, 81.05, 81.06, 81.07, 81.08, 81.09, 81.30, 81.31, 81.32, 81.33, 81.34, 81.35, 81.36, 81.37, 81.38, 81.39, 84.51	T84.019A, T84.029A, T84.039A, T84.049A, T84.059A, T84.069A, T84.099A, T84.498A, T84.119A, T84.129A, T84.199A, T84.498A, T84.50XA, T84.60XA, T84.7XXA, T86.90-T86.92, T86.99, T86.10-T86.12, T86.40-T86.42, T86.20-T86.22, T86.810, T86.811, T86.819, T86.00-T86.02, T86.09, T86.890, T86.891, T86.899, T86.850, T86.851, T86.859, T86.5, T86.890, T86.891, T86.899, T87.0X9, T87.1X9, T87.2, Y83.1, Y83.3, Z99.81, 0RG00J0, 0RG00J1, 0RG00JJ, 0RG00K0, 0RG00K1, 0RG00KJ, 0RG00Z0, 0RG00Z1, 0RG00ZJ, 0RG03J0, 0RG03J1, 0RG03JJ, 0RG03K0, 0RG03K1, 0RG03KJ, 0RG03Z0, 0RG03Z1, 0RG03ZJ, 0RG04J0, 0RG04J1, 0RG04JJ, 0RG04K0, 0RG04K1, 0RG04KJ, 0RG04Z0, 0RG04Z1, 0RG04ZJ, 0RG10J0, 0RG10J1, 0RG10JJ, 0RG10K0, 0RG10K1, 0RG10KJ, 0RG10Z0, 0RG10Z1, 0RG10ZJ, 0RG13J0, 0RG13J1, 0RG13JJ, 0RG13K0, 0RG13K1, 0RG13KJ, 0RG13Z0, 0RG13Z1, 0RG13ZJ, 0RG14J0, 0RG14J1, 0RG14JJ, 0RG14K0, 0RG14K1, 0RG14KJ, 0RG14Z0, 0RG14Z1, 0RG14ZJ, 0RG40J0, 0RG40J1, 0RG40JJ, 0RG40K0, 0RG40K1, 0RG40KJ, 0RG40Z0, 0RG40Z1, 0RG40ZJ, 0RG43J0, 0RG43J1, 0RG43JJ, 0RG43K0, 0RG43K1, 0RG43KJ, 0RG43Z0, 0RG43Z1, 0RG43ZJ, 0RG44J0, 0RG44J1, 0RG44JJ, 0RG44K0, 0RG44K1, 0RG44KJ, 0RG44Z0, 0RG44Z1, 0RG44ZJ, 0RG60J0, 0RG60J1, 0RG60JJ, 0RG60K0, 0RG60K1, 0RG60KJ, 0RG60Z0, 0RG60Z1, 0RG60ZJ, 0RG63J0, 0RG63J1, 0RG63JJ, 0RG63K0, 0RG63K1, 0RG63KJ, 0RG63Z0, 0RG63Z1, 0RG63ZJ, 0RG64J0, 0RG64J1, 0RG64JJ, 0RG64K0, 0RG64K1, 0RG64KJ, 0RG64Z0, 0RG64Z1, 0RG64ZJ, 0RGA0J0, 0RGA0J1, 0RGA0JJ, 0RGA0K0, 0RGA0K1, 0RGA0KJ, 0RGA0Z0, 0RGA0Z1, 0RGA0ZJ, 0RGA3J0, 0RGA3J1, 0RGA3JJ, 0RGA3K0, 0RGA3K1, 0RGA3KJ, 0RGA3Z0, 0RGA3Z1, 0RGA3ZJ, 0RGA4J0, 0RGA4J1, 0RGA4JJ, 0RGA4K0, 0RGA4K1, 0RGA4KJ, 0RGA4Z0, 0RGA4Z1, 0RGA4ZJ, 0SG00J0, 0SG00J1, 0SG00JJ, 0SG00K0, 0SG00K1, 0SG00KJ, 0SG00Z0, 0SG00Z1, 0SG00ZJ, 0SG03J0, 0SG03J1, 0SG03JJ, 0SG03K0, 0SG03K1, 0SG03KJ, 0SG03Z0, 0SG03Z1, 0SG03ZJ, 0SG04J0, 0SG04J1, 0SG04JJ, 0SG04K0, 0SG04K1, 0SG04KJ, 0SG04Z0, 0SG04Z1, 0SG04ZJ
Transplantation	996.80, 6.88, 996.89, 00.91, 00.92, 00.93	T86.5, T86.90-T86.92, T86.99, T86.890, T86.891, T86.899

CNS, central nervous system.
*From Feudtner et al.[40]

Table IV. Medications with known or conditional risk of QT prolongation*

Medication names	GPI-8 code
Known risk of QT prolongation	
AMIODARONE HCL	35400005
ANAGRELIDE HCL	85156010
ARSENIC TRIOXIDE	21700008
AZITHROMYCIN	03400010
BEPRIDIL HCL	34000005
CHLOROQUINE PHOSPHATE	13000010
CHLORPROMAZINE HCL	59200015
CILOSTAZOL	85155516
CIPROFLOXACIN HCL	05000020
CLARITHROMYCIN	03500010
DEXTROMETHORPHAN HBR-QUINIDINE SULFATE	62609902
DISOPYRAMIDE PHOSPHATE	35100010
DOFETILIDE	35400025
DONEPEZIL HYDROCHLORIDE	62051025
DRONEDARONE HCL	35400028
DROPERIDOL	57200030
ERYTHROMYCIN BASE	03100005
ERYTHROMYCIN BASE (COATED)	03100006
ERYTHROMYCIN ESTOLATE	03100020
ERYTHROMYCIN ETHYLSUCCINATE	03100030
ERYTHROMYCIN LACTOBIONATE	03100050
ERYTHROMYCIN STEARATE	03100010
ERYTHROMYCIN-SULFISOXAZOLE	16990002
FLECAINIDE ACETATE	35300010
FLUCONAZOLE	11407015
GATIFLOXACIN	05000082
HALOPERIDOL LACTATE	59100010
LEVOFLOXACIN	05000034
MEMANTINE HCL-DONEPEZIL HCL	62059902
METHADONE HCL	65100050
MOXIFLOXACIN HCL	05000037
ONDANSETRON HCL	50250065
OXALIPLATIN	21100028
PAPAVERINE HCL	40100060
PENTAMIDINE ISETHIONATE	16000045
PIMOZIDE	62000030
PROCAINAMIDE HCL	35100020
PROPOFOL	70400050
QUINIDINE GLUCONATE	35100030
SEVOFLURANE	70200070
SOTALOL HCL	33100045
TERFENADINE	41550040
THIORIDAZINE HCL	59200080
VANDETANIB	21534085
Conditional risk of QT prolongation	
ALISKIREN-AMLODIPINE-HYDROCHLOROTHIAZIDE	36996803
ALISKIREN-HYDROCHLOROTHIAZIDE	36996002
AMANTADINE HCL	73200010
AMITRIPTYLINE HCL	58200010
	58998702
	62990002
	62992002
	62994002
AMPHOTERICIN B LIPID	11000010
ATAZANAVIR SULFATE	12104515
	12109902
BENDROFLUMETHIAZIDE	37600010
CHLORAL HYDRATE	60200020
CIMETIDINE	49200010
	49200011

(*continued*)

Table IV. Continued

Medication names	GPI-8 code
DIPHENHYDRAMINE HCL	41200030
	60300020
	43995702
	43992002
	60309902
	88109904
	88359905
	88109903
	43993002
	43994003
	43995202
	41991002
	43993003
	43994004
	43998903
	43995904
	43998805
	43996804
	43995303
DOXEPIN HCL	58200040
	60400030
ESOMEPRAZOLE MAGNESIUM	49270025
FAMOTIDINE	49200030
	49993503
FUROSEMIDE	37200030
GALANTAMINE HYDROBROMIDE	62051030
HYDROCHLOROTHIAZIDE	36999002
	36991003
	37600040
	36992002
	36991802
	36994002
	36995002
	36994503
	36991002
	37990002
HYDROXYCHLOROQUINE SULFATE	13000020
HYDROXYZINE PAMOATE	57200040
INDAPAMIDE	37600050
ITRACONAZOLE	11407035
IVABRADINE HCL	40700035
KETOCONAZOLE	11404040
LANSOPRAZOLE	49270040
	49270020
LOPERAMIDE HCL	47100020
	47991002
METOCLOPRAMIDE HCL	52300020
METOLAZONE	37600060
METRONIDAZOLE	16000035
	49992003
NELFINAVIR MESYLATE	12104545
OLANZAPINE	59157060
	62995002
OMEPRAZOLE	49270060
	49996002
	85159902
	66109902
PANTOPRAZOLE SODIUM	49270070
PIPERACILLIN SODIUM-TAZOBACTAM SODIUM	01990002
POSACONAZOLE	11407060
PROPAFENONE HCL	35300050
QUETIAPINE FUMARATE	59153070
QUININE SULFATE	13000060

(*continued*)

Table IV. Continued

Medication names	GPI-8 code
RANOLAZINE	32200040
SOLIFENACIN SUCCINATE	54100055
TELAPREVIR	12353085
TORSEMIDE	37200080
TRAZODONE HCL	58120080
	58998002
VORICONAZOLE	11407080
ZIPRASIDONE HCL	59400085

GPI, General Product Identifier.
*Obtained from the CredibleMeds site, https://www.crediblemeds.org/; accessed March 2019.

Table VIII. Sensitivity analyses, allowing for time lags between end of SSRI exposure and index date

SSRI Exposure Category	Unadjusted cOR (95% CI)	Adjusted* cOR (95% CI)
Current SSRI	9.88 (4.48-21.80)	5.11 (1.22-21.37)
Current SSRI + SSRI ending within 30 d pre-index	7.46 (3.73-14.92)	5.69 (1.60-20.22)
Current SSRI + SSRI ending within 60 d pre-index	6.74 (3.42-13.27)	4.42 (1.29-14.93)

non-CV CCC, non-cardiovascular chronic complex condition.
*Adjusted history of mental health diagnoses, history of other cardiac diagnoses, and history of non-cv CCC.