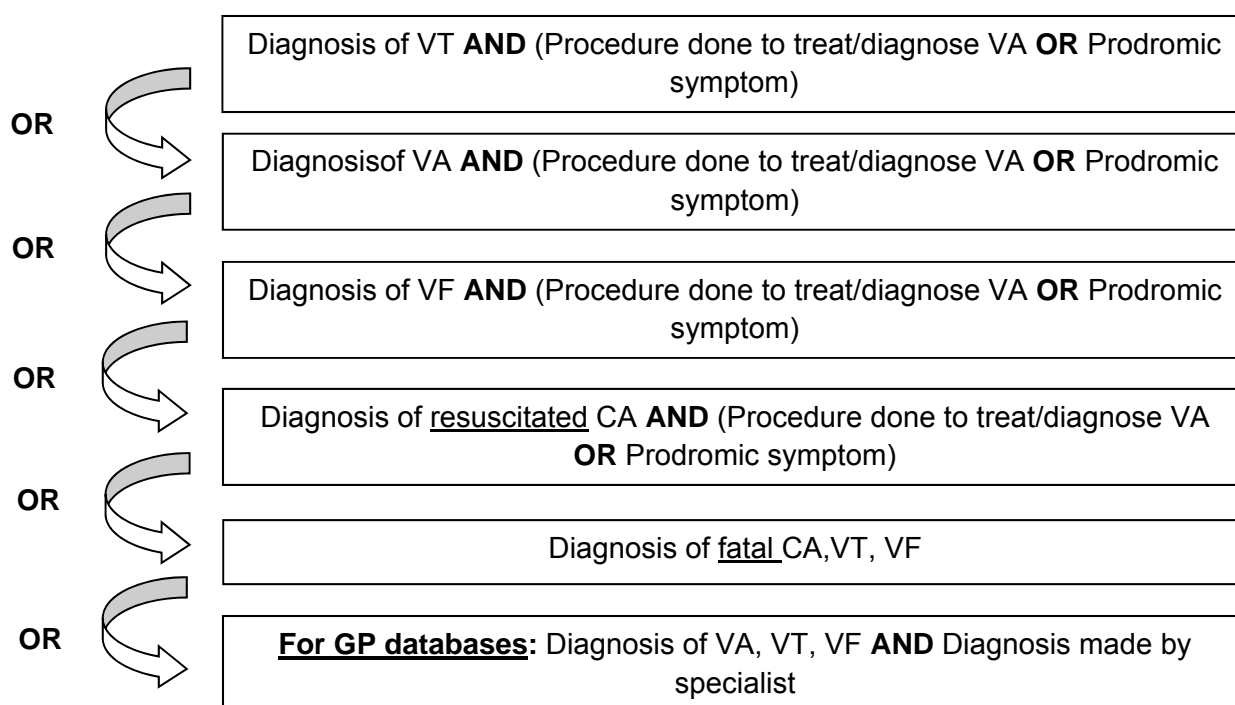


Appendix 1 (as supplied by the authors): Supplementary material

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eFigure 1: Coding algorithm for ventricular arrhythmia identification



Legend: Ventricular Arrhythmia (VA) includes both ventricular tachycardia (VT) and fibrillation (VF). VT is a sequence of three or more beats in a row, with wide QRS complex (QRS ≥ 120 ms) at a ventricular rate exceeding 100 beats/min. If the rhythm lasts more than 30 seconds or requires termination earlier due to hemodynamic instability, it is known as a sustained ventricular tachycardia. If the fast rhythm self-terminates within 30 seconds, it is considered a non-sustained ventricular tachycardia. VT can evolve to VF that is a rapid, chaotic, non-repetitive waveform usually preceded by rapid VT and in which there is uncoordinated contraction of the cardiac muscle of the ventricles. VF is clinically associated with loss of effective blood circulation and, if not immediately treated, leads to death. For this analysis, VA was considered as two separated outcomes: non-fatal and fatal VA with the latter defined as death within 48 hours from the event of interest. In our study, CA was analyzed as part of VA as well as separate outcome. All cases of CA with successful resuscitation were considered as non-fatal VA, while CAs in which the patient died within 48 hours from the beginning of symptoms were considered as fatal VA. **Abbreviations:** CA- cardiac arrhythmia; IV- intravenous; VA- ventricular arrhythmia; VF- ventricular fibrillation; VT- ventricular tachycardia

eTable 1: Unified Medical Language-driven identification of terminology specific codes for ventricular arrhythmia and cardiac arrest

UMLS concept	Preferred term of concept	ICD-9	ICD-10	ICD-10GM	ICPC	RCD v2
Ventricular arrhythmia						
C0085612	Ventricular arrhythmia					328..00, 328Z.00
C0042514	Tachycardia, Ventricular	427.1	I47.2	I47.2	K79005	G571.00
C0030591	Paroxysmal ventricular tachycardia	427.1				G571.11
C0152173	Ventricular Flutter	427.4 2			K80014, K84011	G574100
C0155710	Ventricular fibrillation and flutter	427.4	I49.0	I49.0		G574.00, G574z00
C0349069	Re-entry ventricular arrhythmia		I47.0	I47.0		G57Ya0 0
C0042510	Ventricular Fibrillation	427.4 1			K84020, K80011	G574000 G574011
C0494598	Other cardiac dysrhythmias	427.9	I49.9			G57..00
Cardiac arrest						
C0018790	Cardiac Arrest	427.5	I46, I46.9	I46 I46.9	K84005	G575.00, G575z00
C0340514	Cardiac arrest with successful resuscitation		I46.0	I46.0		G575000
C0340513	Cardiac arrest as a complication of care					SP11000
C0600228	Cardiopulmonary Arrest	427.5				G575.11
C1260909	Cardiorespiratory failure as a complication of care					SP11200
C0397419	Direct current defibrillation					7L1H.00, 7L1H.11, 7L1H.12, 7L1H.13
C0436588	O/E - collapse -cardiac arrest					2241.00
Abbreviations: ICD-9- International Classification of Disease, 9 th version; ICD-10- International Classification of Disease, 10 th version; ICD-10 GM- International Classification of Disease, 10 th version, German modification; ICPC- International Classification of Primary care code; O/E- on examination; RDC v2.- Read code version 2; UMLS- Unified Medical Language System						

eTable 2: Coding algorithms for covariates included in the study			
Well-known risk factors for VA			
Covariate name	Search criteria	Time frame	Notes
Atrial fibrillation/flutter	Dx	Anytime prior to ID	
Cardiomyopathies	Dx	Anytime prior to ID	It includes cardiomyopathies and channelopathies
Cerebrovascular events	Dx	Anytime prior to ID	
Coronary heart disease	Dx or RX	Anytime prior to ID	ATC: C01D* as proxy of disease
Heart failure	Dx	Anytime prior to ID	
Hypertension	Dx or blood pressure measurements or Rx	Anytime prior to ID	ATC: C09A-D*, C07*, C08*, C02A-K*, C02N* as proxy of disease. Two systolic blood pressure measurements exceeding 140 mm Hg were considered to denote hypertension.
Peripheral arterial disease	Dx	Anytime prior to ID	
Antiarrhythmia drug use	Rx	Anytime prior to ID	See eTable 3 for ATC codes
Electrolytic imbalance	Dx or laboratory values	Anytime prior to ID	It includes hypocalcemia, hypokalemia and hypomagnesemia
Use of QT prolonging drugs	Rx	90 days prior to ID	Drugs with established TdP liability, based on CredibleMeds list** See eTable 4 for ATC codes
Concomitant use of medications inducing hypokalemia	Rx	90 days prior to ID	See eTable 5 for ATC codes
Potential risk factors for VA			
Acute and Chronic Renal Failure	Dx	Anytime prior to ID	
Alcohol abuse	Dx	Anytime prior to ID	
Chronic liver disease	Dx	Anytime prior to ID	
Chronic respiratory disease	DX or Rx	Anytime prior to ID	ATC: R03 as proxy of disease
Conduction disorders	Dx	Anytime prior to ID	
Congenital heart disease	Dx	Anytime prior to ID	
Diabetes mellitus	Dx or Rx	Anytime prior to ID	ATC: A10* as proxy of disease
Hyperthyroidism	Dx or Rx	Anytime prior to ID	ATC: H03B* as proxy of disease
Hypothyroidism	Dx or Rx	Anytime prior to ID	ATC: H03A*, H03C* as proxy of disease
Lipid metabolism disorders	Dx or Rx	Anytime prior to ID	ATC: C10* as proxy of disease
Obesity	Dx or BMI ≥ 30 or Rx	Anytime prior to ID	ATC: A08* as proxy of disease
Other cardiac arrhythmias*	Dx	Anytime prior to ID	
Cardiac valve disorders	Dx	Anytime prior to ID	
Abbreviations: Dx- diagnosis; ID- index date; Rx- prescription; VA: ventricular arrhythmia * Except for atrial fibrillation/flutter, conduction disorders, QT prolongation, ventricular arrhythmia and sudden cardiac death. ** CredibleMeds. CredibleMeds webpage. (Accessed January 15, 2014 at https://crediblemeds.org/)			

eTable 3: Anti-arrhythmia drugs	
Anti-arrhythmic drugs, class I and III	ATC code
Quinidine	C01BA01
Procainamide	C01BA02
Disopyramide	C01BA03
Sparteine	C01BA04
Ajmaline	C01BA05
Prajmaline	C01BA08
Lorajmine	C01BA12
Quinidine, combinations excl. psycholeptics	C01BA51
Quinidine, combinations with psycholeptics	C01BA71
Lidocaine	C01BB01
Mexiletine	C01BB02
Tocainide	C01BB03
Aprindine	C01BB04
Propafenone	C01BC03
Flecainide	C01BC04
Lorcainide	C01BC07
Encainide	C01BC08
Amiodarone	C01BD01
Bretylumtosilate	C01BD02
Bunaftine	C01BD03
Dofetilide	C01BD04
Ibutilide	C01BD05
Tedisamil	C01BD06
Dronedarone	C01BD07
Moracizine	C01BG01
Cibenzoline	C01BG07
Vernakalant	C01BG11
Abbreviations: ATC- Anatomical Therapeutic Chemical classification	

eTable 4: Drugs with established torsadogenic liability	
Drug	ATC code
Amiodarone	C01BD01
Arsenic trioxide	L01XX27
Astemizole	R06AX11
Bepridil	C08EA02
Chloroquine	P01BA01
Cisapride	A03FA02
Citalopram	N06AB04
Clarithromycin	J01FA09
Disopyramide	C01BA03
Dofetilide	C01BD04
Domperidone	A03FA03
Erythromycin	J01FA01
Flecainide	C01BC04
Halofantrine	P01BX01
Ibutilide	C01BD05
Levomethadyl	N07BC03
Methadone	N07BC02
Moxifloxacin	J01MA14
Pentamidine	P01CX01
Probucol	C10AX02
Procainamide	C01BA02
Quinidine	C01BA01
Sotalol	C07AA07
Sparfloxacin	J01MA09
Terphenadine	R06AX12
Vandetanib	L01XE12
Abbreviations: ATC- Anatomical Therapeutic Chemical classification	

eTable 5: Drugs known to induce hypokalemia		
Drug class	Drug name	ATC code
Thiazides	Bendroflumethiazide	C03AA01
	Hydroflumethiazide	C03AA02
	Hydrochlorothiazide	C03AA03
	Chlorothiazide	C03AA04
	Polythiazide	C03AA05
	Trichlormethiazide	C03AA06
	Cyclopenthiiazide	C03AA07
	Methyclothiazide	C03AA08
	Cyclothiazide	C03AA09
	Mebutizide	C03AA13
	Bendroflumethiazide and potassium	C03AB01
	Hydroflumethiazide and potassium	C03AB02
	Hydrochlorothiazide and potassium	C03AB03
	Chlorothiazide and potassium	C03AB04
	Polythiazide and potassium	C03AB05
	Trichlormethiazide and potassium	C03AB06
	Cyclopenthiiazide and potassium	C03AB07
	Methyclothiazide and potassium	C03AB08
	Cyclothiazide and potassium	C03AB09
	Chlorothiazide, combinations	C03AH01
Hydroflumethiazide, combinations	C03AH02	
Hydrochlorothiazide, combinations	C03AX01	
High-Ceiling Diuretics	Furosemide	C03CA01
	Bumetanide	C03CA02
	Piretanide	C03CA03
	Torasemide	C03CA04
	Furosemide and potassium	C03CB01
	Bumetanide and potassium	C03CB02
	Ethacrynic acid	C03CC01
	Muzolimine	C03CD01
	Etozolin	C03CX01
	Corticosteroids for systemic use, plain	Aldosterone
Fludrocortisones		H02AA02
Prednisone		H02AB07
Selective beta-2-adrenoreceptor agonists	Salbutamol	R03AC02
	Terbutaline	R03AC03
	Fenoterol	R03AC04
	Rimiterol	R03AC05
	Hexoprenaline	R03AC06
	Isoetarine	R03AC07
	Pirbuterol	R03AC08
	Tretoquinol	R03AC09
	Carbuterol	R03AC10
	Tulobuterol	R03AC11
	Salmeterol	R03AC12

	Formoterol	R03AC13
	Clenbuterol	R03AC14
	Reproterol	R03AC15
	Procaterol	R03AC16
	Bitolterol	R03AC17
	Indacaterol	R03AC18
Catecholamines	Epinephrine	C01CA24
	Norepinephrine	C01CA03
	Dopamine	C01CA04
Abbreviations: ATC- Anatomical Therapeutic Chemical classification of drugs		