APPENDIX

Appendix A – Data sources

In the logistic system in the EDs of the Region of Southern Denmark and the Region of Skåne information regarding triage and presumed diagnoses are shared among the health care personal. The system also provides information on time of arrival to the ED as well as time of discharge. At arrival all patients are registered by main reason for contact. Lund and Helsingborg have 43 somatic contact possibilities, Odense and Esbjerg have 40 contact possibilities. We used these systems to identify patients with suspected poisoning.
From the electronic central ECG databases at the Region of Southern Denmark and the Region of Skåne all ECGs measures were extracted. These databases contain information of all ECGs recorded in any hospital in the respective region.

The Danish National Patient Register was established in 1977. Since 1994 diagnostic information has been recorded in accordance with ICD-10. The content includes information regarding discharge diagnoses from which comorbidities were derived. In Sweden, all health care consultations are recorded in the respective region databases. From the Skåne Healthcare Register, we retrieved information corresponding to information from the Danish National Patient Register. In these regional databases diagnoses from both the primary and secondary health care system are available. Charlson Comorbidity Index was calculated based on data extracted for a 10 year-period ending on the day of contact in the Danish data. From the Swedish database, Charlson Comorbidity Index was calculated for a 2-year period ending on the day of contact to the ED.

The Swedish National Pharmacy Register contains data on all prescriptions dispensed at pharmacies since 2005. Besides date of dispensing, name, amount, and dose of the redeemed medication are accessible from this register. The Danish National Prescription Registry provides similar information of individual-level prescription of medication since 1995. Information of redeemed prescription of QT prolonging drugs (see Appendix c.5) within 90 days before contact was obtained through these registers.

The Danish Civil Registration System contains data regarding birth, emigration, and vital status for the entire populations. Information regarding vital status in Sweden was retrieved from the Swedish population registry. The Danish Civil Registration System was established in 1968, and by law all Danish residents have a unique civil registration number of ten digits. Since 1967, all Swedish residences are assigned a ten-digit personal identity number. These unique numbers allow complete and accurate linkage between registries on an individual level.

Appendix B – Supplementary methods

ECG measurements

All ECGs were recorded and stored either in MUSE® Cardiology Information System (GE Healthcare), or by Philips Diagnostic ECG (Philips). All ECGs in our analysis were 12 lead ECGs. ECGs recorded in MUSE were later processed using the Marquette 12SL algorithm, which calculate the QTc interval using the Bazett Formula, the Fridericia Formula, and the Framingham Formula. In MUSE, the QT interval is measured as a median value from the 12 leads. ECG recorded by Philips were analyzed by the DXL-algorithm. In this algorithm, the QT interval is measured as a median value from reliable leads. A lead is defined as reliable if little variation in beat-to-beat variation. Philips provided QTc intervals corrected by the Bazett Formula and the Fridericia Formula.
To correct for heart rate, we chose the Framingham Formula ($QTc_{Framingham}$ =QT + 0.154 (1-RR)). Because Philips DXL-algorithm does not routinely correct the QT interval using the Framingham Formula, we calculated the $QTc_{Framingham}$ ourselves. As we did not include RR intervals in our analysis, the formula was used in another edition than the original formula. Therefore, we used following formula for correction in ECGs recorded by Philips: $QTc_{Framingham}$ = QT + 154 (1-60/heart rate). The QRS duration was measured as a median value in both algorithms.

The Marquette 12SL algorithm defines onsets as the earliest deflection in any lead, and offsets as the latest deflection in any lead. The QT interval is measured from the earliest detection of depolarization in any lead to the latest detection of repolarization in any lead. Similarly, the QRS duration was measured from the earliest onset in any lead to the latest deflection in any lead. The Philips DXL-algorithm first identifies waveform component and measures every beat in each lead individually. After the approximate waveform locations are known, onsets and offsets are defined. Once the onsets and offsets are known, duration of intervals are calculated.

In both Denmark and Sweden ECG recording is performed by well-educated heath care personals instructed only to accept ECGs of satisfying quality. Otherwise it is considered a routine to record another ECG. If multiple ECGs were recorded in a single individual, the first ECG recorded within 4 hours after arrival was included in the analysis.

Appendix C – Codes and definitions

C.1

Codes for cardiac arrest and codes used in identifying patients with cardiac arrest	
ICD-10 codes	DI46: Cardiac arrest DI46.0: Cardiac arrest with successful recitation DI46.1: Sudden cardiac death DI46.9: Cardiac arrest unspecified
SKS codes*	**Administrative codes** AVAA07: Sudden cardiac arrest AVAA06: Sudden cardiac arrest **Procedure codes** ZZ0401: Standby for cardiac arrest **Treatment codes** BFFA6: Chest compressions BFFA60: External chest compressions BFFA60A: External chest compressions by use of mechanical chest compressions
KVÅ-codes**	DF012: Chest compressions DF017: Mechanical chest compressions DF028: Cardiopulmonary resuscitation

*SKS = Sundhedsvæsenets klassifikations system, available on http://medinfo.dk/sks/brows.php, Danish codes.
**KVÅ= Klassifikation av vårdåtgärder, available on http://www.socialstyrelsen.se/klassificeringochkoder/atgardskoderkva, Swedish codes.

C.2

Poisoning divided into groups by use of ICD-10 codes	
Analgesics and drugs of abuse	T39*-T40*, F110*, F120*, F140*, F150*, F160*
Psychotropic drugs and drugs affecting the central nervous system	T42*-T44*, F130*, F190*
Organic and chemical substances, non-medical substances	T51*-T65*, F100*, F170*, F180*
Others	T36*-T38*, T41*, T45*-T50*
Multidrug	≥2 of the above mentioned poisoning groups

C.3

Charlson Comorbidity Index*		
Condition	**Assigned weight**	**ICD-10 codes**
Peripheral vascular disease	1	I70.x, I71x, I73.1, I73.8, I73.9, I77.1, I79.0, I79.2, K55.1, K55.8, K55.9, Z95.8, Z95.9
Cerebrovascular disease	1	G45.x, G46.x, H34.0, I60.x-I69.x
Dementia	1	F00.x-F03.x, F05.1, G30.x, G31.1
Chronic pulmonary disease	1	I27.8, I27.9, J40.x-J47.x, J60.x-J67.x, J68.4, J70.1, J70.3
Rheumatic disease	1	M05.x, M06.x, M31.5, M32.x-M34.x, M35.1, M35.3, M36.0
Peptic ulcer disease	1	K25.x-K28.x
Mild liver disease	1	B18.x, K70.0-K70.3, K70.9, K71.3-K71.5, K71.7, K73.x, K74.x, K76.0, K76.2-K76.4, K76.8, K76.9, Z94.4
Diabetes without chronic complications	1	E10.0, E10.1, E10.6, E10.8, E10.9, E11.0, E11.1, E11.6, E11.8, E11.9, E12.0, E12.1, E12.6, E12.8, E12.9, E13.0, E13.1, E13.6, E13.8, E13.9, E14.0, E14.1, E14.6, E14.8, E14.9
Hemiplegia or paraplegia	2	G04.1, G11.4, G80.1, G80.2, G81.x, G82.x, G83.0-G83.4, G83.9
Renal disease	2	I12.0, I13.1, N03.2-N03.7, N05.2- N05.7, N18.x, N19.x, N25.0, Z49.0- Z49.2, Z94.0, Z99.2
Diabetes with chronic complications	2	E10.2-E10.5, E10.7, E11.2-E11.5, E11.7, E12.2-E12.5, E12.7, E13.2- E13.5, E13.7, E14.2-E14.5, E14.7
Cancer	2	C00.x-C26.x, C30.x-C34.x, C37.x- C41.x, C43.x, C45.x-C58.x, C60.x- C76.x, C81.x-C85.x, C88.x, C90.x-C97.x
Metastatic cancer	3	C77.x-C80.x
Moderate or severe liver disease	3	I85.0, I85.9, I86.4, I98.2, K70.4, K71.1, K72.1, K72.9, K76.5, K76.6, K76.7
AIDS/HIV**	6	B20.x-B22.x, B24.x

*Diagnostic codes for myocardial infarction and heart failure are not included in the index, but are included in this study as covariates.

** AIDS = acquired immunodeficiency syndrome, HIV = human immunodeficiency virus

C.4

Variables from Charlson Comorbidity Index, included separately in the analysis	
Myocardial infarction	I21.x, I22.x, I25.2
Congestive heart failure	I09.9, I11.0, I13.0, I13.2, I25.5, I42.0, I42.5-I42.9, I43.x, I50.x, P29.0

C.5

List of drugs associated with QT prolongation and risk of TdP*	
Drug category	**ATC-codes****
Alimentary tract and metabolism	Domperidone (A03FA03), Granisetron (A04AA02), Metoclopramide (A03FA01), Ondansetron (A04AA01), Pantoprazole (A02BC02)
Cardiovascular system	Amiodarone (C01BD01), Dronedarone (C01BD07), Flecainide (C01BC04), Furosemide (C03CA01, C03EB01), Hydrochlorothiazide (C03EA01, C09DA01, C09DA06, C09DA04, C09BA02), Indapamide (C03BA11), Isradipine (C08CA03), Ivabradine (C01EB17), Sotalol (C07AA07)
Genito urinary system and sex hormones	Alfuzosin (G04CA01), Mifepristone (G03XB01), Mirabegron (G04BD12), Solifenacin (G04BD08, G04CA53), Tolterodine (G04BD07), Vardenafil (G04BE09)

Systemic hormonal preparations, excl. sex hormones and insulins	Oxytocin (H01BB02), Pasireotide (H01CB05)
Anti-infectives for systemic use	Atazanavir (J05AR15), Azithromycin (J01FA10), Bedaquiline (J04AK05), Ciprofloxacin (J01MA02), Clarithromycin (J01FA09), Erythromycin (J01FA01), Fluconazole (J02AC01), Foscarnet (J05AD), Itraconazole (J02AC02), Ketoconazole (J02AB02), Metronidazole (J01XD01), Moxifloxacin (J01MA14), Posaconazole (J02AC04), Rilpivirine (J05AG05), Ritonavir (J05AE03), Roxithromycin (J01FA06), Saquinavir (J05AE01), Voriconazole (J02AC03)
Antineoplastic and immunomodulatory agents	Anagrelide (L01XX35), Bortezomib (L01XX32), Bosutinib (L01XE14), Ceritinib (L01XE28), Crizotinib (L01XE16), Dabrafenib (L01XE23), Dasatinib (L01XE06), Degarelix (L02BX02), Eribulin mesylate (L01XX41), Fingolimod (L04AA27), Lapatinib (L01XE07), Leuprolide (L02AE02), Nilotinib (L01XE08), Oxaliplatin (L01XA03), Panobinostat (L01XX42), Pazopanib (L01XE11), Sorafenib (L01XE05), Sunitinib (L01XE04), Tacrolimus (L04AD02), Tamoxifen (L02BA01), Vandetanib (L01XE12), Vemurafenib (L01XE15)
Musculo-skeletal system	Tizanidine (M03BX02)
Nervous system	Amantadine (N04BB01), Amisulpride (N05AL05), Amitriptyline (N06AA09), Apomorphine (N04BC07), Aripiprazole (N05AX12), Asenapine (N05AH05), Atomoxetine (N06BA09), Citalopram (N06AB04), Clomipramine (N06AA04), Clozapine (N05AH02), Dexmedetomidin (N05CM18), Doxepin (N06AA12), Droperidol (N05AD08), Escitalopram (N06AB10), Fluoxetine (N06AB03), Galantamine (N06DA04), Haloperidol (N05AD01), Hydroxyzine (N05BB01), Imipramine (N06AA02), Levomepromazine (N05AA02), Lithium (N05AN01), Methadone (N07BC02), Mirtazapine (N06AX11), Nortriptyline (N06AA10), Olanzapine (N05AH03), Paliperidone (N05AX13), Paroxetine (N06AB05), Pimozide (N05AG02), Pipamperone (N05AD05), Propofol (N01AX10), Quetiapine (N05H04), Risperidone (N05AX08), Sertindole (N05AE03), Sertraline (N06AB06), Sevoflurane (N01AB08), Sulpiride (N05AL01), Tetrabenazine (N07XX06), Venlafaxine (N06AX16), Ziprasidone (N05AE04)
Antiparasitic products, insecticides and repellents	Chloroquine (P01BC02), Hydroxychloroquine (P01BA02), Metronidazole (P01AB01), Pentamidine (P01CX01), Quinine sulfate (P01BC01)
Respiratory system	Diphenhydramine (R06AA02), Promethazine (R06AD02)
Various	Perflutren lipid microspheres (V08DA01)

*From QTDrug list, https://crediblemeds.org/, version December 17, 2015. Only drugs available in Denmark are included at our list. The list includes drugs with known risk of TdP, possible risk of TdP, and conditional risk of TdP.
**ATC = Anatomical Therapeutic Chemical

Appendix D – Supplementary results

Results from stratified analysis. Although further strata than shown in this table were preplanned (e.g. stratification on all poisoning groups and age), we only stratified when possible due to a small number of events.

	QTc prolongation QTc ≥450 ms, men QTc ≥460 ms, women	Normal QTc interval <440 ms, men and women	HR* (95% CI)
	Events (n)**	Events (n)**	
Suspected poisoning			
Total	8 (248)	n<5 (496)	3.6 (1.0-12.2)
Male	n<5	n<5	2.7 (0.5-16.3)
Female	n<5	n<5	4.4 (0.8-24.3)
Age ≥50 years	6 (131)	n<5	2.7 (0.7-9.9)
Odense or Esbjerg	n<5	n<5	5.8 (0.6-57.4)
Lund	n<5	n<5	1.7 (0.2-12.2)
Helsingborg	n<5	n<5	4.4 (0.4-49.2)
Confirmed poisoning			
Total	6 (151)	n<5	10.5 (1.2-90.0)
Psychotropic drugs	n<5	n<5	2.0 (0.1-32.5)

Abbreviations: HR; hazard ratio, CI; confidence interval.

*Hazard ratio from Cox regression.

**If the number of events in the analysis was less than 5 (marked by n<5), the number of patients in the strata is not shown.